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RESEARCH AND REVIEWS IN PHARMACEUTICAL AND HEALTH SCIENCES VOLUME I

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PREFACE

In the dynamic realm of pharmaceutical and health sciences, where innovation and discovery intersect with human well-being, the pursuit of knowledge is both an endeavor and a responsibility. As we navigate through the complexities of modern healthcare, the importance of rigorous research and comprehensive reviews cannot be overstated.

This book stands as a testament to the relentless pursuit of excellence in understanding, enhancing, and revolutionizing pharmaceutical and health sciences. Within these pages, readers will embark on a journey through the latest advancements, breakthroughs, and critical analyses shaping the landscape of pharmaceuticals and health. Through meticulous research and insightful reviews, this volume encapsulates the multifaceted dimensions of our discipline, spanning from drug development and clinical trials to public health policies and patient care.

As we delve into the intricacies of pharmaceutical and health sciences, it is essential to recognize the interconnectedness of our endeavors with the broader fabric of society. The implications of our research extend far beyond the confines of laboratories and hospitals, shaping the future of healthcare delivery, accessibility, and equity for generations to come. In a world where the pace of change is ever-accelerating, the need for robust research and critical evaluation has never been more paramount. "Research and Reviews in Pharmaceutical and Health Sciences" seeks to not only capture the present state of our discipline but also to inspire the next generation of researchers, clinicians, and policymakers to continue pushing the boundaries of possibility. As editors, it is our privilege to present this volume to you, dear reader, with the hope that it sparks dialogue, inspires innovation, and fosters collaboration across disciplines and borders. May the insights gleaned from these pages serve as catalysts for transformative change, ultimately leading to improved health outcomes and enhanced quality of life for all.

Together, let us embark on this intellectual voyage, embracing the challenges and opportunities that lie ahead in the pursuit of a healthier, more equitable world.

- **Editors**

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FLAXSEED: THE MIRACLE SEED FOR OPTIMAL HEALTH

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Abstract:

Flaxseed, derived from the flax plant Linum usitatissimum, has garnered significant attention as a functional food due to its rich nutritional profile and abundance of bioactive compounds. This review explores the diverse array of nutrients present in flaxseed, including omega-3 fatty acids, lignans, fiber, and essential vitamins and minerals. Additionally, it investigates the potential health benefits associated with flaxseed consumption, such as cardiovascular protection, anti-inflammatory properties, and potential anticancer effects. The bioactive compounds present in flaxseed, particularly lignans and polyphenols, exhibit promising antioxidant and phytoestrogenic activities, contributing to its therapeutic potential. Moreover, this review highlights the role of flaxseed as a source of functional food in promoting overall health and preventing chronic diseases. Understanding the nutritional value and bioactive components of flaxseed underscores its potential as a valuable herbal functional food source for improving human health.

Keywords: Flaxseed, nutritional food, ALA, protein, dietary fibre, lignans, bioactive compound.

Introduction:

There has been a discernible shift in consumer tastes over the last few decades towards an emphasis on the potential health benefits provided by specific foods and their ingredients. Apart from their basic function of satisfying hunger and meeting basic nutritional requirements, foods are increasingly being sought after for their ability to prevent nutrition-related illnesses and improve people's general physical and mental well-being. The food industry has been pushing to create more functional meals as a result of consumers' growing preference for foods with added advantages; these foods are now a significant category of new food products within the realm of new food products[1]. Foods classified as functional are those that provide additional health

benefits over and above basic nourishment; herbal sources are often included in this category because of the substances they naturally contain that support general health and well-being. Flax seeds' distinct composition and possible health benefits make them a good fit for both of these trends. Flaxseed, or Linum usitatissimum L., is a highly popular food in the modern world because of its high nutritional value and strong biological activity. The main reasons this annual crop is grown are for its oil, fibre, and potential use as food and feed. This crop is being used in many different applications because to the growing awareness of its benefits.[2]

The crop flaxseed, which has bright blue blossoms, produces small, flat seeds that range in colour from golden yellow to reddish brown (Fig. 01). These seeds have a crispy, chewy texture and a delicious nutty flavour. Originally from India, flaxseed has long been grown as a primary food crop in states like Madhya Pradesh, Maharashtra, Chhattisgarh, and Bihar.3. Because of their abundance in vital nutrients, flax seeds are a beneficial supplement to any diet. They are a great source of plant-based protein, healthful fats (especially omega-3 fatty acids), and dietary fibre. Minerals and vitamins like magnesium, manganese, vitamin E, and B vitamins are also included in flax seeds.[4]

Figure 1: Flaxseed flowers & seeds

Nutritional composition of flaxseed

The protein content within flaxseed ranges between 10.5% and 31%. The primary protein constituents found in flax are albumin and globulin. The globulin fraction constitutes a significant portion, accounting for approximately 73.4% of the total, while the albumin component makes up the remaining 26.6% of the protein content. Flaxseed's protein profile is notably rich in amino acids such as arginine, aspartic acid, and glutamic acid, yet it is limited in lysine. The notable presence of cysteine and methionine contributes to heightened antioxidant levels, thereby potentially mitigating cancer risks. Flaxseed stands out as one of the most abundant plant sources of α-linolenic acid (ALA), an omega-3 fatty acid. Furthermore, it encompasses around 28% of dietary fiber. Diets high in dietary fibre may reduce the risk of developing diseases such as diabetes, heart disease, colon cancer, obesity, and inflammation.

Notable amounts of phosphorous (650 mg/100 g), magnesium (350–431 mg/100 g), and calcium (236–250 mg/100 g) can all be found in flaxseed's mineral profile.

On the other hand, there is very little sodium—just 27 mg/100 g. Furthermore, flaxseed has trace amounts of vitamins that are soluble in fat and water. It also contains three different kinds of phenolic compounds: flavonoids, lignans, and phenolic acids. It is especially noteworthy since it is a rich source of phytoestrogens, more especially lignans. Furthermore, the carbohydrate content of flaxseed is very low—just 1 g/100 g.5, 6 Fig. 02 displays the nutritional composition of flax seed.

Health benefits of flaxseed

The plant-based food is abundant in nutrients and has the potential to provide numerous health advantages owing to its blend of beneficial fats, dietary fiber, and a range of bioactive substances. Here are some of the potential health advantages of consuming flaxseeds:

1. Omega-3-Fatty acids: Flaxseeds contain a high concentration of alpha-linolenic acid (ALA), an important omega-3 fatty acid that is vital to human health, making them a superior plant-based supply. Important polyunsaturated fats are omega-3 fatty acids, which are divided into three categories: eicosapentaenoic acid (EPA), docosahexaenoic acid (DHA), and alpha-linolenic acid (ALA). ALA, a precursor to EPA and DHA, is especially abundant in flaxseeds. Flaxseeds contain omega-3 fatty acids, but it's crucial to eat them right to reap the full benefits. Nutrient absorption may be limited by the possibility that whole flaxseeds pass through the digestive system undigested. Before eating, ground flaxseeds to help break down the outer shell and increase the accessibility of their nutrients. Omega-3 fatty acids have anti-inflammatory properties and are beneficial for cardiovascular health because they lower blood pressure, triglyceride levels, and improve general functionality of blood vessels

   They also help to reduce inflammation and prevent the formation of blood clots. When it comes to cognitive health, omega-3 fatty acids are essential for the proper growth and function of the brain. DHA is particularly noteworthy as a key architectural component that is essential to brain structure. Sufficient consumption of omega-3 fatty acids is linked to decreased risk of chronic illnesses as well as enhanced memory, mood control, and cognitive performance.
2. Dietary Fiber: There is an exceptionally high content of dietary fibre in flaxseeds, which includes soluble and insoluble types. Flaxseeds are an excellent complement to a balanced diet because of their high fibre content, which also plays a role in their numerous health advantages. It's best to eat ground flaxseeds to get the full benefits of their high fibre content; you can also add them to smoothies, yoghurt, or muesli to increase your daily dose of fibre.

They can also be added to baked products or tossed over salads. Flaxseeds' blend of soluble and insoluble fibre promotes a healthy digestive system. Insoluble fibre promotes regular bowel movements and helps avoid constipation by giving stool more volume. Because soluble fibre absorbs extra water in the colon, it can aid in the prevention of diarrhoea. Additionally, it lowers total calorie intake, which helps people with diabetes or those at risk of developing type 2 diabetes maintain their weight and avoid overeating.

3. Lignans: Lignans are known to have two distinct properties: they are molecules that resemble oestrogen and antioxidants. These characteristics aid in the body's defence against harmful free radicals. Free radicals are recognised for their increased reactivity and can damage proteins, DNA, and other components of cells. Their capacity for destruction highlights their possible contribution to the development of cancer. The lignans in flaxseeds are converted by the body into substances that may offer a number of health advantages, including preventing cancer.
4. Proteins: By weight, flaxseeds contain between 20 and 25 percent protein. However, it is important to recognise that while flaxseeds contain protein, they are not categorised as a primary source of protein like lentils or beans. Building and mending tissues, especially muscle tissues, require protein. It is necessary for the development, maintenance, and general repair of muscles; it also supports immunological responses and infection prevention, aids in digestion, produces energy, and supports a host of other vital functions.
5. Bone Health: While flaxseeds may not be as well-known as some other foods for their ability to promote bone health, they do include a number of minerals that can help maintain bone health. It contains a lot of magnesium, a mineral that supports healthy bones by interacting with calcium. Magnesium contains phosphorus, which contributes to the overall mineral balance that maintains bone strength. Magnesium is involved in bone mineralization and helps control calcium levels in the body.
6. Cardiovascular Health: While flaxseeds may not be as well-known as some other foods for their ability to promote bone health, they do include a number of minerals that can help maintain bone health. It contains a lot of magnesium, a mineral that supports healthy bones by interacting with calcium. Magnesium contains phosphorus, which contributes to the overall mineral balance that maintains bone strength. Magnesium is involved in bone mineralization and helps control calcium levels in the body.

Incorporating flaxseed into the diet

By including flaxseeds in your diet, you have a great chance to add a powerful dosage of health benefits to your nutrition. These seeds are an excellent source of fibre, omega-3 fatty

acids, and a variety of other nutrients. Here are a few simple ways to include flaxseeds in your diet:

1. Ground flaxseed: Ground flaxseeds are preferable to whole ones since whole flaxseeds may be hard for your body to process. They are available pre-ground or ground at home in a food processor or coffee grinder. You may add ground flaxseeds to a variety of meals without affecting their texture or flavour.
2. Smoothies: One of the easiest ways to incorporate flaxseeds is by adding a tablespoon of ground flaxseeds to your morning smoothie. This adds a nutty flavor and a boost of nutrition.
3. Yogurt or oatmeal: Sprinkle ground flaxseeds on top of your yogurt or oatmeal for added texture and a nutritional kick.
4. Baking: Ground flaxseeds can be added to bread, pancakes, and muffins. They are frequently used in vegan baking as an egg alternative; simply replace one egg in recipes with one tablespoon of ground flaxseed mixed with three tablespoons of water.
5. Salads: For crunch and nutrients, top salads with ground flaxseeds. They complement grain salads and green salads as well.
6. Cereal: For an extra dose of fibre and omega-3 fatty acids, mix powdered flaxseeds into your porridge.
7. Homemade Granola or Energy Bars: Ground flaxseeds can be used to homemade granola or energy bars for extra nutrition and a subtle nutty flavour.
8. Soups & stews: Mix ground flaxseeds into soups and stews right before serving. They can thicken the broth and add nutrients.
9. Flax seed oil: Another option is flaxseed oil, but it lacks the fibre that ground flaxseeds do. Flaxseed oil can be drizzled over cooked vegetables or used in salad dressings.[9,10]
10. Flax seed crackers: Create your own flaxseed crackers by sprinkling a thin layer of the ground flaxseeds mixture onto a baking sheet, adding seasoning, and baking until the mixture becomes crunchy.

Culinary uses and challenges of using flaxseed in cooking

Using flaxseeds in cooking offers various benefits and opportunities, but there are also some challenges to consider.

Uses & benefits:

1. Nutritional boost: Flaxseeds offer an amazing nutritional profile since they are high in fibre, omega-3 fatty acids, and lignans, which have antioxidant qualities. Your diet will have more nutrients if you include them in your meals.

2. Heart health: Omega-3 fatty acids, which are included in flaxseeds, have been linked to heart health advantages like lowering blood pressure, less inflammation, and support for appropriate cholesterol levels.
3. Digestive health: Flaxseeds are an excellent source of dietary fibre that also aid in regular bowel motions, better digestion, and a feeling of fullness.
4. Protien: Flaxseeds are a wonderful choice for vegetarians and vegans who want to up their protein intake because they have a reasonable quantity of plant-based protein.
5. Texture & flavor: Ground flaxseeds offer a nice nutty flavour and slightly crunchy texture to meals like yoghurt, muesli and smoothies.
6. Binding agent in baking: Flaxseeds are suitable for vegan recipes because they may be used in baking as an egg substitute. For those who have dietary restrictions or allergies to eggs, this can be extremely beneficial.

   Challenges:

1. Digestive sensitivity: Because flaxseeds are high in fibre, some people may have pain in their digestive tracts when they consume them. To prevent stomach problems, it's crucial to incorporate them into your diet gradually.
2. Oxidation: Healthy lipids found in flaxseeds can go rancid in the presence of heat, light, and air. To avoid this, crush the flaxseeds as needed and keep them in the refrigerator in an airtight container.
3. Nutrient absorption: While flaxseeds are nutritious, their hard outer shell can make it difficult for the body to absorb all the nutrients they contain. Grinding them before consumption enhances nutrient availability.
4. Allergies & interactions: Flaxseeds may cause allergies or sensitivities in certain people. Furthermore, flaxseeds may interact with some drugs, so if you have any concerns, it's best to speak with a healthcare provider.
5. Taste & texture: The unique nutty flavour of flaxseeds may not be to everyone's taste. If you don't like this flavour, it could make it harder for you to appreciate foods that have flaxseeds added.
6. Calorie density: Because flaxseeds are high in calories, even if they have numerous health benefits, if consumed in excess without taking into account their calorie content, one may gain weight if their intake is not balanced with overall caloric intake.

Recommended daily intake:

Whole flax seeds: One to two tablespoons (about 10–20 grammes) of whole flax seeds should be consumed each day. This gives your body a healthy mix of nutrients without taxing it too much.

Ground flax seeds: When compared to whole seeds, ground flax seeds are easier for the body to absorb and digest. One to two tablespoons of ground flax seeds should be consumed daily.

Contribution of flaxsees compounds to sustaining gut microbiota and human well-being

The crucial roles that the gut microbiota plays in facilitating digestion, synthesising essential nutrients, regulating the immune system, and protecting against harmful infections are all very influential in human well-being. Numerous health problems, including as obesity, metabolic disorders, and inflammatory bowel illnesses, have been connected to imbalances in the gut microbiota.

Flaxseed-derived compounds have been shown to encourage positive changes in the gut microbiota, which may help prevent and treat a variety of illnesses. (Figure 2).

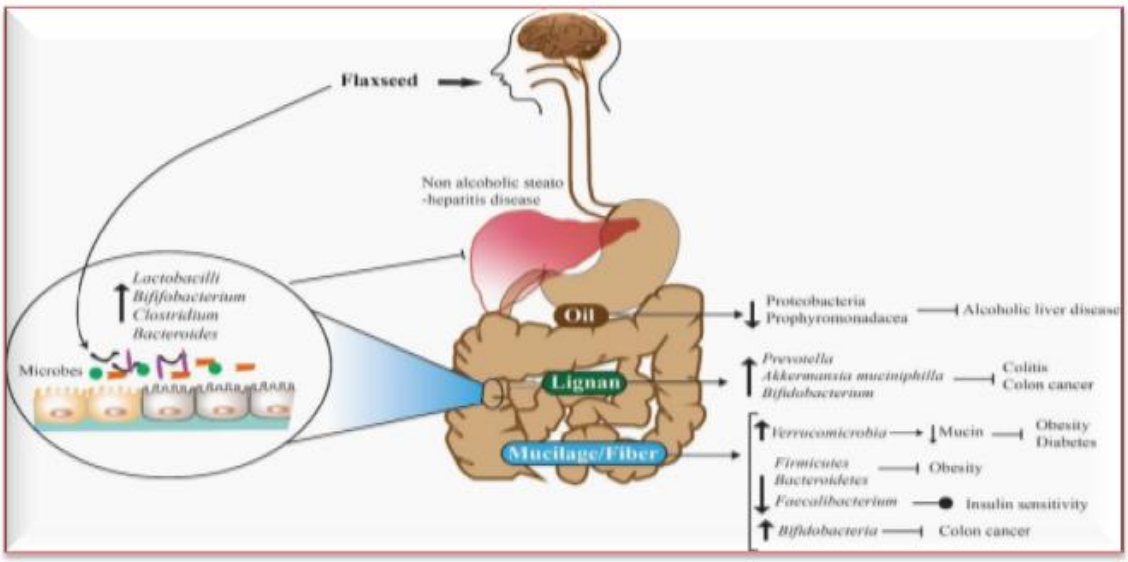

Figure 2: Effect of Flaxseed on gut health

Flaxseeds are high in dietary fibre, which helps to support regular bowel motions and acts as a substrate for the fermentation of good gut bacteria. Short-chain fatty acids (SCFAs), which have anti-inflammatory qualities and support the integrity of the gut lining, are created when gut bacteria ferment dietary fibre. Because they promote the growth of beneficial bacteria, omega-3 fatty acids have been shown to have anti-inflammatory properties and may also affect the composition of the gut microbiota. Lignans, polyphenolic chemicals with antioxidant and possibly hormone-modulating qualities, are found in flaxseeds. According to certain research, lignans may have prebiotic properties that encourage the development of healthy gut flora.

Containing flaxseed, its components have demonstrated their potential to aid in the prevention of obesity in living organisms.[11]

Conclusion:

Flaxseed has nutritional and functional properties. Flax seeds have gained significant focus as a promising herbal functional food source due to their high nutritional profile and bioactive compounds. They are particularly renowned for their high content of essential fatty acids, primarily alpha-linolenic acid (ALA), which is an omega-3 fatty acid with potential cardiovascular and anti-inflammatory benefits. Additionally, flax seeds are rich source of dietary fiber, lignans, and protein. Research has shown that incorporating flax seeds into the diet can contribute to improved heart health, reduced inflammation, and potentially offer protection against certain chronic diseases, such as diabetes and certain types of cancer. To enhance the potential health advantages of flax seeds, research has linked their lignans to antioxidant and hormonal balance. When flaxseed is consumed, it encourages the growth of probiotic bacteria in the stomach. Furthermore, it initiates the production of metabolites that play critical roles in immunological responses, the preservation of homeostasis pathways, and the metabolism of fats and carbohydrates. More research is necessary to better understand the mechanisms by which flaxseed promotes beneficial changes in gut flora and improves a variety of physiological processes. Flax seeds' high nutritional content and bioactive ingredients make them a promising herbal functional food source. Even though the majority of the health advantages are already supported by research, their full potential to improve human health and well-being can only be realised with further study, innovation, and education.

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GRAPE SEED OIL IN MEDICINE: CURRENT INSIGHTS AND FUTURE PROSPECTS

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Abstract:

Grape seed oil, derived from the seeds of grapes, has gained significant attention in recent years for its potential therapeutic benefits. This natural product is rich in polyphenols, antioxidants, and essential fatty acids, making it a valuable resource for various health and wellness applications. This abstract explores the therapeutic benefits of grape seed oil, focusing on its antioxidant properties, potential cardiovascular benefits, skin and hair care applications, and anti-inflammatory effects. Additionally, we discuss the oil's potential in the management of chronic diseases such as diabetes and its role in promoting overall well-being. The research suggests that grape seed oil can be a versatile and beneficial addition to one's daily regimen, offering a wide range of health advantages. However, further studies are needed to comprehensively understand its mechanisms of action and optimal usage for various health conditions.

Keywords: Grape Seed Oil; *Vitis vinifera* L.; Phytochemistry; Bioactive Compounds; Biological Activity

Introduction:

Grape seed oil, derived from the seeds of grapes, has gained significant popularity in recent years due to its numerous health benefits and versatile uses. This oil, extracted through a process of cold-pressing grape seeds, boasts a delicate flavor profile and a high smoke point, making it suitable for various culinary applications and skincare routines alike. In the culinary world, grape seed oil has emerged as a favored alternative to traditional cooking oils due to its neutral taste and light texture. With its high smoke point, typically around 420°F (216°C), grape seed oil is ideal for high-temperature cooking methods such as frying, sautéing, and baking. Unlike some other oils, it retains its nutritional properties even at high heat, making it a healthier choice for cooking.

Nutritionally, grape seed oil is rich in polyunsaturated fats, particularly omega-6 fatty acids, and vitamin E. These essential fatty acids are known for their role in supporting heart health by reducing LDL cholesterol levels and promoting overall cardiovascular function. Additionally, vitamin E acts as a powerful antioxidant, helping to protect cells from damage caused by free radicals. Beyond its culinary uses, grape seed oil has also found a place in skincare and beauty products. Thanks to its lightweight texture and non-greasy feel, it is often used as a moisturizer for both the face and body. Its high concentration of linoleic acid, a type of omega-6 fatty acid, makes it an excellent choice for those with acne-prone or sensitive skin, as it helps to regulate oil production and maintain the skin's natural barrier.[1]

Furthermore, grape seed oil is a common ingredient in cosmetics and hair care products due to its emollient properties. It is often included in formulations such as serums, lotions, and hair masks to help hydrate, nourish, and protect the skin and hair. In addition to its culinary and skincare uses, grape seed oil has been studied for its potential health benefits when consumed as a dietary supplement. Some research suggests that it may help to lower blood pressure, improve circulation, and reduce inflammation throughout the body. However, more studies are needed to fully understand the extent of its therapeutic effects. Grape seed oil offers a wide range of benefits, both culinary and cosmetic [2]. With its neutral flavor, high smoke point, and nutritional profile, it serves as a versatile cooking oil that supports heart health. Meanwhile, its moisturizing and antioxidant properties make it a popular choice in skincare and beauty products. Whether used in the kitchen or as part of a skincare regimen, grape seed oil is a valuable addition to any lifestyle seeking a balance of health and wellness.

Botanical and taxonomical description of *Vitis vinifera* l.

Vitis vinifera L., commonly known as the European grapevine, is a species of flowering plant in the Vitaceae family. This deciduous woody vine is native to the Mediterranean region and has been cultivated for thousands of years for its fruit, which is used in winemaking and eaten fresh.[3]

The plant typically features climbing stems that can reach impressive lengths, often climbing up structures or trailing along the ground. Its leaves are large, palmate, and lobed, with serrated edges. *Vitis vinifera* produces small, greenish flowers that develop into clusters of berries, known as grapes, which come in various colors including green, red, and purple, depending on the cultivar. Taxonomically, *Vitis vinifera* belongs to the kingdom Plantae, the division Magnoliophyta, the class Magnoliopsida, the order Vitales, the family Vitaceae, and the genus Vitis. Its specific epithet, "vinifera," is derived from Latin and means "wine-bearing," highlighting its historical significance in winemaking.[4]

Therapeutic effects of grape seed oil

Grape seed oil, derived from the seeds of grapes, is renowned for its therapeutic effects on various aspects of health and well-being. Rich in polyunsaturated fats, particularly omega-6 fatty acids, and vitamin E, grape seed oil offers a range of benefits:

Cardiovascular health: The omega-6 fatty acids in grape seed oil contribute to heart health by lowering LDL cholesterol levels and reducing the risk of cardiovascular diseases. Additionally, its antioxidant properties help to prevent the oxidation of LDL cholesterol, which can lead to plaque buildup in the arteries.[5]

Anti-inflammatory properties: Grape seed oil contains compounds such as procyanidins and resveratrol, which have anti-inflammatory effects. These compounds help to reduce inflammation throughout the body, potentially alleviating symptoms of conditions such as arthritis and promoting overall joint health.

Skin health: When applied topically, grape seed oil serves as an excellent moisturizer due to its lightweight texture and high concentration of linoleic acid. It helps to hydrate the skin without clogging pores, making it suitable for all skin types, including acne-prone and sensitive skin. Additionally, its antioxidant properties help to protect the skin from free radical damage, reducing the signs of aging such as fine lines and wrinkles.

Hair care: Grape seed oil is often used in hair care products due to its emollient properties. It helps to moisturize the scalp, strengthen hair follicles, and improve hair elasticity, resulting in softer, shinier hair with reduced breakage and split ends.

Therapeutic effects of grape seed oil make it a valuable addition to both dietary and skincare regimens, promoting cardiovascular health, reducing inflammation, and nourishing the skin and hair.[6]

Traditional uses

Grape seed oil has a long history of traditional uses across various cultures, dating back centuries. Some of its traditional uses include:

Culinary application: In Mediterranean cuisine, grape seed oil is a staple cooking oil, prized for its light flavor and high smoke point. It is commonly used for sautéing, frying, and salad dressings.

Medicinal purpose: Traditional medicine systems such as Ayurveda and Traditional Chinese Medicine have utilized grape seed oil for its medicinal properties. It has been used to promote digestive health, alleviate symptoms of arthritis, and support cardiovascular function.

Skin and hair care: Ancient civilizations, including the Egyptians and Greeks, valued grape seed oil for its moisturizing and antioxidant properties. It was used topically to hydrate the skin,

treat wounds, and protect against environmental damage. Additionally, it was applied to the hair to nourish and condition strands, promoting healthy growth and shine.[7]

Massage therapy: Due to its lightweight texture and easy absorption, grape seed oil has been used in massage therapy to moisturize the skin, reduce friction during massages, and deliver therapeutic essential oils deep into the tissues.

These traditional uses highlight the versatility and efficacy of grape seed oil in promoting overall health and well-being.[8]

Anti-hypercholesterolemic and cardioprotective effects

Grape seed oil exhibits anti-hypercholesterolemic and cardioprotective effects, making it beneficial for cardiovascular health. Rich in polyunsaturated fats, particularly omega-6 fatty acids, grape seed oil helps to lower LDL cholesterol levels, reducing the risk of atherosclerosis and heart disease. Additionally, its antioxidant properties, attributed to compounds such as procyanidins and resveratrol, help to prevent the oxidation of LDL cholesterol, which can lead to the formation of plaque in the arteries. Studies have demonstrated that supplementation with grape seed oil can improve lipid profiles, including reducing LDL cholesterol and triglyceride levels, while increasing HDL cholesterol levels, thereby promoting a healthier balance of lipids in the blood. Furthermore, the anti-inflammatory properties of grape seed oil contribute to its cardioprotective effects by reducing inflammation in the cardiovascular system, supporting overall heart function, and lowering the risk of complications associated with chronic inflammation.[9]

Antioxidant potential of GSO

Grape seed oil possesses a potent antioxidant potential due to its rich content of phenolic compounds, including flavonoids, phenolic acids, and procyanidins. These antioxidants play a crucial role in scavenging free radicals and preventing oxidative damage to cells and tissues throughout the body. The primary antioxidant compounds found in grape seed oil, such as procyanidins, exhibit superior free radical scavenging abilities compared to other antioxidants like vitamins C and E. Procyanidins are particularly effective at neutralizing reactive oxygen species (ROS) and inhibiting lipid peroxidation, a process implicated in various diseases and aging.

Studies have shown that the antioxidant activity of grape seed oil contributes to its numerous health benefits, including cardiovascular protection, anti-inflammatory effects, and skin rejuvenation. By combating oxidative stress, grape seed oil helps to reduce the risk of chronic diseases such as heart disease, cancer, and neurodegenerative disorders. The antioxidant potential of grape seed oil extends to its stability as a cooking oil. Its resistance to oxidation at

high temperatures makes it suitable for frying and sautéing without compromising its nutritional value or forming harmful compounds. The antioxidant properties of grape seed oil make it a valuable dietary supplement and skincare ingredient, offering protection against oxidative damage and promoting overall health and well-being.[10]

Antimicrobial effect

Grape seed oil exhibits antimicrobial properties against a range of pathogens, making it a promising natural alternative for combating microbial infections. The antimicrobial effects of grape seed oil are primarily attributed to its bioactive compounds, including polyphenols, flavonoids, and procyanidins. Grape seed oil demonstrates antibacterial activity against various Gram-positive and Gram-negative bacteria, including Staphylococcus aureus, Escherichia coli, and Salmonella species. These bacteria are commonly associated with foodborne illnesses, skin infections, and respiratory tract infections. Grape seed oil's ability to inhibit the growth of these pathogens suggests its potential use as a food preservative and topical treatment for bacterial infections.

Grape seed oil exhibits antifungal properties against fungal species such as Candida albicans, which can cause oral thrush, vaginal yeast infections, and other fungal-related ailments. Its antifungal activity may be attributed to its ability to disrupt fungal cell membranes and inhibit fungal growth. It has been studied for its antiviral effects against certain viruses, although more research is needed to fully elucidate its mechanisms of action and effectiveness against viral pathogens. The antimicrobial effect of grape seed oil highlights its potential as a natural antimicrobial agent for use in food preservation, topical treatments for bacterial and fungal infections, and possibly as a component in antiviral therapies. However, further research is necessary to explore its efficacy, safety, and potential applications in clinical settings.[11]

Cosmetic use

Grape seed oil is prized in cosmetics for its versatile benefits for both skin and hair. As a lightweight and non-comedogenic oil, it serves as an excellent moisturizer, hydrating the skin without leaving a greasy residue. Rich in antioxidants such as vitamin E, grape seed oil helps protect the skin from environmental damage, reducing signs of aging like wrinkles and fine lines. Its gentle nature makes it suitable for all skin types, including sensitive and acne-prone skin.In hair care, grape seed oil nourishes and strengthens hair follicles, promoting healthier strands with increased shine and reduced breakage. It moisturizes the scalp, aiding in dandruff prevention and improving overall scalp health. Whether used as a standalone oil, incorporated into skincare products like serums and creams, or added to hair care formulations like shampoos and

conditioners, grape seed oil is a valuable cosmetic ingredient known for its moisturizing and protective properties.[12]

Conclusion:

In conclusion, grape seed oil has emerged as a promising natural product with a multitude of potential therapeutic benefits. Its rich content of polyphenols, antioxidants, and essential fatty acids make it a valuable resource for promoting health and wellness in various ways. The antioxidant properties of grape seed oil can help combat oxidative stress, potentially reducing the risk of chronic diseases and supporting overall well-being. Its potential cardiovascular benefits, including its role in managing diabetes, further highlight its positive impact on health. Grape seed oil's applications in skincare and haircare underscore its versatility, offering a natural and nourishing option for personal care routines. Additionally, its anti-inflammatory effects add to its potential in managing various health conditions. While the existing research suggests the numerous advantages of grape seed oil, further studies are essential to gain a more comprehensive understanding of its mechanisms of action and the optimal ways to incorporate it into different health regimens. With ongoing research and exploration, grape seed oil may continue to reveal even more of its potential in promoting health and enhancing the quality of life.

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EXPLORING PLANT-DERIVED COMPOUNDS FOR CANCER

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Abstract:

This comprehensive chapter explores the potential of natural products, particularly those derived from plants, as anti-cancer agents. Focused on diverse compounds like alkaloids, flavonoids, terpenoids, and polyphenols, the review delves into their mechanisms of action in combating cancer, emphasizing their multifaceted approach. Alkaloids exhibit cytotoxic effects, interfere with the cell cycle, and possess anti-angiogenic and anti-inflammatory properties. Flavonoids, with antioxidant capabilities, anti-inflammatory effects, and cell cycle regulation impact, offer a varied approach to cancer treatment. Terpenoids demonstrate apoptosis induction, anti-inflammatory modulation, and angiogenesis inhibition. Polyphenols, known for antioxidant activity, anti-inflammatory effects, and signalling pathway modulation, significantly contribute to cancer prevention and treatment. The review outlines mechanisms such as apoptosis induction, cell cycle arrest, angiogenesis inhibition, antioxidant, and anti-inflammatory effects, DNA repair inhibition, signaling pathway targeting, and immunomodulation. Despite promising aspects, challenges like bioavailability and potential side effects necessitate further research for optimized cancer therapies. In this chapter, exploration into natural products presents a dynamic and promising avenue for advancing cancer treatment strategies, uncovering new compounds, and refining existing ones for improved patient outcomes.

