UPI Journal of Pharmaceutical Medical, and Health Sciences

Content Available at www.uniquepubinternational.com ISSN: 2581-4532

Open Access **Review Article**

A REVIEW ON MEDICINAL PLANTS CONTAINING GLYCOSIDES

Badri.Sireesha[1*], P. Pavitra[2], D.Sameena[2], G.Anitha[2], S.K. Asifa[2] , K.Mahesh[2], E.Pushpalatha[2]

[*1] Assistant Professor, Sankar Reddy Institute of Pharmaceutical Sciences, Salakalaveedu(V), Bestavaripeta (M), Prakasam (D), Pincode-523370

[2] B.Pharmacy, Sankar Reddy Institute of Pharmaceutical Sciences, Salakalaveedu(V), Bestavaripeta (M), Prakasam (D), Pincode-523370

Article History

Received: 26-07-2023
Revised: 17-08-2023
Accepted: 12-09-2023

***Corresponding Author**
Badri.Sireesha
Assistant Professor, Sankar Reddy Institute of Pharmaceutical Sciences, Salakalaveedu(V), Bestavaripeta (M), Prakasam (D), Pincode-523370

DOI:https://doi.org/10.37022/jpmhs.v6i3.91

Abstract

Plant-active metabolites are under intensive examination around the world to supplement the drugs with minimal side effects. Thus, there is vast potential to explore the possible medicine from plant sources. Cardiac glycosides are a unique group of secondary metabolites that are considered one of the most useful drugs in therapeutics. In this review, cardiac glycosides and their analogs are presented. The structure and distribution in plants, as well as structure elucidations, synthetic routes, and chemical analysis, are shown. In addition, the pharmacological activities, mode of action studies, and structure-activity relationships are cardiac glycosides.

Keywords: Chemical analysis, Pharmacological activities, SAR, metabolites, plants.

Introduction

Glycosides are the molecules in which a sugar part is bound to some other non-sugar part. Glycosides play numerous important roles in living organisms. Plants store important chemicals in the form of inactive glycosides if these chemicals are needed, the glycosides are brought in contact with water and an enzyme and the sugar part is broken off, making the chemical available for use [1].

Cassava grows well in a tropical climate and is an important root crop in Pacific Isle and countries, Latin America, Africa and regions of Asia. Bamboo shoots grow in a variety of climates and are commonly used in Asian cuisine. However, if either are eaten raw or processed inadequately, their consumption may be potentially harmful due to the presence of cyanogenic glycosides, linamarin in cassava and taxiphillin in bamboo shoots, which break down to produce hydrogen cyanide.

The potential toxicity of cassava and bamboo shoots can be significantly reduced by adequate processing to break down the cyanogenic glycoside and remove the resulting hydrogen cyanide. Traditional preparation techniques reflect the need for removal of the natural toxicants prior to consumption. Cassava is grown for its enlarged starch-filled roots, which contain about 30% starch and very little protein. It is consumed in a number of forms: flour used for cooking; root slices; root chips; baked grated root; steamed grated root; pan fried grated root; steamed whole root; and tapioca pearls made as a pudding. Cassava leaves are also eaten in some countries after extensive boiling. Cassava flour can be produced by either sun drying or heap fermentation. Cassava flour produced by heap fermentation has lower cyanide content than cassava flour produced by sun drying. Sweet varieties of cassava (low cyanide content) are adequately processed by peeling and then fully cooking (e.g. roasting, baking or boiling). Bitter varieties of cassava (high cyanide content) require further processing, involving techniques such as heap fermentation. Bamboo shoots are a traditional component of Asian cuisine. There are approximately 1200 species of bamboo, although only a limited number of these are viable as food. Bamboo shoots may contain significantly higher levels of hydrogen cyanide than cassava tubers, however, the cyanide content is reported to decrease substantially following harvesting. Preparation generally involves boiling for an extended period [2].

Formally ,a glycoside is any molecule in which a sugar group is bonded through its anomeric carbon to another group via a glycoside bond, the sugar group is known as the glycone and the non- sugar group as the aglycone are genin part of the glycoside.

