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Diosgenin: Ethnopharmacology, Mechanism of Actions, and Formulations

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Diosgenin, pharmacological properties, isolation and extraction techniques, ethnobotanical sources, therapeutic potential, biosynthesis pathways

ABSTRACT:

Diosgenin, a unique steroidal saponin, offers a variety of pharmacological benefits due to its distinctive chemical structure. To fully harness its therapeutic potential, it is crucial to thoroughly understand its chemical and physical properties, including its stereochemistry, stability, and spectroscopic characteristics. Further research into its biological activities is essential for the development of effective pharmacological formulations. Diosgenin is extracted and isolated using a collection of processes that incorporate both conventional and contemporary approaches. Maceration and percolation are two procedures that offer simplicity; nevertheless, solvent extraction and supercritical fluid extraction demonstrate a higher level of efficiency. In order to get pure diosgenin for use in a variety of applications, purification in the form of column chromatography and high-performance liquid chromatography is essential. Plants that are rich in diosgenin have been highly regarded in many different cultures due to their medical characteristics, which include the regulation of hormones and the alleviation of pain. A number of species of Dioscorea, Trigonella foenum-graecum, Smilax species, and Costus speciosus are considered to be ethnobotanical sources of diosgenin. It is imperative that further research be conducted to investigate the therapeutic potential of these plants. The pharmacological effects of diosgenin include anti-inflammatory, anticancer, antioxidant, immunomodulatory, and hepatoprotective activities. These features underline the value of diosgenin in the prevention and management of disease. In the context of both medicinal and industrial settings, a comprehensive understanding of its biosynthesis pathways and regulatory mechanisms offers the potential to facilitate the creation of sustainable materials and extend their application.

1. Introduction

Diosgenin, a steroid saponin that occurs naturally in a number of plants, has attracted a lot of interest because of its possible role in cancer treatment. Diosgenin has the potential to inhibit tumor cell development and cause apoptosis, according to research that has examined its effects on cancer cells. Diosgenin is an intriguing topic for oncological research due to the complex molecular pathways that underlie its anti-cancer properties. Diosgenin has also sparked attention in its possible use as a cancer treatment due to its potential as a natural therapeutic agent. The present state of knowledge on the action mechanisms of diosgenin and its possible uses in cancer treatment is the focus of this article. (1,2)

Diosgenin has been the subject of substantial cancer research as of late, leading to a better understanding of its possible utility as a natural anti-cancer agent. Diosgenin has the ability to influence many signaling pathways that are important for the progression and development of cancer, including those involved in cell cycle control, apoptosis, inflammation, and metastasis, according to research. (3)

Diosgenin has the ability to slow tumor cell growth, according to research. This is because it stops the cell cycle, which means it suppresses proliferation.

Journal of Chemical Health Risks

www.jchr.org

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Additionally, it activates intrinsic and extrinsic apoptotic pathways, which aids in the eradication of cancer cells, by inducing apoptosis in cancer cells. (4,5)

On top of that, diosgenin possesses anti-inflammatory qualities, which are critical in creating an unsavory environment for tumor growth. diosgenin helps reduce cancer cell growth and survival by reducing inflammatory signaling and cytokine production (6). Beyond its direct effects on tumor cells, diosgenin has potential uses in cancer therapy. Researchers have looked at its potential to halt angiogenesis, the formation of new blood vessels that tumors rely on for their survival. On top of that, diosgenin makes cancer cells more responsive to standard radiation and chemotherapy treatments. (7–10)

2. Ethnopharmacology of diosgenin

2.1 Traditional Uses

The traditional use of diosgenin spans many civilizations around the globe. Its many medicinal uses have made it an important component of traditional medicine. Here are a few examples of its more conventional uses:

2.1.1 Ayurvedic Medicine

Traditional Ayurvedic medicine has long relied on diosgenin-rich plants for the treatment of a wide range of illnesses. Two such plants are fenugreek ***(Trigonella foenum-graecum)*** and wild yam ***(Dioscorea villosa).*** (11,12)

The restorative and balancing powers of these plants are widely believed. Supporting female reproductive health, alleviating monthly discomfort, and promoting hormonal stability during menopause are prominent uses for herbs that contain diosgenin. In addition to its appetite stimulant and indigestion reliever properties, diosgenin is also thought to be good for digestive health. (13–15)

2.1.2 Traditional Chinese Medicine

The tonifying effects of plants rich in diosgenin, like the Chinese yam ***(Dioscorea opposita),*** have long been coveted in Traditional Chinese Medicine (TCM). Common belief is that these herbs strengthen the digestive tract, provide fuel for the kidneys, and boost energy levels generally. Herbs that contain diosgenin are often suggested as a means to alleviate menopause symptoms, control menstrual cycles, and enhance fertility. Furthermore, diosgenin is used in traditional Chinese medicine to promote good digestion, improve blood circulation, and relieve pain in the joints. (16–18)

2.1.3 Native American Medicine

There is a long history of medical use of plants containing diosgenin among Native American tribes. The Cherokee people, for example, traditionally used the wild yam (Dioscorea villosa) to ease PMS and increase fertility. In a similar vein, the Navajo people used yucca root, sometimes known as soapweed, as a diuretic and a remedy for a number of skin ailments. (19)

For coughs and sore throats, the Iroquois people would use the roots of the common blue violet, or Viola sororia. Native American medicine makes extensive use of plants that are high in diosgenin, as shown by these long-established practices. (19,20)

2.1.4 African Traditional Medicine

The analgesic and anti-inflammatory effects of plants that contain diosgenin have long been prized in traditional African medicine. When used topically, the African yam ***(Dioscorea dumetorum)*** can reduce inflammation and pain associated with rheumatic disorders. Also used to alleviate inflammation and pain in the joints is the African eggplant, scientifically known as ***Solanum anguivi***. The importance of plants rich in diosgenin in pain and inflammatory diseases management in traditional African medicine is highlighted by these practices. (21)

2.1.5 Other Traditional Uses

Many other traditional medicine systems across the world have discovered uses for diosgenin. South American women employ diosgenin-containing plants, such as wild yam ***(Dioscorea spp.),*** to promote fertility, increase libido, and treat menopause symptoms. Traditional European medicine makes use of diosgenin-rich herbs like fenugreek ***(Trigonella foenum-graecum)*** to improve digestion, encourage nursing, and increase general vitality. (15,22–24)

Journal of Chemical Health Risks

www.jchr.org

JCHR (2024) 14(3), 2669-2692 | ISSN:2251-6727

2.2 Ethnobotanical Sources

The plants from which it is derived and the traditional applications of those plants are as follows.

Dioscorea species: diosgenin is mostly found in the yams and other plants of the Dioscorea genus. Several species of Dioscorea, such as ***Dioscorea villosa, Dioscorea bulbifera, Dioscorea composita, and Dioscorea oppositifolia,*** have been found to have high amounts of diosgenin. The Americas, Africa, and Asia are just a few of the many places you might find these plants. The many medicinal uses of Dioscorea species have earned them a place of honor in traditional medicine. To alleviate period cramps, gastrointestinal issues, and rheumatism, for example, Native American cultures have used ***Dioscorea villosa,*** also known as wild yam. Ayurvedic practitioners have also discovered that ***Dioscorea bulbifera*** helps with bronchitis, asthma, and other respiratory issues. (17,25,26)

Trigonella foenum-graecum: Another important source of diosgenin is ***Trigonella foenum-graecum***, which is more often known as fenugreek. This plant is widely grown for its culinary and medicinal uses; it is native to the Mediterranean region. Traditional medicine has long recognized the benefits of fenugreek seeds for a variety of health issues, including improved lactation, better digestion, and diabetic management. (27,28)

Smilax species: Climbing vines of the genus ***Smilax***, often called sarsaparilla, are native to the tropics and subtropics. Many cultures have long recognized the medicinal and therapeutic benefits of these plants, with Ayurveda and traditional Chinese medicine being two of the most prominent examples. Diosgenin is a well-known characteristic of several Smilax species, such as ***Smilax china*** and ***Smilax glabra***. Sarsaparilla has a long history of respect as a diuretic and blood purifier in traditional medicine. It has demonstrated promise in alleviating rheumatism, skin problems, and STDs. Additionally, sarsaparilla has a long history of use as an aphrodisiac and general health enhancer. (29)