Keywords: Cancer, Terpenoids, Alkaloids, Plant

Introduction:

Cancer persists as a formidable global health challenge, necessitating continuous research into novel treatment strategies. Among these, natural products, particularly those derived from plants, have garnered attention for their potential as anti-cancer agents. This review focuses on the exploration of various plant-derived compounds and their mechanisms of action in combatting cancer. The significance of natural products lies in their diverse chemical compositions, offering a rich source of bioactive compounds with potential medicinal properties. By delving into the intricate details of how these compounds modulate cellular pathways, particularly those involved in cell proliferation, apoptosis, angiogenesis, and inflammation,

researchers aim to uncover unique opportunities for intervention. The promise of diversity within plant-derived compounds, spanning categories such as alkaloids, flavonoids, terpenoids, and polyphenols, underscores the multifaceted approach these compounds bring to cancer research. Despite challenges such as bioavailability and potential toxicity, the exploration of plant-derived compounds presents opportunities for refining and optimizing these agents, tailoring them for targeted and effective cancer therapies. In conclusion, the dynamic and promising frontier of natural products in cancer research holds the potential to unveil novel and effective treatments for this global health concern [1].

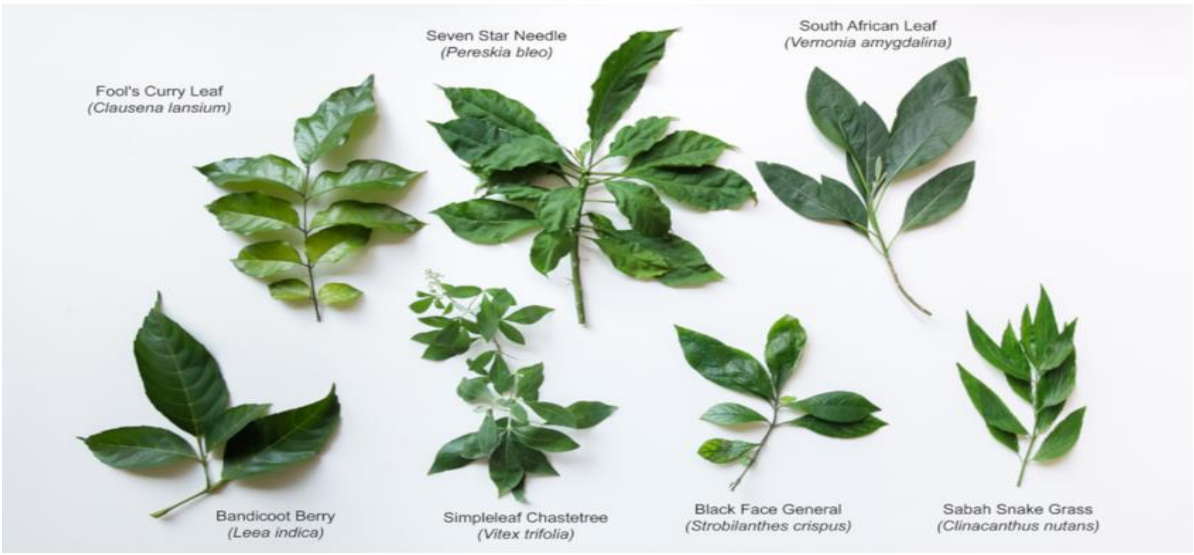

Figure 1: Asian Medicinal plant contain Anti-cancer compound

Plant derived compounds in anti-cancer research

Numerous plant-derived compounds have demonstrated anti-cancer properties, displaying their potential as therapeutic agents. Examples include alkaloids (vinblastine, vincristine), flavonoids (quercetin, epigallocatechin gallate), terpenoids (paclitaxel, artemisinin), and polyphenols (curcumin, resveratrol). These compounds have been studied for their ability to inhibit tumor growth, induce apoptosis, and interfere with various signaling pathways implicated in cancer progression.

1. Alkaloids

Alkaloids, a diverse group of naturally occurring organic compounds found in plants, are gaining attention for their potential role in cancer treatment. These compounds often possess complex structures and exhibit a wide range of pharmacological activities. One notable aspect of alkaloids is their ability to induce cytotoxic effects in cancer cells, contributing to the suppression of uncontrolled cell proliferation. Moreover, certain alkaloids have demonstrated the

capacity to induce apoptosis, a programmed cell death process crucial for eliminating damaged or abnormal cells and preventing cancer progression.

In addition to their impact on cell survival, alkaloids may interfere with the cell cycle progression of cancer cells, leading to cell cycle arrest. This disruption hinders the uncontrolled division of cancer cells. Furthermore, alkaloids have been investigated for their anti-angiogenic effects, meaning they can inhibit the formation of new blood vessels. This is significant in restricting the blood supply to tumors, thereby limiting their growth and potential for metastasis [2].

The anti-inflammatory properties of certain alkaloids are also noteworthy, as chronic inflammation is associated with cancer development. Alkaloids may contribute to reducing inflammation, thereby playing a role in the prevention or control of cancer. Additionally, alkaloids may interact with DNA and inhibit repair mechanisms in cancer cells, leading to genomic instability and increased susceptibility of cancer cells to cell death. Another facet of alkaloids in cancer research involves their modulation of various signaling pathways within cancer cells. This includes pathways related to cell survival, proliferation, and apoptosis. Alkaloids can exert control over these pathways, influencing the behaviour of cancer cells. Furthermore, some alkaloids exhibit immunomodulatory effects, enhancing the body's immune response to identify and eliminate cancer cells [3].

Certain alkaloids demonstrate specificity in targeting particular types of cancer. For instance, vinblastine and vincristine, derived from the Madagascar periwinkle, have been utilized in the treatment of various cancers, including leukemia and lymphoma. Moreover, alkaloids may enhance the effectiveness of other anti-cancer therapies, and combinations with chemotherapy or radiation therapy are being explored for potential synergistic effects to improve overall treatment outcomes [4].

It is crucial to note that while some alkaloids show promise in preclinical studies and early-phase clinical trials, further research is essential to establish their efficacy, safety, and optimal use in cancer treatment. The potential side effects and specific mechanisms of action may vary among different alkaloids. As with any potential cancer therapy, the use of alkaloids in clinical settings should be approached with caution and guided by rigorous scientific investigation [5].

2. Flavanoids

Flavonoids, a diverse group of polyphenolic compounds found in plants, have garnered significant attention for their potential role in preventing and treating cancer. With their intricate structures, flavonoids possess a range of biological activities that contribute to their impact on

various cellular processes. A key attribute of flavonoids is their potent antioxidant properties, enabling them to neutralize free radicals that can induce DNA damage and mutations, factors associated with cancer development. By reducing oxidative stress, flavonoids play a protective role in cellular health.

Beyond their antioxidant capabilities, flavonoids exhibit anti-inflammatory effects, a crucial aspect in cancer prevention. Chronic inflammation is implicated in cancer initiation and progression, and the ability of flavonoids to modulate inflammatory pathways can contribute to limiting these processes. Flavonoids also play a role in apoptosis, or programmed cell death, in cancer cells. This mechanism is essential for eliminating damaged cells, and the induction of apoptosis by flavonoids is a significant aspect of their anti-cancer effects [6].

Flavonoids influence the cell cycle, the series of events governing cell division. Through the modulation of key cell cycle regulators, flavonoids can impede the uncontrolled growth of cancer cells, promoting cell cycle arrest. Additionally, flavonoids have demonstrated anti-angiogenic effects, inhibiting the formation of new blood vessels crucial for tumor growth and metastasis. Their ability to limit the blood supply to tumors contributes to their potential, as anti-cancer agents [7]. Modulation of signaling pathways is another mechanism through which flavonoids exert their anti-cancer effects. By interfering with pathways related to cell survival, proliferation, and metastasis, flavonoids influence the behavior of cancer cells. Some flavonoids induce epigenetic changes, such as DNA methylation and histone modification, which can affect gene expression and contribute to the suppression of cancer-related genes [8].

Flavonoids also showcase immunomodulatory properties, enhancing the body's immune response to recognize and eliminate cancer cells. This interaction with the immune system contributes to an effective anti-cancer response. Furthermore, flavonoids exhibit anti-metastatic effects by interfering with processes involved in cell migration, invasion, and adhesion [9].

While evidence supports the anti-cancer potential of flavonoids, it is crucial to acknowledge that the effectiveness of specific flavonoids may vary, and their role in cancer treatment is complex. Factors such as bioavailability and interactions with other dietary compounds can influence their impact on cancer. Continued research is anticipated to unveil more specific mechanisms and optimal conditions for harnessing the potential of flavonoids in the prevention and treatment of cancer [10].

3. Terpenoids

Terpenoids, a diverse class of naturally occurring compounds derived from isoprene units, have emerged as promising candidates in cancer treatment research due to their multifaceted therapeutic properties. One notable aspect of terpenoids is their ability to induce

apoptosis, or programmed cell death, in cancer cells. This mechanism is pivotal for eliminating damaged or abnormal cells and preventing uncontrolled cell growth. Additionally, terpenoids have demonstrated the potential to inhibit the proliferation of cancer cells by interfering with the cell cycle, disrupting uncontrolled cell division, and impeding tumor growth.

The anti-inflammatory properties of terpenoids constitute another important facet of their potential in cancer treatment. Chronic inflammation is closely linked to cancer development, and terpenoids can modulate inflammatory pathways, reducing the production of pro-inflammatory molecules. This modulation creates an environment less conducive to cancer initiation and progression. Moreover, many terpenoids exhibit antioxidant properties, neutralizing free radicals and reducing oxidative stress. This antioxidant activity contributes to protecting cells from DNA damage, a key factor in cancer development [11].

Terpenoids have been studied for their ability to inhibit angiogenesis, the formation of new blood vessels crucial for tumor growth. By limiting the blood supply to tumors, terpenoids can impede their growth and reduce the potential for metastasis. Additionally, terpenoids can interfere with various signaling pathways involved in cancer development, including those related to cell survival, proliferation, and metastasis. This interference allows terpenoids to exert control over the behavior of cancer cells. Some terpenoids exhibit immunomodulatory effects, enhancing the body's immune response to identify and eliminate cancer cells. This immunomodulation contributes to an effective anti-cancer immune response. Terpenoids may also induce differentiation in cancer cells, promoting a more specialized and less aggressive cell phenotype, thereby reducing the malignancy of cancer cells. Certain terpenoids have direct cytotoxic effects on cancer cells, leading to their destruction, and this cytotoxicity can be selective for cancer cells, sparing normal cells.

Moreover, terpenoids may enhance the efficacy of conventional chemotherapy. Studies suggest that they can sensitize cancer cells to the effects of chemotherapy, potentially lowering the required dosage and reducing side effects. While the anti-cancer potential of terpenoids is promising, it is crucial to acknowledge that their effectiveness may vary depending on the specific compound and cancer type. Additionally, the bioavailability and pharmacokinetics of terpenoids should be considered in their development as potential cancer treatments. Further research is needed to elucidate the specific mechanisms of action and optimize the use of terpenoids in cancer therapy [12].

4. Polyphenol

Polyphenols, a diverse group of naturally occurring compounds found in plants, have garnered considerable attention for their potential in preventing and treating cancer. One key

attribute of polyphenols is their potent antioxidant activity, effectively neutralizing free radicals and reactive oxygen species implicated in DNA damage and cancer initiation. Moreover, these compounds exhibit anti-inflammatory effects by modulating inflammatory pathways, creating an environment less conducive to cancer progression. Polyphenols also play a crucial role in apoptosis, inducing programmed cell death in cancer cells and preventing uncontrolled growth. Their influence extends to the cell cycle, where they inhibit proliferation by disrupting key regulators, hindering tumor development [13].

In addition to their impact on cellular processes, polyphenols contribute to cancer prevention through anti-angiogenic effects, limiting the formation of blood vessels crucial for tumor growth. They interfere with various signaling pathways associated with cancer, affecting cell survival, proliferation, and metastasis. Furthermore, polyphenols induce epigenetic changes, influencing gene expression and suppressing cancer-related genes. Their immunomodulatory effects enhance the body's immune response, aiding in the recognition and elimination of cancer cells. Polyphenols also demonstrate anti-metastatic effects by inhibiting processes involved in cancer spread, such as cell migration and invasion. In hormone-dependent cancers, certain polyphenols, like those found in soy, can modulate hormonal pathways [14].

While preclinical studies and epidemiological evidence support the anti-cancer potential of polyphenols, their effectiveness can vary based on factors such as bioavailability, metabolism, and interactions with other dietary compounds. Continued research is crucial to fully comprehend the specific mechanisms and optimal conditions for harnessing the potential of polyphenols in the prevention and treatment of cancer.

Mechanisms of action:

- ✓ Apoptosis induction: Many plant-derived compounds exhibit pro-apoptotic effects, triggering programmed cell death in cancer cells. For instance, resveratrol has been shown to activate apoptotic pathways, leading to the elimination of cancer cells.
- ✓ Cell cycle arrest: Compounds like paclitaxel interfere with microtubule dynamics, causing cell cycle arrest and inhibiting cancer cell proliferation.
- ✓ Angiogenesis inhibition: Some plant-derived compounds, such as epigallocatechin gallate, target angiogenesis pathways, disrupting the formation of new blood vessels that support tumor growth.
- ✓ Antioxidant and anti-inflammatory effects: Polyphenols like curcumin possess antioxidant properties that mitigate oxidative stress, and anti-inflammatory effects that may contribute to cancer prevention.

- ✓ DNA repair inhibition: Compounds like quercetin may interfere with DNA repair mechanisms in cancer cells, leading to genomic instability and increased susceptibility to cell death.
- ✓ Targeting signaling pathways: Plant-derived compounds often modulate critical signaling pathways, including PI3K/AKT, MAPK, and NF-κb, which play pivotal roles in cancer development and progression.
- ✓ Immunomodulation: Some compounds, like artemisinin, have demonstrated immunomodulatory effects, enhancing the body's natural defences against cancer cells.

Challenges and future directions:

While the potential of plant-derived compounds in cancer treatment is promising, challenges such as bioavailability, specificity, and potential side effects need to be addressed. Additionally, further research is needed to optimize dosage regimens and assess the efficacy of these compounds in various cancer types [15].

Conclusion:

The investigation into natural products as potential anti-cancer agents, with a specific focus on plant-derived compounds, constitutes a highly promising and dynamic area of research. This exploration is driven by the recognition that plants offer a vast array of bioactive compounds that may possess unique properties in combating cancer. The significance of this research lies not only in the identification of novel compounds but also in the comprehensive understanding of the diverse mechanisms through which these natural products exert their anti-cancer effects. Delving into the intricate ways in which these compounds interact with cancer cells, influence signaling pathways, induce apoptosis, or modulate key cellular processes provides invaluable insights. Such insights are instrumental in the development of targeted and effective anti-cancer therapies.

The complexity of cancer demands a multifaceted approach, and natural products offer a rich source of diverse chemical structures that can be explored for their therapeutic potential. As researchers unravel the intricate mechanisms of action of these compounds, they pave the way for the refinement and optimization of existing anti-cancer agents and the discovery of new ones. This continual exploration and refinement are essential for developing strategies that are not only potent in targeting cancer cells but also selective in minimizing adverse effects on normal cells.

The ongoing commitment to research in this field holds the promise of uncovering previously undiscovered compounds with potent anti-cancer properties. Furthermore, the refinement of existing knowledge about plant-derived compounds allows researchers to tailor these agents for improved efficacy and reduced toxicity. Ultimately, the goal is to translate these findings into the

development of advanced and targeted cancer treatment strategies that can enhance patient outcomes.

In summary, the exploration of natural products, especially those derived from plants, as anti-cancer agents is a dynamic and rich area of research. Understanding the intricacies of how these compounds exert their effects provides critical insights, offering the potential for the development of targeted and effective anti-cancer therapies. The continuous dedication to research in this field not only uncovers new compounds but also refines existing ones, holding the promise of advancing cancer treatment strategies for the benefit of patients.

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HERBS USED IN THE MANAGEMENT OF OSTEOPOROSIS

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Abstract:

A major health issue that is known to impact a wide population is osteoporosis. It used to be widely accepted that women would eventually get this illness as they aged, especially during menopause as a result of hormonal imbalances. According to statistics, one in five men and one in three women over 50 may experience osteoporotic fractures at some time in their life. Both bone resorption and production occur continuously during the remodeling process of the adult skeleton. On the other hand, osteoporosis occurs when bone resorption exceeds bone development. Throughout their lives, men and women alike should place a high priority on maintaining healthy bones. Osteoporosis prevention requires addressing variables impacting bone health at every stage. Effective preventative interventions are essential to counteract the rising frequency of osteoporotic fractures, with the goal of optimizing peak bone density. The main objectives of current therapy are to prevent more bone loss and fractures, maintain bone mass, and use drugs such as strontium, bisphosphonates, anabolic steroids, bisphosphonates, and hormone replacement therapy (HRT). It's crucial to remember that several of these medications, including anabolic steroids, bisphosphonates, HRT, and SERMs, may have unfavorable side effects. Thus, the search for safe, natural, economical, and less toxic substances to treat osteopenia and osteoporosis is urgently needed. The key to treating this illness and encouraging improved bone health is locating safer substitutes.

Keywords: Osteoporosis, Bone Resorption, Herbs, Bone Formation

Introduction:

A person is diagnosed with osteoporosis when their bone structure deteriorates and their bone density decreases, making their bones weaker and more prone to breaking. The amount of bone loss and an individual's maximal bone mass are determined by their bone density, which is expressed in grams of mineral content per square centimeter or cubic inch. In essence, bone density is a measure of how much mineral is present in bone tissue. Higher mineral content bones are denser and less prone to break. Numerous factors, such as bone mineralization, the

development of microfractures, bone turnover, and overall architecture, affect the quality of bone. An ongoing loss of bone mass causes osteoporosis, a common chronic metabolic bone disease that makes bones more brittle and prone to breaking. Factors such as menopause and natural aging influence its development, causing bone tissue deterioration and affecting the overall strength of bones. While osteoporosis can affect anyone, it is more prevalent in Caucasians, especially older women. Its prevalence is increasing globally due to an aging population, with over two hundred million people currently affected by the condition. Osteoporotic fractures, striking one in three women and one in five men over 50, underscore the need for early detection and preventative measures. Notably, osteoporosis often remains asymptomatic until it causes fractures, which can be severe and significantly impact morbidity in men. Moreover, osteoporosis has a negative impact on life expectancy modified for disability, quality of life, and places a significant financial strain on healthcare systems. Osteoporosis prevention requires early identification, precise measurement of bone mineral content, and prompt therapy. Because of a number of causes, including inadequate bone formation, rapid bone decay, and inadequate bone growth in proportion to elevated destruction during remodeling, osteoporosis is characterized by brittle bones that are more prone to breaking. Fragile fractures are largely caused by a number of variables like the frequency and type of falls, especially those affecting the hip and wrist. Skeletal fragility is ultimately caused by a breakdown in bone remodeling, which increases bone resorption and decreases production. Various factors, including increased osteoclastic resorption and inadequate bone formation response, can lead to bone fragility, emphasizing the complexity of osteoporosis development.

Herbs used in the management of osteoporosis

Evidence from historical societies indicates a widespread utilization of plants for healing and restoring bodily functions, establishing herbal therapy as one of the earliest forms of healthcare. The current significance of herbs has magnified due to the alarming consequences of processed diets and extensive medication. Their integration into contemporary beverages, cosmetics, and food reflects a broader shift towards lifestyle improvements.

Red sage

Chinese sage, or *Salvia miltiorrhiza*, is another name for red sage, which grows wild in China and Japan's riverbanks and hillsides. It is composed of about 70 chemicals that are separated into lipophilic and hydrophilic groups. Studies reveal that it has the ability to obstruct the RANKL signaling pathway, inhibiting components such as TRAF6 and NFTAc1, as well as dysregulated cathepsin K and calcitonin receptor. Research has shown that SML (a combination of *S. miltiorrhiza* ethanol extract and liquid calcium) can prevent bone loss caused by low

estrogen levels. Many conventional clinical trials that successfully treated osteoporosis used it extensively, which has generated interest in learning more about the precise components of the plant.

Red clover

Trifolium pratense, the scientific name for red clover, is a flowering herbaceous plant of the Fabaceae family. It is native to Europe, Western Asia, and Northwest Africa, and has been widely grown across these continents. This plant has been used historically to treat menopausal symptoms and is well known for its high isoflavone content. The most prevalent kind of osteoporosis is caused by a reduction in ovarian hormones during menopause. In comparison to sham procedures, rats who had ovariectomy had lower bone minerals, femoral weight, femoral volume, higher levels of bone-specific alkaline phosphatase, and more osteoclasts in their femur sections. In contrast, similar to control rats that had ovariectomies, isoflavone treatment significantly increased markers of bone health and reduced osteoclasts. These results demonstrate how red clover isoflavones, which control bone turnover and inhibit bone resorption, may help minimize bone loss resulting from ovariectomy. Research indicates that red clover isoflavone extracts, when given to rats after ovariectomies, can help sustain bone mass.

Horsetail

Equsetum arvense, or horsetail, has an extended tradition of use as a herbal treatment dating back to the times of the ancient Greek and Roman civilizations. This thin perennial has a rhizomatous stem that looks like the tail of a horse. Horsetail was included in a research experiment with 122 Italian women, and those who consumed horsetail showed better bone densities. Horsetail is rich in silicon, a mineral that is well known for its ability to build bones. The most prevalent protein in the body, collagen, contains a significant quantity of silica and is essential for the maintenance of tendons, skin, cartilage, and muscles.

Curcumin

The principal curcuminoid in turmeric is curcumin, which is produced from *Curcuma longa* plants, often known as turmeric within the ginger family (Zingiberaceae). Curcumin is a bright yellow chemical. Turmeric has a long history of use as an anti-inflammatory in traditional Chinese medicine. Osteoporosis can result from long-term glucocorticoid drug use. Curcumin, however, has been shown in trials to prevent bone loss from ovariectomy and to decrease osteoclast generation in mice models. Curcumin has been shown by Yang *et al.* to improve mineral density and bone microarchitecture in transgenic mice. Both in vivo and in vitro studies have demonstrated the efficacy of curcumin in reducing osteoporosis caused by dexamethasone. Studies show that curcumin improves bone mineral density and bone metabolic indicators in rats,

including osteocalcin and collagen type-I fragments. In essential bone-forming cells, it also controls proteins linked to bone maturation and the process of bone differentiation. Additionally, curcumin has been shown to reactivate the Wnt/β-catenin signaling pathway, which may be a factor in its ability to protect bones. These results clearly imply that curcumin prevents osteoporosis caused by glucocorticoids.

Withania somnifera

Ashwagandha, or *Withania somnifera*, is a member of the Solanaceae family of plants and is considered to be one of the most important therapeutic herbs in Ayurveda, an ancient Indian therapeutic tradition that dates back thousands of years. Often used as a Rasayana, ashwagandha is well known for its many health advantages. Ashwagandha is rich in bioactive chemicals, including withanolides, withaferin, cuscohygrine, anahygrine, tropine, pseudo-tropine, and anaferine. Its ability to mimic the actions of estrogen on bones, especially when it comes to withanolides, suggests that ashwagandha may be used as an osteoporosis therapy. The benefits of ashwagandha extract for bone health were demonstrated in a study with ovariectomized rats, which showed elevated levels of ash weight, ash calcium, ash phosphorus, and ash magnesium in the tibia and femur bones.

Terminalia arjuna

Native to the Indian subcontinent, *Terminalia arjuna*, or "arjuna," is a plant that may be found from Sri Lanka to Myanmar. In addition to being valuable in sericulture, wood, fuel, and other applications, it is also used extensively in a number of traditional medical systems, including Yunnan, Siddha, Ayurveda, and Unani. It is occasionally referenced in writings such as the Rig Veda and Artharva Veda, and has cultural connotations with astrology and Hindu mythology. Powdered arjuna bark is mentioned as having astringent and diuretic qualities in the Charka Samhita. Glycosides, tannins, calcium carbonates, and small amounts of aluminum and magnesium may be found in the ethanol extract of Terminalia arjuna bark. The components that have been found include terpenoids such arjumin, arjunic acid, arjunolic acid, and terminic acid, and flavonoids like arjunolone, arjunone, gallic acid, and quercetin. The bark has also yielded chemicals that have been isolated, including tannins, pyrocatechols, punicallin, punicalagin, terchebulin, and casurinin. Its elevated flavonoid concentration has a beneficial effect on antioxidant status, particularly in those with coronary heart disease. The bark is believed to have hypolipidemic, cardiotonic, and anticancer properties. Studies on ovariectomized rats have demonstrated that *T. arjuna* possesses anti-osteoporotic qualities that resemble human postmenopausal osteoporosis symptoms. Because the bark can stimulate the synthesis and distribution of female hormones, it is believed to hold potential for bone remineralization. It

provides postmenopausal women with relief from osteoporosis and other bone-related diseases. *T. arjuna* ethanol extract administration has demonstrated reduction of osteoclast formation and demonstrated benefits, safety, and efficacy in osteoporosis management.

Tinospora cordifolia

A member of the Menispermaceae family, *Tinospora cordifolia* (Willd.) Miers ex Hook. F. and Thoms is a big deciduous climbing shrub that may grow up to 300 meters in height. It is widespread in many parts of China and India, especially in the tropics. In Hindi, it's called Giloy, and in Sanskrit, Guduchi. To learn more about the effects on bone formation, differentiation, and the generation of bone-like matrix, researchers looked at the effects of an alcoholic extract of Tinospora cordifolia on primary osteoblast cells from rat femurs and human osteoblast-like cells, or MG-63. In all of the cell model systems, a 25 g/ml dosage of the extract was demonstrated to have positive effects on osteoblast proliferation, encouraging osteoblastic lineage cell differentiation and enhancing the mineralization of the bone. Additionally, studies on cell morphology demonstrated that an increase in cell quantity had no detrimental effects on the cell's structure. Sarcoma osteogenic $SAOS_2$, human osteoblast-like cells, were used in a study to test the ability of alcoholic and aqueous extracts to stimulate the growth of new bone. The ethanolic extract showed enhanced osteoblast proliferation at a dosage of 25 g/ml, but the aqueous extract had no effect on cell growth. Pro-stimulatory effects of the extract were also seen in osteoblasts. Perhaps because of these research, Ayurveda would advise utilizing the fermented version of this drug for medicinal purposes.

Sesame

Benne, or sesame (*Sesamum indicum*), is an annual plant in the Pedaliaceae family that is prized for its delicious seeds that have a pleasant flavor and perfume. Sesame has been grown for millennia and thrives in tropical, subtropical, and southern temperate climates. 10% sesame oil treatment was shown to significantly reduce tartrate-resistant acid phosphatase activity and modified alkaline phosphatase activity in rats that had ovariectomies. Additionally, this therapy strengthened the microarchitecture of the bone and decreased lytic bone trabeculae, which can be disruptive.

Moringa oleifera

One of the best natural sources of vitamins A, B (1, 2, 3, 6, 7), C, D, E, and K is *Moringa oleifera*, a well-known variation in the Moringa genus of the Moringaceae family. In addition, it has more than 40 naturally occurring antioxidants and important minerals including copper, iron, calcium, potassium, magnesium, zinc, and manganese, all of which have a variety of positive health effects. Many parts of the Moringa plant, including the leaves, pods, seeds, gums, bark,

and flowers, are used in more than 80 countries, including Pakistan, to treat vitamin and mineral deficiencies, promote cardiovascular health, control blood sugar, combat free radicals to reduce the risk of cancer, support anti-inflammatory mechanisms, improve anemia, and strengthen the immune system. In addition, studies on the benefits of moringa for brain health, eye health, and bone strength suggest that it may be especially helpful for women who are facing menopause as well as for those suffering from malnourishment and weakness. Moringa oleifera and its constituents showed a noteworthy impact in reducing bone loss in rats undergoing ovariectomies.

Conclusion:

A metabolic bone disorder called osteoporosis results in decreased bone mass and heightened fracture vulnerability. It impacts a big population. Its severe consequences on quality of life need the development of a successful treatment strategy devoid of adverse effects. Ayurvedic-inspired herbal remedies have shown a great deal of promise in treating osteoporotic changes, offering a practical approach to therapy. These treatments are widely available, straightforward to use, and purportedly devoid of any known negative effects. Completing more clinical research may help to confirm their position as a practical and successful osteoporosis therapy option in clinical settings.

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DEVELOPMENT AND VALIDATION OF STABILITY INDICATING METHOD FOR THE SIMULTANEOUS ESTIMATION OF EMTRICITABINE, TENOFOVIR DISOPROXIL FUMARATE AND EFAVIRENZ IN PHARMACEUTICAL DOSAGE FORMS BY RP-HPLC

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Abstract:

A stability-indicating method was developed for the simultaneous estimation of Emtricitabine, Tenofovir and Efavirenz in pharmaceutical dosage form by reverse phase high-performance liquid chromatography (RP-HPLC) and validated. The chromatographic separation was performed using the Kromasil C_{18} (250mm × 4.6mm, 5µ) column run in an isocratic mode with a flow rate of 1mL/min at ambient temperature. The mobile phase consists of 0.01N Ammonium acetate and Acetonitrile in the ratio 65:35 (v/v/) and is detected at the wavelength 260nm. The retention times for Emtricitabine, Tenofovir and Efavirenz were found to be 2.28min, 4.03min and 2.79min respectively. The drugs obeyed Beer's law in the concentration range of 50µg/mL to 300µg/mL, 150µg/mL to 900µg/mL and 75µg/mL to 450µg/ml respectively. The method was validated as per ICH guidelines for accuracy, precision, specificity, ruggedness, robustness and stability. The standard solution was subjected to stress conditions such as acidic, basic, oxidative, neutral, photolytic and thermal conditions. The net degradation was found to be within the limits.

Keywords: Emtricitabine, Tenofovir, Efavirenz, Stability indicating, Method development, Validation, RP-HPLC.

Introduction:

Emtricitabine (EMT)[1] (Fig.1A), 4-amino-5-fluoro-1-[(2*R*,5*S*)-2-(hydroxymethyl)-1,3-oxathiolan-5-yl]-1,2-dihydropyrimidin-2-one, is a white to off-white powder, soluble in water and methanol and practically insoluble in methylene chloride with pKa value of 2.65. It is used

as antiretroviral drug in the treatment of HIV and AIDS. Tenofovir Disoproxil Fumarate (TDF)[2] (Fig.1B),[[(2R)-1-(6-aminopurin-9-yl)propan-2-yl]oxymethyl-(propan-2-pyloxycarbonyloxymethoxy)phosphoryl]oxymethyl propan-2-ylcarbonate;(E)-but-2-enedioic acid, is a white to off-white crystalline powder, soluble in methanol and dimethyl Formamide, sparingly soluble in water with pKa 3.75. It is used as antiretroviral drug in the treatment of HIV and AIDS. Efavirenz (EFA)[3] (Fig.1C), (4S)-6-Chloro-4-(2-cyclopropylethynyl)-4-(trifluoromethyl)-2,4-dihydro-1H-3,1-benzoxazin-2-one, is a white to slightly pink powder, soluble in methanol with pKa value of 12.52. It acts as antiretroviral agent and used in the treatment of HIV infection and AIDS. According to the literature survey[4-11], very few methods were developed for the simultaneous estimation of Emtricitabine, Tenofovir and Efavirenz in pharmaceutical dosage forms. The present study aimed to develop and validate the stability indicating method for the simultaneous estimation of Emtricitabine, Tenofovir and Efavirenz in pharmaceutical dosage form using RP-HPLC.

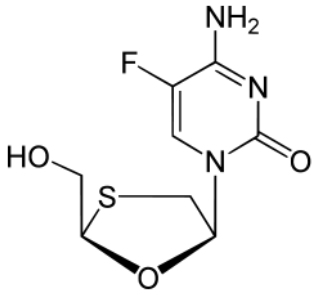

Figure 1A: Chemical Structure of Emtricitabine

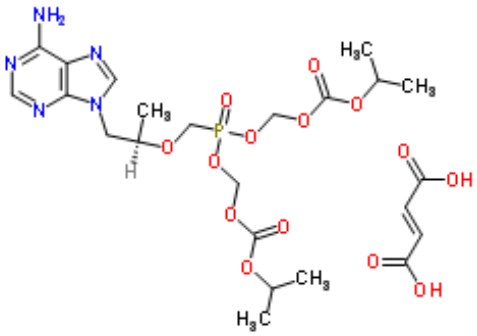

Figure 1B: Chemical Structure of Tenofovir Disoproxil Fumarate

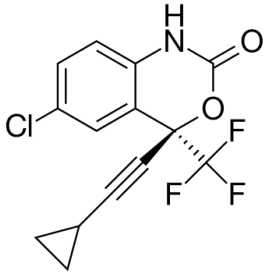

Figure 1C: Chemical Structure of Efavirenz

Materials and Methods:

Emtricitabine, Tenofovir and Efavirenz working standards were supplied by Hetero Drugs Pvt. Ltd., Hyderabad, India as gift samples. The tablets were purchased from local pharmacy. All the chemicals used in the method were of AR grade. All the solvents used were of HPLC grade.