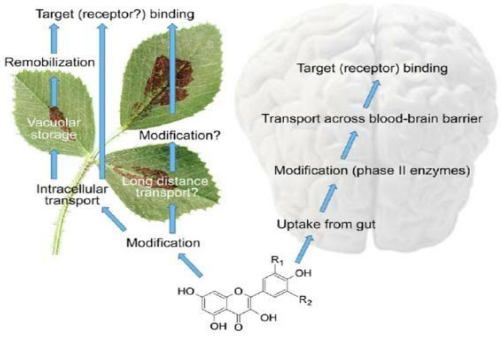
The glycone can consist of

Single sugar group monosaccharide or Several sugar groups oligosaccharide [3].

Glycosidesin medicinal plants

Steroidal cardioactive glycosides :A number of cardioactive glycosides with steroidal aglycones occur in a wide varity of plant species in several plant families. Many of these steroidal gzycosides are of Phazinacological significance and some are important therapeutic agents. In table 1 arelisted some of the better known plant species and the principle glycosides occurring in them. In crude drug from, as dry plnt material, digitalis purpurea, digitalis lanata, urginea maritimea and urginea indica constitute the plant sourecs for certain crude drug substance of the B.P.C.and of the U.S.P. but a number of the individual glycosides which are drug substains [4].

Flavonoid Glycosides



5Derivatives of flavone, isoflavone,flavonol,and flavonone are called flavonoids. Flavone itself is colourless, but many of its hydroxylated. Derivatives are coloured. These flavonoids , either free or linked to sugars(i.e.as glycosides) are of common occurrence in a wide variety of plants 6, particularly in red, blue and yellow pigments of flowers and fruits. Among the glycosides in which the aglycones are flavonoids, rutin, hesperidin,and some of their derivatives have been used as medicinal agents, they are collectively reffred to as bioflavonoids in medicinal preparations. The principal botanical source of rutin is the leaf of bulk-wheat, the annual herb [7].

Bryophyllum ;

Bryophyllum is a group of plant species of the family crassulaceae native to Madagascar. it is a section or subgenus within the genus kalanchoi, and was formerly placed at the level of genus this section is notable for vegitatively growing small plantlets on the fringes of the levels these eventually drop off and root. These plantlets aries from mitosis of meristem type tissue is notches in the leaves [8].

Nerium

Nerium oleander most commonly known as oleander or nerium,is a shrub or small tree cultivated worldwide in temperate and subtropical areas as an ornamental and landscaping plant.9 It is the only species currently classified in the genus nerium, belonging to subfamily apocynoideas of the dogbane family apocynaceae. It is so widely cultivative that no precise region of origin has been identified, thought it is usually associated with the Mediterranean basin [10].

Kalanchoe Pinneta

Kalanchoe pinnata commonly known as cathedral bells,air plant,life plant,miracle leaf,and Goethe plant is a succulent plant native to Madagascar. It is popular houseplant and has become neutralized in tropical and subtiopical areas.the species is distinctive for the profusion of miniature plantlets that form on the margins of leaves,a triait it has in common with some other membars of bryophyllum [11].

Squill

Squill common name drimia maritime is a species of flowering plant in the family as paragaceae, subfamily scilloideas. This species is known by several common names including suill, sea squill, sea onion, and maritime squill. it may also be called red squill, particularly a form which produceds red-tinged flowers instead of white. It is

native to southern europee,western asia, and northern Africa.

Stophanthus

is a genus of flowering plants in the family apocynaceae, first described as a genus in 1802. It is native primarily to tropical Africa extending to south Africa, whith a few species in asia from southern india to new guinea and southern china. The genus name is a compound of the greek word(strophos) twisted and lobes which in some species-notably S. petersianus –resemble long twisted ribbons or threads and can reach a length of 30-35cm. this trait, in addition to colouring involving combination of bright pinks, purples and oranges, combine to make the flowers among the most ornamental in the plant kingdom [12].

Digitalis

Digitalis is native to Europe western Asia and north western Africa. The flowers are tubular in shape, produced on a tall spike and very in colour with species, from purple to spike and vary in colour with species, from purple to pink, white and aloe. The scientific name means finger. The genus was traditionally placed in the figwort family, scrophulariaceae, but phylogenetic research led taxonomists to move it to the veronicaceae in 2001. More recent phylogenetic work has placed it in the much enlarged family plantaginaceae.

Alovera

Alovera known for its lance-shaped leaves with jagged edges, alone vera is a popular houseplant for many reasons:its one of the best air-purifuing plants and has an array of dermatologist-approved benefits like helping to reduve acne and wrinkles healing wounds or easing irritation from sunburns.