Costus speciosus: The perennial herb ***Costus speciosus*** is native to Southeast Asia and goes by several names, including crepe ginger and spiral flag. This plant has a long history of usage in Ayurvedic medicine and is often grown for its aesthetic value. The anti-inflammatory and analgesic effects of diosgenin are highly prized in the rhizomes of Costus speciosus. Traditional medicine has long made use of ***Costus speciosus*** to alleviate inflammatory disorders, such as rheumatism and arthritis. The rhizomes are also used to treat indigestion and flatulence, which are gastrointestinal problems. Costus speciosus also helps with wound healing and acts as a diuretic. (30)

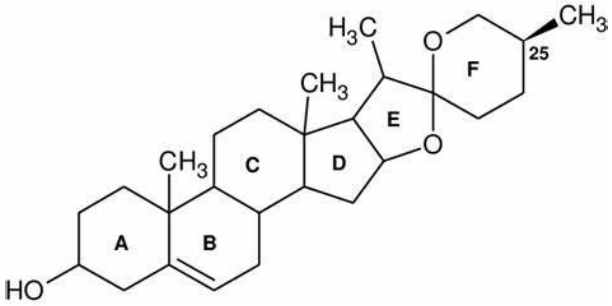
Other Sources: diosgenin does not only occur in the plants listed above, but also in other plant species, but in lower concentrations. A few examples are ***Yucca schidigera, Solanum xanthocarpum***, and ***Asparagus racemosus.*** The medicinal uses of these plants date back many centuries and can help with a wide range of conditions, including infertility and respiratory issues. (13,17)

3. Phytochemistry of diosgenin:

3.1 Chemical Structure and Properties

3.1.1 Chemical Structure

The chemical structure of diosgenin consists of a steroidal nucleus with a spiro ketal ring system. It is composed of a four-ring structure known as the cyclopenta[a] phenanthrene ring system. The core structure consists of three six-membered rings (A, B, and C) and one five-membered ring (D). The A ring is saturated, while the B and C rings are partially unsaturated. The D ring contains a ketone group at position 3 and a hydroxyl group at position 17. Diosgenin also possesses a sugar moiety attached to the hydroxyl group at position 3, which can vary depending on the plant source. (31)



Chemical structure of diosgenin

Journal of Chemical Health Risks

www.jchr.org

JCHR (2024) 14(3), 2669-2692 | ISSN:2251-6727

3.1.2 Physical Properties

The melting point of diosgenin, a white crystalline powder, lies between 204 and 207 degrees Celsius. Organic solvents like acetone, methanol, ethanol, and chloroform make it soluble, but water barely dissolves it. Around 414.6 g/mol of the chemical is its molecular weight. (32)

3.1.3 Stereochemistry

Stereochemistry diosgenin's biological actions are greatly influenced by its stereochemistry. The chemical has many chiral centers, such as C-5, C-6, C-22, and C-25. distinct plant sources of diosgenin can have diosgenin with distinct pharmacological characteristics due to differences in the configuration of its chiral centers. Several factors, such as the biosynthetic pathway and the enzymatic activities involved in diosgenin production, determine its stereochemistry. (17)

3.1.4 Chemical Properties

Because of its hydroxyl and ketone functional groups, diosgenin can be described as having acidic and basic characteristics. Oxidation, reduction, esterification, and glycosylation are among the chemical reactions that the molecule can experience. By modifying and derivatizing diosgenin, its pharmacological characteristics can be enhanced, leading to the development of new therapeutic candidates. (25)

3.1.5 Stability

Consistency variables like light, pH, and temperature affect diosgenin's stability. While it retains its integrity under typical storage circumstances, it may degrade in harsh environments. The bioavailability and efficacy of the chemical can be compromised by hydrolysis, oxidation, and photodegradation. Maintaining diosgenin's stability and ensuring its efficacy in pharmaceutical formulations need proper storage and management. (33)

3.1.6 Spectroscopic Properties

Spectroscopic methods such as mass spectrometry (MS), infrared (IR) spectroscopy, and nuclear magnetic resonance (NMR) spectroscopy can be used to characterize diosgenin. By measuring diosgenin's chemical shifts and coupling constants, NMR spectroscopy reveals important structural details. The compound's functional groups can be located using infrared spectroscopy by analyzing their unique absorption bands. The molecular weight and fragmentation pattern of diosgenin can be determined using MS analysis, which assists in both its identification and structural elucidation. (34)

3.2 Isolation and Extraction Methods

To get pure and strong diosgenin from plants, isolation and extraction techniques are vital. Several plant species, such as Dioscorea species, Trigonella foenum-graecum, and Costus speciosus, contain diosgenin, a steroidal saponin. Because of their high diosgenin content, these plants have a long history of medical use. (17)

3.2.1 Traditional Methods

Conventional approaches for ages, people have relied on time-honored techniques to extract diosgenin from plants. Extracting the plant's active components is the goal of these techniques, which employ solvents like water, ethanol, or methanol. Prior to extraction, the plant material is typically dried and ground into a fine powder. The maceration method has been around for a while, and it involves soaking plant material in a solvent for a set amount of time in order to extract diosgenin. The percolation method is another option; in this process, the solvent is slowly but steadily pushed through the plant material in order to release the active chemicals. Though they are easy to implement and inexpensive, these conventional approaches might not produce enough pure diosgenin to meet current demands. The quantity and purity of diosgenin have been enhanced by the use of more contemporary extraction procedures. (17)

3.2.2 Modern Extraction Techniques

The efficiency and yield of diosgenin extraction have been enhanced by the development of new extraction processes, made possible by developments in technology. These procedures include a variety of approaches, including solvent extraction, microwave-assisted extraction, and supercritical fluid extraction. (24)

Journal of Chemical Health Risks

www.jchr.org

JCHR (2024) 14(3), 2669-2692 | ISSN:2251-6727

One of the most used approaches in current extraction techniques is solvent extraction. This process includes removing diosgenin from plants using organic solvents like ethanol, chloroform, or methanol. The solvent's polarity and solubility of the desired chemical are the determining factors in its selection. In order to improve the extraction process, the plant material is usually soaked in the solvent and then mixed with agitation or sonication. Diosgenin can be isolated by further purification of the crude extract, which is obtained after the solvent is evaporated. (35)

Supercritical fluid extraction (SFE): Another cutting-edge method that has been more popular recently is supercritical fluid extraction (SFE). As an extraction solvent, it makes use of supercritical fluids like carbon dioxide. The special characteristics of supercritical fluids make them a great choice as a solvent for the extraction of bioactive chemicals. When compared to traditional solvents, they are able to permeate plant materials more effectively due to their low viscosity and high diffusivity. The capacity to extract heat-sensitive chemicals, reduced extraction time, and improved extraction efficiency are only a few of the benefits offered by SFE. (36)

Microwave-assisted extraction (MAE) is a way to speed up and improve the extraction process by using microwave energy. This technique involves irradiating plant matter using microwaves after mixing it with an appropriate solvent. Diosgenin is more soluble and diffuses more quickly after being heated by the microwave, which speeds up the extraction process. Extraction time, yield, and selectivity can all be enhanced by MAE, among other benefits. (37)

3.4 Biosynthesis Pathways

Diosgenin is biosynthetized from the cholesterol molecule as shown in figure 1.