The HPLC analysis was performed using Waters 2998 model equipped with an autosampler, Photo Diode Array detector and done on empower software. Column used was Kromasil C18 (250mm × 4.6mm, 5µ).

Preparation of buffer (0.01N Ammonium Acetate): Transfer 0.77g of ammonium acetate in to a 1000mL volumetric flask; add about 100ml of milli-Q water and mix. Finally make volume up to the mark with milli-Q water.

Preparation of mobile phase: Mixture of Buffer and Acetonitrile in the ratio 65:35 (v/v) respectively.

Preparation of diluent: Mixture of water and acetonitrile in the ratio 50:50 (%v/v) respectively

Preparation of standard solution: (200µg/mL Emtricitabine, 600µg/mL Efavirenz & 300µg/mL Tenofovir Disoproxil Fumarate) 20mg of Emtricitabine, 60mg of Efavirenz and 30mg of Tenofovir Disoproxil Fumarate working standards were accurately weighed and transferred into a 10mL volumetric flask. 7mL of diluent was added, sonicated to dissolve and make up to final volume with diluent. From the above stock solution, 1mL was pipetted into a 10mL volumetric flask and the volume was made up to mark with diluent.

The standard solution was injected into the HPLC system and chromatogram was recorded (Fig.2A).

Preparation of sample solution:

20 tablets (Atripla) were weighed accurately and the average weight was calculated. Then the tablets were crushed and fine powder was collected. An amount equivalent to 20mg of Emtricitabine was weighed and transferred into 10mL volumetric flask. 7mL of diluent was added and sonicated for 30min with intermediate shaking. Volume was made up with diluent. The above solution was filtered using HPLC filters. 1mL of the above solution was pipette into 10mL volumetric flask and made up with diluent.

The sample solution was injected into the HPLC and chromatogram was recorded (Fig. 2B). A blank solution was also injected and chromatogram was recorded (Fig.2C).

Method validation[12]:

The standard solution was injected into the HPLC system six times and system suitability parameters were noted in the table 1.

The specificity study was conducted using placebo solution. The placebo interference with the peaks of drugs is to be noted (Fig.3).

Precision (%RSD) was determined by injecting the six samples of solution.

To determine the accuracy of the test method, samples were prepared by spiking drug materials with the equivalent amount of placebo at 50%, 100% and 150% of the target concentration. The average % recoveries were determined.

Linearity was determined by preparing the series of standard solutions and injecting into the HPLC system. A graph is plotted to concentration versus peak area, results and graphs were summarized in table 2 and figures 4A, 4B and 4C. LOD and LOQ were determined using the formula mentioned in ICH guidelines, based on calibration curves.

Ruggedness (%RSD) was determined by analyzing the samples on different days. Robustness was determined by varying the optimum conditions such as ±5% of organic phase, ±0.2mL/min flow rate and ±5ºC column oven temperature with respect to test method.

The stability of drugs in solution was determined by repeated analysis of samples during the course of experimentation on the same day and also after storage of drug solution for 24h under laboratory conditions.

Forced degradation studies[13] were conducted by exposing the standard solution to the stress conditions like acidic (hydrochloric acid), basic (sodium hydroxide), oxidative (hydrogen peroxide), neutral (water), photolytic (UV light) and thermal (heat) conditions. The chromatograms were recorded (Fig. 5) and results were summarized in table 3.

Results:

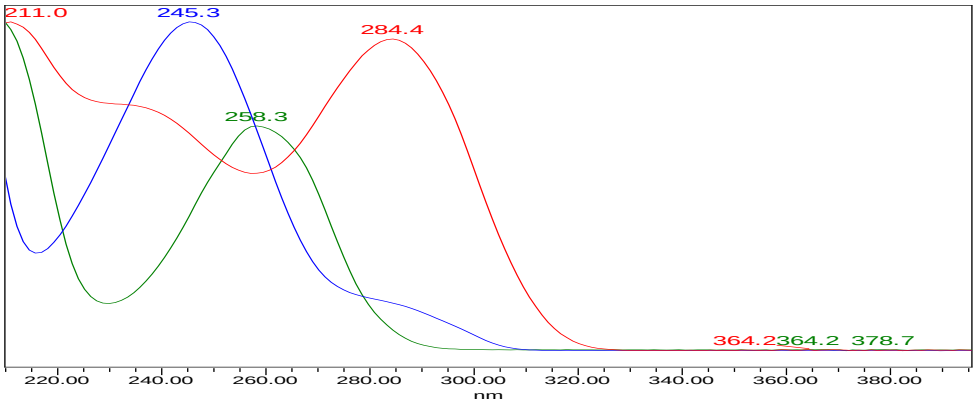

Figure 2: Overlay UV Spectrum of EMT, TDF and EFA

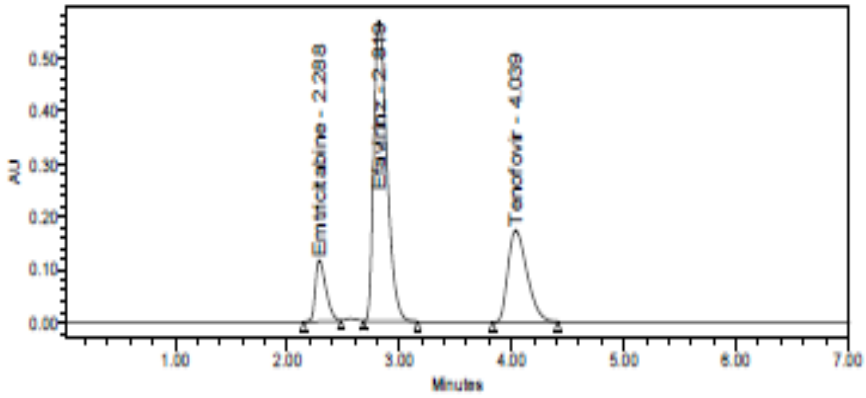

Figure 2A: Standard chromatogram

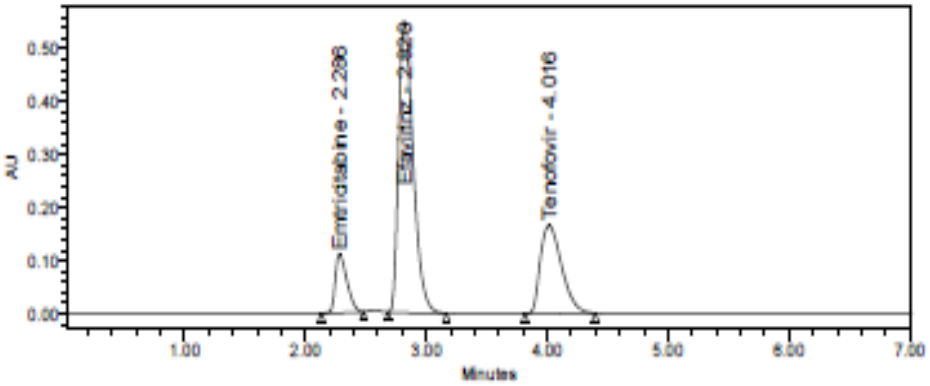

Figure 2B: Sample chromatogram

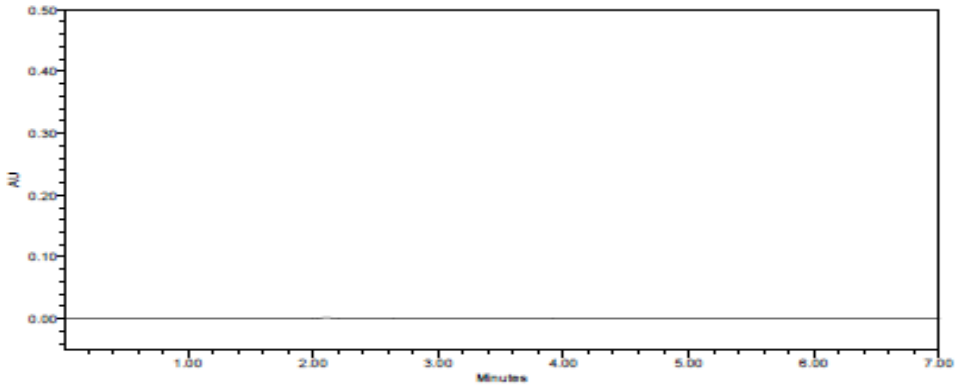

Figure 2C: Blank chromatogram

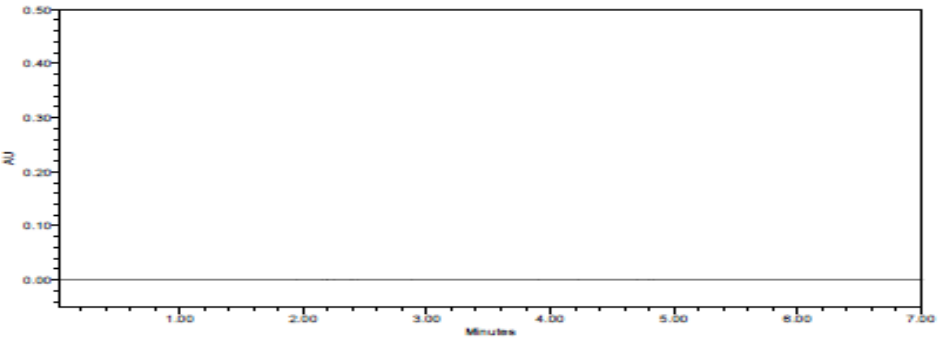

Figure 3: Placebo chromatogram

Table 1: System suitability and validation parameter results

Parameter	Emtricitabine	Efavirenz	Tenofovir
Specificity	Specific	Specific	Specific
Precision (%RSD)	0.5	0.5	0.6
Accuracy (% Recovery)	99.60%-100.07%	99.02%-99.60%	99.60%-100.14%
Linearity range (µg/ml)	50-300	75-450	150-900
Correlation coefficient, r	0.9998	0.9996	0.9996
Limit of Detection (µg/ml)	0.32	1.23	0.15
Limit of Quantitation (µg/ml)	0.96	3.73	0.46
Ruggedness (%RSD)	0.9	0.7	0.6
Robustness	Robust	Robust	Robust
Stability	Stable	Stable	Stable
USP Plate Count	3331	2979	2947
USP Tailing factor	1.41	1.44	1.21
USP Resolution		2.7	5.2

Table 2: Linearity results

Parameter (Unit)	Emtricitabine	Efavirenz	Tenofovir
Linearity range (µg/mL)	50-300	75-450	150-900
Regression equation, y=mx+c	y=3685.1x+9178.7	y=7917.5x+45083	y=7102.4x+15511
Slope, m	3685	7917	7102
Regression coefficient, r^2	0.9996	0.9993	0.9992
Correlation coefficient, r	0.9998	0.9996	0.9996

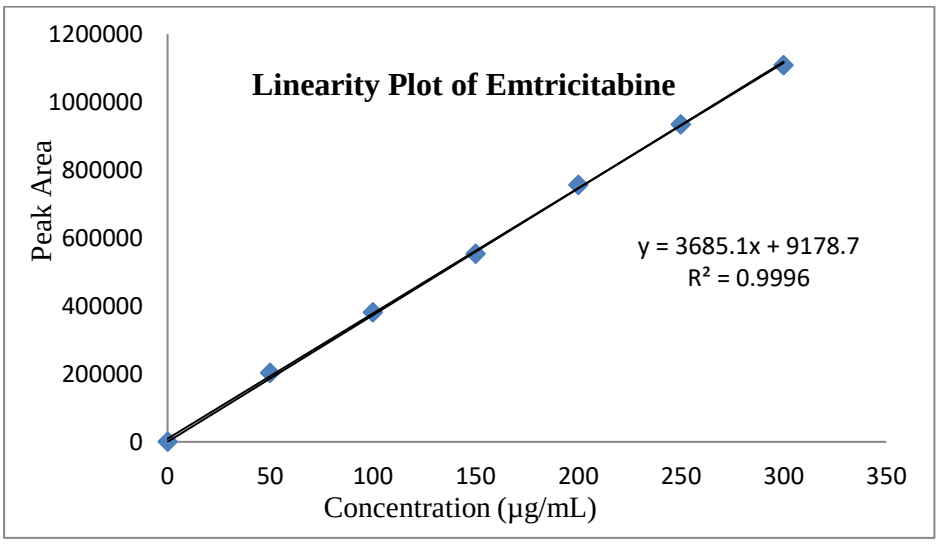

Figure 4A: Linearity plot of Emtricitabine

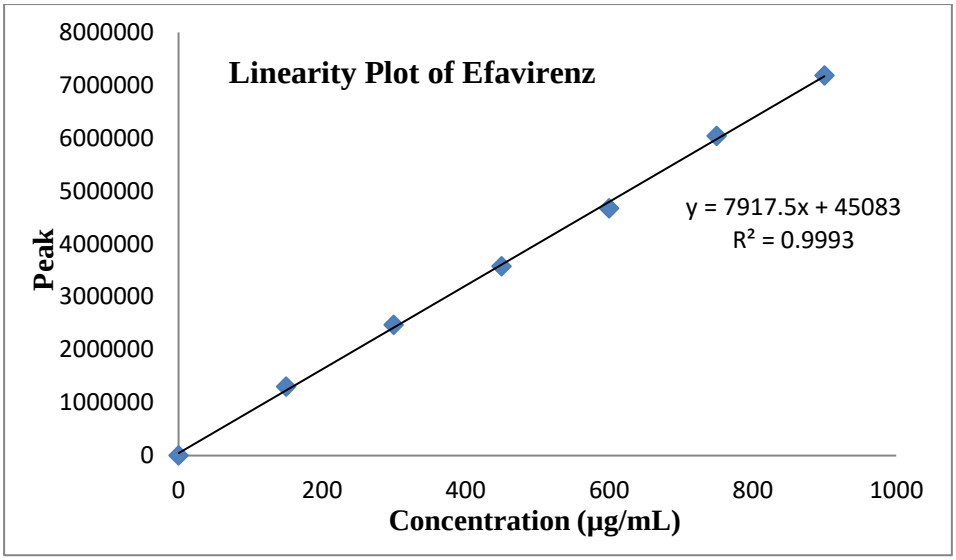

Figure 4B: Linearity plot of Efavirenz

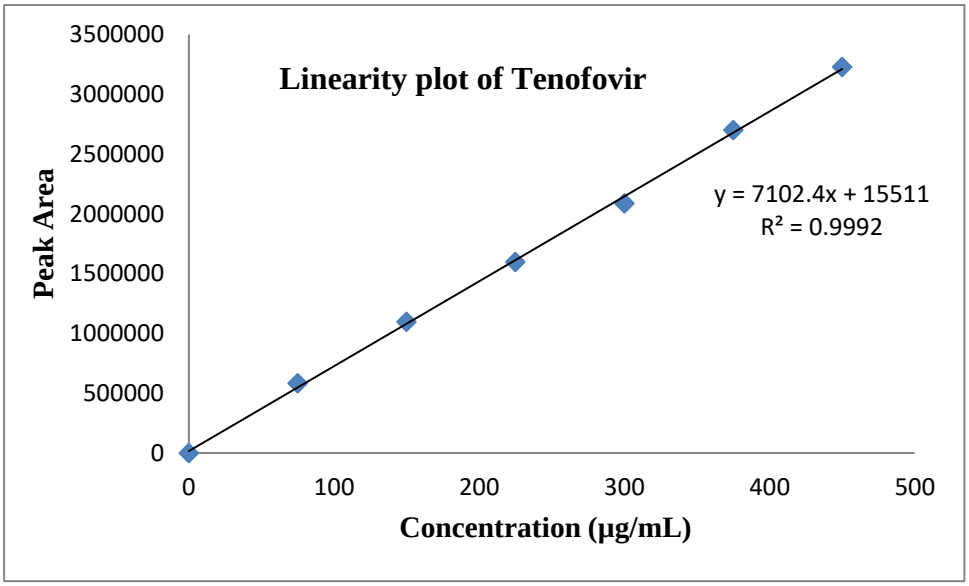

Figure 4C: Linearity plot of Tenofovir

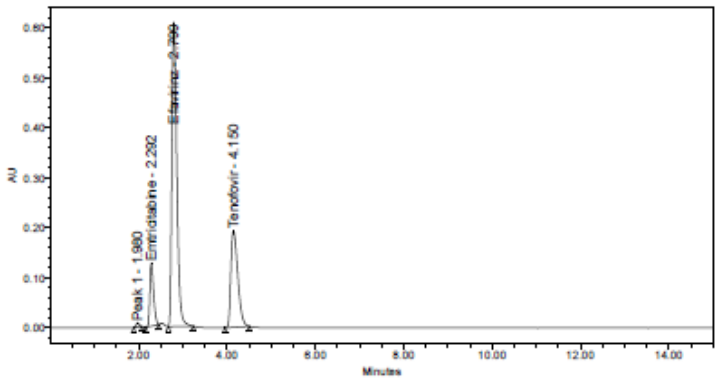

Figure 5A: Acid Degradation study chromatogram

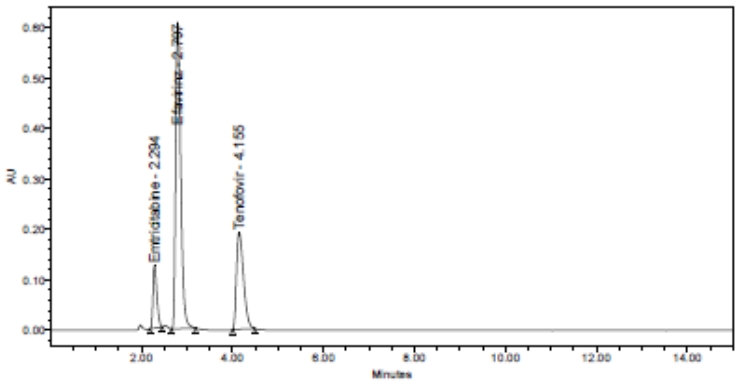

Figure 5B: Base Degradation study chromatogram

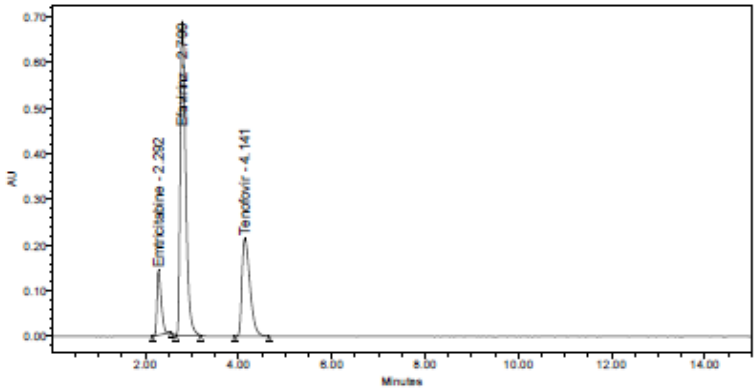

Figure 5C: Oxidative Degradation study chromatogram

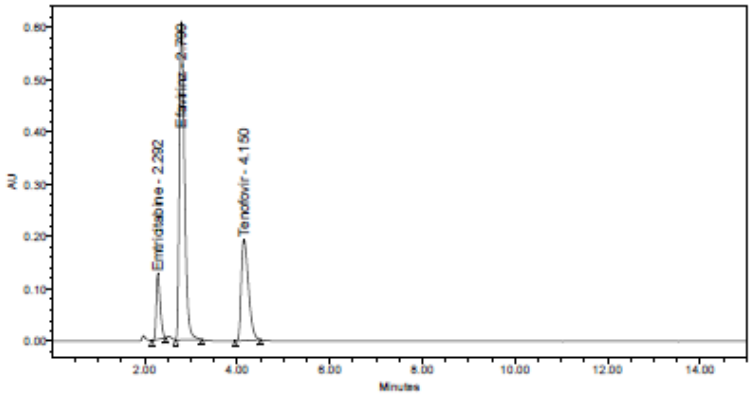

Figure 5D: Neutral Degradation study chromatogram

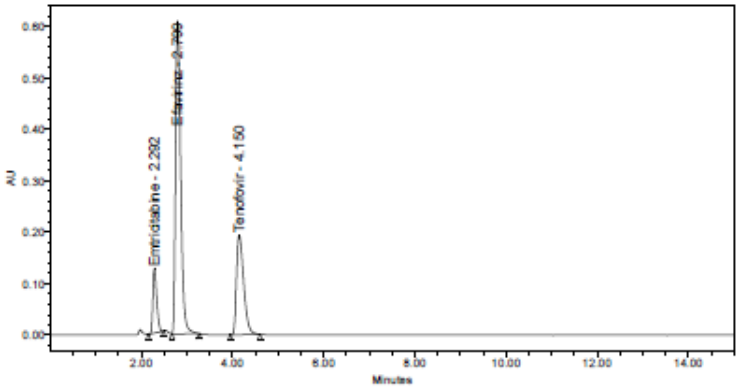

Figure 5E: Photolytic Degradation study chromatogram

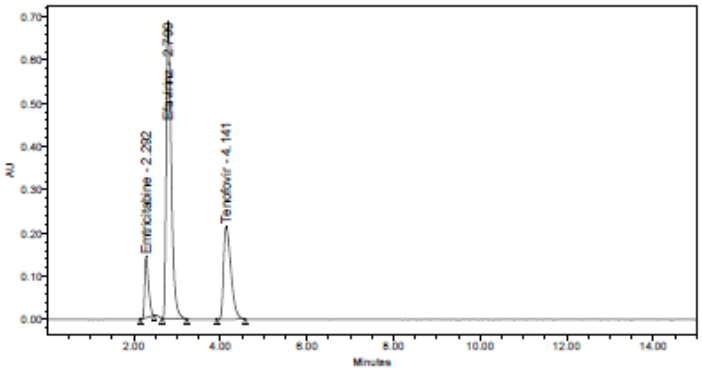

Figure 5F: Thermal Degradation study chromatogram

Table 3: Forced degradation studies results

Drug	Parameters	Stress Condition					
		Acidic heat	Basic	Oxidative	Photolytic	Neutral	Dry
	% Assay	95.49	97.04	98.06	99.44	99.32	99.18
Emtricitabine	Purity Angle	3.073	2.972	1.863	1.571	0.073	7.726
	Purity Threshold	4.273	3.268	2.280	2.280	0.273	8.27
	% Assay	95.21	97.28	98.45	99.40	99.29	99.18
Efavirenz	Purity Angle	0.520	0.720	0.742	0.563	0.120	0.806
	Purity Threshold	1.284	1.283	0.995	0.785	0.284	1.295
Tenofovir	% Assay	95.30	97.22	98.53	99.31	99.20	99.14
Disoproxil	Purity Angle	0.097	0.090	0.131	0.105	0.097	0.121
Fumarate	Purity Threshold	1.309	1.303	0.312	0.318	0.309	1.306
% Area of	degradation Peak	0.51	-	-	-	-	-

Discussion:

At the starting, various mobile phase ratios were tried to separate the drugs. Based on their peak parameters, run time and resolution, optimized conditions were determined. The standard solution of 10µg/mL was prepared and scanned in the range of 200-400nm. 260nm was selected as detection wavelength based on the overlay UV spectrum (Figure 6). The chromatographic separation was performed using Kromasil C18, 250mm × 4.6mm, 5µ column. 0.01N Ammonium acetate: acetonitrile (65:35) run in isocratic mode and flow rate 1.0ml/min was selected. Emtricitabine, Efavirenz and Tenofovir Disoproxil Fumarate were found to be 2.28min, 2.79min and 4.03min respectively

A linear response was observed in the concentration range of 50µg/mL – 300µg/mL for Emtricitabine, 150µg/mL – 900µg/mL for Efavirenz and 75µg/mL – 450µg/mL for Tenofovir with correlation coefficient of 0.999.

The %RSD for Emtricitabine, Efavirenz and Tenofovir Disoproxil Fumarate were found to be 0.5, 0.5 and 0.6 respectively. The % recoveries were found to be 99.90% - 100.07% for Emtricitabine, 99.02%-99.60% for Efavirenz and 99.60%-100.14% for Tenofovir Disoproxil Fumarate.

The results of ruggedness, robustness and stability confirmed that the developed method is rugged, robust and stable up to 24h.

The forced degradation studies confirmed that the drugs were stable under stress conditions such as acidic, basic, oxidative, neutral, photolytic and thermal conditions. The net degradation was found to be within the limits. The peak purity angle is less than the peak purity threshold.

Conclusion:

A stability indicating RP-HPLC method was developed for the simultaneous estimation of Emtricitabine, Efavirenz and Tenofovir in bulk drug and pharmaceutical dosage form. The method was validated according to ICH guidelines. The method was found to accurate, precise, specific, stable, rugged and robust. From the degradation studies, it is concluded that the drugs were stable in stress conditions. The proposed method is used for the simultaneous estimation of Emtricitabine, Efavirenz and Tenofovir in routine and quality control analysis of tablet formulations.

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OVERACTIVE FORCES: NAVIGATING THE REALM OF HYPERTHYROIDISM

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Abstract:

Hyperthyroidism, a common endocrine disorder, results from an excessive production of thyroid hormones, primarily thyroxine (T4) and triiodothyronine (T3). This dysfunction leads to a state of metabolic overdrive, impacting various physiological systems. This abstract provides a comprehensive overview of hyperthyroidism, exploring its etiology, clinical manifestations, diagnostic approaches, and available treatment modalities.

Keywords: Hyperthyroidism, Thyroid hormones, Etiology , Clinical manifestations, Diagnosis, Thyroid function tests , Treatment modalities, Antithyroid drugs, Radioactive iodine therapy, Thyroidectomy

Introduction:

Hyperthyroidism stands as a prevalent and clinically significant endocrine disorder, marked by an excessive production of thyroid hormones by the thyroid gland. The thyroid hormones—thyroxine (T4) and triiodothyronine (T3)—play a fundamental role in regulating the body's metabolic rate, impacting various physiological processes. When this delicate balance is disrupted, a cascade of symptoms ensues, affecting nearly every organ system.[1]

The etiology of hyperthyroidism is diverse, encompassing autoimmune conditions, nodular thyroid diseases, and, to a lesser extent, thyroiditis. Graves' disease, an autoimmune disorder characterized by the production of stimulating antibodies, is a primary contributor to hyperthyroidism. Toxic nodular goiter, marked by the presence of hyperfunctioning thyroid nodules, represents another significant cause. Understanding the underlying causes is pivotal for tailoring effective treatment strategies and addressing the unique challenges presented by each patient.

Clinical manifestations of hyperthyroidism are wide-ranging, reflecting the profound influence of thyroid hormones on bodily functions. Patients commonly present with symptoms such as palpitations, weight loss, heat intolerance, tremors, and anxiety. The challenge for clinicians lies in recognizing these manifestations, often mimicking other medical conditions, and conducting a thorough diagnostic evaluation to ascertain the root cause of hyperthyroidism.

Accurate diagnosis involves a combination of clinical assessment and specialized laboratory tests. Measurement of thyroid-stimulating hormone (TSH), free T4, and free T3 levels serves as the cornerstone of diagnostic evaluation. Imaging studies, such as thyroid scintigraphy, aid in identifying the specific etiology, guiding subsequent treatment decisions. The diagnostic process is not only crucial for confirming hyperthyroidism but also for determining its underlying cause, as the treatment approach may vary based on the specific diagnosis.

Etiology:

The etiology of hyperthyroidism, the condition marked by an excess production of thyroid hormones, is multifaceted and often involves disruptions in the delicate regulatory mechanisms of the thyroid gland. Several underlying factors contribute to the development of hyperthyroidism, with autoimmune disorders, nodular thyroid diseases, and less commonly, thyroiditis, playing prominent roles.[2]

1. **Graves disease**: The most prevalent cause of hyperthyroidism is Graves' disease, an autoimmune disorder where the immune system mistakenly produces antibodies that stimulate the thyroid gland. These thyroid-stimulating immunoglobulins (TSIs) bind to the thyrotropin receptor on thyroid cells, leading to an uncontrolled release of thyroid hormones.
2. **Toxic nodular goiter (Plummer's disease)**: Nodular thyroid diseases, particularly toxic nodular goiter, contribute significantly to hyperthyroidism. In this condition, one or more thyroid nodules become hyperfunctional, producing excessive amounts of thyroid hormones independently of the regulatory feedback mechanisms.
3. **Subacute thyroiditis**: Although less common, subacute thyroiditis can cause transient hyperthyroidism. This condition is often preceded by inflammation of the thyroid gland, resulting in the release of stored thyroid hormones into the bloodstream. Subacute thyroiditis can be triggered by viral infections or other inflammatory processes.
4. **Thyroiditis**: Inflammation of the thyroid gland, known as thyroiditis, can lead to the release of stored thyroid hormones. This can occur in several forms, including Hashimoto's thyroiditis (an autoimmune condition that typically causes hypothyroidism but can temporarily result in hyperthyroidism during the early stages) and postpartum thyroiditis.
5. **Excessive iodine intake**: Elevated iodine levels, whether from dietary sources, medications, or contrast agents used in medical imaging, can contribute to hyperthyroidism, particularly in susceptible individuals. This phenomenon, known as the Jod-Basedow effect, is more likely to occur in regions with iodine deficiency.

6. **Thyroid cancer**: Certain thyroid cancers, such as follicular or papillary carcinoma, may lead to hyperthyroidism as a result of uncontrolled thyroid hormone production by malignant cells.

Epidemiology:

Hyperthyroidism, a common endocrine disorder, has a notable prevalence worldwide, affecting individuals across various age groups and demographics. The epidemiology of hyperthyroidism involves considerations of incidence, prevalence, risk factors, and demographic patterns.

1. **Incidence and prevalence:**

- Global Prevalence: Hyperthyroidism is more prevalent than previously thought, with estimates varying globally. It is reported to affect approximately 1-2% of the general population.
- Geographical Variations: Incidence rates may vary in different regions, often influenced by iodine intake levels. Regions with iodine deficiency may have a higher incidence of hyperthyroidism due to increased autoimmune thyroid disorders.

2. **Age and gender distribution:**

- Age-Related Patterns: Hyperthyroidism can occur at any age, but it is more commonly diagnosed in individuals between 20 and 40 years old. There is also an increased risk in older adults.
- Gender: Graves' disease, a leading cause of hyperthyroidism, demonstrates a clear gender bias, predominantly affecting women. The female-to-male ratio for Graves' disease is approximately 5:1.

3. **Risk factors:**

- Autoimmune Factors: Graves' disease, an autoimmune condition, constitutes a significant proportion of hyperthyroidism cases. Family history and genetic predisposition are important risk factors.
- Iodine Intake: Both iodine deficiency and excess can contribute to the development of hyperthyroidism, emphasizing the importance of balanced iodine intake.
- Other Autoimmune Conditions: Individuals with a history of other autoimmune disorders, such as type 1 diabetes or rheumatoid arthritis, may be at an increased risk.

4. **Pregnancy and hyperthyroidism:**

- Gestational changes: Pregnancy can influence thyroid function, and hyperthyroidism may occur or exacerbate during gestation. Conditions like postpartum thyroiditis can also lead to transient hyperthyroidism in the postpartum period.

5. **Thyroid disorders in elderly:**

- Increased prevalence: Hyperthyroidism is more prevalent in the elderly population, often due to conditions like toxic nodular goiter. Diagnosis can be challenging in this age group due to atypical presentations.