Senna

Senna the sennad, is a large genus of flowering plants in the legume family this diverse genus is native throught the eropics, with a small number of species in temperate regions. The number of species is estimated to be form about 260to 350 the type species for the genus is senna alexandrina. Above 50 specues of denna are known in cultivation [13].

Milkweed

Asclepias is a genus of herbaceous,perennial, flowering plants known as milkweeds, name for their latex a milky substance containing cardiac glycosides termed cardenolides, exuded where cells are damaged.most species are toxic to humans and many others species, primarly due to the presence of cardinolides. However,as whith many such plants some species feed upon them or from them. The most notable of them is the monarch butterfly, which used and requires certain milkweeds as host plant for their larvae.

Meadowsweet

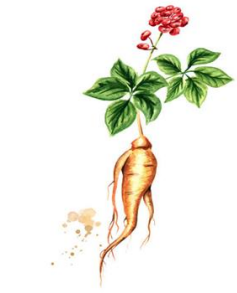
Filipendula ulmaria, commonly known as meadowsweet or mead wort, is a perennial herbaceous plant in the family rosaceae that grows in damp meadows. It is native throught mosy of Europe and western asia. It has been introduced and naturalized in noeth America.

Asian Ginseng

Panax ginseng, ginseng, also known as Asian ginseng chinese ginseng, Japanese gingseng or Korean ginsing, is a species of plant whose root is the original source of ginseng. It is a perentak plant that grows in the mountains of east asia [14].

Ginseng Root

GINSENG (TRI TERPENOID SAPONIN) Dried roots of Panax ginseng (Korea) and other species of Panax Source P. japonicas (Japan), P. pseudoginseng (Himalaya), P. quinquefolius (American), P. trifolius (Dwarf), P. vietnamensis (Vietnamese), P. notoginseng (Chinese) Family Araliaceae Syn. Ninjin, Pannag, Energofit Image G.S. Korea, China, Russia now cultivated in Japan, Canada & US The term panax (derived from greek) panaceae = cure all History The term ginseng (derived from chinese) shen sang = man root Shape of human body - Ginsenosides, Panaxosides and Chikusetsu Saponins. Chemical-Ginsenoside consists of aglycone dammarolConstituents - Panaxoside have aglycone as oleanolic acid - Starch, Gum, Resin, volatile oil, flavonoids, sesqui terpenoids USES-important immunomodulatory drug, increase natural resistance and overcome illness -both stimulant & sedative property Uses -aphordiasic & adrenal & thyroid dis funtioning -blood sugar, anaemia, gastritis etc. Roots of Panax quinquefolius (American Ginseng) & P.ginseng (A sianginseng), Araliaceae. Contains acomplex mixture of triterpenoid al saponins with tetracyclic (steroids) or pentacyclic structure (in its cork)



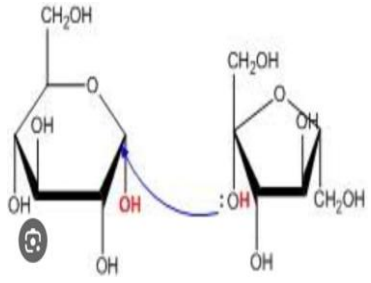
Bacopa

Source: Fresh leaves and stem of Bacopa monnieri (Herpestis monnieri) Family Scrophulariaceae Syn. Jalbrahmi, Neerbrahmi G.S. Throughout India in wet, damp & marshy places up to 1200 m elevation – ChemicalConstituents: saponin glycosides known as bacoside A and bacoside B - on acid hydrolysis triterpenoid aglycone bacogenin A and bacogenin B – Asiatic acid and brahmic acid ChemicalConstituents - treatment of insanity and epilepsy, asthma Uses - potent nervetonic, cardiotonic and diuretic - mild laxative.PA.

Hydrocotyl

Source: dried aerial parts of Centella asiatica (Hydrocotyl asiatica) Family Umbelliferae Syn. Indian pennywort, Mangosteen, Mandukparni G.S.: India, Pakistan, Srilanka, Madagaskar ChemicalConstituents: Tri terpenoid saponin glycoside in form of α-amyrin derivative: asiaticoside, madecassoside - Asiaticoside hydrolysis asiatic acid + 2 glucose + rhamnose -Madecassoside hydrolysis madecassic acid + 2 glucose + rhamnose Chennai & Lucknow variety Brahmoside, Brahminoside hydrolysis brahmic acid & iso brahmic acid , arabinose, glucose, rhamnose USES -nervine tonic, spasmolytic, anti anxiety, anti-stress, sedative Uses –skin diseases, leprosy, syphilis [15].