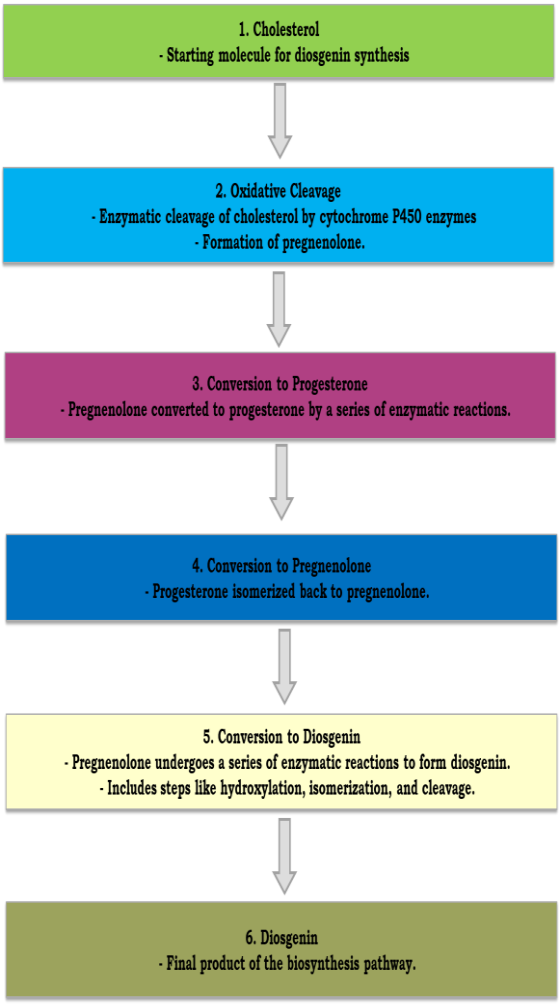


Figure 1: Schematic Representation of the Diosgenin Biosynthesis Pathway

3.4.1 Biosynthesis in Dioscorea Species

The majority of diosgenin comes from yams and other plants in the Dioscorea genus. Traditional medicinal remedies have made use of the tubers of Dioscorea species, which are rich in diosgenin. diosgenin is biosynthesized in Dioscorea species by an intricate enzymatic cascade (38). Making pregnenolone from cholesterol is the first stage in making diosgenin. The cholesterol side-chain cleavage enzyme (CYP11A1) is responsible for catalyzing this conversion. The 3β-hydroxysteroid dehydrogenase (3β-HSD) enzyme converts pregnenolone into progesterone. The enzyme CYP17A1 allows progesterone to be further metabolized to 17α-hydroxyprogesterone. The next stage of the biosynthetic process is turning 17α-

Journal of Chemical Health Risks
www.jchr.org
JCHR (2024) 14(3), 2669-2692 | ISSN:2251-6727

hydroxyprogesterone into diosgenin. The action of enzymes such as 5α-reductase, 3β-hydroxysteroid dehydrogenase, and Δ5-3β-hydroxysteroid dehydrogenase mediates this conversion. Enzymes like these are vital for the process of diosgenin synthesis from progesterone derivatives. Several factors control diosgenin production in Dioscorea species. These factors include precursor molecule availability and the expression of critical biosynthetic genes. Environmental factors, including light, temperature, and nutrition availability, impact the expression of genes involved in the biosynthetic pathway. The control of diosgenin biosynthesis is also affected by the existence of certain regulatory elements and transcription factors. (38–40)

3.4.2 Biosynthesis in Other Plant Sources

The production mechanism in Dioscorea species is comparable to that in **fenugreek,** where diosgenin begins with the conversion of cholesterol to pregnenolone. Nevertheless, in the following stages, certain enzymes, such as cytochrome P450 and glycosyltransferases, convert pregnenolone to diosgenin (41)(38). The biosynthesis of diosgenin in ***Smilax species*** follows an enzymatic pathway that begins with the conversion of cholesterol to pregnenolone and then to diosgenin. No complete characterization of the enzymes participating in these processes has yet been completed. Crepe ginger, or ***Costus speciosus,*** is another plant that contains diosgenin. Additional research is needed to fully understand the process by which this plant produces diosgenin. (39,42)

3.4.3 Regulation of Biosynthesis Pathways

There is a complicated interaction between genetic, environmental, and physiological factors that affect the diosgenin production pathways in various plant sources. Various regulatory elements, including transcription factors, control the expression of essential metabolic genes. Light, temperature, and the availability of nutrients are some of the environmental elements that impact diosgenin production. In addition, many hormones and signaling molecules affect diosgenin production. It has been found that plant hormones such as gibberellins and jasmonates can influence the expression of genes that are involved in the manufacture of diosgenin. Furthermore, diosgenin can be produced by plants in response to certain elicitors, such as bacterial or fungal infections. In order to increase plant diosgenin production, it is essential to comprehend the control of biosynthetic pathways. Improving diosgenin synthesis is possible through the use of genetic engineering and biotechnological methods that alter the expression of important biosynthetic genes. Increased diosgenin output in plant sources can also be achieved by adjusting climatic conditions and nutrient availability. (39)

4. Biological Activities of diosgenin

Various biological activities of diosgenin are illustrated as follows:

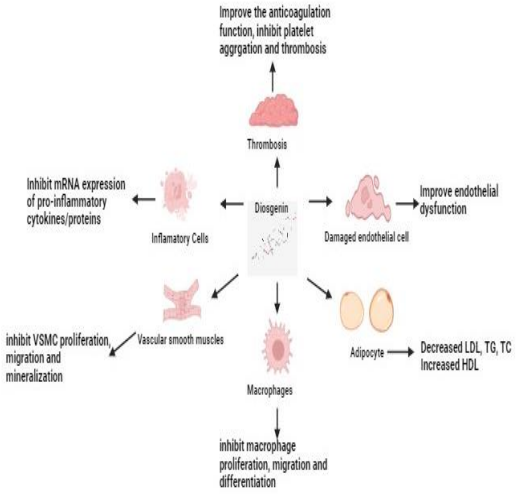


Figure 2: Diagrammatic Representation of Diosgenin's Biological Activities

4.1 Anti-inflammatory Effects

The body's innate reaction to pathogens or injuries is inflammation. There are a lot of immune cells and mediators involved in the mechanism. Chronic inflammation, in contrast to acute inflammation, can cause a host of diseases, such as autoimmune disorders, cardiovascular disease, and neurological disorders. Consequently, there has been a lot of focus in recent years on finding natural chemicals that have anti-inflammatory capabilities.
Many investigations, both in the lab and in humans, have shown that diosgenin can reduce inflammation and its symptoms by regulating the immune response. (13,17)

Journal of Chemical Health Risks

www.jchr.org

JCHR (2024) 14(3), 2669-2692 | ISSN:2251-6727

4.1.1 Modulation of Inflammatory Mediators

Research has demonstrated that diosgenin can reduce the synthesis of cytokines, chemokines, and prostaglandins, all of which are known to contribute to inflammation. When it comes to starting and keeping the inflammatory response going, these mediators are key players. Diosgenin has been found to inhibit the production and release of inflammatory cytokines, such as TNF-α, IL-1β, and IL-6, according to academic research. Diosgenin helps to reduce the inflammatory cascade by blocking the generation of these cytokines. In addition, diosgenin can block the production of prostaglandins, powerful inflammatory mediators, by inhibiting the activity of the enzyme cyclooxygenase-2 (COX-2). diosgenin has anti-inflammatory properties because it inhibits COX-2 activity, which in turn lowers prostaglandin synthesis. (43,44)

4.1.2 Suppression of Inflammatory Signaling Pathways

Nuclear factor-kappa B (NF-κB) and mitogen-activated protein kinases (MAPKs) are two of the signaling pathways that control inflammation. NF-κB is an essential transcription factor that controls the expression of genes that promote inflammation. Inflammatory mediators are produced when NF-κB is activated. Research has demonstrated that diosgenin can reduce the expression of genes associated with inflammation by blocking the activation of NF-Kb. (45,46)

Diosgenin also modulates MAPK signaling pathways, such as p38 MAPK, c-Jun N-terminal kinase (JNK), and extracellular signal-regulated kinase (ERK). Regulatory of inflammatory reactions is a function of these mechanisms. diosgenin reduces the synthesis of pro-inflammatory mediators by blocking the activation of these MAPKs. (47)

4.1.3 Antioxidant Activity

When the body's antioxidant defense mechanism is overwhelmed by the generation of reactive oxygen species (ROS), a condition known as oxidative stress, unfolds, leading to inflammation. Free radicals (ROS) have the potential to harm cells and have a role in the onset of inflammatory disorders. Research has demonstrated that diosgenin has strong antioxidant properties, making it useful in preventing ROS damage. Research has shown that diosgenin can prevent oxidative damage to cells by scavenging free radicals and blocking lipid peroxidation. Another factor contributing to diosgenin's antioxidant benefits is its ability to improve the activity of natural antioxidant enzymes including catalase and superoxide dismutase (SOD). (44,48)