6. **Thyroid cancer:**

- Association with hyperthyroidism: Certain thyroid cancers, although less common, can be associated with hyperthyroidism. The epidemiology of hyperthyroidism may be influenced by the prevalence of thyroid malignancies. [3]

Pathophysiology:

The pathophysiology of hyperthyroidism involves a disruption in the finely regulated feedback mechanisms that control thyroid hormone production, leading to an excessive release of thyroxine (T4) and triiodothyronine (T3) from the thyroid gland. The primary contributors to hyperthyroidism are autoimmune disorders, toxic nodular goiter, and thyroiditis. [4]

1. **Autoimmune disorders - Graves' disease:**
   - **Stimulating antibodies:** Graves' disease, the most common cause of hyperthyroidism, is characterized by the production of autoantibodies, particularly thyroid-stimulating immunoglobulins (TSIs) or thyroid-stimulating antibodies (TSAb).
   - **Thyroid stimulation:** These antibodies mimic the action of thyroid-stimulating hormone (TSH), binding to the TSH receptors on thyroid follicular cells. This leads to continuous stimulation of the thyroid, causing an uncontrolled synthesis and release of thyroid hormones.
2. **Toxic nodular goiter (Plummer's disease):**
   - **Hyperfunctioning Nodules:** In toxic nodular goiter, one or more thyroid nodules become hyperfunctional and operate independently of normal regulatory feedback.
   - **Autonomous hormone production:** These nodules autonomously produce and release thyroid hormones, disrupting the balance of the hypothalamic-pituitary-thyroid axis.
3. **Thyroiditis:**
   - **Inflammation and hormone release:** Thyroiditis, inflammation of the thyroid gland, can lead to the release of stored thyroid hormones due to damage to thyroid follicular cells. This can result from various causes, including viral infections.
   - **Transient hyperthyroidism:** In conditions like subacute thyroiditis, the initial inflammation causes a transient phase of hyperthyroidism, followed by a hypothyroid phase as the gland heals.

4. **Iodine-induced hyperthyroidism:**
   - **Jod-Basedow effect:** Excessive iodine intake, whether from diet, medications, or contrast agents, can lead to hyperthyroidism, known as the Jod-Basedow effect.
   - **Increased hormone synthesis:** High levels of iodine stimulate the thyroid gland, leading to increased synthesis and release of thyroid hormones. This is more likely to occur in individuals with underlying thyroid disorders or iodine deficiency.
5. **Thyroid cancer:**
   - **Autonomous thyroid hormone production:** Certain thyroid cancers, such as follicular or papillary carcinoma, can lead to hyperthyroidism by autonomously producing thyroid hormones.
   - **Disruption of normal regulation:** Malignant thyroid cells may disrupt the normal regulatory mechanisms, contributing to uncontrolled hormone production.

The excessive thyroid hormone levels in hyperthyroidism have widespread effects on various organ systems. Increased metabolism leads to symptoms such as weight loss, heat intolerance, and increased heart rate. The cardiovascular, gastrointestinal, and neuromuscular systems are also affected. Additionally, the chronic state of hyperthyroidism can have long-term consequences, emphasizing the importance of early diagnosis and appropriate management to prevent complications.

Clinical presentation:

The clinical presentation of hyperthyroidism reflects the profound impact of elevated thyroid hormone levels on various organ systems. The symptoms are diverse and can range from subtle to severe. The following is a comprehensive overview of the clinical manifestations associated with hyperthyroidism:

1. **Cardiovascular symptoms:**
   - **Tachycardia:** Increased heart rate is a hallmark of hyperthyroidism, leading to palpitations, a sensation of rapid or irregular heartbeat.
   - **Atrial fibrillation:** In severe cases, persistent high heart rates may contribute to the development of atrial fibrillation, a cardiac arrhythmia.
2. **Metabolic symptoms:**
   - **Weight loss:** Despite an increased appetite, individuals with hyperthyroidism often experience unexplained weight loss.
   - **Increased Basal Metabolic Rate (BMR):** Elevated thyroid hormone levels boost the body's metabolic rate, leading to increased energy expenditure.

3. **Heat intolerance:**
   - **Intolerance to heat:** Hyperthyroid individuals may have difficulty tolerating heat, sweating excessively, and feeling uncomfortably warm.
4. **Gastrointestinal symptoms:**
   - **Increased bowel movements:** Hyperthyroidism can accelerate gastrointestinal transit, leading to more frequent bowel movements and even diarrhea.
   - **Increased appetite:** Some individuals may experience an increase in appetite, contributing to weight loss.
5. **Musculoskeletal symptoms:**
   - **Muscle weakness:** Hyperthyroidism can lead to muscle weakness and fatigue.
   - **Tremors:** Fine tremors, especially in the hands, may be noticeable.
6. **Neuropsychiatric symptoms:**
   - **Anxiety and irritability:** Individuals with hyperthyroidism may experience heightened levels of anxiety, nervousness, and irritability.
   - **Insomnia:** Difficulty falling asleep or staying asleep can be a symptom of hyperthyroidism.
7. **Reproductive symptoms:**
   - **Menstrual Irregularities:** Women may experience changes in their menstrual cycles, with irregularities in timing and flow.
8. **Ophthalmic symptoms (Graves' ophthalmopathy):**
   - **Proptosis (Eye bulging):** Graves' disease, a common cause of hyperthyroidism, may be associated with ophthalmic manifestations, including proptosis.
   - **Eye irritation:** Dryness, redness, and a feeling of grittiness in the eyes may occur.
9. **Dermatological symptoms:**
   - **Warm and moist skin:** The skin may feel warm and moist due to increased sweating.
10. **General symptoms:**
    - **Fatigue:** Despite the increased metabolic rate, individuals may still experience fatigue and weakness.
    - **Emotional lability:** Mood swings and emotional lability can be observed.

It is important to note that the severity and combination of symptoms can vary among individuals. Additionally, some cases of hyperthyroidism may present with atypical or subtle symptoms, making the diagnosis challenging. Timely recognition and appropriate management are crucial to alleviate symptoms and prevent complications associated with prolonged hyperthyroidism. [5]

Diagnosis:

The diagnosis of hyperthyroidism involves a combination of clinical evaluation, laboratory tests, and, in some cases, imaging studies. The goal is to assess thyroid function, identify the underlying cause, and determine the appropriate course of treatment. The following are key components of the diagnostic process:[6]

1. **Clinical assessment:**
   - **Medical history:** A thorough medical history is crucial, including information about symptoms, their duration, and any factors that might contribute to hyperthyroidism.
   - **Physical examination:** A comprehensive physical examination helps identify signs associated with hyperthyroidism, such as an elevated heart rate, tremors, goiter (enlarged thyroid), and eye changes (in Graves' disease).
2. **Thyroid function tests:**
   - **Thyroid Stimulating Hormone (TSH) test:** TSH levels are typically the first-line test. In hyperthyroidism, TSH levels are suppressed due to the negative feedback loop – the thyroid gland doesn't respond to the high levels of thyroid hormones.
   - **Free Thyroxine (FT4) and Free Triiodothyronine (FT3) tests:** Elevated levels of these hormones confirm hyperthyroidism. FT4 and FT3 are more accurate indicators of thyroid function than total T4 and T3.
3. **Antibody tests (Graves' disease):**
   - **Thyroid Stimulating Immunoglobulins (TSIs) or Thyroid Receptor Antibodies (TRAb):** Positive results indicate autoimmune hyperthyroidism, specifically Graves' disease.
4. **Radioactive Iodine Uptake (RAIU) test:**
   - **Iodine Uptake by Thyroid Gland:** This test measures the amount of radioactive iodine taken up by the thyroid. Increased uptake indicates overactivity. It helps differentiate between causes like Graves' disease and toxic nodular goiter.
5. **Thyroid ultrasound:**
   - **Imaging of the thyroid gland:** Ultrasound can help visualize the thyroid gland, identifying any nodules or structural abnormalities.
6. **Thyroid scintigraphy:**
   - **Imaging with radioactive tracers:** This test provides a functional assessment of the thyroid gland and helps determine if the hyperthyroidism is diffuse (Graves' disease) or focal (toxic nodular goiter).

7. **Fine Needle Aspiration (FNA):**
    - **Biopsy of thyroid nodules:** If nodules are detected, an FNA biopsy may be performed to rule out thyroid cancer.
8. **Additional tests:**
    - **Complete Blood Count (CBC):** Anemia and other blood abnormalities may be associated with hyperthyroidism.
    - **Liver function tests:** Hyperthyroidism can affect liver function, and these tests help assess liver health.

The diagnosis is typically confirmed by the combination of low TSH levels, elevated FT4 and FT3 levels, and supporting information from antibody tests or imaging studies. It's important to note that the specific diagnostic approach may vary based on individual cases and the suspected underlying cause of hyperthyroidism. A collaborative effort between healthcare professionals, including endocrinologists and radiologists, is essential for an accurate diagnosis and appropriate management.

Treatment:

The treatment of hyperthyroidism aims to normalize thyroid hormone levels, alleviate symptoms, and address the underlying cause of the condition. The choice of treatment depends on factors such as the severity of hyperthyroidism, the underlying cause, the presence of coexisting medical conditions, and patient preferences. The main treatment modalities include: [7]

1. **Antithyroid medications:**
    - **Propylthiouracil (PTU) and Methimazole (MMI):** These medications inhibit the synthesis of thyroid hormones. Methimazole is often preferred due to its longer duration of action, but PTU may be used in specific situations, such as during the first trimester of pregnancy.
    - **Monitoring:** Regular monitoring of thyroid function is essential during antithyroid drug therapy to adjust the dosage and assess for potential side effects.
2. **Radioactive iodine therapy:**
    - **Radioactive Iodine (I-131) treatment:** This approach involves the oral administration of radioactive iodine, which selectively accumulates in the thyroid gland. The emitted radiation gradually destroys thyroid tissue, leading to a reduction in hormone production.
    - **Advantages:** Radioactive iodine therapy is a common and effective treatment for hyperthyroidism, especially in cases of Graves' disease.
    - **Considerations:** This treatment may result in hypothyroidism over time, necessitating lifelong thyroid hormone replacement.

3. **Thyroidectomy (Surgical removal):**
    - **Partial or total thyroidectomy:** Surgical removal of part or all of the thyroid gland is reserved for cases where antithyroid medications or radioactive iodine therapy is contraindicated or not well-tolerated.
    - **Advantages:** Thyroidectomy provides a rapid resolution of hyperthyroidism, but it carries the risk of surgical complications and requires lifelong thyroid hormone replacement.
4. **Beta-blockers:**
    - **Symptomatic relief:** Beta-blockers such as propranolol can help manage symptoms like tachycardia, tremors, and anxiety. However, they do not address the underlying cause of hyperthyroidism.
    - **Short-term use:** Beta-blockers are often used as a temporary measure before more definitive treatments take effect.
5. **Supportive care:**
    - **Fluid and electrolyte management:** In severe cases, hyperthyroidism may lead to dehydration and electrolyte imbalances. Supportive care may involve intravenous fluids and electrolyte monitoring.
    - **Management of complications:** Addressing complications such as thyroid storm, a life-threatening exacerbation of hyperthyroidism, requires intensive care and specific interventions.
6. **Pregnancy considerations:**
    - **Special considerations:** The management of hyperthyroidism in pregnant women requires careful consideration, and antithyroid medications like propylthiouracil are often preferred to minimize potential harm to the developing fetus.

Individualized treatment plans are crucial, and decisions should be made collaboratively between patients and healthcare providers. Regular follow-up is essential to monitor thyroid function, adjust treatments as needed, and address any potential side effects or complications. Successful management of hyperthyroidism often involves a multidisciplinary approach, with endocrinologists, surgeons, and primary care physicians working together to optimize patient outcomes.

Conclusion:

In conclusion, hyperthyroidism represents a complex endocrine disorder with diverse etiologies and a wide spectrum of clinical manifestations. The disruption in thyroid hormone balance, whether stemming from autoimmune conditions like Graves' disease, toxic nodular goiter, or thyroiditis, profoundly affects multiple organ systems. The clinical presentation of

hyperthyroidism is varied, encompassing cardiovascular, metabolic, neuropsychiatric, and ophthalmic symptoms.

The diagnosis involves a thorough clinical assessment, including medical history and physical examination, coupled with specific laboratory tests and imaging studies. Identifying the underlying cause is crucial for tailoring an appropriate treatment strategy, considering options such as antithyroid medications, radioactive iodine therapy, or thyroidectomy. Symptomatic relief through beta-blockers may be employed, especially in the short term.

Successful management requires a nuanced approach, taking into account the severity of hyperthyroidism, the presence of complications, and individual patient characteristics. Regular monitoring and collaboration among healthcare professionals are essential to fine-tune treatment plans, address potential complications, and ensure optimal outcomes.

As our understanding of hyperthyroidism continues to evolve, ongoing research and advancements in therapeutic options promise to refine diagnostic approaches and treatment strategies. Ultimately, a patient-centered and multidisciplinary approach remains fundamental in managing hyperthyroidism effectively, promoting improved quality of life, and preventing long-term complications associated with this challenging endocrine disorder.

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OVERVIEW ON PANDEMIC DISEASE COVID -19: EPIDEMIOLOGY, SYMPTOMS, TRANSMISSION, TESTS, TREATMENTS – A REVIEW

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Abstract:

Thousands of new patients with Covid-19 present for care each day, and many can be quickly enrolled in pragmatic clinical trials. The most relevant clinical outcomes for evaluating these drugs including death, hospitalization, number of days spent in intensive care, and need for a ventilator are readily assessed and available within days or weeks COVID-19 is a pandemic disease, it effects globally hence World health organization was listed this in Pandemic disease and announced medical emergency throughout the world. However in India, compare to other countries it's severely affected. United States of America was reported highest positive Cases as well as Deaths. WHO reported that the American region highest Covid-19 6,397,230 positive cases and 279,857 death cases. Least cases were recorded in the Western Pacific region positive cases and death cases as follows 239,111 and 7,563. All over the world COVID-19 was infected the human beings all over the world except 33 countries. In India from the reported date of first case to till date 11 July 2020, there are 820,916 positive cases and 22,674 deaths cases were reported. Sikkim State and Lakshadweep were not reported even a single case. Most of the affected cases were spread of virus through clustered in time, geographic location or by common exposure. 3 states were reported no death case. Till date there is no medicine or vaccine to treat COVID-19, the only thing to prevention is to maintain physical distance from each other. The present study briefly noted information of epidemiology, symptoms, transmission/spread, diagnosis methods, treatments/ drugs and situation were mentioned.

Keywords: COVID-19, Pandemic disease, Plasma therapy, Social distancing, Quarantine

Introduction:

Corona viruses are a large family of viruses that can cause a range of illnesses from common cold all the way up to more severe diseases such as the Middle East Respiratory Syndrome (MERS) and the Severe Acute Respiratory Syndrome (SARS), which are known to

lead to critical respiratory and intestinal illnesses. Corona viruses belong to the family *Corona viridae* and are positive single-stranded RNA viruses surrounded by an envelope. They are divided into four genera: *Alpha-*, *Beta-*, *Gamma-*, and *Deltacoronavirus*. The *Alphacoronavirus* genus includes *HCoVNL63* and *HCoV-229E*, while the *Betacoronavirus* genus comprises *HCoV-OC43*, *HCoV-HKU1*, *SARS-CoV* (severe acute respiratory syndrome coronavirus), *MERSCoV* (Middle East respiratory syndrome-related coronavirus), and the unique *SARS-CoV-2* (severe acute respiratory syndrome coronavirus. SARS-CoV and MERS-CoV are zoonotic in origin; they cause severe respiratory syndrome and are often fatal. Neoteric coronavirus was tentatively named 2019-nCoV, now SARS-CoV-2 based on the Coronavirus Study Group of the International Committee on Taxonomy of Viruses. SARS-CoV belongs to Betacornavirus. The genome size of the SARS-CoV varies from 29.0 kb to 30.2 kb which can encodes structural proteins Spike, envelope (E), membrane (M), N proteins and non-structural proteins papain-like protease(s) (PLpro), chymotrypsin-like protease (3CLpro), RNA-dependent RNA polymerase (RdRp) and helicase (Hel). Haemagglutinin-esterase gene is absent from the genome of SARS-CoV.

Spike protein structure

The coronavirus spike protein is a class I fusion protein. The development of an α-helical coiled-coil shape is characteristic of this class of fusion protein, which comprise in their C-terminal part locations predicted to have an α-helical secondary structure and to manifestation coiled-coils. The S2 subunit is the most economized region of the protein, whereas the S1 subunit deviates in sequence even amidst species of a single coronavirus. The S1 carries two subdomains, a N-terminal domain (NTD) and a C-terminal domain (CTD). Both are capable to function as receptor binding domains (RBDs) and bind diversity of proteins and sugars. Coronavirus spike proteins hold two heptad repeats in their S2 domain, a feature typical of a class I viral fusion proteins. Heptad repeats constitute a repetitive heptapeptide with a and d being hydrophobic remnant feature of the formation of coiled-coil that participate in the fusion process. For SARS-CoV and MHV, the post-fusion structures of the HR have been solved; they form the characteristic six-helix bundle. The operational involvement of MHV and SARS-CoV HR was persistent by mutating key residues and by restraint experiments using HR2 peptides.

The spike protein is the frequent target for nullifying antibodies and vaccines. Spike protein encompasses two subunits, S1 and S2. S1 contains a receptor binding domain (RBD), which is reliable for grasping and binding with the cell surface receptor. S2 subunit holds other basic elements required for the membrane fusion. SARS-CoV-2 (2019-nCoV) can contaminate the human respiratory epithelial cells throughout interaction with human ACE2. Indeed, the recombinant spike protein can bind with recombinant ACE2 protein. The Nucleocapsid Protein

(N-protein) is the most packed protein in coronavirus. The N-protein is an extremely immunogenic phosphoprotein, and it is typically much conserved. The N protein of coronavirus is frequently used as a marker in diagnostic assays. The spike (S) protein is the particularly significant antigen of SARS-CoV. It is constituted of two subunits; the S1 subunit contains a receptor-binding domain (RBD) that engages with the host cell receptor angiotensin-converting enzyme 2 (ACE2) and the S2 subunits mediates fusion between the viral and host cell membranes. The S protein plays key parts in the induction of neutralizing-antibody and T-cell responses, as well as protective immunity, during infection with SARS-CoV (Hayes K.H. Luka, 2019).

Epidemiology effect of pandemic COVID-19

The director-general of the World Health Organization, Doctor Tedros Ghebreyesus, announced on January 23rd that "the emerging COVID-19 is an emergency in China only and not considered as Public Health Emergency of International Concern (PHEIC)" (WHO Guidelines 2020). The outbreak was declared a Public Health Emergency of International Concern on 30 January 2020. On 11 February 2020, WHO announced a name for the new coronavirus disease: COVID-19. On March 11, 2020, the World Health Organization designated "coronavirus disease 2019" (Covid-19) a global pandemic. The present study discussed about the situation from the first COVID-19 confirmed case to till date.

WHO regions

Heads of state, ministries of health, hospitals, clinics, and community health organizations are taking immediate action. As the pandemic makes its first in roads, several nations have potently pursued containment achievements including identifying, assessing, and isolating people with suspected cases and close contacts of each infected person. Countries are also organizing virtual learning networks to circulate information to the departments of health and community persons.

First case of novel coronavirus outside of China confirmed 13 January 2020 Officials confirmed a case of the novel coronavirus in Thailand. The worldwide spread of COVID-19 is multiply day by day as per the World Health Organization situation report (WHO, 2020). As stated in the data updated globally, as of 10:00 CEST, 11 July 2020, there have been 12,322,395 confirmed cases of COVID-19, including 556,335 deaths. WHO categorized 6 regions; highest positive cases and deaths were reported in the American region 6,397,230 and 279,857 deaths. European region reported 2,888,850 positive cases and 202,837 death cases. Positive cases 1,255,977 and 30,145 death cases were reported in the Eastern Mediterranean region. In the South East Asia region was reported positive cases and death cases as follows 1,097,074 and 27,990. Africa region reported 443,412 positive cases and death rate was low and the number of

death cases 7,930. Comparatively all the regions, Western Pacific Region reported 239,111 positive cases and deaths 7,563. Data were shown in the Table 1.

Epidemiology of COVID-19 in India

In India on 30th January 2020, first positive case of Novel Coronavirus patient, of a student studying in Wuhan University, has been reported in Kerala. On 2nd and 3rd February 2020 second and third the patient has tested positive for Novel Coronavirus has been reported in Kerala and they were in isolation in the hospital. The patient is stable and is being closely monitored. After reported of first cases new cases were reported on 3rd and 4th March six cases with high viral load have been detected during sample testing in Agra. These are the ones who have come in contact with the COVID-19 patient from New Delhi, reported. They have been kept in isolation. First death case on 13th March 2020 was reported. Death of a 68 year old female from West Delhi (mother of a confirmed case of COVID 19), is confirmed to be caused due to co-morbidity (diabetes and hypertension). She has also tested positive for COVID-19. She had history of contact with a positive case (her son who had travel history to Switzerland and Italy between 5th to 22rd February, 2020). Religious tourism and weddings: potential coronavirus clusters in India. Places of religious gathering such as temples, mosques and churches can be clusters for coronavirus transmission in India, where religious tourism is high and community gatherings for celebrating festivals are huge. ISKCON, one of the popular Hindu religious organisations running temples that attract foreign devotees, is reported to have advised foreigners from the coronavirus-affected countries not to visit for two months, as a precautionary measure. Agra, another popular hotspot for tourists including foreigners, is a potential cluster. One more potential coronavirus cluster in India is weddings where the average guest counts run from few hundreds to more than a thousand.

Ministry of Health and Family Welfare is constantly and rigidly working with States/UTs to reinforce the health infrastructure in the country. As follows, a total of 602 facilitated COVID-19 hospitals with 106,719 isolation beds and 12,024 ICU beds have been arranged. Additionally, 1919 dedicated COVID-19 hospitals have been established at both Centre and State level which includes: 672 Dedicated COVID Hospitals (DCH) (with 107,830 sheltered private beds and 14742 ICU beds), 1247 Dedicated COVID Health Centres (DCHC) (with total of 65916 isolation beds and 7064 ICU beds) Hence a total of 1919 facilities having 173,746 isolation beds and total ICU beds 21,806 are available. In the battle against COVID-19, Government of India has awaked numerous preventive efforts, which are being enforced throughout the country with the collaboration of State/UT governments. As a remarkable preventive measure, the Union Government has earlier launched an application called Aarogya Setu. The Ministry of Electronics and IT has developed the Aarogya Setu Mobile App. To increase the testing capacity

for COVID-19 at the National Centre for Disease Control (NCDC), the Empowered Group 2 recommended the procurement of a high throughput machine, which has been approved. The Cobas 6800 testing machine has been successfully installed at NCDC and is currently supporting the testing of samples from Delhi, NCR, Ladakh, J&K, and other states as needed. The testing capacity at NCDC has been significantly enhanced with the Cobas 6800, which has the capacity to test around 1200 samples in 24 hours, compared to the current capacity of 300-350 tests per day.

ICMR has explicitly stated that there are currently no approved therapies for COVID-19, including plasma therapy, as mentioned earlier. Plasma therapy is just one of the numerous experimental treatments being explored. Nevertheless, there is currently no substantiated evidence to validate its effectiveness as a treatment. To evaluate the therapy's efficacy, ICMR has initiated a National Study. However, it is crucial to emphasize that until ICMR concludes its study and robust scientific evidence is available, plasma therapy should only be utilized for research and trial purposes. It is important to note that the use of plasma therapy may pose life-threatening complications. In order to provide comprehensive guidance on the use of plasma therapy outside the scope of the study, ICMR has already issued detailed guidelines.

The mortality rate for COVID-19 is of 3.3%. Further analysis of the data indicates that out of the deceased, the age distribution reveals that 14.4% of individuals fall within the 0-45 years age bracket, while 10.3% belong to the 45-60 years age group. Furthermore, 33.1% are classified in the 60-75 years age range, and the remaining 42.2% are aged 75 years and above. These statistics indicate that a significant majority, amounting to 75.3% of the cases, are attributed to individuals aged 60 years and older. Additionally, it is noteworthy that 83% of the cases exhibited co-morbidities. These findings reinforce the earlier emphasized notion that older adults and individuals with underlying health conditions are more susceptible to higher risks. As on 12 July 2020, 08:00 IST (GMT+05:30) total confirmed cases 849,553, active cases 292,258 and 22,674 death cases were reported, in this 534,620 cases were recovered (MoHFW 2020). State wise data was shown in the Table 4.

Symptoms and incubation period of COVID-19

COVID-19 affects various people in different ways. Most infected people will develop mild to moderate illness and recover without hospitalization. Infected persons were observed the common symptoms of high body temperature, dry cough, and tiredness. Few of the symptoms were expected to towards the suspected or carriers of the COVID-19 such symptoms are body pains, headache, tasteless or sore throat, diarrhea conjunctivitis. In children rash on skin or discoloration of finger toes was observed as a symptom to recognize as infected. Difficulty to take breath, chest pain and loss of speech were serious symptoms of the Covid-19.

Incubation period

The estimated duration of the incubation period ranges from 2 to 15 days and transmission from asymptomatic cases has been reported (Tang *et al.,* 2020). It is anticipated that there will be a surge in COVID-19 cases in the near future due to heightened screening and detection measures. The paramount concern is the potential spread of the virus by infected persons who may be mobile. The incubation period is important for defining the period of public health observation of exposed contacts of confirmed cases. The understanding of the incubation period plays a crucial role in various significant public health endeavors aimed at combating infectious diseases. These endeavors include active monitoring, surveillance, control, and modeling. To ensure active monitoring, individuals who may have been exposed are urged to promptly notify local health authorities about their health condition on a daily basis. Understanding the length of active monitoring needed to limit the risk for missing SARS-CoV-2 infections is necessary for health departments to effectively use limited resources. The current period of active monitoring recommended by the U.S. Centers for Disease Control and Prevention (14 days) is well supported by the evidence (The White House 2020). Symptomatic disease is frequently associated with transmissibility of a pathogen. However in light of the latest findings on SARS-CoV-2 transmission by individuals with mild symptoms or no symptoms at all. (Rothe *et al.,* 2020).

Spread of COVID-19

The determination is made by evaluating various factors, encompassing but not restricted to: substantial quantities of cases not linkable to transmission chains; large numbers of cases from sentinel lab surveillance. 53 countries were affected through the spread of COVID-19 through community transmission.

Clusters of cases: COVID-19 spread through this, 88countries experiencing cases, clustered in time, geographic location and/or by common exposures.

Sporadic cases: in this most of the cases spread through imported or locally infected persons. Totally 52 countries detected the positive cases as sporadic cases.

Community transmission: experiencing larger outbreaks of local transmission

Diagnosis for COVID-19

Collection of samples

Collection of specimens from the surface of the respiratory mucosa with nasopharyngeal swabs is a procedure used for the diagnosis of Covid-19 in adults and children (MedlinePlus 2020). The procedure is also commonly used to evaluate patients with suspected respiratory infection caused by other viruses and some bacteria.

Tests for diagnosis of COVID-19

There exists a duo of test classifications for diagnose the COVID-19:

- Serology based tests
- Molecular based tests

Serology based tests

Serology testing for SARS-CoV-2 is at increased demand in order to better quantify the number of cases of COVID-19, including those that may be asymptomatic or have recovered. Serology tests are blood-based tests that analyze the immune response of individuals to determine if they have been exposed to a specific pathogen, such as COVID-19. These tests can detect cases of the virus, including those who may not show symptoms or have already recovered. On the other hand, the RT-PCR tests, which are widely used for diagnosing COVID-19, can only confirm the presence of viral material during an active infection and will not indicate if a person was infected and subsequently recovered. These tests can give greater detail into the prevalence of a disease in a population by identifying individuals who have developed antibodies to the virus. In this different types of serological assays were used to diagnose the virus. i.e**.** Rapid diagnostic test (RDT), Enzyme linked immune sorbent assay (ELISA), Neutralization assay and Chemiluminescent immune assay. Each sample test can look for multiple types of antibodies, including IgG, IgM, and IgA.

Molecular based Tests for COVID-19

The diagnostic testing field for COVID-19 is rapidly evolving and improving in quality every day, with many tests focused on diagnosing patients with active viral infections. Molecular-based diagnostics are commonly utilized to identify present and ongoing infections, providing valuable insights to researchers regarding the existence of the pathogen. These diagnostics employ various techniques, such as detecting the genetic material or distinctive markers specific to the pathogen. In the case of SARS-CoV-2, the viral genomic material is ribonucleic acid (RNA), which is present in the body solely during the replication phase of the virus. There are also rapid antigen tests in development that act by detecting specific surface markers on the outside of the virus; none of these tests have received FDA emergency use authorization (EUA), nor are any available on the market at this time. Molecular diagnostics usually require samples from the patient that are likely to contain virus, such as nasopharyngeal swabs or sputum samples. Some pathogens can also be identified in feces, urine, or blood. In the case of respiratory illnesses such as COVID-19, nasopharyngeal swabs have been deemed the most reliable method as they target the specific area of the respiratory tract where the virus initially infects an individual. This region is relatively accessible compared to the final site of viral infection, which is the lower respiratory tract. As a result, the nasopharyngeal tract is likely

to have both active virus replication and sufficient viral quantities to be detected in testing kits. Many tests currently available or under development can utilize saliva or nasal swabs, which offer simpler sampling procedures for healthcare providers and patients.

Types of molecular and antigen tests

Reverse transcriptase quantitative polymerase chain reaction (rRT-qPCR): Identifies and quantifies the presence of infectious agents in a sample through the process of detection, amplification, and output measurement. The proximity of an active infection, by targeting distinct gene sequences of SARS-CoV-2. This can be quantitative but is usually qualitative. It usually has a very low limit of detection, over 100 viruses /mL. Limitation: Efficient completion of the test requires adequate time, skilled professionals, and specialized tools for result analysis. Duration for test 2-4 hours

Reverse transcription loop-mediated isothermal amplification (RT-LAMP): Rapid amplification of viral genomic material coupled with a color- or light-based readout, and it can be performed at a single temperature, unlike rRT-PCR. The presence of an active infection, by targeting specific gene sequences of SARS-CoV-2. This is typically qualitative. It depends on especially elective primers that help generate the looped structures needed for amplification. It is very rapid and does not always require special equipment (can be measured by eye in some cases). It has a very low limit of detection of 125 viruses/mL.

Recombinase polymerase amplification (RPA): The recombinase enzyme is utilized to identify DNA sequences with high accuracy by separating DNA strands and amplifying particular viral genes. This technique targets specific gene sequences of SARS-CoV-2 to determine the presence of an active infection, providing a qualitative result. The recombinase enzyme enables a swift and straightforward process that does not always necessitate specialized equipment. Moreover, it boasts a remarkably low limit of detection of 125 viruses/mL.

Rapid antigen test: Detects easy-to-find surface markers on the outside of the virus and avoids extraction and amplification steps. Researchers or clinicians collect samples from easy to reach areas where the virus tends to replicate the most. Detection of particular viral proteins in a patient sample is used to determine the existence of an ongoing infection. This is commonly combined with lateral flow assays to produce visible outcomes that can be interpreted visually. Requires very careful design of synthetic antibodies, deep knowledge of viral proteins produced in various tissue environments, and may yield false negatives if the viral protein production is low.

Spread /transmission of coronavirus

The global health community has been alarmed by the outbreak and transmission of the 2019-nCoV, a new strain of coronavirus that originated in Wuhan, China (Zhu N, Zhang D,

Wang W, *et al.*, 2020). In the wake of its detection in December 2019, numerous countries have documented isolated cases of the virus among individuals who have recently traveled from China. (WHO2020).

Virus stability in aerosols

Virus stability in aerosols was resolved and described earlier at 65% relative humidity (RH) and 21-23°C (Fischer *et al.*, 2016).

Virus stability on surfaces

Surface stability was estimated on plastic (polypropylene, Plastics), AISI 304 alloy stainless steel (Metal Remnants), copper (99.9%) (Metal Remnants) and cardboard (local supplier) representing a variety of household and hospital statuses and was accomplished as described formerly at 40% RH and 21-23°C using an inoculum of 105 TCID50/mL (van Doremalen *et al.*, 2013).

The stability of SARS-CoV-2 varied across different surfaces, with plastic and stainless steel exhibiting greater stability compared to copper and cardboard. It was observed that viable virus particles could still be detected on these surfaces for up to 72 hours after initial application. A study conducted by van Doremalen (2020) suggested that both aerosol and fomite transmission of SARS-CoV-2 are plausible, as the virus can remain infectious in aerosols for several hours and on surfaces for several days, depending on the amount of initial inoculum. These findings align with earlier research on SARS-CoV-1, where both aerosol and fomite transmission played a significant role in nosocomial spread and super-spreading events. These insights are crucial for informing effective strategies to mitigate the ongoing pandemic.

Treatment for COVID-19

World populations are currently facing an unprecedented health crisis caused by the spread of an infectious virus, the coronavirus-induced pneumonia, known as the Novel Coronaviruses disease (COVID-19), which has seriously affected human health worldwide (Yang, Y, Shen, C, Li, J *et al*,.2020). Patients infected with this virus suffer from potential damage to vital organs especially the lungs, heart, liver and kidney (Valizadeh *et al.*, 2020 and Yalameha *et al.*, 2020).