Glycosidic Bond



A glycosidic bond is a certain type of a functional group that joins alcoholic group of a carbohydrates molecule to an aglycone molecule. A substance containing a glycosidic bond is glycoside By glycones The glycone group of glycoside is glucose, then the molecule is glucoside .if it is fructose, then the molecule is a fructoside. It is glucuronic acid, then the molecule is glucuronide.

Classification of glycosides

General Characters of glycosides:

S. No.	Class	Examples
1.	Anthraquinone glycosides	Senna, Aloe, Rhubarb, etc.
2.	Sterol or Cardiac glycosides	Digitalis, Thevetia, Squill, etc.
3.	Saponin glycosides	Dioscorea, Liquorice, Ginseng, etc.
4.	Cyanogenetic and Cyanophoric glycosides	Bitter almond, Wild cherry bark, etc.
5.	Thiocynate and Isothiocynate glycosides	Black mustard
6.	Flavone glycosides	Ginkgo
7.	Aldehyde glycosides	Vanilla
8.	Phenol glycosides	Bearberry
9.	Steroidal glycosides	Solanum
10.	Bitter and Miscellaneous glycosides	Gentian, Picrrohiza, Chirata, etc.

1. Widely distributed in higher plants.
2. Bitter, acrid taste & sternutatory (irritant to mucousmembranes).
3. Form colloidal solutions in H2O→ foam onshaking→ lowers surface tension in aqueous solution.
4. Destroy RBCs→blood haemolysis.
6. Toxic by i.v.injection & harmless by oral route.

Physical Characters

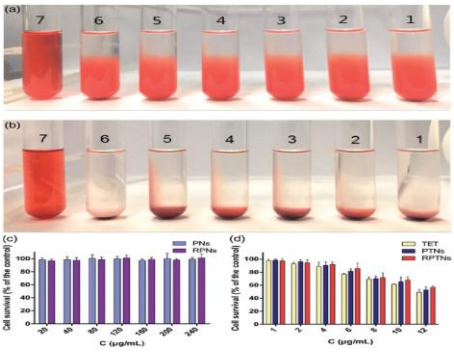
1.Rarely crystalline & generally amorphous powder with high MPs
2. Soluble in water and form colloidal solutions
3. Soluble in ethyl & methyl alcohol
4. Insoluble in organic solvents like petroleum ether, chloroform and acetone etc.
5. Bitter in taste
6. Non-alkaline in nature
7. Produce sneezing and have property of lowering surface tension
8. Hydrolysed by acids, alkalies to yield aglycone called sapogenin

Physiological Properties:

- Very dilute solution of saponins hemolyses RBC (hemolysis takes place due to theformation of complex with the cholesterol or erythrocyte membrane causing itsdestruction (chief property of saponin, very rarely shown by any other plantproduct.
- Accelerate the germination and growth of the seeds.
- Showsfungicidal, antifertility, molluscidal, blood purifying, abortifacient, anthelmintic, sedative & antispasmodic effects [16].

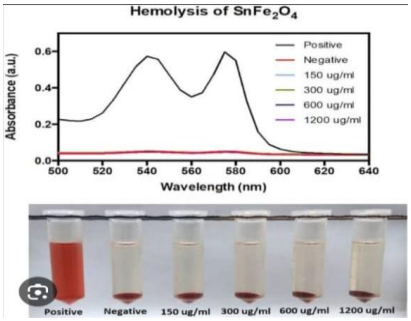
Tests for Identificatio

1. Froth test:



1 ml of aqueous solution of saponin or plant extract + shake →persistent & voluminous froth

2. Hemolysis test:



Suspension of RBCs in normal saline + equal volume of plant extract in normal saline+ Shake gently →clear red solution indicating heamolysis of RBCs (compared with bla DIOSCOREA (STEROIDAL SAPONIN) Dried tubers of Dioscorea deltoidea, D. composita & other species of Source Dioscorea Family Dioscoreaceae Syn. Yam, Rheumatism root

