Review Article

Therapeutic applications of glycosides obtained from medicinal plants

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Abstract

Due to the wide range of therapeutic uses for glycosides generated from medicinal plants, recent years have seen a substantial increase in interest. These organic substances, which are identified by the presence of a sugar moiety connected to a non-sugar aglycone, display a variety of biological functions that have been exploited for therapeutic benefit. The therapeutic potential of glycosides derived from medicinal plants is thoroughly discussed in this review paper. We look at their functions in terms of cardiovascular, antibacterial, anticancer, anti-inflammatory, and neurodegenerative illnesses. Discussions of the mechanisms underlying these compounds' bioactivity give information on how they interact with cellular targets and signalling networks. Additionally, the difficulties and possibilities related to glycoside extraction, isolation, and characterization are discussed. The potential for creating new and strong therapeutic interventions is underlined by the synergy between glycosides and other bioactive substances found in medicinal plants. Overall, this review highlights the significance of glycosides as promising drug development candidates and highlights the necessity of more study to fully realize their therapeutic potential.

Key words

Glycosides, Types, Therapeutic applications, Mechanism of action.

Introduction

Since ancient times, medicinal plants have played a crucial role in maintaining human health and wellbeing because they are a rich source of bioactive substances with a variety of pharmacological activities. Glycosides, one of the several components found in these plants, have distinguished themselves as an intriguing class of substances with tremendous potential as therapeutic interventions. Glycosides can be extracted from both plant and animal sources. Glycosides, which have a special chemical structure that consists of a sugar moiety (glycone) and a non-sugar aglycone or genin, have drawn a lot of attention for their diverse bioactivities and possible use in contemporary medicine [1, 2].

Glycosides have unique physicochemical features due to the complex interaction between glycone and aglycone, which makes it easier for them to interact with biological systems. These compounds produce one or more sugar moieties and the aglycone upon enzymatic or acid hydrolysis, opening up a wide range of therapeutic options. The intricate connectedness between the glycone and aglycone is further highlighted by the glycosidic linkages, which include S-, N-, C-, and O-glycosidic bonds. This connectivity affects the biological activity and stability of the molecules [3, 4].

The therapeutic potential of glycosides derived from medicinal plants has been the focus of research in recent years. These substances have shown amazing health benefits for a variety of ailments, including antibacterial and anticancer effects as well as anti-inflammatory, cardiovascular, and neurological capabilities. Their methods of action include interactions with certain biomolecules, modification of important cellular signalling pathways, and control of a range of physiological processes. Additionally, the structural variety of glycosides and their capacity for synergistic interactions with other bioactive components found in medicinal plants make their therapeutic uses more complex.

In order to give a thorough overview of the therapeutic uses for glycosides derived from medicinal plants, this review article. We aim to highlight the promise of these natural chemicals as sources of novel therapeutic agents by examining their various bioactivities, clarifying underlying mechanisms, and talking about difficulties connected with their extraction and characterization. The complex interaction between glycosides and cellular functions emphasizes their significance in contemporary drug research and creates opportunities for cutting-edge therapies. A deeper comprehension of the chemical and biological aspects of glycoside-based therapies promises to open the door to the creation of efficient and long-lasting interventions for a variety of health disorders.

Overview of glycosides

A glucose molecule linked to an aglycone makes up glycosides. Glycone, aglycone, and the kind of glycosidic bond are used to represent glycosides. When the glycosidic bond of glycosides is hydrolyzed by an enzyme or an acid, one or more sugar moieties and non-sugar entities are released. The non-sugar part is referred to as aglycone or genin, whereas the sugar moiety is known as glycone. The attachment of an aglycone to the anomeric carbon (C-1 carbon) of a glycone, which defines the glycoside structure, is what gives these compounds their wide range of characteristics and biological functions. The primary structural component of glycosides, the glycosidic bond, is amenable to enzymatic cleavage, which is frequently aided by -glucosidases or acid hydrolysis. Glycosyl transferases, which alter secondary metabolites by attaching sugar moieties to particular places on the aglycone, control the synthesis of glycosides in plants. To give glycosides the correct chemical structure and pharmacological effects, extra metabolic processes like oxidation, acylation, or degradation may occasionally be required during manufacturing [5, 6].