4.1.4 Modulation of Immune Response

A number of studies have shown that diosgenin can control the immune response by influencing the way cells like lymphocytes and macrophages function. Both the start and the end of inflammation are mediated by macrophages. Evidence suggests that diosgenin blocks macrophage activation and the secretion of pro-inflammatory cytokines.
In addition, diosgenin can alter the function of T cells, which are lymphocytes that play a role in the adaptive immune response. According to research, diosgenin can reduce the immunological response by preventing T cells from proliferating and activating. (31,42)

4.1.5 Animal and Clinical Studies

Clinical trials and animal models have both looked at diosgenin's anti-inflammatory properties. Research on animals has demonstrated that diosgenin can alleviate inflammation in many models of inflammation, including paw edema caused by carrageenan and arthritis generated by adjuvant. The results of these investigations on diosgenin's possible use as a treatment for inflammatory disorders are very encouraging. Additionally, diosgenin has been shown in human clinical trials to have anti-inflammatory properties. Supplemental diosgenin, for instance, alleviated pain and enhanced joint function in osteoarthritis patients, suggesting that it may have anti-inflammatory properties. (49)

4.2 Anticancer Properties

Numerous studies have explored the effects of diosgenin on different types of cancer cells, revealing promising results.

4.2.1 Mechanisms of Action

Diosgenin is an adaptable chemical in the fight against cancer since it displays its anticancer effects through several pathways. The capacity to cause cancer cells to

Journal of Chemical Health Risks
www.jchr.org
JCHR (2024) 14(3), 2669-2692 | ISSN:2251-6727

undergo apoptosis, also known as programmed cell death, is one of the main processes. Critical for controlling cell proliferation and removing defective or aberrant cells, apoptosis is an essential cellular mechanism. Evidence suggests that diosgenin triggers apoptotic signaling pathways, ultimately resulting in cancer cell death. In addition, diosgenin can stop the cell cycle at various points, which means it can slow the growth of cancer cells. Diosgenin stops cancer cells from dividing and proliferating excessively by interfering with the cell cycle. When it comes to stopping cancer in its tracks, this quality is crucial. (31,44,50)

The anticancer benefits of diosgenin are enhanced by its strong anti-inflammatory capabilities. The onset and advancement of cancer are strongly linked to chronic inflammation. Diosgenin helps hinder the growth of cancer cells by decreasing inflammation. (42,51,52)

The anticancer benefits of diosgenin are enhanced by its strong anti-inflammatory capabilities. The onset and advancement of cancer are strongly linked to chronic inflammation. Diosgenin helps hinder the growth of cancer cells by decreasing inflammation. (45)

4.2.2 Effects on Different Types of Cancer

Diosgenin has shown promise in preventing the proliferation of certain cancer cell types, according to the research. Diosgenin inhibits cancer cell multiplication and triggers cell death in breast cancer. By preventing breast cancer cells from migrating and invading, it also has anti-metastatic characteristics. (53)

Research on prostate cancer has shown that diosgenin can induce cell cycle arrest and decrease the development of cancer cells. Another indicator often used to track the evolution of prostate cancer, prostate-specific antigen (PSA), may be reduced to some extent as well. (54)

The use of diosgenin to treat colon cancer has also demonstrated encouraging results. According to research, it can cause colon cancer cells to die off and slow their growth. Further research has shown that diosgenin can stop the production of some enzymes that contribute to colon cancer.
In addition, diosgenin inhibits cell growth and induces apoptosis, resulting in anticancer benefits in lung cancer. Additionally, it can increase the efficacy of chemotherapy by making lung cancer cells more sensitive to these medications.

4.2.3 Synergistic Effects and Combination Therapy

Researchers have looked into the possibility of synergistic effects between diosgenin and other anticancer drugs. Research has demonstrated that diosgenin can increase the effectiveness of chemotherapy medications, allowing them to destroy cancer cells with greater precision. The capacity of diosgenin to overcome drug resistance and sensitize cancer cells to chemotherapy is responsible for this synergistic impact. Additionally, diosgenin improves the efficacy of radiation therapy for cancer treatment. It increases the radio sensitivity of cancer cells, making them more vulnerable to radiation's destructive power. There is hope that this combination therapy method will improve cancer treatment outcomes. (55)

4.2.4 Preclinical and Clinical Studies

Additional study is necessary to confirm the effectiveness of diosgenin in clinical settings, despite the encouraging results of preclinical studies on its anticancer characteristics. There has been a dearth of research into the safety and effectiveness of diosgenin in cancer patients. Nonetheless, diosgenin shows promise as a cancer treatment agent based on the evidence that is now available. (55)

4.3 Antioxidant Activity

An important function of antioxidants is to keep the body's reactive oxygen species (ROS) generation and neutralization mechanisms in check. Damage to cells and tissues caused by reactive oxygen species (ROS) can result in a number of diseases and the aging process. Extensive research on the antioxidant action of diosgenin, a naturally occurring component in several plants, has been conducted. (13,56)

4.3.1 Mechanism of Antioxidant Action

There are a number of pathways that diosgenin uses to achieve its antioxidant properties. Free radical scavenging is one of the main mechanisms. Damage to DNA, proteins, and lipids, among other physiological components, can be caused by free radicals, which are

Journal of Chemical Health Risks

www.jchr.org

JCHR (2024) 14(3), 2669-2692 | ISSN:2251-6727

unstable chemicals. In order to protect cells from free radical damage, diosgenin functions as a powerful scavenger.

In addition, diosgenin boosts the efficiency of the body's natural antioxidant enzymes, including catalase, glutathione peroxidase, and superoxide dismutase (SOD). In order to protect cells from oxidative stress, the body relies on these enzymes, which convert reactive oxygen species (ROS) into molecules with lower reactivity. (44)

4.3 Immunomodulatory Effects

By "immunomodulation," we mean a substance's capacity to control the immune system, whether it by increasing or decreasing its activity. diosgenin has the potential to be a therapeutic agent for a number of immune-related illnesses, according to research that has demonstrated encouraging results in its capacity to modify the immunological response. (57)

4.4.1 Mechanisms of Immunomodulation

It is thought that diosgenin's immunomodulatory actions are mediated through many pathways. The capacity to control the number and function of several types of immune cells—including T cells, B cells, and natural killer (NK) cells—is one of the main strategies. Evidence suggests that diosgenin promotes T cell proliferation and differentiation, which in turn increases cytokine production—a key signaling molecule in immune control. (58)

In addition, diosgenin has the ability to influence the function of macrophages, an essential kind of immune cell that helps clear the body of harmful microbes and releases chemicals that cause inflammation. According to research, diosgenin can decrease inflammation and speed up tissue regeneration by increasing the phagocytic activity of macrophages and the production of anti-inflammatory cytokines.