- G.S. North western Himalaya, USA, Mexico Non-edible as very bitter.
- Chemical Constituents : Rhizome: 75% starch &phenol; Roots: Diosgenin (4-6%) steroidal sapogenin, glycoside: smilagenin, epismilagenin, B-isomer of yammogenin, Enzyme: sapogenase;
- The group contains the sapogenins with pentacyclic triterpenoids nucleus which is linked with sugars and uronic acids. The sapogenins are further divided in to αamyrin, β-amyrin & Lupeol.
- Important derivative of this group is triterpenoid acid formed via substitution of carboxylic acid group at C4, C17 & C20 positions

Chemical Constituents

Glycyrrhizin (6-8%) is found to be 50 times as sweet as sugar. – Glycyrrhizin upon hydrolysis loses its sweet taste and gives rise to the aglycone glycyrrhetinic acid (glycyrrhetic acid) together with two moles of -Color of drug is due to Chalcone glycoside-isoliquiritin -A host of other chemical constituents essentially include are namely: coumari derivatives e.g., umbelliferone and herniarin; flavonoid glycoside e.g., liquiritoside; isoliquiritoside, liquiritin; isoliquiritin, rhanoliquiritin, and rhamnoisoliquiritin; Usparagines; 22-33-dihyrostigmasterol; glucose; mannitol and about 20% of Interestingly, carbenoxolone, which is an oleandane Chemicalderivative Section/Powder + 80% H2SO4 orange yellow color Test (transformation of flavones glycoside liquiritin to chalcone glycoside isoliquiritin USES -demulscent and expectorant; -as a masking agent for bitter drugs in pharmaceutical formulations, such as: Uses quinine, aloe, ammonium chloride etc. -Ammoniated glycyrrhiza: as a flavouring agent in beverages, pharmaceuticalsand confectionary.

- The presence of glycyrrhetinic acid exert mineralocorticoid activity andhence it is used in the treatment of inflamations, rhematoid arthritis and Addison's disease.

- liquid extract: as a foam stabilizer in the foam type-fire-extinguisher
- In the treatment of peptic ulcer.
- In Europe the glycyrrhetic acid: in dermatological formulations;
- Anti- iinflammatory properties [17].

Aromatic and Medicinal Plants - Back to Nature

Characteristically have an A/B cis and B/C, trans orientation. Although cardiac glycosides are more abundant than aglycones, some aglycones of cardiac glycosides are used for conges-tive heart failure and commercially available like digoxigenin, gitoxigenin, strophanthidin, and ouabagenin as shown in Figure 2. The most commercially important plant sources of cardiac glycosides are digitalis purpurea, D. lanata, Strophanthus gratus, and Strophanthus kombé . Figure 2 shows the structure of some common cardiac aglyconesThe sugar moieties are mostly attached to the aglycone at C-3 by β-linkage and are composedof up to four sugar units. It may include glucose or rhamnose together with other deoxy sugars whose natural occurrence is, so far, known only in association with cardiac glycosides.Figure 3 shows the structures of some examples of sugar residues attached to cardenolides, Figure 3. Examples of sugar residues attached to cardenolides.

Uses

- Diosgenin is hydrolytic product of saponin dioscin. Source of STEROIDS (in manufacturing progesterone, steroidal drugs, contraceptive) & in treatment of arthritis Licorice Root(RADIX GLYCYRRHIZAE)
- Botanical origin: The dried peeled or unpeeled roots and stolons of Glycyrrhizaglabra L. and its varieties (Family Leguminosae).
- Geographical Source: Licoriceisnative to the Mideterrane an region, as Spain, Italy, England, France Germany, U.S.A., Russia and Egypt.
- Deep well cultivated fertile moistened retentive soil for good root production -prefers a sandy soil with abundant moisture and does not flourish in clay. -slightly alkaline condition gives best production [18].
- Cultivation -thrives in maritime climate –propagated using seeds and roots -seeds are presoaked for 24 h in warm water and then sown in spring or autumn in a green house -The roots are usually harvested after 3 to 4 years from its plantation when they mostly display enough growth.
- The rhizomes and roots are normally harvested in the month of October, particularly from all such plants that have not yet borne the fruits, thereby ascertaining maximum sweetness of the sap.
- The rootlets and buds are removed manually and
- Preparation -The drug is first dried under the sun and subsequently under the shade till it loses almost 50% of it sinitial weight. -The large thick roots of the Russian Liquorice are usually peeled before drying. -It is a usual practice in Turkey, Spain and Israel to extract a substantial quantity of the drug with water, the resulting liquid is filtered and evaporated under vacuo and the concentrated extract is molded either into sticks or other suitable forms.