Due to the outbreak of the global pandemic, clinicians and the Food and Drug Administration (FDA) are under immense pressure to efficiently expedite the availability of medications to patients. Currently, there are no approved antibodies or drugs specifically designed to treat coronaviruses, posing challenges in the treatment and management of diseases caused by the 2019-nCoV and its associated pandemic. In an effort to discover potential drugs to combat the 2019-nCoV, we utilized a computational approach to screen existing commercial medications that could potentially act as inhibitors for the Mpro of 2019-nCoV. Previous

investigations aiming to predict drugs for the Mpro of SARS-CoV successfully identified two HIV-1 protease inhibitors, namely lopinavir and ritonavir, as promising candidates. These inhibitors bind to the same target site of Mpro, underscoring their potential efficacy. Clinical application of these drugs on 2019-nCoV patients has shown promising results, emphasizing the significance of the drug binding site in suppressing the activity of the 2019-nCoV Mpro enzyme.

Currently, there are no approved medications available for the treatment or prevention of this particular infection. Effective management involves isolating the patient, implementing strict hand hygiene measures, utilizing face masks, and other sanitary precautions to prevent the spread of respiratory aerosol/droplet infection. These measures significantly reduce the risk of transmission to caregivers and close contacts. A clinical trial is currently underway in Nebraska, USA (NCT04257656) to evaluate the efficacy of a new antiviral drug, remdesivir (Gileads Sciences Inc.), in hospitalized adults. This investigational drug has previously shown promising results in animal models infected with Ebola virus, SARS, and MERS virus (Wit E, Feldmann F, Cronin J, *et al.*, 2020). Remdesivir works by inhibiting RNA polymerase, which is essential for viral replication in host cells. When administered as pre-exposure prophylaxis and therapeutic treatment in rhesus macaques, remdesivir significantly reduced disease severity, virus replication, and lung damage.

Plasma therapy

Convalescent plasma therapy for COVID-19

The US Food and Drug Administration (FDA) have recently confirmed the use of plasma therapy from retrieved COVID-19 patients to treat hypercritical nauseous patients. As per FDA recommendations, the plasma must be collected from a donor who showed no symptoms for the last 14 days and had negative recent COVID-19 results (Tanne, JH.2020 and FDA 2020). The initial pilot study on CP treatment was carried out in three affiliated hospitals, involving 10 critically ill COVID-19 patients who received a sole administration of 200 ml CP. The findings demonstrated a substantial elevation or sustained presence of neutralizing antibodies in patients, accompanied by a swift amelioration of clinical symptoms within a span of 3 days (Duan, K, Liu, B, Li, C *et al.*, 2020). After COVID-19 was declared a global pandemic, many scientists suggested that CP could be used as a capable therapeutic approach to mitigate the infection's symptoms (Casadevall, A, Pirofski, LA 2020, Chen, L, Xiong, J, Bao, L *et al.*, 2020 and Shen, C, Wang, Z, Zhao, F *et al.*, 2020). Based on these fundamental results, USA-based John Hopkins University is currently leading a randomized trial (Phase 2) on 150 older participants undergoing CP treatment with a titer of neutralizing antibody > 1:64 for post-exposure prevention (NCT04323800, 2020). A Mayo Clinic-sponsored phase 2 trial investigating CP treatment with a titer > 1:64 is also currently recruiting (NCT04325672, 2020). A thorough examination of the

antibody responses during the progression of the disease was conducted by analyzing the outcomes of 173 patients in a recent study. Periodic antibody detection demonstrated that antibody presence was less than 40% in patients during the initial week of COVID-19 infection. However, it exhibited a rapid escalation to 100% for Ab, 79.8% for IgG, and 94.3% for IgM from the second week onwards after the onset of infection. This emphasizes the significance of regular testing in the context of COVID-19 infections (Zhao, J, Yuan, Q, Wang, H *et al.*2019). Additionally, it was observed that female patients exhibited a higher average level of IgG antibodies compared to male patients, especially in severe cases. This disparity in COVID-19 outcomes between genders could potentially be attributed to this difference. (Zeng, F, Dai, C, Cai, P *et al.*2020).

Plasma therapy derived from individuals who have successfully recovered from COVID-19 displays promising prospects for both safety and efficacy in treatment, according to the existing data. Given the present circumstances, the critical need for viable treatment methods for COVID-19 is of utmost importance. As the efficacy of antiviral drugs undergoes evaluation, the utilization of CP emerges as a primary consideration in combating this ongoing pandemic. The attainment of successful therapeutic approaches necessitates collaborative involvement and coordination among various entities, including blood banking specialists, virologists, hematologists, and other healthcare professionals, to ensure accurate assessment of the severity of the disease.

Lopinavir/ ritonavir

The viral protease enzyme is inhibited by two drugs that are commonly used to treat HIV. Studies conducted on in vitro and animal models have demonstrated their effectiveness in combating SARS and MERS CoV. These drugs have been found to bind to the Mpro enzyme, which is utilized by CoV for replication. Based on pre-clinical data, these drugs are recommended for use against COVIDB. 19. A retrospective cohort study of hospitalized patients reviewing clinical course and risk factors for mortality included 29 patients who received lopinavir; ritonavir. No difference was noted in the duration of viral shedding after treatment with lopinavir; ritonavir. However, few critical COVID-19 patients were found to be recovered by treatment with these two drugs. The risk factors for these drugs include cardiac arrhythmias and are avoided for administration to patients with hepatic disease or hepatitis. It also has significant drug interactions like chloroquine and hydroxychloroquine (Cao et al., 2020).

Tocilizumab: This particular substance is a monoclonal antibody that functions as an inhibitor for the interleukin-6 receptor. Due to its ability to release cytokines, it has been proposed for use in combating COVID-19. By competitively binding to both the soluble and membrane-bound interleukin-6 receptors, it effectively regulates the cytokine release signaling system. As a result,

it is employed as a standard supplementary therapy for COVID-19 treatment. Ongoing investigations are being conducted to gather additional data on its clinical effectiveness against COVID-19. However, it is important to note that there are potential risks associated with its usage, including gastrointestinal perforation and hepatotoxicity. Additionally, it is not recommended for patients with thrombocytopenia and neutropenia. It has infusion-related reactions (Smith *et al.,* 2020).

Bacillus Calmette-Guerin (BCG) vaccine is implemented in many vaccine plans across Latin America, in Brazil, to induce protection against tuberculosis and leprosy. In recent years, several clinical studies have highlighted another crucial effect of BCG, which is its ability to provide heterologous protection against infections that are not related. Recent findings suggest that BCG can trigger the release of specific cytokines, resulting in the activation of CD4+ and CD8+ memory T cells. (Berg RE, *et al.,* 2002). Another proposed mechanism is to induce a more active innate immune response through several epigenetic modifications in *IL-6 and TNFA* genes, and activation of human monocytes that can protect against a non-related viral infection mediated by IL-1β (Arts RJW *et al.,* 2017). BCG vaccination could be an important factor also to protect health professionals against SARS-CoV2 infection.

The Indian Council of Medical Research, under the Ministry of Health and Family Welfare, has recommended chemoprophylaxis with hydroxychloroquine (400 mg twice on day 1, then 400 mg once a week thereafter) for asymptomatic healthcare workers treating patients with suspected or confirmed COVID-19, and for asymptomatic household contacts of confirmed cases (MOHF 2020). The document states "its use in prophylaxis is derived from available evidence of benefit as treatment and supported by preclinical data". Although some in-vitro evidence supports the antiviral activity of hydroxychloroquine and its precursor chloroquine, there is no peer-reviewed publication that evaluates either drug for exposure prophylaxis of SARSCoV-2 infection. Even for treatment of diagnosed cases, only one small study reported faster nasopharyngeal viral clearance, with no data for clinical improvement (Gautret *et., al* 2020). This evidence, or the lack thereof, hardly justifies state-endorsed, widespread use of hydroxychloroquine for prophylaxis.

Remdesivir

This compound, currently under investigation, is an investigational nucleoside analogue that demonstrates a broad spectrum antiviral activity in vitro. It also exhibits specific inhibitory activity against a wide variety of CoVs. Acting as a monophosphoramidate prodrug of remdesivir-triphosphate, it functions as an adenosine analog that effectively inhibits RNA-dependent RNA polymerases. By competing with adenosine-triphosphate for incorporation into nascent viral RNA chains, it effectively inhibits viral RNA production. Additionally, once

incorporated into the viral RNA, it terminates RNA synthesis without immediate chain termination, thus evading proofreading by viral exo-ribonuclease activity. Encouragingly, clinical administration of this drug to several hundred COVID-19 positive patients in the USA, Europe, and Japan has resulted in satisfactory recovery rates. Notably, it possesses a high genetic barrier to resistance and demonstrates efficacy against a wide variety of CoV strains. Its EC50 value was determined to be 0.77 μM, with a half-cytotoxic concentration (CC50) exceeding 100 μM, resulting in a selective (Ko *et al.*, 2020).

Azithromycin

This macrolide antibacterial drug effectively hinders the growth of bacteria, making it a valuable tool in combating infections. Additionally, it has been observed to possess immune-modulatory properties, further enhancing its therapeutic potential. In clinical studies focusing on pulmonary inflammatory disorders, the drug has demonstrated highly satisfactory results. By down-regulating inflammatory responses and reducing excessive cytokine production associated with respiratory viral infections, it effectively alleviates symptoms. However, its direct impact on viral clearance remains uncertain. The drug's immuno-modulatory mechanisms include inhibiting cytokines, particularly IL-8, which reduces the chemotaxis of neutrophils to the lungs. It also inhibits mucus hypersecretion, decreases the production of reactive oxygen species, accelerates neutrophil apoptosis, and blocks the activation of nuclear transcription factors. When used in conjunction with hydroxychloroquine, its efficacy is further enhanced, making it a valuable adjunct therapy. Although it shows promise against COVID-19, clinical trials are currently underway to investigate its full potential. It is important to note that the drug carries a risk of cardiac arrhythmias and significant drug interactions. (Science News, 2020).

In the midst of a pandemic where the rates of illness and death are skyrocketing, it is understandable to feel the urge to provide unproven therapies without waiting for extensive clinical trial data. However, it is important to note that well-executed randomized, controlled trials can be conducted rapidly even in severely ill patients. With a constant influx of thousands of new Covid-19 cases daily, many individuals can be efficiently enrolled in pragmatic clinical trials.

Preventions

Wash hands frequently with soap or 70% alcohol based sanitizer at least for 20 seconds to remove invisible microbial agents. When moving into the public places use face mask and must maintain physical distance of 6feet distance, avoid mass gathering. Isolation of confirmed or suspected cases with mild illness at home is recommended. To ensure the elimination of viruses, it is essential to maintain proper ventilation in the household, preferably with exposure to sunlight. Patients should be instructed to wear a simple surgical mask and follow cough

hygiene practices. Caregivers, meanwhile, should wear a surgical mask when in close proximity to the patient and practice hand hygiene every 15–20 minutes. Don't spit in public. It's not just rude, but it can spread harmful particles. Explain to your child why he/she should not engage in public spitting. Do it in a tissue that you can safely dispose of. Droplet and contact precautions prevent direct or indirect transmission from contact with contaminated surfaces or equipment (i.e. contact with contaminated oxygen tubing/interfaces). Use Personal Protective Equipment (PPE) (triple layer surgical mask, eye protection, gloves and gown) when entering room and remove PPE when leaving. Avoid contaminating environmental surfaces that are not directly related to patient care (e.g. door handles and light switches). Ensure adequate room ventilation. Avoid movement of patients or transport. Perform hand hygiene. High Risk People age group above 60 yrs., Diabetes Mellitus, Renal Failure, Chronic Lung disease and Immuno compromised persons.

Healthcare workers should receive fit tested N95 respirators, as well as protective suits and goggles. Precautions against airborne transmission should be implemented during procedures that generate aerosols, such as intubation, suction, and tracheostomies. Given their increased risk of exposure to the virus, healthcare providers are particularly susceptible to emotional distress during the current pandemic. They also face concerns about infecting and caring for their loved ones, shortages of personal protective equipment (PPE), longer work hours, and involvement in emotionally and ethically challenging resource-allocation decisions. To address these challenges, prevention efforts should prioritize screening for mental health problems, providing psychoeducation, and offering psychosocial support to at-risk groups. The Covid-19 pandemic has significant implications for both individual and collective health, as well as emotional and social functioning. In addition to providing medical care, healthcare providers play a crucial role in monitoring psychosocial needs and delivering psychosocial support to their patients, fellow healthcare providers, and the general public. These activities should be integrated into overall pandemic healthcare efforts.

Conclusion:

COVID-19 is a pandemic disease. Till date there is no medicine or vaccine was not developed. Scientist and researcher observed the different types of genetic modification in the victims. These modifications vary from different regions of the world. It's spreading throughout the world day by day very rapidly. The only prevention is to avoid mass gathering of crowded places, maintain physical distance and use of mask. This pandemic situation mostly affected the developed countries. European region was recorded maximum positive cases and deaths compared to the rest of the world. In India most of the cases were spread through cluster of cases. During this global pandemic, Plasma therapy emerges as a promising option to explore

while antiviral drugs are undergoing testing. The development of effective therapies necessitates the collaboration and coordination of various entities, including blood banking specialists, virologists, hematologists, and other healthcare professionals. Their collective efforts are crucial in accurately assessing the severity of the disease. It is worth noting that the Remdesivir drug has shown potential in evading viral exo-ribonuclease activity, thus making it a viable treatment option. Encouragingly, the clinical administration of this drug to numerous COVID-19 positive patients in the United States, Europe, and Japan has yielded satisfactory recovery rates. This paper will give the brief information on the updated epidemiology of COVID-19 and diagnosing tests treatment for pandemic disease COVID-19.

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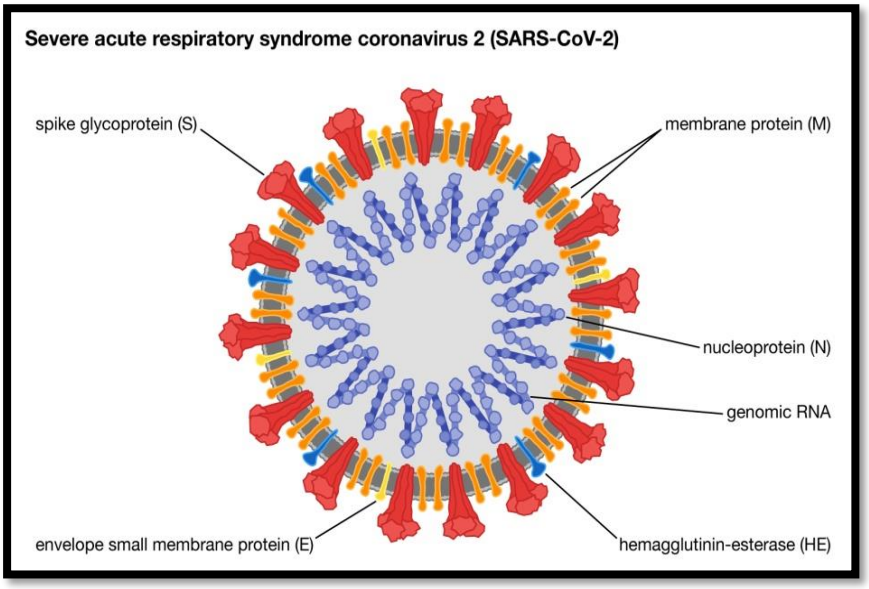

Figure 1: Corona Virus

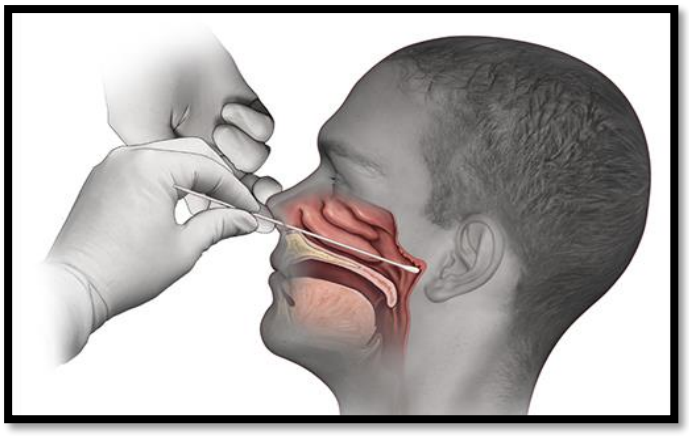

Figure 2: Collection of sample using nasopharyngeal swabs

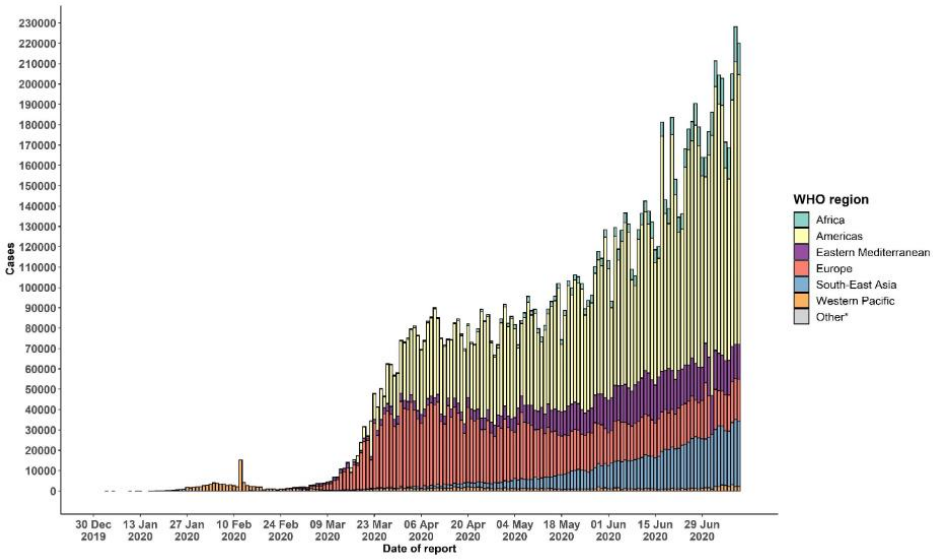

Figure 3: Reported cases (Source: WHO)

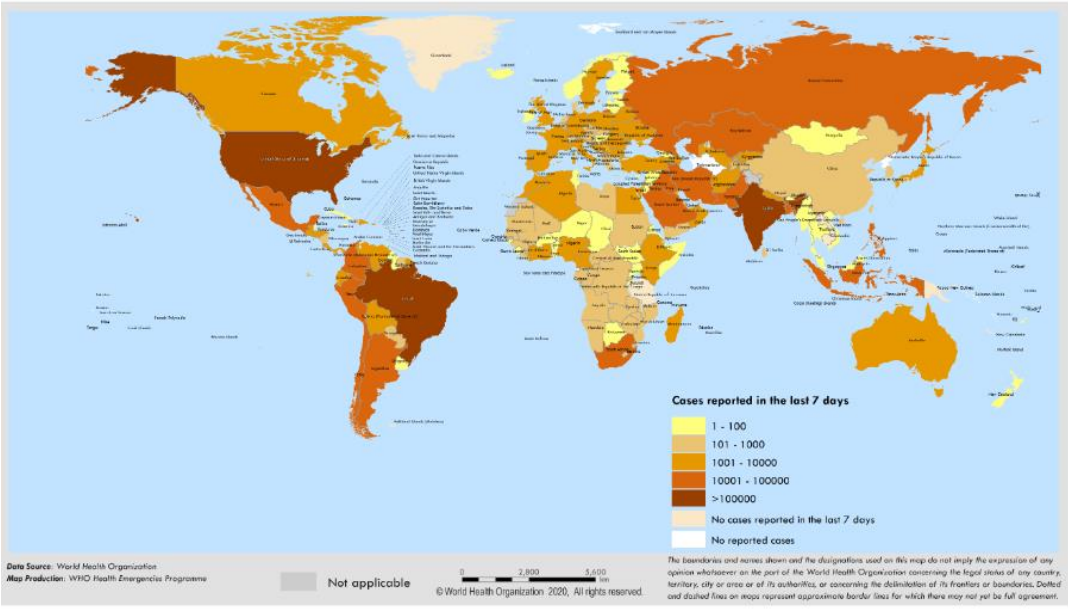

Figure 4: Global situation (Source: WHO)

Table 1: Reported Confirmed cases and Death cases

Reported Confirmed Cases and Deaths-WHO Regions			
S.No	**Region**	**Cases**	**Deaths**
1	Africa	443412	7930
2	America	6397230	279857
3	Eastern Mediterranean	1255977	30145
4	Europe	2888850	202837
5	South East Asia	1097074	27990
6	Western Pacific	239111	7563

Table 2: Top ten Countries Reported Confirmed cases and Death cases

S.No	**Country**	**Confirmed Cases**	**Death Cases**
1	United States of America	3,097,300	132,683
2	Brazil	1,755,779	69,184
3	India	820,916	22,123
4	Russian Federation	92,0547	11,205
5	Peru	316,448	11,314
6	Chile	309,274	6,781
7	The United Kingdom	288,137	44,650
8	Spain	253,908	28,403
9	Mexico	282,283	33,526
10	Iran	252,720	12,447

Table 3: State wise list of Covid-19 cases in India

S. No.	**Name of State / UT**	**Active Cases***	**Cured/Discharged/Migrated***	**Deaths****	**Total Confirmed cases***
1	Andaman and Nicobar Islands	70	93	0	163
2	Andhra Pradesh	12,533	14,393	309	27,235
3	Arunachal Pradesh	214	125	2	341
4	Assam	6,351	9,150	35	15,536
5	Bihar	4,557	10,685	131	15,373
6	Chandigarh	135	413	7	555
7	Chhattisgarh	810	3,070	17	3,897

8	Dadra & Nagar Haveli and Daman & Diu	245	226	0	471
9	Delhi	19,895	87,692	3,334	110,921
10	Goa	928	1,428	12	2,368
11	Gujarat	10,260	28,649	2,032	40,941
12	Haryana	4,891	15,394	297	20,582
13	Himachal Pradesh	263	908	11	1,182
14	Jammu & Kashmir	4,092	5,895	169	10,156
15	Jharkhand	1,347	2,243	23	3,613
16	Karnataka	20,887	14,716	613	36,216
17	Kerala	3,446	3,963	29	7,438
18	Ladakh	148	928	1	1,077
19	Madhya Pradesh	3,878	12,679	644	17,201
20	Maharashtra	99,499	136,985	10,116	246,600
21	Manipur	750	843	0	1,593
22	Meghalaya	139	66	2	207
23	Mizoram	77	150	0	227
24	Nagaland	435	313	0	748
25	Odisha	4,105	8,360	61	12,526
26	Puducherry	629	690	18	1,337
27	Punjab	2,352	5,040	195	7,587
28	Rajasthan	5,376	17869	503	23,748
29	Sikkim	71	80	0	151
30	Tamil Nadu	46,413	85,915	1,898	134,226
31	Telangana	12,135	20,919	348	33,402
32	Tripura	572	1,375	2	1,949
33	Uttarakhand	653	2,718	46	3,417
34	Uttar Pradesh	11,490	22,689	913	35,092
35	West Bengal	9,588	17,959	906	28453
	Cases being reassigned to states	3,024			3,024
	Total#	292,258	534,621	22,674	849,553
*(Including foreign Nationals), **(more than 70% cases due to comorbidities)					
#States wise distribution is subject to further verification and reconciliation #Our figures are being reconciled with ICMR					

A SCHEMATIC REVIEW ON EVOLUTIONARY ECOLOGICAL INSIGHTS OF SARS-CoV2 VIRUS AND VACCINES

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Abstract

Background: The genesis of replicated viral protein with adjuvant against SARS-CoV2 is widely overcoming the positive results all around the world. The outbreak of new strains during this vaccination retracts the new subtypes of regulatory proteins that are activated on inhalation by contact human to human. There are no records of transmission in an aspect of zoonosis except human society.

Methods: The omnipotent characters of monoclonal antibodies in human plays the significant role to control the safety margin with vaccine potency. The vaccine therapy of boosting module is undergoing the process to develop their immunological status to protect from other viral epitopes of the adenoviral family throughout the world. The development of analytical research of artificial immunogenetic is carried out by different vaccine agencies developing RNA extracted immunogens in synthetic recombinant or inactivated form.

Results: The diagnosis protocol on physiological and hematological conformation is screened by testing antigen-antibody titer level before immunization to determine the surface viral antigen in concentrated plasma. The development of the concept from community health status at Assam is required to study the statistical alignment of evolution to examine the three stages of progressive continuation of immunogenetic depending on host immune antigen-antibody titer levels.

Conclusion: The effects of modern displays are very visionary to play a role for the current herd immunized population to understand. The migratory part of the third wave is now directed by reforming to monoclonal resistance whereas polyclonal should be launched in the future for immunization status.

Keywords: Auto-immunization, DNA vaccine, Interleukin-6, Viral vector.

Introduction:

The SARS-CoV2 transmission is important after a long term of vaccination in a mass population. The development of preventive strategies is profound as a key reservoir of transmission in the previous year (2). However, the samples from hematological analysis derived from human plasma showed positive result s for viral RNA detection (1). The current reviewers initially focused on chain transmission of a viral pandemic but not about cross-transmission along with an immunized environment (3). The cross-transmission along with the potency of having vaccine implementations is raised a lot of contraindicated tasks among the immunized and non-immunized population (4). The variety of different viral strains could not be featured out due to modified transmission during this certain period (5). So the crucial and significant challenges are turning with or without vaccines against the emerging of a virus as an epidemic (6). The immune-genetics of RNA vaccine, recombinant vaccine, different types of peptide vaccines, and live or attenuated vaccines plays the same potency level from their immunogenetic rate of different safety margins (7). Studies revealed the epidemiological scenario for the phenomena of vaccine efficacy after genomic verity of novel-corona virus finding (8). Two leading RNA vaccines have not been reported for asymptomatic infections. The vaccines have been more than effective in preventing symptoms of COVID-19 along with immune boosters (9). The DNA vaccines have to be balanced to come down to cost-benefit analysis. The scale of the pandemic played a crucial to have more than one dose for each individual. The world occupies lots of several vaccines as the recommendation followed to implement after Cyto-toxicity trials (10). The lingering question is whether the vaccine can be assured for perfect immunization (15). The key shaping of the course module in mass vaccination is a complete immunization process following three doses. The Oxford-AstraZeneca team plays the role to develop three leading vaccines monitored for asymptomatic infections for trials. The working module on immunogenic artificial protein or RNA or DNA has demonstrated for vaccine regimens to migrate in a potential range.

On the platform of vaccine potency the immunization process in Assam circumflex into two objectives

a) Immunization against chain transmission of the virus

b) Marginal safety range of immunization potency

Methods

Table 1: Enlisted vaccines with their wide range of components are tabulated to feature the immunogenic potency for mass populations (Source: ourworldindata.org).

Name of Vaccine (Trade name)	Immunogenic components
Comirnaty Moderna	m RNA based vaccine, m RNA 1273
Astrazeneca (AZD 1222)	Adenovirus Vaccines
Sputunik V	Recombinent Adenovirus Vaccines (r Ad26 and r Ad5)
Janssen Vaccine	Non replicating viral vector
Corona Vac	Inactivated vaccine
Epi Vac Corona	Peptide Vaccine
Covidicea	Adeno virus types with five vector components
Co-vaxin	Inactivated Vaccine
NVX-CoV 2373	Nano particle Vaccine
ZyCoV-D	Plasmid DNA Vaccine
UB 612	Multiple peptide vaccine

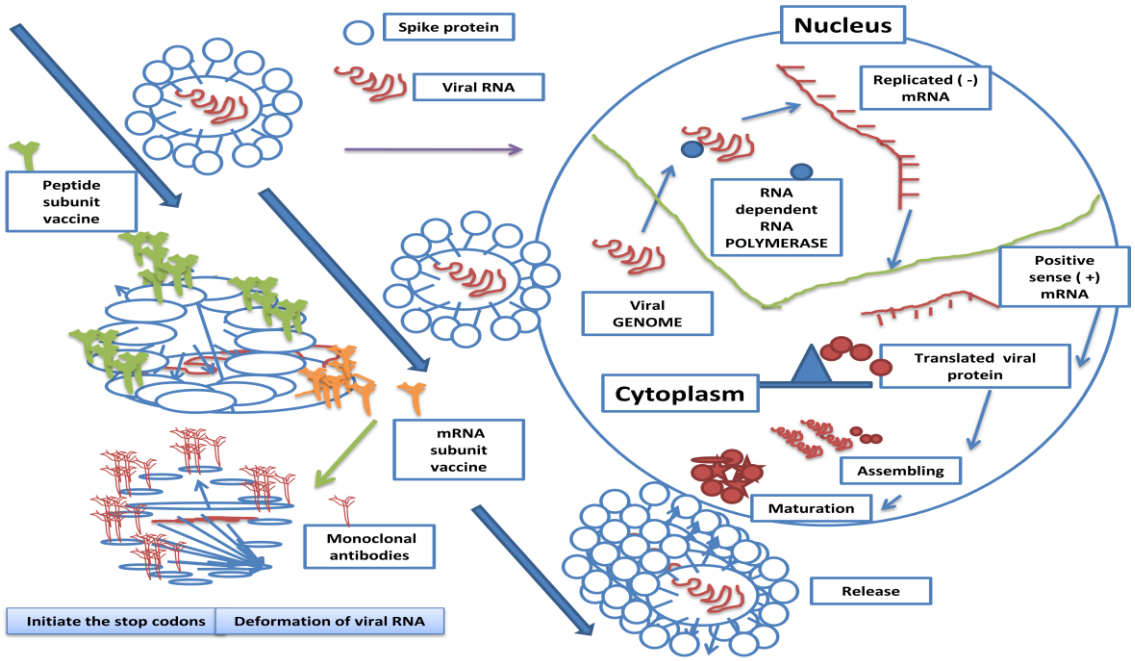

Figure 1: The diagram is the portrait for designing the immunization against viral multiplication

The migration potency of different vaccines is scheduled for different categories due to their experimental results and outcomes. The pandemic scenario from continental regions was being catastrophic from seasonal influences of transmission. The immune potency drugs against viral antigens were provoked to prevent the early migration of viral strains from individual to respective hotspots zone (14). So the early vaccination methods are very challenging and crucial for underdeveloped countries to distribute in a huge entity for cost-effectively reconstructing auto-immunization.

In this diagram, (Figure and Table 1) Europe is leading to growing faster the immunogenic conversion ratio rather than the largest continent Asia and Africa. The second growth is very prominent to migration potency in South America and North America.

Results:

The studies were conducted to evaluate the therapeutic potential of administrating the neutralization antibodies of critically ill patients without any deaths. The dosages have convincingly standardized protocols to eliminate the other effects of hypertension, cardiovascular diseases, cerebrovascular diseases, hepatitis, diabetes, chronic renal failure, and pulmonary diseases. The examined necessities were already be furnished following the efficacy of safety margin with the mechanical ventilation, high flow nasal cannula oxygenation, or the low flow nasal cannula oxygenation to the Covid 19 patient during trials.

Immunization is the continuous boosted therapy against COVID 19 pandemic already certified to progress for implementation. The physiological response of human patients played the omnipotent response by their autoimmune criteria against a viral antigen, modified strains, and chain transmission (11). The genesis of molecular degeneration on the cellular transporter of vaccinated components is concerned with the activation of monoclonal antibodies by the artificial secondary immune responses (12). Analytical research for the study of artificial immunogenesis is framed to construct depending on the presence of surface antigen to clarify the titre level in plasma (13). The following table has been tabulated for highlighting the well-ranked vaccines that are profiling as materials of immunization in mass populations. The diagram is portrait to clarify the immunogenic transformation in host defence against viral spike proteins.

The vaccine patterns from different modules showed no notable differences to develop immunogen for long-term synchronization of antibody interactions. Normalization of the body temperature and absorption of pulmonary lesions is signified to be tested negative for insert artificial immunization for regenerating antibodies in host cells. The reported experiments from trials were demonstrated for the viral loads after 7-37 days following the reduction in the procalcitonin and interleukin 6 (IL-6). The observations are established for increasing the

antibody titer-specific IgG and IgM at post convalescent plasma therapy significantly. The prospective potency impedes the conclusive statement about the vaccine evolution against the SARS-CoV2 virus from the apart of successive immunizations.