Diosgenin also has immunomodulatory effects because of its antioxidant capabilities. When the body's antioxidant defense mechanism is overwhelmed by the formation of reactive oxygen species (ROS), a condition known as oxidative stress sets in, and the immune system becomes dysfunctional. Research has demonstrated that diosgenin has strong antioxidant properties, which aid in lowering oxidative stress and shielding immune cells from harm. (59)

4.4.2 Immunomodulatory Effects in Autoimmune Diseases

An overreaction of the immune system to harmless cells and tissues is the hallmark of autoimmune disorders. Diosgenin has the ability to modulate the immune system, which means it could be used to treat autoimmune illnesses. Diosgenin has shown promise in a number of autoimmune diseases, including rheumatoid arthritis, multiple sclerosis, and systemic lupus erythematosus, according to a number of research. (60)

Research has demonstrated that diosgenin can reduce the production of inflammatory cytokines such tumor necrosis factor-alpha (TNF-α) and interleukin-6 (IL-6), which are crucial in the development of rheumatoid arthritis. The activation of the transcription factor NF-κB, which is important in the regulation of inflammatory reactions, can be inhibited by diosgenin. It has been suggested that diosgenin may modulate the immune response in multiple sclerosis by increasing the production of anti-inflammatory cytokines and decreasing the production of pro-inflammatory cytokines. This safeguards nerve fibers from damage by reducing the autoimmune response and preserving myelin sheaths. (61)

4.4.3 Immunomodulatory Effects in Cancer

Cancer research could possibly benefit from diosgenin's immunomodulatory capabilities. Cancer cells have the ability to elude detection by the immune system and continue to multiply unchecked. Through activating immune cells like cytotoxic T lymphocytes (CTLs) and natural killer (NK) cells, diosgenin improves the immune response against cancer cells. The immune response to cancer relies on NK cells, which identify and destroy cancer cells. Research has demonstrated that diosgenin increases cancer cell death by boosting the cytotoxic activity of natural killer (NK) cells. More than that, diosgenin boosts the development and activity of cytotoxic T lymphocytes (CTLs), which are specific immune cells that target and destroy cancer cells. Also, by triggering apoptosis, a form of programmed cell death, diosgenin reportedly slows the development

Journal of Chemical Health Risks
www.jchr.org
JCHR (2024) 14(3), 2669-2692 | ISSN:2251-6727

and spread of cancer cells. The development of drug resistance is a significant obstacle in cancer treatment; this helps eradicate cancer cells while doing so. (1,61–63)

5. Mechanism of Action

Primary mechanisms and effects of diosgenin described in Table 1.

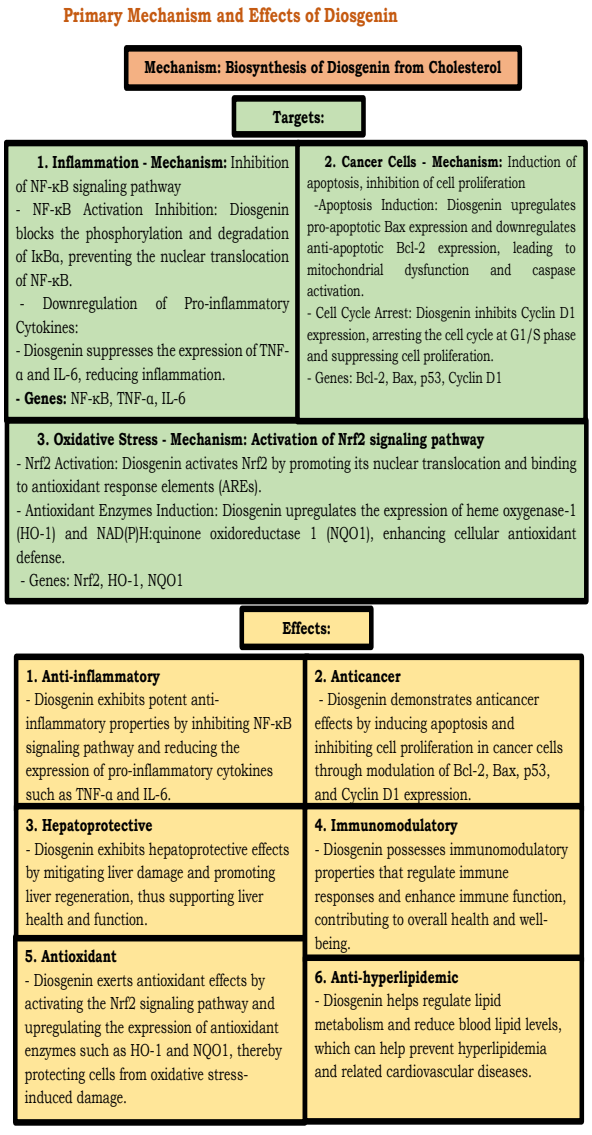


Table1: Systematic Representation of Diosgenin's Primary Mechanisms and Effects.

5.3.1 Modulation of Signaling Pathways

Diosgenin modulates numerous signaling pathways in the body, which is one of the main ways it exerts its pharmacological effects. The ability of diosgenin to regulate cellular processes has been demonstrated by its ability to activate or inhibit particular signaling pathways.

Diosgenin hits the nuclear factor-kappa B (NF-κB) pathway, a significant signaling route. An essential part of inflammation and immunological responses is the transcription factor NF-κB. The generation of inflammatory mediators and pro-inflammatory cytokines can be decreased due to diosgenin's ability to block NF-κB activation. (17,42)

One more thing diosgenin can do is change the way the MAPK signaling complex works. MAPKs play an important role in cell death, differentiation, and proliferation, among other biological events. In order to affect cell proliferation and survival, diosgenin controls MAPK events.

In addition, the peroxisome proliferator-activated receptor gamma (PPARγ) pathway has been discovered to be activated by diosgenin. The nuclear receptor PPARγ is vital for controlling the metabolism of both glucose and lipids. The insulin sensitivity and lipid profile can be improved through diosgenin's activation of PPARγ, which makes it a possible therapeutic agent for metabolic disorders like diabetes and dyslipidemia. (64)

5.3.2 Anti-inflammatory Effects

One of the most important steps in the development of many diseases, including autoimmune disorders and chronic inflammatory conditions, is inflammation, a multifaceted biological reaction. An abundance of research has focused on diosgenin's anti-inflammatory effects.

One way diosgenin reduces inflammation is by blocking certain chemicals that the body uses to do so. Research has demonstrated that diosgenin has the ability to reduce the synthesis of inflammatory cytokines such IL-1β, IL-6, and TNF-α. Diosgenin can lessen the inflammatory response by decreasing the synthesis of these cytokines.

On top of that, diosgenin can stop the inflammatory mediator-making enzymes cyclooxygenase-2 (COX-2) and inducible nitric oxide synthase (iNOS) from doing their thing. Key mediators of inflammation, prostaglandins and nitric oxide, can be reduced by

Journal of Chemical Health Risks

www.jchr.org

JCHR (2024) 14(3), 2669-2692 | ISSN:2251-6727

diosgenin by reducing the activity of these enzymes. (65–68)

5.3.3 Anticancer Properties

Unchecked cell growth and proliferation characterize cancer, a complicated disease. Research into diosgenin's possible usage in cancer prevention and treatment has yielded encouraging results due to its anticancer characteristics.

To induce apoptosis, or programmed cell death, is one-way diosgenin carries out its anticancer actions. Researchers have discovered that diosgenin triggers the apoptotic process by activating caspases. Diosgenin inhibits tumor growth by inducing the death of cancer cells by caspase activation.

In addition, diosgenin can stop the cell cycle at certain points, which means it can slow the growth of cancer cells. Research has shown that diosgenin can stop cancer cells from proliferating and advancing through the cell cycle by inducing cell cycle arrest at the G1 phase.

Angiogenesis, the formation of new blood vessels to deliver nutrition to tumors, is inhibited by diosgenin. To stop cancers from growing and spreading, diosgenin blocks angiogenesis, which means it limits blood flow to tumors. (69,70)

5.3.4 Immunomodulatory Effects

The immune system is vital in keeping the body protected from harmful substances and infections. Diosgenin may have immunomodulatory properties due to its demonstrated ability to alter the immune response. The immune cell type known as natural killer (NK) cells is essential for the clearance of cancerous and infectious cells, and research has shown that diosgenin can boost their activity. Diosgenin can boost the immune response to cancer cells and infections by increasing the activity of NK cells.