Morphology

Color Unpeeled Liquorice-Externally, yellowish brown or dark brown; and internally, yellowish Shape Unpeeled drug—Straight and nearly cylindrical Peeled drug—Mostly angular Size Length 20 to 50 cm; Diameter 2 cm, Taste Sweet Fracture Fibrous in bark; and splintery in the woodnk) [19].

Chemical analysis

The analytical methods for cardiac glycosides can be divided into two groups, which are classical and sensitive methods. The classical methods (μg range) including photometry and chromatography have an importance in the pharmacopoeias and are widely employed in control laboratories for quantitative determination of the content and purity of glycoside preparations. Sensitive methods (ng range) include pharmacokinetic investigations, which require sophisticated apparatus. They comprise gas chromatography coupled to a mass spectrometer (GC-MS) and HPLC coupled to a sensitive detector (MS or fluorescence detector).Such method affords reliable measurements in the ng range , whereas the classical methods require preliminary purification usually by chromatography In classical methods, direct measurement by UV led to the absorption maxima for cardenolides at 217 nm (εmol = 16,595) and for bufadienolides at 300 nm (εmol = 5250, εmol is the molar extinction coefficient)ʒ For qualitative and quantitative determination of the cardiac glycosides, it must therefore be converted into colored derivatives as shown in Figure 4. It can be converte into colored derivatives by reaction with polynitroaromatic derivatives in alkaline solution, with Keller-Kiliani or xanthydrolin acidic medium or by treatment with strong acids andthese can be measured by conventional photometers or fluorimeter

Extraction and purification of cardiac glycosides

The isolation and identification of pure cardiac glycosides from their crude mixture faced some difficulties in the past due to its low quantity or its presence as a complex mixture. Reich stein's group suggested the defatting of dried and powdered seeds, and/or leaves with petroleum ether followed by digestion with water at 0°C to extract polysaccharides and hydrolytic enzymes.20 One of the most common methods of extraction of cardiac glycosides

is the prior protection of plant material by its maceration in toluene and allowing it to stand for many days at 25–37°C to avoid the enzymatic hydrolysis. Then, it is followed by exhaustive extraction with water alcohol mixture. The aqueous extract could be evaporated to a small volume under vacuum at 50°C. Fats could then be removed by extraction with petroleum ether and the aqueous syrup of glycosides is diluted with an equal volume of water. Tannic acid and other polyphenolic and acidic products are precipitated with freshly prepared lead hydroxide and the mixture is filtered through HyfloÕSuper Gel. The clear filtrate is adjusted to pH 6, concentrated under vacuum and subjected to fractional extraction: first with ether, then chloroform, and finally with chloroform alcohol, 2:1 and 3:2. For isolation of glycosides of high solubility in water, the residual aqueous phase is half saturated with sodium sulfate and then extracted with chloroform alcohol. The less polar fractions are separated by chroma tography on neutral alumina The more polar fractions are usually chromatographed after acetylation or benzoylation and the free glycosides recovered by hydrolysis with bicarbonate. Reversed phase column chromatography are widely accepted in many fields including HPLC of cardiac glycosides with RP8 or RP18 column and acetonitrile/water or methanol/ water as an eluent, followed by UV detector at 220 nm.The employment of HPLC tech niques also led to the isolation of large number of cardiac glycosides [21].

Conclusion

The results revealed the presence of medicinally important constituents in the plants studied. Many evidences gathered in earlier studies which confirmed the identified phytochemicals to be 14 RNS Yadav and Munin Agarwala bioactive. Several studies confirmed the presence of these phytochemicals contribute medicinal as well as physiological properties to the plants studied in the treatment of different ailments. Therefore, extracts from these plants could be seen as a good source for useful drugs. The traditional medicine practice is recommended strongly for these plants as well as it is suggested that further work should be carried out to isolate, purify, and characterize The active constituents responsible for the activity of these plants. Also additional work is encouraged to elucidate the possible mechanism of action of these extracts.

Funding

No Funding

Conflict of Interest

No Conflict of Interest

Inform Consent and Ethical Considerations

Not Applicable

Author Contribution

All authors are contributed equally.

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