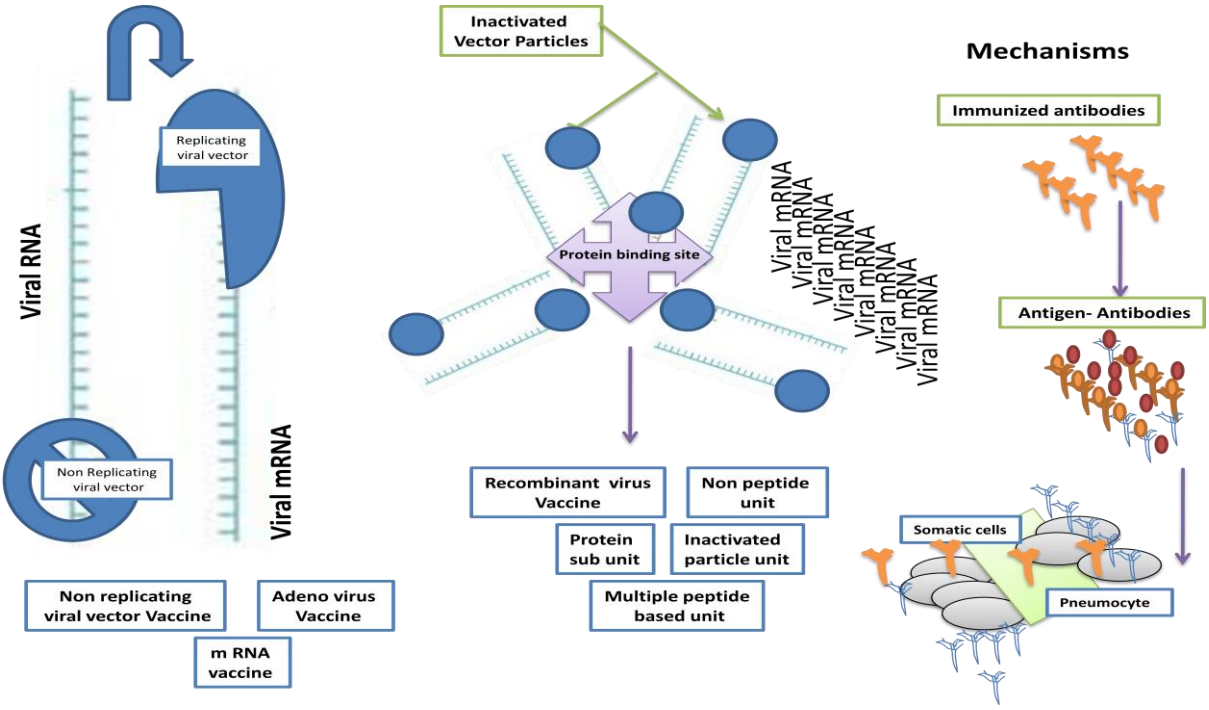

Figure 2: Molecular genesis and mechanisms of marginal safety potency from Novel Corona vaccines are defined to host defense systems.

Human metagenomic antibodies from plasma have been found to bind with the spike protein of SARS-CoV2, stipulating as regulatory response as a prospective therapeutic agent. The combinatorial effect of monoclonal antibodies recognizes different epitopes of the viral surface, can be considered for the neutralization of the virus to prevent the viral escape. Live attenuated vaccines are required for extensive accessories margin in the highest peak to generate secondary immune responses to establish safety and efficacy (Figure 1). But the probability of nucleotide substation during replication of the virus is controlled with prolific contents of subunit peptide or whole virus DNA vaccines (Table 1, 2 & Figure 2, 3). Safety issues are concerned with several trials reported for various RNA-based vaccines showing instability and few are reported for reactogenicity. The artificial isolating gene encoded the antibodies responsible for the neutralization of the SARS-CoV2. These genes will be employed to foster the recombination of recombinant antibodies replicate by homogenized molecular mimicry. The booster doses fabricate the antibodies as a library from the cells of convalescent plasma.

Discussion:

The monoclonal antibodies originated from human cells, creates the unique parent to bind a single epitope. The basic implement of developing and generating monoclonal antibodies

cognates with the convalescent plasma differs with various titer levels. The terms related to post-vaccination refers to the specificity, safety, low risk of blood-borne infection, and other arrays of hematological disorders to the host or post treated COVID 19 patients. The artificial immunogenic peptide contains the valid contents to implement against anti-tumor, anti-platelet, or anti-viral therapy before or post-secondary boosting (Figure 1, 2 and Table 1). Intercellular adhesion molecule cognates with interferon-gamma inducible protein counteract against the cytokine storm of SARS-CoV2 viral protein invasion. Anti interleukin receptor antibody is used to control the hyper pulmonary inflammation reducing the Cytotoxic receptor of the spike protein. The interleukin junction blocks the cytokine axis to enhance the effectiveness of the monoclonal antibodies (Table 2, Figure 3, 4). The chemokine degeneration and interleukin storm are carried out from the inflammatory cascade of pneumocytes after boosting of concentrated immunogenic peptide artificially. The safe and effective COVID-19 vaccine induces an appropriate immune response to terminate the pandemic from all over the world. The eradication should have priority to spot the international funding agencies for the development and manufacturing of coronavirus vaccines. The stockpiling of the vaccines is very much in need to serve as for the mass population of underdeveloped countries. The vaccination schedule and the recommendation should play as the guidepost strictly by the population. A pan-corona-virus vaccine is urgently required to assist the morbid patients and prohibit pre-infected deaths. In this circumstance, the conceptual model on immunogenetics of vaccine is required to provide SARS-CoV2 prone regions by the statistical alignments and assessments of the affected population in pandemic migratory sites.

Conclusion:

The new migration of second wave is gradually transformed in host defence mechanisms causing a mild havoc to the immunized community at Assam. So the desirable polyclonal vaccines are required for near implementation to prevent accessories infection occurred by native variants. The current epidemiological studies are portrait to view the concurrent infectious migrations throughout the Assam by these analytical studies in background of immunology.

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THE SWEET MENACE: EXPLORING THE HEALTH IMPLICATIONS OF EXCESSIVE SUGAR CONSUMPTION ON OBESITY

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Abstract:

The article reveals how sugar has negative effects on one's health. Sugar is associated with obesity, metabolic syndrome, and dental caries. Excessive consumption of sugar leads to malnutrition, sudden bursts of energy, obesity, and the accumulation of glucose and triglycerides in cholesterol. Research indicates that individuals who frequently consume fast food and sugary drinks have a higher propensity to develop obesity and diabetes. Administering these compounds orally can modify the frequency of meals, thereby decreasing symptoms of diabetes and obesity. The detrimental effects of sugar consumption on health have prompted international public health organisations to implement measures. The World Health Organisation (WHO) has issued guidelines regarding dietary intake, and numerous countries have implemented taxes on beverages with high sugar content. Nevertheless, alterations in market regulation and a deceleration in worldwide demand have resulted in an excess supply of sugar, leading to a decrease in prices.

Research indicates a robust correlation between sugar consumption, energy intake, and body weight. Many times, sugary confectioneries are used as substitutes for healthier options, resulting in a lack of essential vitamins, minerals, and fibre in the body. This impacts the sensation of satiety and the metabolism of energy. In order to disrupt the sugar cycle, it is advisable to restrict the consumption of added sugars, carefully examine food labels, practise mindful eating, and engage in regular physical activity. To ensure a balanced and healthy relationship with sugar, consuming nutrient-rich whole foods and developing responsible habits to manage weight and enhance overall well-being is essential.

Keywords: Metabolic health, Obesity, Sugar intake, MUFA, ATP, Metabolic Biomarkers

Introduction:

Increased sugar intake has been implicated in several diseases, such as obesity, metabolic syndrome and dental caries. With increased sugar intake from processed foods and sweetened beverages, these health problems have also shown an evident surge. Overeating sugar brings poor nutrition and short-term high energy, leading to obesity and accumulating glucose and

triglycerides in cholesterol (Vranceanu *et al.,* 2017). In addition, it is also the source of visceral fat and liver fat. Studies have also confirmed that those who eat fast food or consume sweet drinks regularly are at extreme risk of obesity and diabetes. Studies have also shown that orally administering these compounds can alter the number of meals a person has, which is known to aid in lowering symptoms of diabetes and obesity. Faced with this link between large amounts of sugar and negative health outcomes, global public health organisations are taking action. The World Health Organization recently released dietary guidelines that include reducing the consumption of processed sugars; countries around the globe have begun to implement measures such as levying taxes on sales of sweetened beverages into law (Bélanger-Gravel *et al.,* 2022).

As the detrimental effects of overeating sugar on health become known, awareness about unnecessary consumption has been further enhanced by a severe increase in chronic diseases. Furthermore, alternative sweeteners have been actively developed to overcome the undesirable effects of sugar on health. But these efforts have effects both for health and the sugar market itself. Changes in market regulations and slower growth in world demand have created an oversupply of sugar globally, which has driven prices downward. What is obvious from this starting point, plus the boost in diseases linked to excessive intake of sugar, like diabetes and cardiovascular problems, has led. It can be said that there's a rising awareness about health and calls for a reduction in foods rich with nutrition or taste, such as sugar, salt and fat. Consequently, there has been a change in consumer lifestyles, and people have become more willing to get exercise and eat healthier (Critchlow *et al.,* 2020).

In addition, research has indicated a close relationship between the impact of sugars on body weight and energy intake. Sugar and portions It appear that sugar consumption can result in increased body weight, but only when an excess of overall energy intake accompanies it; otherwise, people eat more to compensate for the extra calories from sugars. This is particularly so given that recent controversy has arisen over whether sugar intake affects metabolically unhealthy factors like dyslipidaemia and insulin sensitivity.

It has been confirmed that high-carbohydrate, low-saturated fat diets can help control the blood glucose levels of type 2 diabetics (Yang *et al.,* 2022). This effect is possibly due to the changes in metabolic pathways and insulin secretion. The macronutrient content of the diet and its influence on metabolic control has also been stressed.

Although steps are being taken to deal with the side effects of excessive sugar consumption, attempts must be made at various levels to find substitute sweeteners and other methods for adjusting people's diets to combat such terrible illnesses effectively.

The role of sugar in the human body

Sugars are an important source of energy in the human body. Glucose is the foremost form of glucose in cells and is used to produce ATP. From this, we can see that an important job the sugars have to do is supplying the energy for physiological activity. However, the effect of various kinds of sugar on the body is quite different. Studies have disclosed that sugars are related to cardiovascular disease, obesity, and metabolic conditions. On the other hand, fruits contain mostly simple sugars that are less likely to be pro-inflammatory and usually come paired with much-needed nutrients or fibre (Angelopoulos *et al.,* 2016). In discussing the impact of sugar on body weight, energy expenditure must also be considered. Research has also indicated that sugar intake can influence body weight when combined with an excessive energy balance. This emphasises the need to consider overall energy consumption when discussing the connection between sugar and weight.

According to studies, dietary fibre increases with the consumption of certain types of fats that can be used instead of carbohydrates in foods for diabetics. By doing so, it would be possible to increase blood glucose control levels. While researching the influence of different types of sugars on metabolic functions and what proportion can be ingested, human diets must gradually move to balance out these risks with alternative sweeteners or dietary adjustments that minimise their negative effects. Sugars are different, and especially when one examines their effects on body weight and metabolic function, there is obvious and frequent interaction with other aspects of a diet. Studies have also pointed out the connection between a large intake of sugar, along with excessive energy consumption and adverse health consequences like obesity or metabolic disorders (Seferidi *et al.,* 2018).

In addition, there is evidence that sugar has been related to body weight after noting the correlation between calories consumed and calorie requirement. However, a higher intake of pure sugar does not affect weight so long as the overall energy input remains constant. This reflects how sugar intake affects energy balance and metabolic health. In addition to the effect on body weight, studies have suggested that dietary sugars may affect metabolic health-related conditions like dyslipidaemia and insulin sensitivity. Consequently, much controversy exists regarding the relationship between sugar consumption and metabolic function. Dietary macronutrients and their ratio of saturated fatty acid (SFA), mono-unsaturated fatty acid (MUFA) and poly-unsaturated fatty acids have been demonstrated to be related to metabolism (Ibrahim *et al.,* 2005). For instance, high carbohydrate consumption and the relationship of dietary fat to blood glucose control and insulin activity have all been connected with changes in these conditions. This has mainly applied to sufferers of type 2 diabetes.

The relationship among sugars, overall dietary makeup and metabolic health is so complicated that only through continued research can one understand how all these factors interact at a deeper level. For instance, whether a diet's macronutrients (fibre and fat types) affect metabolic health or glucose regulation remains to be studied. While the scientific community is just beginning to unravel this challenging feedback loop, it increasingly seems valid to ask what other effects sugar intake has on health and whether dietary measures that provide metabolic balance can be found (While, 1997). Lastly, the current research regarding dietary sugars indicates that further study is still required to fathom their impact on body fat, metabolic conditions, and other chronic illnesses. The interactive effects of sugars, diet composition, and metabolic factors can help us further understand their relationship to health outcomes. This would allow for more rigorous, evidence-based dietary decisions.

Correlation between sugar intake and weight gain

Sugar has always been the subject of great controversy but an inescapable facet of our lives. The sweetness of its voice tempts us to enjoy rich flavours, but the voices in the background also hint at hidden temptations that are not quite so delightful. Perhaps one of the most commonly used arguments for people to cut out sugar is that there is considerable evidence showing its connection with weight gain (Maqsood *et al.,* 2020).

- **Calorie conundrum:**

But fundamentally, the problem is one of basic arithmetic. Sugar, mainly processed foods and drinks with added sugars, is a calorically dense food. If they are not offset by exercise or a limited intake of calories through dietary control measures, these calories create a positive energy balance. Getting rid of this surplus energy by converting it into fat results in weight gain over time.

- **Beyond the scale:**

But the calorie count is only part of a long story. There are many physiological and metabolic factors influencing sugar's effect on weight gain. Here's a closer look at some key culprits:

Insulin rollercoaster: In the cells, sugar stimulates insulin secretion to carry glucose out of the blood into cells to burn it. However, too much sugar can cause cells to become resistant and unable to respond. This, in turn, can lead to weight gain by impairing glucose metabolism and encouraging the storage of fat.

Hunger hormones hijacked: Sugar has a deceptive charm. It may create sensations of pleasure and reward, but it's only momentary. But after the sugar rush passes, it can cause a rebound in appetite and make one crave more calories than they should be consuming. This interference in regulating hunger hormones often makes it difficult to keep one's weight under control.

- **Nutrient displacement:**

But foods that are high in sugar generally replace other nutritious choices. When sugar-laden treats replace fruits, vegetables and whole grains, the body is robbed of many crucial vitamins, minerals, and fibre (Compher, 2021). All three have direct effects on satiety while indirectly affecting metabolism.

- **The evidence speaks:**

The sugar-weight connection isn't just theoretical. Numerous studies have shown a close positive correlation between the two. For example, a 2013 review of each study in Advances in Nutrition examined 68 prospective trials. It concluded that sugar-sweetened beverages" are a decisive risk factor for weight gain among children and adolescents.

In addition, in another paper that the New England Journal of Medicine published this year, which followed more than 120,000 people for years and divided them into groups based on whether they had increased their intake to unchanged levels as previously, the study discovered that those who raised their intake had higher rates of weight gain (McCarthy, 2014).

- **Breaking the sugary cycle:**

Thus, the sugar effect and weight gain are apparent, but each person's factors, such as genetic makeup, metabolic rate or even overall diet, will differ. Yet admitting the connection is the first step in making rational choices. Here are some ways to navigate the sugary landscape and keep your weight in check:

Limit added sugars: Only eat simple, natural foods, and don't fall for refined sugars hidden in processed foods. Replace sugar-rich desserts with sweet-tasting fruit.

Read food labels: Always pay particular attention to the added sugar content of foods. Go for products with low sugar content or unsweetened ones.

Practice mindful eating: Take pleasure in your eating and observe hunger signals. Do not engage in meaningless snacking and emotional eating, which result in overeating.

Embrace physical activity: The first is exercise's ability to use up calories and control weight. Engaging in moderate-intensity activity for at least 150 minutes per week is recommended.

But, as always, a healthy relationship to sugar balance is key. After all, having the occasional treat is perfectly okay. However, emphasising whole foods rich in nutrients and responsible consumption habits will ensure healthy weight control and well-being.

Understanding the truth beneath, we can choose how to face up to sweets once we get a handle on their science. How can we break the vicious cycle of sugar dependence and stroll along a road to lasting health and equilibrium with food?

Relation of sugar intake and metabolic biomarkers

Because sugar intake affects metabolic function, whether there's a correlation with other biomarkers of metabolism besides adiposity needs to be clarified. The study was designed to determine whether consuming either added or free sugars leads Japanese adolescents 'blood glucose levels and other biomarkers to change even if their body weight remains unchanged. Investigation of that relationship showed an association between sugar intake and metabolic indicators, most notably in blood pressure and lipid levels (Okuda *et al.*, 2020). The association was noted regardless of absolute calorie intake numbers, which suggests that the relationship between sugars and metabolic outcomes is direct. This shows how the relationship between dietary sugars and metabolic health is complicated.

In addition, dietary sugar poses a unique challenge to medical professionals in understanding its role as a risk factor for adolescents at high risk of cardiometabolic complications. At the same time, as some metabolic illnesses are associated with sugar consumption, their effects differ depending on the type of sugar (Grimes *et al.*, 2013). To design appropriate interventions to reduce adolescents 'cardiometabolic risks, we need a better understanding of these finer points in sugar consumption. What's more, results from another special data showed a correlation between the sugar-drinking habit of children and lipid level differences, which may be used as risk indicators for cardiovascular disease in the future. Even more important was that the relationship was partially mediated by adiposity, suggesting a complex interplay between sugar and metabolic disease through fat. The results also show that healthier beverage habits in childhood can prevent later cardiometabolic risks, regardless of weight status.

Relation of sugar intake, adipocyte mass, and cardiometabolic risk

In particular, changes in steatosis grades were seen across tertiles of visceral fat volume, implying a relationship between sugar intake and adipocyte hypertrophy, leading to an increase in liver lipids (Hallgreen & Hall, 2008). Capturing this relationship is key to explaining the cardiovascular and metabolic risks of sugar consumption.

Research links between sugar intake and adipocytes within the visceral compartment are significant for understanding how high-sugar diets adversely affect metabolism. Further research into such considerations will provide data for designing appropriate dietary interventions and primary prevention to reduce the risk of heart disease.

Possible ill effects of overeating sugar

In light of the concerns about sugar being detrimental to health, researching how increased consumption relates mechanistically to cardiometabolic risk factors is very important. Previous studies have mapped out some possible mechanisms, such as the direct pathway

involving abnormal hepatic uptake and uncontrollable fructose metabolism or the indirect one related to weight gain and fat accumulation (Fahs & Swank, 2017). These pathways help create and combine cardiometabolic risk factors, further revealing the superseding effect of added sugar in beverages.

Sugar-sweetened beverages' effect on teenage metabolic health in overweight and obese adolescents. The excess weight magnifies the adverse effects of added sugar. Besides obesity, high sugar intake is also linked to lower diet quality and a higher risk of becoming overweight; these facts all suggest that the overall impact on health results from diets with too many sugar-sweetened drinks (De Koning *et al.,* 2012). Even to behave rationally, it is necessary to understand the relationship between added or free sugar intake and adverse metabolic biomarkers other than fat. It compared groups with similar energy intake but differed in blood pressure and lipid profile. After adjusting for total calorie intake, the study revealed a direct effect of sugar on metabolic outcomes; it also indicated who would be at high risk of developing cardiometabolic disorders whose causes were related to what they consumed.

While research contributes even more light to the complex connections between sugar intake and metabolic health, further in-depth studies must be conducted on possible associations among people with different body types (according to adiposity) at higher or lower risk for cardiometabolic diseases. Through greater awareness of the diversity and interactions among different sugars, we can learn more about metabolism and thus design appropriate interventions to improve health outcomes.

Research shows that the adverse effects of sugar on obesity are not only due to energy balance. The link between sugar intake and obesity risk brings to the forefront how much remains unknown about the effects of different sugars on fat in humans (Klingenspor, 2019). The results of the systematic review and sample met analysis are additional evidence that points to an association between intake of sugars and body weight, blood pressure, and some aspects related to a person's lipid profile. The results reinforce that pure sugars directly impact metabolic outcomes and show the many elements they affect, which concerns weight gain and cardio metabolism risks.

The key to improving metabolic health is that by learning how various types of sugar can affect our biochemistry rates, it should be possible to refine medical treatment and nutritional advice aimed at remedying specific derangements in blood chemistry caused by its consumption. It appears that this targeted approach should be able to reduce cardiometabolic risks associated with high sugar consumption among young people.

Efficient ways to cut down on sugar use

- **Implementing behavioral interventions**

Behavioural treatments are an important means of combating sugar abuse and re-educating people about healthy diets. Through cognitive-behavioural methods and educational opportunities, people can acquire skills to make appropriate choices about how much sugar they take in. Fostering eating habits like reading food labels and learning about the amount of sugar in processed foods gives people some way to address this problem independently.

In addition, promoting a dietary environment that encourages consuming foods in their natural state and appreciating the sweetness found within fruits can help promote sustained reductions in added sugar intake (Survey, 2007). Public education for adults and children can increase appreciation of how sugar harms health, promoting a habit of informed choice along with long-term behavioral change.

- **Policy measures and regulatory frameworks**

Policy measures and regulations can also stop rampant sugar consumption. In what form? Such measures might include taxing sweetened drinks and encouraging the production and consumption of healthier options. Policy interventions like these can create environments that push people toward healthy food choices and away from excessively sweet products, so they complement behavioural approaches to the public health challenge of sugar intake.

- **Behavioural interventions to tackling sugar addiction**

One case supports behavioural interventions in controlling sugar intake, presenting a comprehensive response to promoting healthier diets. Behavioural science principles can be employed to provide tailored behaviour guidance modules which educate consumers about the consequences of high sugar intake (Kienzle, 2018). Furthermore, adding behavioural methods like cognitive reconditioning and environmental adjustments can establish a supportive environment for people to control their sugar intake. However, evidence-based behavioural interventions can increase awareness and bring about sustainable changes in dietary habits to reduce the impact of sugar-related metabolic disorders.

- **Nutritional education and gastronomic**

Nutritional education and culinary detours are thus empowering tools by which people can get what they crave--the knowledge to make correct dietary choices and the satisfaction of knowing that they have something good on their menus. With these kinds of programs, people will understand the secret of a pimple in their eating formation and have new ways to find creative solutions for low-calorie cooking. We can only encourage a kind of nutritional vocabulary and gastronomic creativity that will allow people to adopt dietary changes to enhance metabolic health while making good sense. This method fosters a long-term, healthy decline in

the amount of sugar people consume and, therefore, aims to help prevent metabolic disorders and cardiometabolic diseases stemming from overconsumption.

- **Empowering healthcare professionals**

Hastening the rise of healthy living values by empowering healthcare professionals to give evidence-based guidance about sugar consumption and dietary patterns, citizens will gain support in taking control (Lumsdaine, 2016). Most importantly, incorporating assessment and counselling of sugar consumption into clinical care can provide an opportunity for early interventions while helping physicians make dietary recommendations tailored toward individual patients 'needs.

In addition, strengthening the linkages between health care providers and public health agencies on the one hand and community groups in various positions of authority on the other will facilitate the widespread provision of educational resources and related support systems to stand up against sugar's assault.

Through a comprehensive combination of behavioural interventions, policy incentives and medical care empowerment, we can indeed map out an effective path towards conquering sugar overuse and its negative health effects. With these collaborative efforts, there is reason to hope for a society that moves toward more wholesome dietary habits and fosters lifelong metabolic health.

Sugar and its influence upon diet

Investigating how to reduce sugar intake and encourage healthier food habits effectively. Besides understanding the possibly positive effects of ketosis, implementing good methods to control sugar intake and improve dietary habits is also extremely important. Through evidence-based methods, we can counter the effects of excessive sugar consumption on metabolic health and help people adopt healthy diets.

Studies on behavioural and environmental treatments provide useful information for the design of countermeasures against excessive sugar intake (Avena *et al.,* 2008). Additionally, looking at the effectiveness of public health interventions, education programs, and policy measures can help guide efforts to create environments conducive to lower sugar intake. So, in this way, we can help build an all-round framework that fosters healthy eating habits, slowing the spread of sugar-related ailments.

Exposing the sugar lobby's influence on dietary culture

At the same time as seeking to develop means of controlling sugar consumption, it is also crucial to analyse in depth how the sugar industry has influenced dietary habits and public health. By seeing how sugar has made its way into the food supply through historical, economic and

sociopolitical factors, we can understand why people have become dependent on it. This may help in understanding ways to deal with its harmful health consequences.

Only an in-depth examination of how the sugar industry contributed to dietary recommendations, marketing strategies, and policy creation will put today's ubiquitous role for sweet stuff into perspective.

Shifting paradigms: Sugar in the spotlight

In addition, looking back at evolving ideas about sugar and health allows us to re-evaluate where the discussion of sugar lies in today's dietary guidelines and public policy. From changing science and the reappraisal of dietary advice, we can do our bit to allow people better grasp what sugar consumption may mean for metabolism and chronic diseases.

Comparing changing patterns in sugar consumption can provide useful information for public health education and advice, diets and lifestyles--steering consumers away from what is not beneficially linked with metabolic balance (Damman & Timmermans, 2012). Third, paying attention to changes in sugar-related research is one way of promoting the use of evidence-based methods aimed at helping people adopt healthy lifestyles.

Conclusion:

In sum, reconciling sugar consumption and metabolic health requires various elements in balance--including methods to cut back on the amount of sugar consumed, dealing with industry interference, and moving away from old viewpoints about food. Through creative efforts that tell a coherent tale by weighing the dangers of eating sugar against calls for healthier living, we can construct environments to promote individual autonomy in deciding matters concerning diets and ultimately help prevent metabolic maladaptation due to sugars.

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UNFOLDING THE USAGE OF NEW GENERATION TECHNOLOGIES: A PHYSIOTHERAPIST'S PERSPECTIVE

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Abstract:

Physiotherapy is a primary care health profession providing services to individuals and populations to develop maintain and restore maximum movement and functional ability throughout the lifespan. As the technologies are turning advanced, the health sector has also found out a number of ways to use emerging technologies for the advancement in the field of healthcare services. Emerging technologies are showcasing promising results in published trials or have well-defined research going on. Therefore in the future arena, physiotherapy professionals shall have novice technologies with rapid advancements within the rehabilitation space to make use of, in the superior treatment of their patients and contribute more in the ever-developing health sector.

Keywords: Artificial Intelligence, Next Generation Technologies, Physiotherapy, Virtual Reality

Introduction:

Physical therapy (or physiotherapy) is a primary care health profession, with physical therapists (or physiotherapists) providing services to individuals and populations to develop maintain and restore maximum movement and functional ability throughout the lifespan. Physical therapy management commonly includes prescription of or assistance with specific exercises, manual therapy, education and other interventions. Physiotherapy has many specialties namely Orthopedic, Neurologic, Cardopulmonary, Paediatrics, Geriatrics and many more areas where the physiotherapists get engaged in treating the patients. Physical therapists use an individual's history and physical examination to arrive at a diagnosis and establish a management plan and, when necessary, incorporate the results of laboratory and imaging studies. Electrodiagnostic testing (e.g., electro-myograms and nerve conduction velocity testing) may also be of assistance. [1]

Content:

The primary objective of this study is to unveil and analyze the application of modern technologies in the field of physiotherapy and rehabilitation from a Physiotherapist's point of view. As the technologies are turning advanced, the health sector has also found out a number of ways to use emerging technologies for the advancement in the field of healthcare services. The technologies such as Artificial Intelligence (AI), Virtual Reality (VR), and robotics are being utilized to provide better facilities which can be more beneficial for the individuals in need. The next generation technologies are also being used and are providing positive outcomes for the Physiotherapists in the world of rehabilitation.

New-generation computers are now manufactured with "machine learning", which is the capacity to learn and think without explicit programming. This learning and thinking capacity of the computer is known as Artificial intelligence (AI). Health tracking apps in almost every smart phone creates the perfect conditions for widespread technological change in the field of physical therapy. [2]

Physiotherapists use knowledge of similar patients to produce a differential diagnosis. Deep learning is one specific type of such supervised learning where layers of algorithms (neural networks) process information in a manner similar to how the brain works. [3] The success of machine learning depends on the accuracy and amount of data available to teach the system. Predictive modelling where prediction of an event or outcome based upon the available data is done and can be a useful tool in providing preventive and immediate care for patients having certain conditions. [4]

AI has been extensively used in physiotherapy assessment, the common example of which can be gait analysis. Recent progress in video analysis driven by machine learning has shown that computers are able to automate the diagnosis of gait abnormalities and underlying pathology, for example, the use of AI in the gait lab or motion analyzer system, as it will be able to track the human motions and detect any anomalies or underlying pathological cause. It can also be used to measure progress before and after in patients during the therapeutic interventions. The usage of AI has been deployed in the field of rehabilitation to enhance the quality and accuracy of treatment. For example; The Physiotherapists in the near future will find themselves working with a large scale of data and it won't be easy for them to deal with such massive figures. To solve this problem, AI can come to the rescue with its cognitive function capability which will not only be able to identify the type of conditions but might also help with the assessment and treatment plans using its cognitive memory from the vast data stored within it. Also, we struggle with trying to support our clients in adherence to different exercise regimens

that in many cases are meant to be lifelong activities, which could become easier for the patients with the cognitive assistance from the AI and VR. Physical therapy in Parkinsonism is also very beneficial as it makes the individual's life a better one and in which the physical therapists may include various treatment protocols which assists to improve the patients daily life activities like breathing, and relaxation, and reducing freezing moments that may cause falls and injuries.The long term goals may also include maintaining, correcting, and/or improving functional ability, strength, flexibility, posture, and balance.

There are several studies of non-pharmacological physiotherapy interventions among older adults usually between 60 and 80 years old with Parkinson's disease, often accompanied with robot assistance or virtual reality tools that have been evaluated as interventions to enhance walking and physical performance even for home sessions. These procedures include a wide range of approaches, focusing on posture, upper extremity function, balance, and gait combined with the use of cognitive movement and exercise strategies to maintain and improve quality of life. [5]

The impact of VR in the field of Physiotherapy can be beneficial as to encourage and train the individual or a group of individuals with specific exercise programmes and it can as well be beneficial with the specific virtual reality games, which can assist in patients regaining balance, coordination, posture and gait enhancements. The benefits of rehabilitation robots in the physiotherapy sector have been emerging with its updated advancements in the forms of therapeutic and assistive robots. Both these types deliver high intensity and high dosage treatment training for the patients requiring rehabilitation in localised or generalised ways. They provide direct control of specific joints, which can reduce abnormal posture or movement.

Some of the emerging PT tech employs next-generation hardware and robotics. It won't replace the intelligence and emotional care of a dedicated therapist, but from AI and exoskeleton suits to VR and video games, advanced technology is already improving patient outcomes, reducing physical therapist burnout, and making clinics more efficient. The application of next generation wearable hardware may be beneficial for the patients as it helps to improve the movements, quality of life and functional independence with balancing exercises, gait training, postural corrections, motion and biometric capturing and virtual biofeedback.

To conclude, emerging technologies are showcasing promising results in published trials or have well-defined research going on. Therefore in the future arena, physiotherapy professionals shall have novice technologies with rapid advancements within the rehabilitation space to make use of, in the superior treatment of their patients and contribute more in the ever-developing health sector. In the near future, the usage of technologies such as AI, VR, and

Robotics will be accelerated at a very high speed due to the increased workload of the physiotherapists and the promising functions of the various modern technologies.

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THE USES OF TRADITIONAL PLANT-BASED REMEDIES IN MODERN WOUND CARE TREATMENT IN CURRENT PHARMACEUTICAL HEALTH RESEARCH

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Abstract:

A break in the cellular, anatomical, or functional continuity of live tissue is referred to as a "wound." Tissue damage brought on by chemical, physical, thermal, microbiological, and immunological causes is the cause of it. Many plants and plant-based items have been used as wound cures since ancient times. Plant extracts from a number of species show great promise in the treatment of wounds. Plant-based extracts promote blood coagulation, granulation, contraction, and epithelization of skin tissue, all of which hasten the healing process of wounds. This chapter's aim is to present a list of plants, plant parts, ayurvedic formulations, and cutting-edge wound healing therapies that are undergoing pre-clinical and clinical testing. The popularity and signs of continued use of these old traditions demonstrate that there are still important lessons to be learned from them.