In addition, diosgenin controls how immune cells make cytokines. Research has demonstrated that diosgenin has the ability to enhance IL-2 synthesis, which in turn enhances the proliferation and activation of immune cells. To improve immune system function and control the immunological response, diosgenin modulates cytokine production. (71–74)

5.3.5 Other Mechanisms

Several other pathways have been identified by which diosgenin exerts its pharmacological effects. One example is diosgenin, which may shield cells from oxidative stress and lessen the likelihood of developing chronic diseases due to its antioxidant characteristics. In addition, diosgenin can alter the activity of enzymes that are involved in the metabolism of xenobiotics and pharmaceuticals. Diosgenin has the ability to affect the pharmacokinetics and pharmacodynamics of other medications by modifying the activity of these enzymes. This could result in drug interactions. In sum, diosgenin's action mechanism is intricate and multidimensional. Its antioxidant capabilities, anti-inflammatory effects, modulation of the immunological response, inhibition of cancer cell proliferation, and modulation of signaling pathways are some of its many pharmacological activities. The complex processes via which diosgenin exerts its therapeutic benefits and its possible uses in a range of illness situations require additional research. (35)

5.4 Drug Interactions

Interactions between pharmaceuticals change the way they work in the body; this phenomenon is known as a drug interaction. Reduced efficacy or increased toxicity are two examples of the unexpected and sometimes dangerous effects that might result from these interactions. diosgenin is a naturally occurring chemical with multiple pharmacological properties, thus it's crucial to be aware of the possible drug interactions it may cause. (75)

5.4.1 Interactions with Anticoagulant Drugs

According to reports, diosgenin has anticoagulant qualities. This means it could potentially interact with other medications that have the same effect. Warfarin, heparin, and aspirin are a few examples of these medications. There is a higher risk of bleeding since diosgenin may make these medications more effective anticoagulants. Thus, before utilizing diosgenin supplements or goods, it is essential for individuals using anticoagulant drugs to contact with their healthcare professional. (76)

5.4.2 Interactions with Antiplatelet Drugs

Diosgenin has the potential to interact with antiplatelet medications like clopidogrel and aspirin, just like

Journal of Chemical Health Risks
www.jchr.org
JCHR (2024) 14(3), 2669-2692 | ISSN:2251-6727

anticoagulant medicines. To avoid the risk of blood clots, antiplatelet medications are frequently recommended. Because diosgenin is anticoagulant, it may increase the risk of bleeding caused by these medications. Before utilizing diosgenin supplements, people using antiplatelet drugs should talk to their doctor. (77,78)

5.4.3 Interactions with Hormonal Medications

Due to its estrogenic properties, diosgenin may cause unwanted side effects when taken with other hormonal drugs, such as oral contraceptives and HRT. The estrogenic actions of diosgenin could potentially cause hormonal imbalances or reduce the effectiveness of these drugs. To ensure proper treatment of their illness, patients taking hormonal drugs should discuss the usage of diosgenin with their healthcare professional. (35)

5.4.4 Interactions with Immunosuppressant Drugs

People with autoimmune diseases or who have received an organ transplant often take immunosuppressant medications. These drugs may have their effectiveness affected by diosgenin's immunomodulatory actions. To avoid lowering immune system function, people receiving immunosuppressant medications should talk to their doctor before using diosgenin products or supplements. (79)

5.4.5 Interactions with Antidiabetic Medications

It is possible that diosgenin interacts with insulin and metformin, two antidiabetic drugs, due to its hypoglycemic effects. The hypoglycemic effects of diosgenin may amplify the impact of these drugs, resulting in a substantial drop in blood sugar levels. People with diabetes who are taking medication to control their blood sugar levels should be careful when taking diosgenin supplements. (80)

5.4.6 Interactions with Antihypertensive Drugs

Because of its antihypertensive properties, diosgenin may interact with other drugs that lower blood pressure, including beta-blockers and angiotensin-converting enzyme inhibitors. Because of its antihypertensive characteristics, diosgenin has the potential to enhance the blood pressure-lowering effects of these medications. To avoid dangerously low blood pressure, anyone using antihypertensive medicine should talk to their doctor before taking diosgenin supplements. (81)

5.4.7 Interactions with Antidepressant Drugs

Diosgenin may interact with other antidepressants, including SSRIs and tricyclic antidepressants, due to its purported antidepressant-like properties. An elevated risk of serotonin syndrome may result from the synergistic actions of certain antidepressant drugs with diosgenin. It is important for those using antidepressants to consult with their doctor before using diosgenin to make sure their condition is well-managed. (82,83)

5.4.8 Interactions with Anti-inflammatory Drugs

Because of its anti-inflammatory properties, diosgenin may have an adverse interaction with NSAIDs like ibuprofen and naproxen. Potentially elevating the risk of gastrointestinal bleeding and renal damage, diosgenin's anti-inflammatory characteristics may amplify the effects of these medications. diosgenin supplements should be used with caution by anyone taking nonsteroidal anti-inflammatory drugs (NSAIDs) without first consulting their healthcare professional.(83,84)

5.4.9 Interactions with Anticancer Drugs

Researchers are looking into diosgenin because of its possible anticancer effects, which could interact with chemotherapy medications. The anticancer actions of diosgenin could potentially increase the toxicity of these medications or reduce their effectiveness. To get the most out of their cancer treatments, people should talk to their doctors before taking diosgenin supplements. (1,13)

6. Formulation and Delivery Systems of diosgenin

6.1 Pharmaceutical Formulations

In order for medications to reach their intended target in the body, pharmaceutical formulations are vital. The creation of appropriate pharmaceutical formulations is crucial for the stability, bioavailability, and therapeutic effectiveness of diosgenin, a naturally occurring chemical with tremendous medicinal potential. This section delves into the several diosgenin pharmaceutical formulations that have been investigated, covering both traditional and cutting-edge delivery techniques. (85)

Journal of Chemical Health Risks

www.jchr.org

JCHR (2024) 14(3), 2669-2692 | ISSN:2251-6727

6.1.1 Conventional Formulations

To improve the solubility, stability, and bioavailability of diosgenin, conventional pharmaceutical formulations have been devised. Tablets, capsules, ointments, gels, and creams are all part of these compositions. The oral dose forms of diosgenin that are most typically used are tablets and capsules. Oral administration of the substance is made easier and more standardized with their help. In order to make sure that diosgenin is released and absorbed properly in the GI tract, binders, diluents, and disintegrants are utilized in the formulation of tablets and capsules. (86)

Another common way that diosgenin is applied topically is in the form of lotions, ointments, and gels. Therapeutic effects, such as anti-inflammatory or wound healing capabilities, can be delivered locally by means of these formulations. To make sure diosgenin gets through the skin efficiently, they have the right bases and penetration enhancers in the formula. (87)

6.1.2 Nanotechnology-based Delivery Systems

To improve the bioavailability, stability, and solubility of poorly soluble meds like diosgenin, delivery techniques based on nanotechnology have recently attracted a lot of interest. Nanoemulsions, solid lipid nanoparticles, liposomes, and nanoparticles are all examples of such delivery methods. (88,89)

Solid colloidal particles that range in size from one hundred to one thousand nanometers are known as nanoparticles. To prevent diosgenin's breakdown, they can be made utilizing a variety of polymers, including chitosan or poly(lactic-co-glycolic acid) (PLGA). Various routes of administration, including oral, intravenous, and topical delivery, are possible for nanoparticles. (90,91)

Lipid bilayers form the vesicular structure known as a liposome. Diosgenin is one of many hydrophilic and hydrophobic medications that they can encapsulate. One promising method for delivering diosgenin to particular cells or tissues is via liposomes, which have the dual benefits of regulated release and targeted drug delivery. (92,93)

Diosgenin and other lipophilic medications can be encapsulated in solid lipid nanoparticles (SLNs), which are nanoparticles derived from lipids. The therapeutic efficacy of diosgenin is enhanced by SLNs, which provide increased drug stability and regulated release. Biocompatible lipids, like phospholipids or triglycerides, can be used to formulate them. Emulsions containing oil and water or water and oil with droplet sizes in the nanometer range are called nano-emulsions. They enhance the bioavailability of hydrophobic medicines like diosgenin by solubilizing them. Nanoemulsions show promise as a delivery strategy for diosgenin due to their facile production and stability. (94–96)

6.1.3 Lipid-based Delivery Systems

Extensive research into lipid-based delivery methods for diosgenin has been conducted. Liposomes, nanostructured lipid carriers, and self-emulsifying drug delivery systems (SEDDS) are all examples of such systems.