Glycosides have water solubility due to the glycone moiety, which increases their bioavailability and makes it easier for them to interact with biological systems. Typically, glycone is made up of monosaccharide units, most frequently glucose but also sometimes di-, tri-, or tetrasaccharides. The most common monosaccharide, glucose, is usually found as a component of glycone, which has led to the nomenclature of glucosides for glycosides synthesised with glucose. In addition to glucose, glycosides can be grouped according to the particular glycone unit they contain, such as rhamnose (which produces rhamnosides), fructose (which produces fructosides), arabinose (which produces arabinosides), and glucuronic acid (which produces glucuronides). Indicating the structural diversity that glycosides are capable of, classification based on the number of saccharide units in the glycone results in names like monodesmosides or monosides (with one sugar unit), bidesmosides or biosides (with two sugar units), and tridesmosides or triosides (with three sugar units) [7, 8].

Classification of glycosides

The type of sugar moiety and the nature of the aglycone are the main factors used to categorize glycosides. O-glycosides, N-glycosides, and S-glycosides are the three primary subcategories of glycosides according to one widely used classification scheme. O-glycosides, which are frequently found in plant secondary metabolites including flavonoids, anthraquinones, and cardiac glycosides, involve a glycosidic bond between the glycone and aglycone through an oxygen atom. N-glycosides, on the other hand, are typically found in alkaloids like morphine and quinine and include a glycosidic link to the aglycone through a nitrogen atom. S-glycosides, which are less frequent but play a part in substances like thioglycosides, involve a sulphur atom in the glycosidic connection.

Glycosides can also be divided into groups according on the kind of sugar moiety they contain. While oligosaccharide glycosides have several sugar units, monosaccharide glycosides only have one sugar unit in its glycone. Glycosides can be further divided into glucosides, galactosides, xylosides, and other types depending on the individual sugar moiety, with each giving the resulting molecules unique properties. Glycosides have a variety of biological properties that have been used to develop medicinal uses. For instance, cardiac glycosides from plants like Digitalis purpurea have been utilized to treat congestive heart failure due to their beneficial inotropic effects on the heart. Additionally, antimicrobial glycosides like salicin from willow bark have been traditionally utilized as homoeopathic treatments for fever and pain.

Therapeutic applications of glycosides

Glycosides have become a versatile family of natural chemicals with a wide range of medicinal uses. They are distinguished by their characteristic glycone-aglycone structure. Their involvement in treating a range of health issues, including their antibacterial and anticancer effects as well as their anti-inflammatory [9], cardiovascular, and neuroprotective capabilities, highlight their potential as useful sources of therapeutic compounds derived from medicinal plants, as shown in the accompanying table (**Table - 1**).

Anti-microbial activity

Glycosides have several and varied anti-microbial actions. Some glycosides damage microbial membranes, causing cellular contents to seep out and ultimately causing cell death. Others disrupt cellular or microbial activities, impairing critical processes including protein synthesis and DNA replication. Glycosides are excellent possibilities for battling diseases that have developed drug resistance because of their distinctive chemical structures that allow them to engage with particular microbial targets.

Table - 1: Types of glycosides with therapeutic applications.

Glycosides	Therapeutic applications
Alcoholic glycosides	Analgesic, anti-pyretic and anti-inflammatory
Anthraquinone	purgative and laxative effects
Anthocyanins	Anti-inflammatory, antibacterial, and rheumatoid, it gives flowers their distinctive colour.
Cardiac glycosides	Great effectiveness for a variety of heart conditions, including arrhythmia and congestive heart failure.
Cyanogenic glycosides	Provides defence by making themselves unpleasant to predators.
Coumarin	coronary artery dilation, calcium channel blockage, antispasmodics, and antibiotics
Flavonoid glycosides	reduce blood capillary fragility and increase antioxidant activity to strengthen them
Phenolic glycosides	Effect of urinary antiseptics
Steviol glycosides	Natural sweetener
Thioglycosides	antiseptic and allopathic effects

A well-known class of glycosides called saponins has demonstrated broad-spectrum anti-microbial action. These substances stand out for their capacity to damage microbial cell membranes, which cause the lysis and demise of microorganisms [10]. Cardiac glycosides with antibacterial characteristics have been studied, including digitoxin and digoxin. Certain bacterial strains, such as Staphylococcus aureus and Escherichia coli, can have their growth inhibited by these substances, according to studies; because they interfere with bacterial membrane integrity and ion transport processes [11]. Another class of glycosides found in large quantities in plants, flavonoids, has proven anti-microbial properties. These substances have anti-inflammatory and antioxidant characteristics, which help them, fight off microbial infections. For instance, it has been demonstrated that quercetin glycosides from plants like Sophora japonica can stop the growth of harmful bacteria like Helicobacter pylori [11]. Anthraquinone glycosides have anti-microbial capabilities against a variety of bacteria and are present in plants like Rheum palmatum and Cassia species. These substances have been researched for their capacity to prevent the development of bacterial growth and biofilms, making them promising candidates for the creation of novel anti-microbial agents [12].