Keywords: Wound, Microbiological, Traditional, Plants

Introduction:

Plants are frequently used in traditional and contemporary medicine to treat and prevent disease. For more than 5,000 years, India's "Ayurvedic" system of natural healthcare has employed plants to both prevent and treat illness. Traditional Chinese medicine, which has been used for at least 3,000 years and use a large range of plant species, is practiced in Eastern Asian nations (1). Modern science has studied many of the plant species that have traditionally been used as medicine in order to understand more about their bioactive components and develop new drugs. Studies on the pharmacological mechanism governing the action and effectiveness of these plant-derived chemicals indicate that many of them are pharmacologically safe. This encourages more research in preclinical studies and clinical trials. While a sizable portion of the

world's population cannot afford these pricey medications, these patient groups may benefit from the use of herbal remedies (2). Using traditional herbs, several formulations for skin conditions including burns, wounds, and cuts have been developed throughout the years (3). According to some study, traditional herbal remedies account for around one-third of the treatment options available for cutaneous wounds, whereas only a small percentage of drugs found in Western pharmacopoeias have been used to treat such wounds (4). According to scientific research, traditional plants that have been used historically in folklore to treat wounds may be a better option because they are more reasonably priced and do not have any negative side effects when compared to conventional synthetic techniques, which can have costly and unavoidable side effects (5). According to the organisation for wound healing, a wound is an injury to the body that causes a break or opening in the skin and interferes with the normal structure and function of the skin. Skin injuries are caused by the epithelium rupturing its continuity, but the underlying connective tissue also fails (6). It consists of three phases: remodelling, proliferation, and inflammation. These stages overlap. Any type of disruption can cause abnormalities in wounds (7). In general, wounds are classified according to the underlying cause of the wound. There are several kinds of wounds, such as 8–9. ;

1. Acute wounds: During the tissue damage phase of an acute wound, there is often a systematically time-reparative phase that efficiently restores the integrity of both function and structure. Surgical incisions or other trauma often result in acute wounds.

2. Closed wounds: Plasma can travel through the blood circulation system through a closed wound, but it remains within the body. Injuries and scars are obviously visible.

3. Open wounds: Blood is streams from the body when there is an open wound, making the bleeding easier to notice. Depending on where the damage originated, the open wound can be further classified as follows:

a) **Incised wounds:** This incision shows little to no tissue loss or injury. The primary causes are sharp items like knives and razors.

b) **Laceration or tear wounds:** When combined with other forms of stress, this non-surgical damage leads to tissue deterioration.

c) **Abrasions or superficial wounds:** Sliding across a rough surface produces abrasion to the surface. Using this method, the epidermis—the skin's outermost layer—is scraped off, exposing nerve endings and causing an acute injury.

d) **Puncture wounds:** These infections happen when an item, particularly a sharp object or pointy object, comes into contact with the skin's surface. Given the possibility of dirt getting far into the incision, infection is quite possible.

e) **Penetration wounds:** These infections happen when an item, particularly a sharp object or pointy object, comes into contact with the skin's surface. Given the possibility of dirt getting far into the incision, infection is quite possible.

f) Gunshot wounds: Injuries might result from a bullet or another item entering or passing through a bodily component.

4. Chronic wounds: These chronic wounds are ones that are not healing normally at this time and instead need to go through a pathologic inflammatory process, which usually takes longer to heal. The most common causes of chronic wounds include localised infections, low oxygen levels, trauma, foreign objects, and systemic diseases including diabetes, obesity, immunological deficiencies, malnutrition, or drug side effects. Venous leg ulcers, pressure ulcers, and diabetic foot ulcers are a few instances of persistent sores.

Factors influencing the healing of wounds:

Oxygenation: Nearly all wound healing mechanisms and the metabolic activity of cells, particularly the ATP-based energy generating process, are dependent on oxygen. It promotes the growth of blood vessels, boosts the differentiation, migration, and re-epithelialization of keratinocytes, quickens the production of collagen and fibroblasts, and expedites the healing of wounds. Additionally, it keeps wounds from getting infected. Significant oxygen depletion occurs in the initial wound environment, and active metabolic cells absorb hypoxia. Two systemic diseases that cause reduced vascular flow and inadequate oxygen in the tissue are ageing and diabetes. This, together with inadequate oxygenation, results in a persistent wound that is incapable of healing.

Infections: Microorganisms that are commonly confined on the skin's surface get access to the layers of tissue below unless the skin layer is disturbed. Depending on whether the wound has been classified as inflamed, colonised, locally invaded/critically colonised, or spreading invasive, the infection's present stage and the microorganism's capacity for replication vary. Whereas colonisation is the presence of replicating bacteria on the wound without causing tissue damage, contamination is the emergence of non-replicating organisms. An intermediary step is local infection/critical colonisation, which includes microbial proliferation and the start of local tissue activities. In a wound, microorganisms proliferate and cause damage to the host's body. We call these invasive infections. Inflammation is an essential component of wound healing and is required for the removal of infectious microorganisms. But even in the absence of adequate disinfection, inflammation may continue because of inadequate microbial clearance. Two pro-inflammatory cytokines that are raised over time and prolong the inflammatory process by encouraging the development of bacteria and endotoxins are interleukin-1 (IL-1) and TNF-alpha.

Should this continue, the injury may become chronic and cease to heal. Long-term inflammation also leads to an increased concentration of matrix metalloproteases (MMPs), a class of proteases that may degrade the extracellular matrix. Protease activity rises in tandem with a reduction in the quantity of naturally produced inhibitory protease. Proliferative factors seen in chronic wounds may rapidly disintegrate as a result of this shift in protease equilibrium (10).

Elderly age: Ageing has been associated with a delay in wound healing. Research has demonstrated that in older individuals with wounds, there is a fall in fibroblast proliferation and activity, a slowdown in collagen formation, and a decrease in wound contraction (11).

Psychological stress modulates healing processes: The way individuals interact with one another in social settings is significantly impacted by stress. Numerous diseases, such as diabetes, cancer, poor wound healing, and cancer, are linked to stress. Numerous studies have indicated that the neuroendocrine-immune system's dysfunction caused by stress is crucial for good health. People who are under stress are more likely to engage in unhealthy behaviours such as sleeplessness, eating poorly, exercising seldom, and smoking, using goods that contain nicotine, or abusing other substances. This is on top of the direct impacts that anxiety and depression disorders have on immunological and endocrine systems (12).

Body type: The body's physical makeup can have an impact on how rapidly wounds heal. For example, inadequate blood supply to the adipose tissue in an obese patient may impede wound healing. Many obese people also experience a protein shortage, which impedes their ability to heal. However, if a patient is extremely malnourished and oxygen-depleted, this may impede the healing of wounds.

Chronic diseases: Wound healing can be slowed down by long-term medical disorders such diabetes mellitus, peripheral vascular disease, coronary heart disease, and stroke. Patients with chronic diseases should be monitored often during their treatment regimen in order to implement the optimal approach.

Nutrition: For almost a century, it has been known that food significantly affects how quickly wounds heal. The most apparent reason is that, after trauma and surgery, nutritional deficits can have a substantial influence on wound healing. Patients who are malnourished, have non-healing wounds, or have chronic wounds need extra vital vitamins and minerals. Therefore, the way the body uses energy, carbohydrates, proteins, fats, vitamins, and minerals affects the healing process (13).

Improper diet: In order to function, anabolic processes such as wound healing require both energy and nutritional substrates. Reportedly, a serum albumin level of 3.5 gm/dl or more is necessary for a successful recovery (14). Protein is required for the creation of collagen if a

wound is present. Malnutrition may result in an inadequate amount of protein, which might hinder the production of collagen, reduce the tensile strength of wounds, or increase the risk of infection (15).

Mechanism

In the intricate process of healing wounds, there are three simultaneous phases: remodelling, propagation, and an allergic response. The inflammatory process initiates a proliferative wound-healing response, which is further differentiated by vascular mechanisms such as hemostasis and blood coagulation. Leukocyte invasion, the release of cytokines, and the use of antibiotics are examples of cellular activity. Granulation tissue then grows to fill the wound region after the proliferative phase, during which the epithelium forms to cover the wound surface. Fibroblast proliferation, collagen deposition, the formation of new blood vessels, and the deposition of more extracellular matrix all contribute to the production of granulation tissue (16). When new connective tissue develops inside the incision, the tissue's structural integrity and functional competence are restored, signalling the start of the remodelling phase. However, the three separate phases of wound healing require varying amounts of time and do not follow a straight line. Acute wounds that heal quickly include burns, wounds following surgery, and other severe injuries. A typical acute wound is an incisional surgical wound that is neat, uninfected, and approximated by operational sutures. Even while organised healing seeks to rebuild tissues with the same structure and capabilities as skin that has been maintained, regeneration is seldom achieved, with some notable exceptions such as early foetal repair. A product that is both physically and functionally acceptable but not exactly the same is produced by healing. The rate at which wounds heal is frequently strictly regulated by several growth hormones and cytokines released at the wound site. Modifications that hinder rapid, regulated healing increase tissue damage and lengthen the healing process (17).

A. **Inflammatory phase:** As soon as damage is sustained, the inflammatory phase begins and typically lasts for 24 to 48 hours, although it can sometimes last for up to two weeks. The inflammatory phase initiates the hemostatic mechanisms, which stop bleeding from the wound site quickly. Cardinal indicators of inflammation that may be clinically observed are dolor (pain), calor (warmth), tumour (swelling), and rubor (redness). During this phase, vasoconstriction and platelet aggregation lead to blood clotting, which is quickly followed by phagocytosis and vasodilation, which produce inflammation at the site of the wound.
B. **Proliferative phase:** The following stage of wound healing is called the proliferative phase, and it can continue anywhere from two to three weeks after the inflammatory phase. The stages of granulation, contraction, and epithelialization make up the complete process.

During the granulation stage, fibroblasts produce a collagen bed and new capillaries. Among the various substances produced by fibroblasts, glycosaminoglycans and collagen are essential for wound healing (18). In order to eliminate anomalies, wrapped ends close together during the contraction phase. Over the wound site, new epithelial tissues grow in the third stage.

C. **Remodeling phase:** This time span might be anywhere from two years to three weeks. New collagen develops at this stage (19–20). Tissue tensile strength is increased by the intermolecular cross-linking that collagen creates via hydroxylation depending on vitamin C. The surrounding tissues get 80% stronger than the original tissue as a scar flattens.

Utilising medicinal herbs to heal wounds:

For centuries, several medicinal herbs have been utilized to control and cure multiple types of wounds (21). Despite significant advancements in the field of contemporary medicine, medicinal plants continue to be an important part of the current approach to wound treatment (22). The Plant *Bacopa Monnieri* (faster re-epithelialization) is one of the medicinal herbs claimed to speed up wound healing (23), *Acalypha Indica* (boosts cell division) (24), *Calotropis gigantea* is a plant that can help in scar reduction (25). *Aloe vera* can promote new blood vessel growth (26), *Curcuma longa* can speed up re-epithelialization (27), *Malva sylvestris* can help the body's blood vessels proliferate (28), Makes wound contraction; *glycyrrhiza glabra* (29).

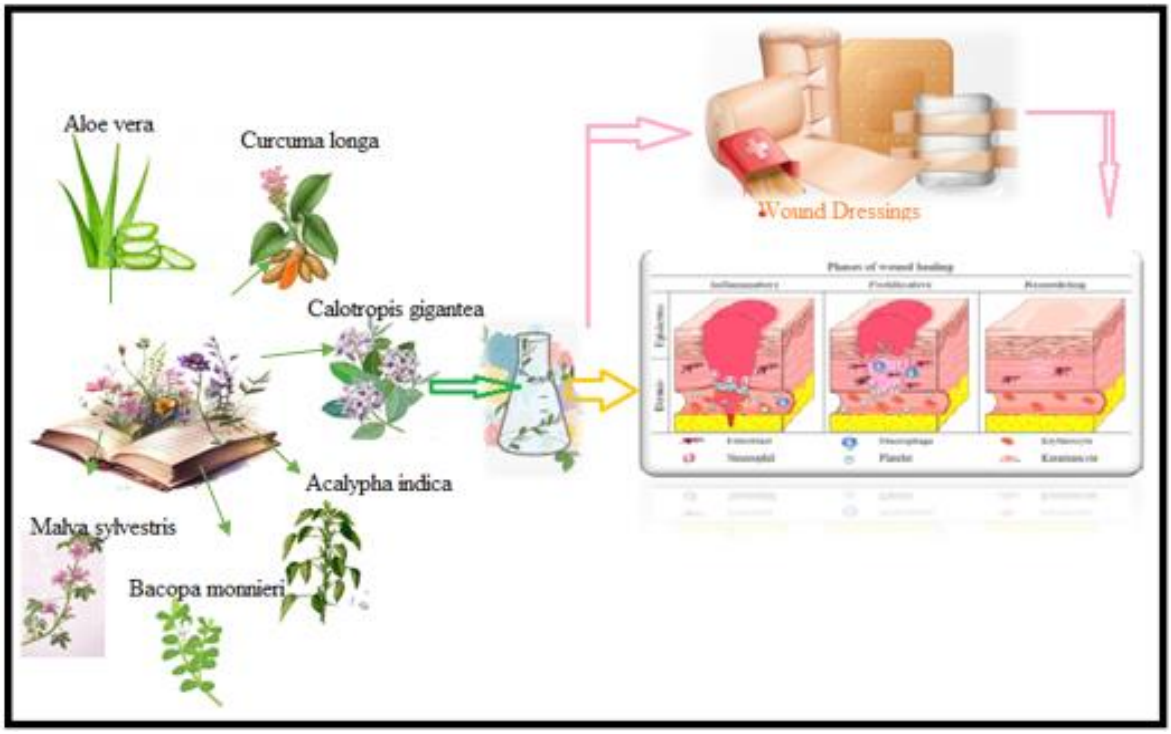

Figure 1: Some medicinal plants and their capacity to treat wounds

Table 1: Some illustrations of medicinal plants and their capacity to treat wounds (30-44)

Sr. No.	Medicinal plants	Part used	Bioactivities	Clinical Uses	Formulation
1	*Aloe vera*	Leaves	Immuno-modulatory Antidiabetic, Anti-inflammatory	Wound healing	Gel
2	*Arctium lappa*	Leaves Whole root	Antimicrobial, Antiviral	Burns, Rashes	Ointment
3	*Astragalus propinquus Rehmannia glutinosa*	Roots	Anti-inflammatory	Diabetic foot ulcer	Herbal drink
4	*Ampelopsis japonica*	Root tuber	Anticancer Neuroprotective	Burns, Ulcers	Wound plaster
5	*Blumea balsamifera*	Leaves	Antifungal, Antiobesity Antiplasmodial, Antitumour	Dermatitis, Eczema Skin bruises Skin injury	Oil
6	*Calendula officinalis*	Flower	Antifungal, Anti-inflammatory Antioxidant Antiviral	Burns, Dermatitis Wounds	Topical spray Oil
7	*Celosia argentea*	Leaves	Antimicrobial Antioxidant Hepatoprotective	Skin sores Ulcers	Poultice of stems and leaves [topically]
8	*Centella asiatica*	Aerial parts	Anti-inflammatory, Antioxidant Proangiogenic	Wounds	Oral form (tablets, drops) Topical medication (ointments and powder) Injections (subcutaneous and intramuscular

9	*Commiphora myrrha*	Leaves and resin	Analgesic Antibacterial Anti-inflammatory, Antioxidant	Wounds and pain	Oil
10	*Curcuma longa Jiang H*	Rhizomes	Antibacterial Anti-inflammatory, Antioxidant	Wounds	Capsules
11	*Daphne genkwa*	Flower Root	Anti-inflammatory Antitumour	Wounds	Not available
12	*Ganoderma lucidum*	Fruiting body	Anti-infective Anti-inflammatory	Ulcer	Not available
13	*Panax ginseng*	Leaves, root, and whole plant	Antiaging Antiallergic Anticancer Anti-inflammatory Antimicrobial, Antioxidant	Wound healing	Not available
14	*Panax notoginseng*	Leaves, flowers, roots, and rhizome	Anticancer Antidiabetes Anti-inflammatory Antioxidative	Trauma	Powder on wound Spray on wound
15	*Lithospermum erythrorhizon*	Roots	Antibacterial Anti-inflammatory	Wounds	Oil formulations, gel

Conclusion:

Given the substantial significance of wound healing in both economics and patient care, it is not unexpected that the field of wound healing research is quite active. Molecular biology and materials science, among other seemingly unrelated topics, are the source of many recent studies on wound healing. Many herbal plants have great promise for medical use in wound healing because of their inherent ability to heal wounds. Many isolated phytoconstituents and herbal extracts are used nowadays because of their ability to promote wound healing. Modern technology has made it possible to treat wounds with a wide variety of ayurvedic, allopathic, and herbal treatments. Herbal medicines and formulations are gaining popularity in developed countries due to their safety compared to allopathic treatments.

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RECENT ADVANCES IN NOVEL DRUG DELIVERY SYSTEMS FOR ANTICANCER DRUG

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Abstract:

Novel drug delivery systems (NDDS) have many benefits, which include improved therapy byincreasing the efficacy and duration of drug activity, increased patient compliance through decreased dosing frequency and convenient routes of administration and improved targeting for a specific site to reduce unwanted side effects. The challenge for both drug and drug delivery companies is to deliver both existing and emerging drug technologies in a manner that improves the benefits to the patients. Over the past several years, great advanceshave been made on development of novel drug delivery systems of anticancer drug (NDDS). The variety of novel formulations like polymeric nanoparticles, nanocapsules, liposomes, phytosomes, nanoemulsions, microsphere, hydrogels has been reported using bioactive and plant extracts. The novel formulations are reported to have remarkable advantages over conventional formulations of anticancer which include enhancement of solubility, bioavailability, protection from toxicity, enhancement of pharmacological activity, enhancement of stability, improved tissue macrophages distribution, sustained delivery, and protection from physical and chemical degradation. The present review highlights the current status of the development of novel formulations and summarizes their method of preparation, type of active ingredients, size, and entrapment efficiency, route of administration, biological activity and applications of novel formulations.

Keywords: Hydrogel, Anticancer, Drug Delivery, Nanoparticles, Microspheres, Liposomes.

Introduction:

Cancer is a worldwide public health problem and presently 24.6 million people are suffering from this deadly disease [1]. Despite significant advancements in early diagnosis and treatment, successful cure rates for cancer remain alarmingly low. With over 100 different types, cancers are typically named according to the organ or type of cell where they originate. They can be broadly categorized into three main types: Carcinoma (originating in skin or tissues lining internal organs), Sarcoma (arising in bone, cartilage, muscle, blood vessels, or other supportive

tissues), and Leukemia (beginning in blood-forming organs like the bone marrow, leading to the production of abnormal blood cells).

In current cancer therapy, drugs are typically administered via intravenous or oral routes using conventional formulations such as tablets, capsules, or injectables. However, there is a growing need for sustained and targeted delivery of anti-cancer agents to maximize their efficacy during tumor growth while minimizing exposure to healthy cells and reducing toxicity. Achieving a steady infusion of drugs into the tumor interstitium is also desirable to enhance exposure to dividing cells and promote tumor regression [2]. Conventional oral and injectable forms of anti-cancer drugs face limitations such as short biological half-life, narrow therapeutic index, low oral bioavailability, and formulation challenges like poor water solubility, stability, and high molecular weight [3]. Recent advancements in drug delivery systems have led to the utilization of various colloidal carriers like liposomes, niosomes, microemulsions, nanoemulsions, microspheres, and polymeric micelles for the sustained and targeted delivery of anti-cancer drugs. The emergence of nanotechnology has further fueled optimism for the rationalized delivery of these agents, promising higher efficacy. Pharmaceutical industries are actively researching the development of novel drug delivery systems for anti-cancer drugs, driven by the high cost of treatment, the need for repeated administrations over prolonged periods, and the escalating number of cancer patients. Commercial products like Nanoxel(R), a nanoparticle-based formulation for paclitaxel from Dabur, and Abraxane(R), an albumin-based formulation for paclitaxel from Abraxis Oncology, exemplify these efforts. Various approaches have been explored for achieving sustained and targeted delivery of anti-cancer agents.

Nanoparticles

The development of nanoparticles for drug delivery began in the 1960s [4]. Nanoparticles (NPs) are particles ranging from 10 to 1000 nm in size, containing drugs either encapsulated or absorbed. These drugs may be attached to a nanoparticle matrix or dissolved, encapsulated, and entrapped, resulting in terms like nanoparticles, nanospheres, or nanocapsules—all indicating their common feature of being nano-sized particles. Anti-cancer agent-loaded nanoparticles offer a highly versatile drug delivery system, capable of overcoming physiological barriers and directing drugs to specific cells or intracellular compartments via passive or ligand-mediated targeting mechanisms [5-8]. Nanoparticle anticancer drug delivery pass through the smallest capillary vessels because of their ultra-tiny volume and avoid rapid clearance by phagocytes so that their duration in blood stream is greatly prolonged [9]. Nanoparticles can also penetrate cells and tissue gap to arrive at target organs such as liver, spleen, lung, spinal cord and lymph. Mu and Feng [10] proposed d- tocopheryl polyethylene glycol 1000 succinate (Vitamin E TPGS) a

novel surfactant as well as matrix material with other biodegradable polymers for fabrication of nanoparticle formulation of paclitaxel. Finally, it was concluded that Vitamin E TPGS is advantageous either as emulsifier or as matrix material blended with PLGA for the manufacture of nanoparticles for controlled release of paclitaxel. In another study, Feng *et al.* [11] have developed paclitaxel loaded nanospheres formulation to achieve better therapeutic effects with minimum side-effects. Phospholipids as well as other natural emulsifiers such as cholesterol and vitamins may have greater advantage for preparation of polymeric nanospheres for controlled release of paclitaxel as well as other anti-cancer drugs.PEG-coated biodegradable polycyanoacrylate nanoparticle (PEG-nanoparticles) conjugated to transferrin, for sustained and targeted delivery of paclitaxel. In further study, Zhang and Feng [12] reported the use of poly(lactide) tocopheryl polyethylene glycol succinate (TPGS) (PLA-TPGS) as novel synthesized copolymers having desired hydrophobichydrophilic balance for delivery of paclitaxel. Nanoparticle formulation of paclitaxel using PLA-TPGS copolymer was prepared and characterized *in vitro* and *ex-vivo*. Paclitaxel is one of the best found anti-cancer drug and current commercial formulation employed Cremophor EL as adjuvant for its solubilization.

PEG-coated biodegradable polycyanoacrylate nanoparticle (PEG-nanoparticles) conjugated to transferrin, for sustained and targeted delivery of paclitaxel was studied by Xua *et al.* [13]. They found the sustained release profile of paclitaxel from developed nanoparticle formulation and release was sustained over 30 days (81.6%) period of time. Nanoparticle formulation was also found to exhibit a markedly delayed blood clearance in mice, and the paclitaxel level from conjugated nanoparticles remained much higher at 24 h compared with that of free drug from paclitaxel injection. The biodistribution profiles of nanoparticles in S-180 solid tumor bearing mice after intravenous administration showed the tumor accumulation of paclitaxel increased with time, and the paclitaxel concentration in tumor was found to be 4.8 and 2.1 times higher than those from paclitaxel injection and PEG-nanoparticles at 6 h after intravenous injection. Authors hypothesized that PEG-coated biodegradable polycyanoacrylate nanoparticle conjugated to transferrin could be an effective carrier for paclitaxel delivery. In further study, Shenoy and Dinesh [14] evaluated and compared the biodistribution profile of tamoxifen administered intravenously (i.v.) as a simple solution and encapsulated in polymeric nanoparticulate formulations, with or without surface stabilizing agents. Poly(ethylene oxide)-modified poly(ethylene oxide-caprolactone) (PEO-PCL) nanoparticles with an average diameter of 150–250 nm, having a smooth spherical shape, and a positive surface charge was obtained with the formulation procedure. Authors have found about 90% drug encapsulation efficiency when tamoxifen was loaded at 10% by weight of the polymer. The primary site of accumulation

for the drug-loaded nanoparticles after i.v. administration was the liver, though up to 26% of the total activity was recovered in tumor at 6 h post-injection for PEO-modified nanoparticles. PEO-PCL nanoparticles exhibited significant increase in tumor localization as well as extended their presence in the systemic circulation than the controls (unmodified nanoparticles or the solution form). Lu *et al.* [15] have evaluated tissue distribution, acute toxicity and therapeutic efficiency against breast cancer and its lymph node metastases of formulated Bovine serum albumin (BSA) and chitosan (CS) nanospheres of mitoxantrone (MTO). After local injection in rats, MTO nanospheres (NS) showed a slower elimination rate and a much higher drug concentration in lymph nodes compared with MTO solution, and a lower drug concentration in other tissues. There was no observed acute toxicity to the main tissues of Kunming mice after local injection of MTO-BSA-NS. The inhibition rate of the nanospheres against breast cancer was much higher than that of MTO solution, and lymph node metastases was efficiently inhibited by the nanospheres, especially MTO-BSA-NS. The results showed that nanospheres seem to be a promising carrier system for delivery of anti-tumor agents to breast cancer and especially for its lymph node metastases. Dries *et al.* [16] **s**tudied human albumin serum (HAS)nanoparticles for delivery of doxorubicin. The influence on cell viability of the resulting nanoparticles was investigated in two different cell lines UKF-NB-3 and IMR-32. The anticancer effect of the drug-loaded nanoparticles was found to increase significantly in comparison to doxorubicin solution. HSA nanoparticles represent promising drug carrier systems for anti-cancer drug delivery and may diminish their toxicity, optimize body distribution and overcome multi drug resistance.

1. Solid lipid nanoparticless

Solid lipid nanoparticles (SLN) have been introduced as a novel drug delivery system for delivery of drugs in various application routes [17]. SLN consist of drug trapped in biocompatible lipid core and surfactant at the outer shell, offering a good alternative to polymeric systems in terms of lower toxicity [18]. Moreover, the production process can be modulated for desired drug release, protection of drug degradation and avoidance of organic solvents [19]. First report for use of SLN as carrier for delivery of paclitaxel came before a decade when Cavalli *et al.* [20] developed stealth and non-stealth solid lipid nanospheres (SLNs) as colloidal carriers for paclitaxel delivery. Formulation contained bioacceptable and biodegradable lipids, tripalmitin and phosphatidylcholine, and incorporate amounts of paclitaxel upto 2.8%. Stealth and non-stealth loaded SLNs were in the nanometric size range and can be sterilized and freeze dried. Thermal analysis demonstrated that drug was not crystallize in the SLNs. Release kinetics of paclitaxel from SLNs showed first pseudo zero order and the amount

of paclitaxel released over time was very slow when administered intravenously. Authors concluded that SLNs could therefore be considered as a slow releasing carrier for delivery of paclitaxel. Recently, Zhenghong *et al.* [21] **s**tudied docetaxelloaded hepatoma-targeted solid lipid nanoparticle (tSLN). The cellular cytotoxicity, cellular uptake, subcellular localization, *in vivo* toxicity, therapeutic effect, biodistribution and histology of tSLNs were investigated. The tSLNs was found to have the particle size about 120 nm with higher encapsulation efficiency >90%, a low burst effect within the first day and a sustained release for the next 29 days *in vitro*. The tSLNs also showed better tolerant and anti-tumor efficacy in murine model bearing hepatoma. The histology demonstrated that tSLNs have no detrimental effect on both healthy liver and liver with fibrosis. These results implied that this targeted nanocarrier of docetaxel could enhance its anti-tumor effect *in vivo* with low systemic toxicity for the treatment of locally advanced and metastatic hepatocellular carcinoma. Not much work has been done using SLNs as carrier for anti-cancer delivery but it is expected that drug delivery scientist will explore this as potential carrier in future due to lesser toxicity, easy preparation method and highly lipophilic nature of commonly used anti-cancer drugs.

Liposomes

Tiny pouches made of lipids, or fat molecules surrounding a water core widely used for clinical cancer treatment. Several different kinds of liposomes are widely employed against infectious diseases and can deliver certain vaccines. During cancer treatment they encapsule drugs, shielding healthy cells from their toxicity, and prevent their concentration in vulnerable tissues such as those of patient kidneys and liver. Liposomes can also reduce or eliminate certain common side effects of cancer treatment such as nausea and hair loss. They are form of vesicles that consist either of many, few or just one phospholipid bilayers. The polar character of liposomal core enables polar drug molecules to be encapsulated. Amphiphilic and lipophilic molecules are solubilised within phospholipid bilayer according to their affinity towards phospholipids.

1. Liposomes for sustained and targeted delivery

5-Fluorouracil (5-FU) is highly hydrophilic anti-cancerdrug and its liposomal formulation has problem of poor encapsulation efficiency and drug leaking during storage. Vesicular phospholipid gels (VPG) which is highly concentrated liposomal dispersions containing high amount of phospholipids (30% w/w) for 5-FU delivery was prepared and investigated [22]. This formulation was found to solve the problem of poor entrapment efficiency of 5-FU prepared by high pressure homogenization techniques. The entrapment efficiency of formulation was found to be 40% after redispersion of the gel to liposomal dispersion. The results of *in vitro* drug

release study at Ph 8.0 showed the initial higher release for first 20 min followed by sustained release to 6 h period of time. Authors suggested that 5-FU loaded VPG could be used as implants for sustained release of 5-FU. Potential lipophilic prodrug of 5-fluorouracil–N3-Otoluyl-fluorouracil (TFu) was synthesized and liposomal formulation was prepared with objective to improve the bioavailability and therapeutic efficacy of 5-Fu by oral and intravenous administration [23]. Author found 10 fold increase in entrapment efficiency of prodrug TFu in comparison to hydrophilic 5-Fu in liposomal formulation. *In vitro* drug release profile of TFu loaded liposomes demonstrated that liposomal formulation followed bi-exponential release pattern, initial higher release followed by slow release. Pharmacokinetic studies showed bioavailability of TFu loaded liposomes was nearly 2.0-fold higher than the suspension after oral administration, and was bioequivalent comparing with TFu 50% alcohol solution after i.v. administration. Authors hypothesized that TFu-loaded liposomes can develop as alternative for oral and i.v. administration. Hao *et al.* [24] studied fluid and solid liposomal formulations of topotecan (TPT) with different composition for *in vitro* stability and biodistribution behavior**.** Authors found that compared with the 'fluid' liposome (S-Lip) composed of soybean phosphatidylcholine (SPC), the 'solid' liposome (HLip) composed of hydrogenated soybean phosphatidylcholine decreased the leaking efficiency of TPT and enhanced the *in vivo* stability of liposomes. The results of biodistribution studies in S180 tumor-bearing mice showed 5 and 19 fold increase in the TPT area under curve (AUC) for S-Lip and H-Lip formulation, respectively. PEG-modified H-Lip (HPEG) showed 3.7-fold increase in AUC compared with HLip, but there was no significant increase in tl/2 and AUC for PEG-modified S-Lip (S-PEG) compared with S-Lip. Lyophilized negatively charged paclitaxel magnetic liposome was studied as a potential carrier for sustained and targeted delivery to breast carcinoma *via* parenteral administration [25]. Encapsulation of paclitaxel in magnetoliposomes produced significant difference in pharmacokinetic over the drug in Cremophor EL/ethanol with an increased t1/2 to 19.4 h against 4.1 h. The biodistribution pattern was also found to significantly higher in tumor tissue with magnetoliposomes than lyophilized conventional liposomes or Cremophor EL/ethanol. This study demonstrated that paclitaxel magnetoliposomes can effectively delivered to tumor and exerted a significant anticancer activity with fewer side effects in the xenograft model. Vodovozova *et al.* [26] synthesized a lipid conjugate of the anti-cancer agent methotrexate (MTXDG) and found that the conjugate successfully encapsulated in the lipid bilayer of liposomes. The liposomal formulation of MTXDG was found to overcome the resistance of tumor cells *in vitro* to methotrexate. Authors have performed the cytotoxic activities

(IC50) of MTX in cultures of the human T-lymphoblastic leukemia cell line CEMCCRF and the MTX-resistant subline CEM/MTX and found better anti-cancer activity of developed formulation. Mechanism of drug release from liposome is shown in figure 2.