When diluted in water, SEDDS—which are isotropic combinations of lipids, surfactants, and co-surfactants—can create small oil-in-water emulsions in the digestive tract. SEDDS improve the bioavailability of diosgenin and other poorly soluble medications by increasing their solubility and absorption. Because of their convenient oral delivery and facile formulation, they are a good choice for this purpose. Research has demonstrated that SEDDS enhance diosgenin's oral bioavailability by making it more soluble and boosting its absorption in the gastrointestinal system. (97)

The two main components of NLCs, which are lipid nanoparticles, are a solid lipid matrix and a liquid oil or lipid. Controlled release can be achieved by encapsulating hydrophobic medicines, such as diosgenin. The drug stability and bioavailability of NLCs are superior to those of traditional lipid nanoparticles. (98,99)

Liposomes, as mentioned earlier, are vesicular structures composed of lipid bilayers. They can encapsulate diosgenin and improve its solubility and stability. Liposomes can be formulated using various lipids and can be modified to target specific tissues or cells, making them a versatile delivery system for diosgenin. (92,93)

Journal of Chemical Health Risks

www.jchr.org

JCHR (2024) 14(3), 2669-2692 | ISSN:2251-6727

6.1.4 Polymeric Delivery Systems

The development of diosgenin has also included investigations into polymeric delivery techniques. Micelles, hydrogels, and polymeric nanoparticles are all examples of such systems.
Some biodegradable polymers that can be used to make polymeric nanoparticles are poly (lactic-co-glycolic acid) (PLGA) and polyethylene glycol (PEG). Encapsulating diosgenin and delivering it in a sustained release form can enhance its medicinal effectiveness. The use of polymeric nanoparticles has the dual benefit of preventing the degradation of diosgenin and allowing for controlled medication release.
Micelles are structures that self-assemble from amphiphilic polymers. They enhance the bioavailability of hydrophobic medicines like diosgenin by solubilizing them. Micelles are ideal for a variety of delivery methods due to their ease of formulation and administration.
Diosgenin can be encapsulated and released slowly into the body using hydrogels, which are networks of hydrophilic polymers in three dimensions. One benefit of hydrogels is that they may be produced as either injectable or topical formulations, which allows for localized drug delivery. (100–102)

6.2 Nanotechnology-based Delivery Systems

Nanotechnology has provided novel approaches to overcoming the drawbacks of traditional drug delivery technologies, thereby transforming the area of drug delivery. The pharmaceutical industry has recently shown a lot of interest in delivery methods based on nanotechnology since they can improve the therapeutic effectiveness and safety of medications. The possibility of using diosgenin, a naturally occurring chemical with several pharmacological effects, in delivery systems based on nanotechnology has also been investigated. (102–104)

6.2.1 Nanoparticles

Among the many nanotechnology-based delivery strategies for diosgenin, nanoparticles have received the most amount of research attention. These particles, which can be made from a variety of materials like metals, polymers, and lipids, usually have a size range of 1-1000 nanometers. Increased medication stability, enhanced bioavailability, and tailored drug administration are only a few of the benefits offered by nanoparticles. (102)

6.2.1.1 Lipid-based Nanoparticles

Diosgenin delivery has been explored using lipid-based nanoparticles like SLNs and liposomes. While SLNs are solid lipid particles, liposomes are spherical vesicles that contain bilayers of lipids. Encasing diosgenin in their hydrophobic core or lipid bilayers, these lipid-based nanoparticles can make it more soluble and preserve it from destruction. In addition, these nanoparticles can have their surfaces altered to deliver drugs to particular cells or tissues. (105)

6.2.1.2 Polymer-based Nanoparticles

Diosgenin delivery using polymer-based nanoparticles, such as polymeric micelles and nanoparticles, has also been investigated. Biocompatible and biodegradable polymers, such poly(lactic-co-glycolic acid) (PLGA) and polyethylene glycol (PEG), make up these nanoparticles. Nanoparticles made of polymers can encapsulate diosgenin in their matrix, allowing for the drug's sustained release. It is also possible to alter the nanoparticles' surfaces to make them more stable and to direct them towards particular cells or tissues. (106,107)

6.2.2 Nanocarriers

Another promising class of delivery technology based on nanotechnology for diosgenin is nanocarriers. The medication can be encapsulated and protected by these carriers, which enable controlled release and focused distribution. Nanoparticles of mesoporous silica, carbon nanotubes, and dendrimers are among the most prevalent nanocarriers for diosgenin. (108,109)

6.2.2.1 Dendrimers

Diosgenin can be encapsulated within the internal cavities of dendrimers, which are highly branching, three-dimensional macromolecules. The potential to target particular tissues or cells, regulated release, and a high drug-loading capacity are only a few of the benefits offered by these nanocarriers. To improve dendrimers' targeting capabilities, they can be functionalized with ligands or antibodies. (109,110)

Journal of Chemical Health Risks

www.jchr.org

JCHR (2024) 14(3), 2669-2692 | ISSN:2251-6727

6.2.2.2 Carbon Nanotubes

Structured like a hexagonal lattice, carbon nanotubes are cylindrical and made of carbon atoms. To make diosgenin more soluble, these nanocarriers can be modified to encapsulate it. Carbon nanotubes are well-suited for use in medication delivery because to their exceptional mechanical strength and large surface area. Still, more study is required to find the sweet spot between drug-loading capability and possible toxicity. (110)

6.2.2.3 Mesoporous Silica Nanoparticles

Mesoporous silica nanoparticles have a huge number of pores and a big surface area, making them very porous. Adsorption or covalent attachment can be used to load diosgenin onto these nanocarriers. Targeted drug delivery is possible with functionalized mesoporous silica nanoparticles, which provide controlled drug release. Prior to clinical translation, however, extensive evaluations of their biocompatibility and cytotoxicity are required. (111,112)

6.2.3 Nanogels

Diosgenin can be encapsulated within the hydrogel matrix of nanogels, which are three-dimensional networks of cross-linked polymers. Advantages of these nanogels include regulated release, a high drug-loading capacity, and the capacity to react to environmental cues. The release of diosgenin from nanogels can be controlled by changes in pH, temperature, or enzyme activity, enabling the administration of drugs to precise sites. (113,114)

6.2.4 Challenges and Future Perspectives

While delivery systems based on nanotechnology hold a lot of potential for diosgenin, there are a number of obstacles that must be overcome before they can be used in clinical settings. Improving manufacturing processes for larger batches to guarantee repeatability and scalability is a big obstacle. It is also important to assess these nanocarriers' safety and stability over the long term to reduce any potential toxicity.
To improve diosgenin delivery methods based on nanotechnology, additional research is required in the future. As part of this effort, we are investigating new materials with the potential to improve drug-loading capacity and targeted drug delivery. In addition, there is significant promise for personalized medicine and synergistic therapeutic effects from the creation of multifunctional nanocarriers that can integrate diosgenin with additional imaging or therapeutic molecules. (88,115)

6.3 Lipid-based Delivery Systems

The use of lipid-based delivery methods to transport bioactive substances like diosgenin has recently attracted a lot of interest. Among the many benefits offered by these systems is an increase in the bioavailability, stability, and solubility of the encapsulated molecule. The following are some examples of lipid-based delivery systems for diosgenin and the drugs they may deliver:

6.3.1 Liposomes

Liposomes are bilayer vesicles made of lipids that can encase hydrophilic and hydrophobic substances. They have a spherical shape. Their biocompatibility and versatility in encapsulating pharmaceuticals have led to much research into their potential as drug delivery systems. Liposomes have been utilized to enhance the solubility and stability of diosgenin. They can be generated utilizing a variety of techniques, including thin-film hydration, reverse-phase evaporation, and sonication. When compared to free diosgenin, studies reveal that liposomal versions of the drug have better therapeutic efficacy and increased cellular absorption. The therapeutic potential of liposomes can be further enhanced by adding targeting ligands, which allow diosgenin to be delivered to the site of action of interest. (92,115)

6.3.2 Solid Lipid Nanoparticles (SLNs)

Nanoparticles made of solid lipids suspended in aqueous solution are known as solid lipid nanoparticles (SLNs). Controlled release, increased bioavailability, and better stability are just a few of the benefits they provide. A wide variety of lipid components, including waxes, phospholipids, and triglycerides, can be used to make SLNs.
To improve diosgenin's limited bioavailability and poor water solubility, SLNs have been investigated as potential carriers. Evidence suggests that SLNs can enhance the oral bioavailability of diosgenin by