Anti-cancer activity

Glycosides have numerous anti-cancer strategies that interact with various cellular elements and signalling pathways. Numerous glycosides impact mitochondrial activity, activate caspases, and control Bcl-2 family proteins to cause apoptosis in cancer cells. Others halt the cell cycle to prevent the multiplication of cancer cells, frequently by concentrating on cyclin-dependent kinases. Additionally, it has been noted that glycosides can influence angiogenesis by impairing vascular endothelial growth factor (VEGF) signalling and preventing the development of new blood vessels [13].

Digoxin and digitoxin are cardiac glycosides that have demonstrated anti-cancer effect by focusing on important cellular functions. These substances interact with the Na+/K+-ATPase pump to raise intracellular calcium levels, which then cause apoptotic pathways to be triggered in cancer cells. Cardiac glycosides have been shown to reduce tumor size, trigger apoptosis, and make cancer cells more susceptible to treatment. Oleandrin, a cardiac glycoside derived from Nerium oleander, has also demonstrated potential in slowing the expansion of several cancer cell lines [14-16]. Other class flavonoids glycosides, quercetin glycosides have been demonstrated to trigger apoptosis and cell cycle arrest in cancer cells in addition to having antioxidant capabilities. Additionally, these substances block a number of signalling pathways that contribute to the development of cancer [17]. Kaempferol glycosides have shown anti-proliferative properties and angiogenesis suppression, which raises the possibility that they could be used as anti-cancer drugs [18]. Saponins have demonstrated anti-cancer efficacy through a variety of pathways, and they are distinguished by their amphiphilic nature. Triterpenoidsaponins from plants like Panax ginseng have demonstrated regulation of immunological responses, activation of apoptosis, and suppression of cancer cell proliferation [19]. By focusing on several signalling pathways and reducing angiogenesis, ginsenosides, particular saponins present in ginseng, have shown anti-cancer benefits [20].

Anti-inflammatory activity

Glycosides have a variety of anti-inflammatory mechanisms that interact with various cellular targets. Numerous glycosides work by altering important signalling pathways that are involved in inflammation, including NF-B, MAPKs, and the Janus kinase-signal transducer and activator of transcription (JAK-STAT) pathways. These substances frequently prevent the synthesis of pro-inflammatory cytokines, chemokines, and enzymes, which reduces the inflammatory response.

Saponins are proven to have powerful anti-inflammatory properties. These substances are well known for their capacity to control immunological responses and prevent the synthesis of mediators that promote inflammation. Triterpenoidsaponins, for instance, have demonstrated anti-inflammatory efficacy by inhibiting the production of cytokines and chemokines associated with inflammation [21] in plants like Panax ginseng. Additionally, Quillajasaponariasaponins have demonstrated anti-inflammatory benefits by reducing nitric oxide (NO) generation and COX-2 expression. Flavonoids are proven to have strong anti-inflammatory effects. The nuclear factor-kappa B (NF-B) signalling pathway and the production of pro-inflammatory genes are both suppressed by quercetin glycosides, which are present in many plant sources and have been demonstrated to block inflammatory pathways. By regulating the generation of inflammatory cytokines and lowering oxidative stress, kaempferol glycosides have shown anti-inflammatory benefits [22-24]. Anthraquinone glycosides, which are present in plants like Rheum palmatum, have a variety of anti-inflammatory effects. These substances have been shown to suppress the expression of COX-2 and inducible nitric oxide synthase (iNOS), as well as the generation of inflammatory cytokines including interleukin-1 (IL-1) and tumor necrosis factor-alpha (TNF-) [25].

Immunomodulatory activity

Glycosides' immunomodulatory mechanisms are complex and involve interactions with a number of immune system organs. By influencing cell proliferation, differentiation, and activation, glycosides can modify the roles of immune cells, including T cells, B cells, NK cells, dendritic cells, and macrophages. These substances also have an impact on cytokine synthesis, which is essential for determining immunological responses.