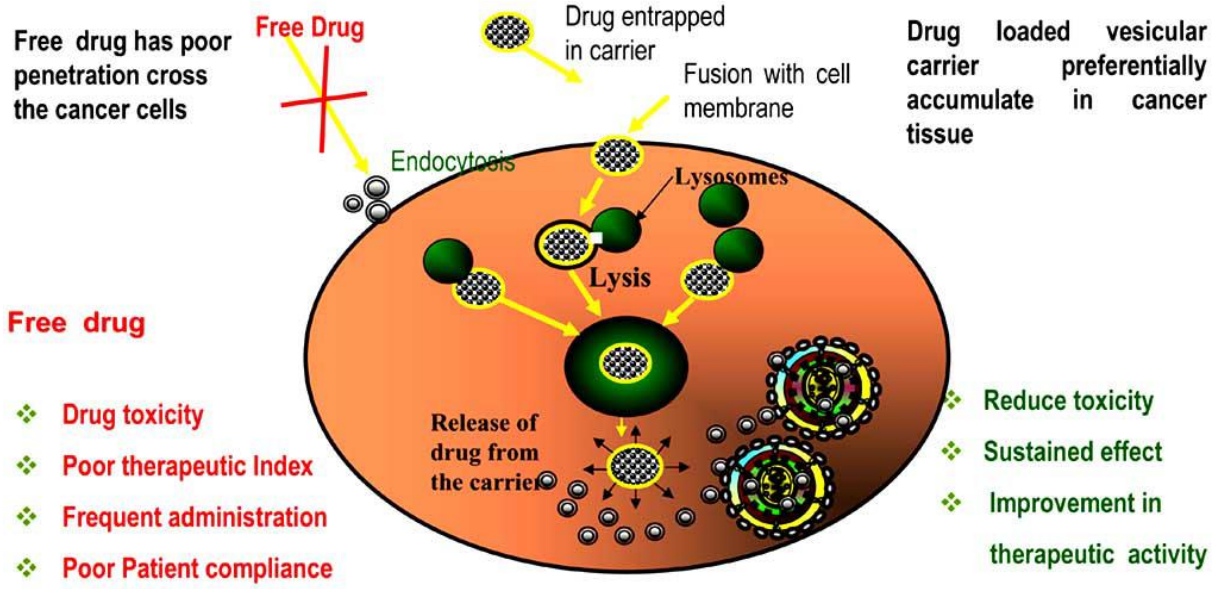

Figure 2: Mechanism drug release form liposome delivery of anti-cancer agents

2. Liposomes for increasing the solubility of drug

First time, Liu *et al.* [27] Cholesterol-free liposomes, composed of egg phosphatidylcholine and poly(ethylene glycol)-conjugated distearoyl phosphatidylethanolamine (DSPE-PEG 2000), were developed for delivering the highly lipophilic anti-cancer agent ML220. ML220 has low water solubility and high lipophilicity. The liposomal formulation increased the water solubility of ML220 by 50,000 fold with an 83% loading efficiency. Subacute toxicity tests in C3H mice showed no signs of toxicity. Pharmacokinetic analysis in Balb/C mice revealed a biexponential drug plasma concentration pattern. In vivo studies in a human colon HT29 carcinoma model demonstrated a significant delay in tumor growth. This research underscores the potential of cholesterol-free liposomes as a formulation approach for highly lipophilic drugs like ML220 and paclitaxel.

In similar studies Zhang *et al.* [28] a notable increase in solubility and encapsulation efficiency of the new anti-cancer agent Camptosar® (SN-38) was reported in a liposomal formulation. SN-38, the active metabolite of irinotecan (CPT-11), is significantly more cytotoxic than irinotecan (200-2000 fold). However, its poor solubility in pharmaceutically acceptable solvents has hindered its use as an anti-cancer drug. Solubility enhancement and sustain release by various systems for anticancer drugs summarized in table 1 and 2.

Table 1: Novel drug delivery systems reported for increasing the solubility of anti-cancer drugs

Drug Name	System	Finding
Paclitaxel	Nanoparticles	High encapsulation efficiency and Enhanced solubility
Paclitaxel	Nanospheres	Prolonged release of paclitaxel, upto 3 months
ML 220	Liposomes	50,000-fold increase in the water solubility
SN-38	Liposomes	Enhanced entrapment efficiency upto 95%.

Table 2: Novel drug delivery systems for sustained and controlled delivery of anti-cancer drugs

Drug Name (System)	Finding
Paclitaxel (Nanoparticles)	Higher therapeutic effects than Taxol®
Paclitaxel(Nanospheres)	Sustained release of paclitaxel upto 20 h.
Paclitaxel (Polymeric Micelles)	Sustained release of paclitaxel upto 20 h.
Paclitaxel (Solidlipid Nanospheres)	Sustained delivery of paclitaxel
5- Fluro Uracil	Showed 4.5-fold increase in half-life
Paclitaxel(Vesicular phospholipids gels)	81.6% paclitaxel was released in 30 days.
Paclitaxel (PEGylated Immuno Liposomes)	Biological half-life increase from 5.05 to 17.8 h
Paclitaxel (Emulsion system)	Slow release of drug in comparison to Taxol®

3. PEGylated liposomal formulation

PEGylation of liposomal formulations has been shown to prolong circulation time by avoiding rapid clearance by the reticuloendothelial system (RES), resulting in favorable pharmacokinetics and effective tumor targeting. Studies by Pakunlu *et al.* demonstrated successful cellular uptake of PEGylated liposomes for cytoplasmic and nuclear delivery of anticancer drugs, enhancing in vitro cytotoxicity and in vivo antitumor activity. Li *et al.* encapsulated Mitoxantrone into PEGylated liposomes, observing faster drug release in smaller-sized formulations with reduced toxicity compared to free Mitoxantrone. Yang *et al.* compared PEGylated immunoliposomes and PEGylated liposomes for targeted delivery to human breast cancer cells, showing higher cellular uptake in HER2-overexpressing cells and prolonged circulation time in rats. These findings suggest the potential of PEGylated immunoliposomes for tumor-specific therapy in HER2-overexpressing breast cancers [29, 30].

Microspheres:

Microspheres are an example of a drug delivery system that has been evaluated extensively in cancer chemotherapy. They are essentially solid porous particles (1 - 100 μm diameters) which can both target their drug cargo by physical trapping in blood vessels (chemoembolisation) and sustain the action of a therapeutic agent through controlled release. Microspheres can be made from a broad range of polymeric materials, including proteins, polysaccharides, polyesters and lipids by a variety of different techniques (emulsification, heat stabilisation, coacervation and phase inversion technology). Their diversity identifies the microsphere as a drug delivery system with considerable flexibility. Examples are cited of different approaches adopted with cytotoxic drugs (chiefly doxorubicin, mitomycin C, cisplatin and 5- fluorouracil) to achieve particular drug delivery profiles. However, it is clear that certain cytotoxic drugs are encapsulated in systems with pharmaceutical properties inappropriate for the particular mechanistic class. Microspheres have made to delivery of immunomodulating cytokines, protein vaccines, antisense oligonucleotides and gene therapy. For these applications, new matrix materials such as bioadhesive polymers and more gentle methods of preparation have had to be developed to preserve the native conformation of these easily denatured biological molecules. Microspheres are anticipated to contribute significantly in the future to the systemic, oral and loco-regional treatment of cancer with cytotoxic drugs and biological response modifiers [31, 32].

Dendrimers

Interest in utilizing polymeric carriers for delivering unaltered natural products is widespread. Dendritic polymers have recently emerged as promising candidates for encapsulating hydrophobic compounds and delivering anticancer drugs. Dendrimers are highly branched macromolecules with a well-defined core, interior region, and numerous end groups. Their physical characteristics, such as monodispersity, water solubility, encapsulation ability, and functionalizable peripheral groups, make them ideal for drug delivery applications [33, 34]. Currently, there are three methods for using dendrimers in drug delivery: (a) the drug is covalently attached to the periphery of the dendrimer to form dendrimer prodrugs, (b) the drug is coordinated to the outer functional groups via ionic interactions, or (c) the dendrimer acts as a unimolecular micelle byencapsulating a pharmaceutical through the formation of a dendrimerdrug (i.e., host–guest) supramolecular assembly.

Hydrogels

Hydrogels are three-dimensional, cross-linked networks of water-soluble polymers. Hydrogels can be made from virtually any water-soluble polymer, encompassing a wide range of

chemical compositions and bulk physical properties. Furthermore, hydrogels can be formulated in a variety of physical forms, including slabs, microparticles, nanoparticles, coatings, and films. As a result, hydrogels are commonly used in clinical practice and experimental medicine for a wide range of applications, including tissue engineering and regenerative medicine [35], diagnostics, cellular immobilization, separation of biomolecules or cells, and barrier materials to regulate biological adhesions [36]. Several terms have been coined for hydrogels, such as 'intelligent gels' or 'smart hydrogels'[37]. The smartness of any material is the key to its ability to receive, transmit or process a stimulus, and respond by producing a useful effect [38]. Hydrogels form depot formulations that slowly elute drugs, maintaining high local concentrations over time. Hydrogels are biocompatible, resembling the native extracellular matrix and can be designed for biodegradability. However, their low tensile strength limits load-bearing applications. Recent advancements include in-situ hydrogel formation, allowing minimally invasive procedures, utilizing physical and chemical cross-linking mechanisms such as hydrogen bonding, hydrophobic interactions, and electrostatic interactions.

Drug-impregnated wafers enable localized chemotherapy

In 1987, Henry Brem and col-leagues inserted these drug impregnated wafers, layered at the surface of the brain, into the tumor resection cavity following tumor removal. The drug is slowly released from these wafers for approximately 3 weeks to destroy any residual tumor. Because the drug is delivered locally, rather than systemically, harmful side effects that normally occur with carmustine were minimized. In 1996, this therapy was approved by the U.S. FDA for patients with recurrent glioblastoma, the first new brain cancer therapy approved in over 20 years. In 2003, the FDA extended its approval to include initial surgery for malignant glioma, based on two additional randomized prospective studies that demonstrated improved survival and safety [39].

To avoid uncomfortable to life threatening toxicity of chemotherapy, approaches have been developed to deliver these drugs locally, with the goal of improving both their safety and efficacy. Delivery of a polymer-drug conjugate during cancer surgery would have the advantage of enhancing the benefit of surgery while minimizing the systemic toxicity that is usually associated with standard drug treatments. This approach has now been successfully exploited, most notably in brain cancer surgery. The ability to deliver chemotherapeutic drugs to this organ via traditional systemic routes is severely restricted by the presence of the blood-brain barrier, which limits transport to this organ. Novel polymers, such as polyanhydrides in the form of wafers, have now been used to deliver chemotherapeutic drugs, such as carmustine (BCNU), local-ly to treat brain cancer.

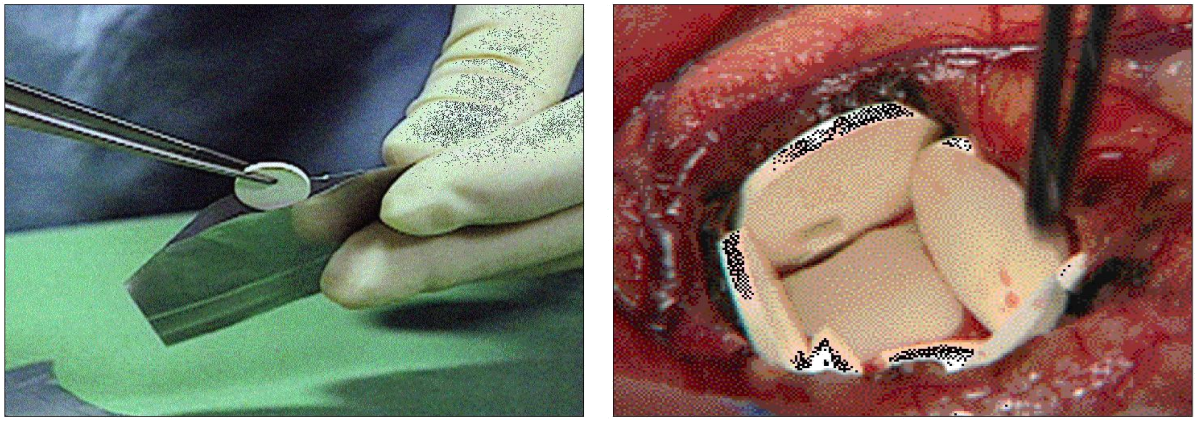

Figure 2: Drug-impregnated wafers

Implantable drug-releasing micro-chips

Efforts to effectively target and deliver chemotherapeutic agents to tumors are ongoing, with challenges remaining in optimal drug diffusion within cancerous tissues and potential interactions between drugs and delivery vehicles. Smarter drug delivery systems are being developed to tackle these issues. For instance, John Santini and Robert Langer have created a controlled-release microchip capable of storing and delivering various drugs on demand, essentially acting as a "pharmacy on a chip." This system can be programmed to release drugs at specific times, patterns, and rates, allowing for novel combination therapies. For example, targeting endothelial cells with angiogenesis inhibitors before administering chemotherapeutic drugs to suppress remaining tumor cells, followed by maintenance on antiangiogenic therapy. To ensure patients with cancer benefit from these advances, equal attention must be given to developing more potent and specific cancer chemotherapeutics, along with optimizing drug delivery systems.

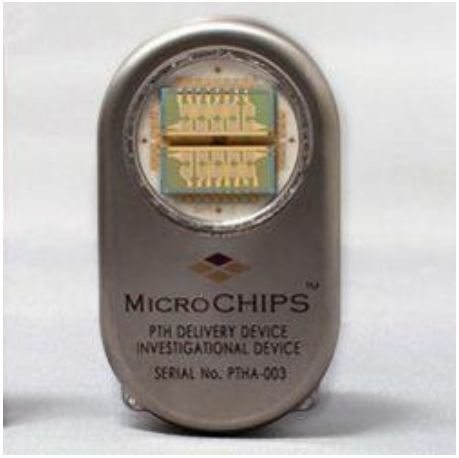

Figure 3: Implantable drug-releasing micro-chips

Implantable drug-releasing microchips, as depicted in Figure 3, can provide hundreds of doses over their lifetime, lasting from months to years (Microchips, Inc., Bedford, MA). These

microchips feature reservoirs capable of storing one or multiple drugs, which can be released on demand through a preprogrammed schedule or external control [39].

Transdermal systems provide sustained systemic drug delivery

Small lipophilic drugs have shown to have the ability to cross the skin quite efficiently. A variety of trans-dermal patches have now been developed, tested, and approved for several different drugs and conditions. These patches are composed of polymers impregnated with drug that diffuse through the polymer and skin to reach the systemic circulation. Among the transdermal patches currently available are scopolamine for motion sickness, nitroglycerine for angina, fentanyl for pain, and clonidine for hypertension. Transdermal delivery also has played an important role in both cancer therapy and prevention. Most compelling is the use of nico-tine patches in preventing smoking and prolonging life [39].

Controlled delivery is possible with drug diffusion from polymers

Biologically active peptides and polypeptides face a challenge due to their short in vivo half-lives. However, controlled drug-delivery systems have overcome this hurdle by providing physical and biochemical protection to these drugs, enabling their successful therapeutic use. In 1976, Robert Langer and Judah Folkman addressed the difficulty of large molecule diffusion through polymer materials in conventional drug delivery systems by embedding molecules into polymers, creating a network of pores for drug diffusion. This innovation led to the development of polymers for sustained protein release, initially using nondegradable polymers like ethylene-vinyl acetate copolymer and later degradable polymers like lactic-glycolic acid copolymers. For instance, analogs of luteinizing hormone-releasing hormone (LHRH) are effectively delivered in the treatment of advanced prostate cancer using this method.

Previously, administering these drugs orally or nasally resulted in low bioavailability and inconsistent blood levels. Embedding the drugs into polymers resolved these issues, resulting in injectable delivery systems like Lupron®, Zoladex®, and Decapeptyl®, which now last from 1 to 4 months and are successfully used in prostate cancer treatment. Another approach to prolong drug lifetimes is by chemically binding the drug to water-soluble polymers like polyethylene glycol (PEG), reducing immunogenicity and extending biological activity. This method has been employed for delivering drugs like asparaginase, interferon, and granulocyte colony-stimulating growth factor (G-CSF) [39,40].

Magnetic-drug targeting

Magnetic-drug targeting can offer a unique opportunity to treat malignant tumors locoregionally. Alexiou *et al.* have treated squamous cell carcinoma.*in vivo* with the injection of magnetic nanoparticles.(ferrofluids) bound to mitoxantrone, as a chemotherapeutic agent, that

was locally induced to concentrate by means of a magnetic field. The intratumoral accumulation of the particles can additionally be visualized by means of MRI [41]. Drug delivery systems currently used for cancer treatment are summerized in table 3.

Table 3: Drug delivery systems currently used for cancer treatment

Delivery Name	Drug	Cancer Treatment	
Injectable Polymer Rod/Microsphere			
Z o l a d ex*	LHRH analog	Advanced prostate cancer	
Lypron depot†	LHRH analog	Advanced prostate cancer	
Decapeptyl†	LHRH analog	Advanced prostate cancer	
Implantable Wafer			
Gliadel	Carmustine	Malignant gliomas	
Liposomes			
Doxil	Doxorubicin	Ovarian cancer, AIDS-related Kaposi's sarcoma	
AmBisome	Amphotericin	Fungal infections in chemotherapy patients	
Daunoxome	Daunorubicin	AIDS-related Kaposi's sarcoma	
Polymer-Drug Complex			
SMANCS–lipiodol emulsion	Zinostatin stimalamer	Hepatocellular carcinoma	
PEGylated Drug			
Oncaspar	L-Asparaginase	Acute lymphoblastic leukemia	
PEG Intron	□- Interferon	Various cancers	
Neulasta	G - CSF	Prevention of chemotherapy-related neutropenia	
Transdermal Patch			
Duagesic	Fentanyl	Pain management	
Habitrol	Nicotine	Smoking cessation (cancer prevention)	
Nicotrol	Nicotine	Smoking cessation (cancer prevention)	
Nicoderm	Nicotine	Smoking cessation (cancer prevention)	
Prostep	Nicotine	Smoking cessation (cancer prevention)	
Lipid Depot in CSF			
Depoctye	Cytarabine	Carcinomatous meningitis	

Commercially Available Novel Drug Delivery System based Formulations for Anti-Cancer Drugs are summerized in table 4.

Table 4: Commercially available novel drug delivery system based formulations for anti-cancer drugs

Drug Name	Novel System	Brand Name	Company
Paclitaxel	Albumin bound particles	Abraxane	Abraxis Bioscience LLC
Paclitaxel	Polymeric nanoparticles gel	Nanoxel	Dabur India Ltd
Doxorubicin	Liposomal injection	Doxil	Ortho Biotech
Doxorubicin	PEGylated liposomal inj.	Lip-Dox	TTY Biopharm
Doxorubicin	Liposomal Injection	Caelyx	Schering-Plough
Doxorubicin	PEGylated liposomal inj.	Myocet	Cephalon Inc
Doxorubicin	PEGylated liposomal inj.	Lipo-dox	Sun pharmaceuticals
Cytarabine	Liposomal Injection	Depocyt	Enzone Pharmaceutical

Conclusion:

The novel anticancer drug delivery systems effectively modulate drug release, target the tumor cells, reduces toxic effects of chemotherapy, provides better patient compliance, reduces dosing frequency and dose. The novel anticancer systems can significantly reduce and controls the cancer with more safety.

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RECENT ADVANCES IN SCIENCE AND MEDICINE

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Abstract:

Chronic pain exerts a significant physical, emotional, and socioeconomic toll on millions of patients worldwide. Traditional pharmacological interventions are often inadequate in providing lasting and effective pain relief for patients suffering from severe chronic pain. However, in recent years, intravenous ketamine infusion therapy has emerged as a promising and alternative treatment modality. The effectiveness of intravenous ketamine infusion therapy in treating chronic pain has been investigated in various pain conditions, such as neuropathic pain, fibromyalgia, complex regional pain syndrome (CRPS), and phantom limb pain. However, varied patient demographics, different endpoints for measuring analgesia, and inconsistent numbers of patients in studies have led to conflicting results. The objective of the present inquiry is to undertake a contemporary updated meta-analysis of the application of IV ketamine infusion therapy in the context of persistent pain.

Introduction;

Recent years have seen a revolution in the domain of medical science, with ground-breaking discoveries changing health care as we once knew it. These advances have considerably improved disease diagno- sis, treatment, and management, improving patient outcomes and quality of life. These innovations range from the creation of novel medications and treatments to the utilization of cutting-edge technologies. For instance, gene editing technologies like Clustered Regularly Interspaced Palindromic Repeats (CRISPR-Cas9) have opened up new treatment options for genetic illnesses, while the development of mRNA vaccines has offered a desperately needed response to the coronavirus disease 2019 (COVID-19) pandemic. Moreover, wearable technology and telemedicine have improved accessibility, convenience, and personalization of health care, whereas 3D printing and nanotechnology breakthroughs have made it possible to create individualized implants and drug delivery systems. This article examines some of the most recent developments in medical research and how they might completely change health care delivery.

The selection process for identifying the latest advances in medical sciences for this article was as follows. We aimed to showcase ground-breaking developments with the potential to revolutionise health care practices and significantly impact patient outcomes. We extensively searched reputable scientific journals, conferences, and reports from recognized health care organisations and institutes. We included the novelty and significance of the advancements, their ability to address existing health care challenges, the level of scientific evidence supporting their efficacy, and their poten- tial for widespread adoption and implementation. By utilizing this process, we ensured that the selected advancements represent diverse medical fields and have the capacity to drive significant advancements in patient care, di- agnostics, treatment modalities, and health care delivery.

Methods:

A search was conducted, adhering to the PRISMA guidelines, to compare the efficacy of IV Ketamine infusion versus control (placebo, midazolam, gabapentin, hydromorphone, and pregabalin) among individuals with chronic pain. During the analysis, Medline, Cochrane, and Embase were thoroughly searched. Two independent investigators identified randomized double-blind and nonrandomized trials comparing IV Ketamine infusions with controls. Review Manager 5.4.1 was used to scrutinize the data, with the main focus on pain scores. Secondary outcomes such as quality of sleep, as well as side effects such as nausea, hallucinations, and sedation, were also analyzed. Sixteen studies were included involving 1080 patients.

Regenerative therapy treatment

Regenerative medicine is a rapidly growing field that seeks to restore, replace, or regenerate damaged tissues and organs using a variety of approaches, including cell therapy, tissue engineering, and gene therapy.

This field has the potential to revolutionise the treatment of many diseases and injuries that are currently incur- able or difficult to treat. For example, stem cell therapy has been shown

to be effective in treating spinal cord injuries. with several studies reporting significant improvements in motor function and sensory percep- tion. Tissue engineering approaches are being developed to replace damaged or diseased organs using 3D printing, such as the liver, pancreas, and heart. Gene therapy is being used to target genetic disorders, such as sickle cell anaemia and cystic fibrosis, with promising results. The development of regenerative medicine has the potential to transform the treatment of many diseases and injuries, providing hope for patients with conditions that are currently considered untreatable

Development of implantable artificial organs

Various replacement or augmentation devices for organs, such as the eyes, kidneys, heart, muscle, liver, skin, and brain, have been developed due to the creation of implantable artificial organs. Artificial organs can be developed from a number of substances, such as polymers and biological tissues, and are intended to mimic the shape and functionality of actual organs. For instance, the Wearable Artificial Kidney (WAK) has promise for enhancing the quality of life for individuals with end-stage of re- nal illness. The creation of artificial hearts, such as the Total Ar- tificial Heart (TAH), has the potential to extend the lives of patients awaiting heart transplants.

Advancements in nanotechnology in health science

Another fast expanding and highly promising area of use for nanotechnology is in the field of medicine. Drugs and other therapeutic substances can be delivered directly to a disease site using nanoparticles because they can target particular cells or tissues in the body. This technology may improve the efficacy of therapies, lessen their negative effects, and potentially enable the treatment of previously incurable diseases.

Current developments in nanotechnology have demonstrated considerable promise for the medical field. A study by Foglizzo and Marchio. created a multifunctional nano platform that delivered chemotherapeu- tic medication and an immunomodulatory substance to tumour cells, increasing antitumor activity and min- imizing adverse effects. Using nanotechnology, a magnetic resonance imaging (MRI) contrast agent that can specifically target and image pancreatic cancer cells was created. Moreover, nanotechnology has dem- onstrated promise in the treatment of diseases like brain tumours that were previously incurable. A study by Chen et al. created a nano platform that specifically targeted and delivered medications to brain tumour cells, improving survival rates in a mouse model. These recent developments show how nanotechnology has the potential to enhance therapeutic efficacy, lessen adverse effects, and broaden the scope of diseases that can be treated.

Development of CRISPR-Cas9 gene editing technology

A rapidly developing technique called gene editing could revolutionise medicine by enabling researchers to change cells' genetic makeup. CRISPR-Cas9, a promising method for gene editing, allows for accurate targeting and editing of particular regions of the genome. Genetic disorders like cystic fibrosis and sickle cell anae- mia, which were once thought to be incurable, could potentially be cured because of this technique. Also, scientists are looking at its therapeutic potential for a number of illnesses, such as Alzheimer disease, hu- man immunodeficiency virus (HIV), and cancer.

Yet there are also moral questions raised by using gene editing on people, so it's important to use the technol- ogy sensibly and morally. Until the hazards and moral issues surrounding germline editing, which edits the genes that can be passed on to future generations, are better known, a group of scientists called for a morato- rium on its clinical usage in 2019.

Artificial Intelligence (AI) for medical science

Recent years have seen considerable advancements in the use of artificial intelligence (AI) and machine learn- ing in the health care industry. In order to find trends and forecast health outcomes, AI systems can evaluate enormous amounts of medical data, including images, test results, and patient records. This may result in more accurate diagnosis, individualized treatment strategies, and effective patient monitoring.

The promise of AI in health care has been proved by a number of studies. For instance, Esteva et al, created an AI model with skin cancer detection accuracy on par with dermatologists. Rajkomar et al.use of machine learning to forecast patient mortality and hospital readmission rates may aid health care professionals in identifying pa- tients who need more care. Moreover, Chung et al. created an AI algorithm that could anticipate the onset of psychosis in individuals who had clinical high-risk signs. Predicting the risk of cardiovascular illness using AI has also shown promise. For example, Khera et al. developed a model using machine learning to identify patients with a high risk of developing heart disease, potentially allowing for early intervention and preventative measures.Yet, there are also issues with using AI in health care that need to be resolved, such as the requirement for strong data protection and ethical concerns with the use of AI algorithms to clinical decision-making Chimeric Antigen Receptor (CAR) T-cell therapy to treat cancer Chimeric Antigen Receptor (CAR) cell therapy, a form of immunotherapy that employs T cells to recognize and target cancer cells, depends heavily on genetically transformed T cells Recent studies have demon-strated that CAR T treatment is very effective in treating a range of lymphoma types, including diffuse large B-cell lymphoma and mantle cell lymphoma.Despite the positive outcomes, CAR T therapy has draw- backs, such as a high price

and risk for toxicity. In order to increase the effectiveness and safety of CAR T treat- ment and broaden its use to treat additional cancer types, research is now being done by Ren et al. For in- stance, a recent study by Yang et al. discovered that multiple myeloma, a kind of blood cancer, that has re- lapsed or become resistant to treatment, can be effectively treated with CAR T therapy that targets the B-cell matu- ration antigen (BCMA). Researchers are also investigating combination therapies, which couple CAR T therapy

Development of mRNA vaccine

The development of mRNA vaccines has been a significant milestone in the fight against COVID-19. The Pfizer-BioNTech and Moderna mRNA vaccines have demonstrated remarkable efficacy and safety profiles in preventing COVID-19 infection and its complications. The mRNA technology used in these vaccines has several advantages over traditional vaccine production methods, including faster development and manu- facturing times, lower production costs, and greater flexibility in responding to emerging viral variants.

Clinical trials of the Pfizer-BioNTech and Moderna vaccines have shown high levels of protection against CO- VID-19. A study by Polack et al. found that the Pfizer-BioNTech vaccine had an efficacy rate of 95% in preventing COVID-19 infection, while a study by Baden et al. reported a similar efficacy rate of 94.1% for the Moderna vaccine. Additionally, real-world data has confirmed the high effectiveness of mRNA vaccines in preventing severe disease, hospitalization, and death caused by COVID-19.

Another company that has been working on developing mRNA vaccines for COVID-19 is Novavax. The company's vaccine candidate combines mRNA technology with nanoparticles to enhance the body's immune response. In clinical trials, the vaccine demonstrated efficacy against both the original strain of COVID-19 and certain variants of the virus.

Companies such as Moderna and BioNTech are now exploring the potential of mRNA vaccines for a wide range of illnesses, including cancer and influenza. The development of mRNA vaccines also holds promise for creating rapid responses to new and emerging infectious diseases, as the technology allows for quick adapta- tion to new viral strains.

Overall, the development of mRNA vaccines for COVID-19 represents a significant breakthrough in vaccine technology, with potential implications for future disease prevention and treatment.

Advances in 3D printing for medical applications

The development of complex anatomical models, prostheses, implants, and drug delivery systems has been made possible by advances in 3D printing technology. 3D printing has enabled the development of custom-made implants, reducing the need for invasive surgeries and

improving patient outcomes. The successful implanta- tion of 3D printed titanium-mesh implants for the repair of bone deformities was described in a study by Ma et al. Anatomical models that have been 3D printed have been proven to be useful for planning surgeries and advancing medical knowledge. The use of 3D printed models for surgical planning in complicated cranio-facial patients was reported in a study by Charbe et al. The development of 3D printing technology has the potential to revolutionise the medical industry by enabling more individualized and efficient patient care.

Telemedicine to provide remote care

Over the past few years, telemedicine – the use of technology to deliver medical treatments remotely – has grown in popularity, especially during the COVID-19 pandemic Telemedicine allows health care pro- viders to offer virtual consultations, monitor patients remotely, and provide access to medical services in areas with limited health care resources. Telemedicine was linked to better health care access and outcomes for patients with cardiovascular disease during the COVID-19 pandemic. Telemedicine also has the potential to lower medical expenses and raise patient satisfaction. High levels of patient satisfaction with teleconsulta- tions for dermatology services were observed in a study by Nicholson *et al.* Telemedicine use is antici- pated to increase over the next few years, which might have a significant impact on how health care is deliv- ered in the future.

Vertual reality in medical training

Medical students can practice and hone their skills in a safe and controlled environment with the help of vir- tual reality (VR), which has grown in popularity in recent years. Students can practice medical proce- dures and scenarios using VR technology, which helps them become more adept at diagnosing and treating patients. According to a recent study by Yiasemidou et al., medical students' performance and con- fidence improved when VR was used for surgical instruction. Moreover, using VR technology can replace ani- mal or cadaveric models in training for less common medical operations. The effective use of VR technology in training for transesophageal echocardiography was described in a study by Arango et al. The use of virtual reality (VR) in medical education has the potential to raise the standard of medical instruction and in- crease patient safety.

Development of wearable devices for health monitoring

The development of wearable health monitoring technology has completely revolutionised how people track and manage their health. Individuals can receive real-time feedback on their health state by using wear- able devices, such as fitness trackers and smartwatches, which can gather data on physical activity, heart rate, blood oxygen saturation,

sleep habits, and other health markers. These devices capture data that can be analysed to find trends and patterns that can provide important information about a person's general health and wellbeing. According to research by Patel et al. adult users of wearable technology had increases in physical activity and weight loss. Moreover, wearable technology can be used to monitor patients with chronic illnesses remotely, enabling health care professionals to monitor patient progress and take appropriate action as needed. According to a study by Gautam et al. wearable devices are useful for remotely moni- toring patients with heart failure. By encouraging early disease identification and prevention, wearable health monitoring technology has the potential to enhance health outcomes and save health care costs.

Results:

The pain score was significantly reduced by IV Ketamine (Mean difference −1.05; 95% CI −1.72, −0.39; p = 0.002), while the quality of sleep (Mean difference 0.00; 95% CI −0.12, 0.12; p = 1.00) was not significantly different between studies.

Nausea (risk ratio 1.42; 95% CI 0.84, 2.39; p = 0.19), hallucinations (risk ratio 1.08; 95% CI 0.67, 1.76; p = 0.75), and sedation (risk ratio 1.05; 95% CI 0.24, 4.54; p = 0.95) outcomes were not significantly different among the studies.

Conclusions:

In conclusion, the most recent developments in medical science have the potential to completely revolutionise the way health care is provided and greatly enhance patient outcomes. With the advent of modern technolo- gies like telemedicine, gene editing, and artificial intelligence, doctors are now able to detect and treat illnesses more precisely and effectively. Moreover, the application of nanotechnology, 3D printing, and regenerative medicine is bringing about ground-breaking treatments for previously incurable diseases. The advances being made in medical science are genuinely astonishing and give hope for a healthier future, even though there are still obstacles to be addressed. In the years to come, we may anticipate even more interesting advances with ongoing innovation and investment.

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