Journal of Chemical Health Risks

www.jchr.org

JCHR (2024) 14(3), 2669-2692 | ISSN:2251-6727

encapsulating it. Diosgenin is protected from degradation and its sustained release is facilitated by the solid lipid matrix, resulting in extended therapeutic benefits. (96)

6.3.3 Nanostructured Lipid Carriers (NLCs)

Lipidomic nanoparticles called nanostructured lipid carriers (NLCs) combine a solid lipid matrix with a liquid lipid or oil. Among the many benefits of NLCs are their increased stability, controlled release, and increased drug loading capacity. Triglycerides, fatty acids, and phospholipids are only a few of the lipid components that can be used to make them. Because of its low bioavailability and poor water solubility, diosgenin has been studied as a possible carrier for NLCs. diosgenin can be efficiently encapsulated and its oral bioavailability increased by NLCs, according to studies. Improved drug release kinetics and higher drug loading are both made possible by the liquid lipid phase that exists in NLCs. In addition, targeting ligands can be applied to the surface of NLCs to improve the targeted distribution of diosgenin to the target region. (95,116)

6.3.4 Lipid-based Microemulsions

Microemulsions made of lipids are isotropic blends of oil, water, surfactant, and co-surfactant; they are also thermodynamically stable. They have better solubilization capacity, more stability, and more medication absorption, among other benefits. Triglycerides, fatty acids, and phospholipids are just a few examples of the lipid components that can be used to create microemulsions.
One possible delivery mechanism for diosgenin that has been investigated is microemulsions, which could increase its bioavailability and solubility. Diosgenin can be more easily dissolved and absorbed when taken orally via microemulsions, according to the available research. Microemulsions enhance drug release kinetics and increase drug surface area due to their small droplet size. Another advantage of microemulsions is how quickly they may be transformed into different dosage forms, such tablets and capsules. (117)

6.3.5 Lipid-based Nanocarriers

Diosgenin delivery has been studied using a variety of lipid-based nanocarriers, including microemulsions, SLNs, NLCs, lipid nanoparticles, and lipid nanocapsules. Benefits such as controlled release, targeted delivery, and enhanced stability are exclusive to these nanocarriers.
Diosgenin and other hydrophobic medications can be encapsulated in solid lipid nanoparticles. The medicinal efficacy of diosgenin is boosted because they increase its solubility and bioavailability. However, lipid nanocapsules are a type of liquid nanoparticle that can encase hydrophobic as well as hydrophilic medications. To increase diosgenin's solubility and stability, they have been investigated as potential carriers. All things considered, diosgenin's formulation and distribution could benefit from lipid-based delivery systems. The therapeutic efficacy of diosgenin can be improved by using these systems, which improve its solubility, stability, and bioavailability. Optimizing the formulation characteristics and investigating the potential uses of lipid-based delivery systems for diosgenin in different disease circumstances require additional research and development in this area. (86,105,118)

6.4 Polymeric Delivery Systems

Because of its adaptability, biocompatibility, and controllability over therapeutic agent release, polymeric delivery systems have attracted a lot of interest in the realm of drug delivery. To improve diosgenin's bioavailability, stability, and targeted administration to particular tissues or cells, polymeric delivery methods provide an encouraging strategy.
In order to create a successful delivery system for diosgenin, it is essential to select an appropriate polymer. The use of chitosan, alginate, poly (lactic-co-glycolic acid) (PLGA), and polyethylene glycol (PEG) are among the synthetic and natural polymers investigated for this use. The particular needs of diosgenin delivery might be satisfied by modifying these polymers' distinctive characteristics.
One polymer that has been explored extensively for drug delivery applications is PLGA, which is biodegradable and biocompatible. diosgenin can be released gradually over a long period of time thanks to its adjustable breakdown rate. Contrarily, chitosan is an ideal vehicle for the oral and mucosal administration of diosgenin due to its exceptional mucoadhesive qualities and its origins in chitin. (107,119,120)

Journal of Chemical Health Risks

www.jchr.org

JCHR (2024) 14(3), 2669-2692 | ISSN:2251-6727

6.4.1 Formulation Approaches

Nanoparticles, microparticles, hydrogels, and films are some of the polymeric delivery strategies for diosgenin that can be developed. The therapeutic efficacy of diosgenin can be enhanced, stability can be improved, and target-specific release patterns can be achieved with these formulations.
Due to their tiny size and capacity to encapsulate hydrophobic medicines like diosgenin, nanoparticles—including polymeric and lipid nanoparticles—have garnered significant attention in the field of drug delivery. Adding ligands or targeting moieties to these nanoparticles can further increase their absorption by cells and allow for site-specific administration.
In contrast, microparticles come in a variety of bigger forms, such as microspheres or microcapsules. Some of the benefits they provide include preventing the degradation of diosgenin and ensuring its continued release. For regulated release of diosgenin in reaction to environmental stimuli or enzymatic breakdown, it can be encapsulated in hydrogels, which are three-dimensional networks of hydrophilic polymers.
diosgenin can be administered transdermally through films made of polymeric matrices. By placing these films on the skin, diosgenin can be released gradually over a long period of time. (121,122)

6.4.2 Encapsulation Techniques

Evaporation of emulsions or solvents, coacervation, electrostatic assembly, and self-assembly are some of the methods that can encapsulate diosgenin within polymeric delivery systems.
When using an immiscible solvent to emulsify a polymer solution containing diosgenin, a typical procedure is emulsion/solvent evaporation. After the solvent is evaporated, polymeric nanoparticles or microparticles loaded with diosgenin are formed.
During coacervation, a polymer solution separates into two phases: one with a high concentration of polymers and another with a lower concentration. The polymer-rich phase can enclose diosgenin and solidify into microspheres or microcapsules.
Diosgenin and polymers with opposite charges interact electrostatically during electrostatic assembly. It is possible to encapsulate diosgenin within the polymeric matrix by modifying the solution's pH or ionic strength.
Polymers and diosgenin can self-assemble into micelles or vesicles and other nanostructures. Benefits of this method include ease of use and scalability. (123–125)

6.4.3 Targeted Delivery

Diosgenin can be delivered to particular tissues or cells by further modifying polymeric delivery methods. Improving the therapeutic efficiency of diosgenin can be achieved by surface-modifying nanoparticles or microparticles with ligands, antibodies, or peptides. This enhances their affinity for target receptors or cells.
Diosgenin can also be delivered site-specifically by means of stimuli-responsive polymers. Specific stimuli, including pH, temperature, or enzymes, cause these polymers to change their physicochemical properties. Diosgenin release can be initiated at the target site with minimal off-target effects by integrating stimuli-responsive polymers into the delivery system. (126,127)

6.4.4 Biocompatibility and Safety

Biocompatibility and safety are important considerations for polymeric delivery methods. For the sake of minimizing side effects, the chosen polymers should not only be biodegradable but also non-immunogenic and non-toxic. To determine whether polymeric delivery systems are immunogenic, cytotoxic, or genotoxic, thorough biocompatibility and safety studies are required.
It is also important to assess diosgenin's stability within the polymeric matrix before storing or transporting it to guarantee its quality. Many variables, including the polymer composition, the manner of formulation, and the storage conditions, might affect the efficiency, release kinetics, and stability of diosgenin. (101,128,129)

Conclusion

In conclusion, diosgenin presents itself as a promising natural compound with a rich history of traditional use and scientific inquiry. This review has provided a comprehensive examination of diosgenin's traditional uses, chemical properties, extraction methods, and pharmacological effects. While diosgenin shows great potential as a novel therapeutic agent, further research is essential to fully understand its pharmacokinetics, safety, and optimal formulation for medical applications. Exciting opportunities lie ahead in exploring diosgenin's potential as a nutraceutical and

Journal of Chemical Health Risks

www.jchr.org

JCHR (2024) 14(3), 2669-2692 | ISSN:2251-6727

medicinal agent, underscoring the importance of standardized extraction procedures and robust clinical trials to validate its efficacy and safety across diverse therapeutic contexts.

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Conflict of interest.

The authors declare no conflicts of interest relevant to this article.

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