Significant immunomodulatory effects were seen in saponins. These substances have adjuvant qualities that boost immune responses by activating antigen-presenting cells (APCs) and encouraging the release of cytokines. For instance, it has been demonstrated that ginsenosides, a type of saponin produced from Panax ginseng, increase T-cell proliferation, boost the activity of natural killer (NK) cells, and encourage macrophage phagocytosis. Researchers have looked into the immunostimulatory properties of astragalusmembranaceussaponins, which could improve immune cell performance [26]. Flavonoids possess immunomodulating qualities. For instance, quercetin glycosides have been shown to affect immunological responses by controlling T-cell differentiation, reducing the generation of inflammatory cytokines, and increasing the activity of regulatory T cells [27]. Additionally, these glycosides help control immune-related signalling pathways. Through its interactions with immune cells and cytokine networks, triterpenoid glycosides like ginsenosides and gypsosaponins have showed immunomodulatory effects. Ginsenosides have demonstrated potential in stimulating cytokine release, modulating immune cell trafficking, and boosting immune cell proliferation [4]. By modulating macrophage activation and fostering the generation of antibodies, gypsosaponins, which are produced from Gypsophila species, have demonstrated immunomodulatory effects [28].

Neuroprotective activity

Glycosides have a variety of neuroprotective processes that involve interactions with a range of cellular and molecular targets. Numerous glycosides have antioxidant and anti-inflammatory properties that help them work by lowering oxidative stress and inflammatory reactions in the brain. Additionally, these substances have the ability to alter intracellular signalling pathways, including the PI3K/Akt and MAPK pathways, which are essential for the survival and plasticity of neurons.

The neuroprotective effects of flavonoids are exhibited through a number of ways. Flavonoids influence the activity of several signalling protein pathways, including ERK and PI3-kinase/Akt, and as a result, have positive neuroprotective effects [29].When it comes to a number of CNS conditions like stroke, Alzheimer's disease, Huntington's disease, and Parkinson's disease, saponins have neuroprotective properties [30].

Anti-oxidant activity

Glycosides have a variety of antioxidant mechanisms that interact with different cellular targets and signalling cascades. In order to neutralize ROS and RNS, several glycosides work as free radical scavengers by donating electrons. Additionally, antioxidant enzymes including superoxide dismutase (SOD), catalase, and glutathione peroxidase, which are essential for cellular defence against oxidative stress, can be modulated by glycosides.

The powerful antioxidant properties of flavonoids are widely known. For instance, the exceptional free radical-scavenging abilities of quercetin glycosides contribute to their capacity to shield cells and tissues from oxidative damage.In the form of a red color, anthocyanin is a flavonoid glycoside that can be found in leaves, fruits, and flowers. It has been demonstrated to be an antioxidant and to guard against liver cell damage [31]. Strong antioxidant properties are exhibited by phenolic glycosides. These substances lessen cellular oxidative stress by scavenging reactive oxygen species (ROS) and reactive nitrogen species (RNS). Through the suppression of lipid peroxidation and the improvement of cellular antioxidant defenses, oleuropein, a phenolic glycoside found in olive leaves, has been demonstrated to possess powerful antioxidant properties [32]. Known for their vivid colors and antioxidant qualities, carotenoid glycosides are essential in preventing oxidative cell damage. For instance, astaxanthin glycosides have strong antioxidant activity because they scavenge peroxyl radicals and quench singlet oxygen. These glycosides help keep cellular redox equilibrium in check.

Particularly capable of quenching singlet oxygen are carotenoids. Antioxidants can neutralize free radicals through two different mechanisms: hydrogen atom transfer (HAT) and single electron transfer (SET) [33].

Conclusion

The broad body of research summarized in this review reveals the various ways that glycosides exert their therapeutic effects, frequently by regulating important cellular pathways and molecular targets. Intricate connections between glycosides and biological systems are still being uncovered by researchers, and this is expected to open up new possibilities for the development of novel drugs. Although the therapeutic promise of glycosides is clear, difficulties still exist in their separation, purification, and clinical formulation. In order to overcome these challenges, advancements in analytical methodologies and extraction procedures are essential. Further research into the interactions between glycosides and other phytochemicals found in medicinal plants may improve therapeutic results and minimize negative effects. In conclusion, research into the therapeutic uses of glycosides derived from medicinal plants has considerable promise for the creation of cutting-edge therapies in contemporary medicine. To fully utilize the potential of these natural substances and transform their advantages into efficient medicines for a variety of health disorders, further study and collaboration between scientists, pharmacologists, and clinicians will be necessary.

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