

SAPONIN: A WONDER DRUG FROM *CHLOROPHYTUM* SPECIES

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ABSTRACT

A wide range of herbs from the genus *Chlorophytum* (*Asparagaceae*) are known for their therapeutic potential with a vast range of pharmacologically important saponins. The important plants of the genus like *C. borivilianum*, *C. malayense*, *C. comosum*, and *C. arundinaceum* have steroidal saponins which has attracted much attention due to their structural diversity and therapeutic capability. The saponins from *C. borivilianum* have aphrodisiac property and popularly used as a safe alternative for Viagra while saponins from *C. malayense* and *C. comosum* have anti-tumor properties and cytotoxicity against cancerous cell line. The review presents an approach to different chemical constituents and gives a brief outline of the various therapeutic properties showed by the saponins from the genera *Chlorophytum*.

KEY WORDS: Saponins, *Chlorophytum*, steroid, anti-cancer, phyto-nutrients, anti-edemic, flavonone glycoside.

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INTRODUCTION

Saponins are a vast group of structurally diverse glycosides of the plant kingdom widely distributed in nature; their surface-active properties distinguish them from other glycosides (Lasztity *et al.*, 1998). They are non-volatile primary compounds, when dissolved in aqueous solution they form soap like foaming on shaking. They are referred to as steroidal glycosides and triterpenes consisting nonpolar aglycones coupled with one or more monosaccharide moieties (Oleszek, 2002). This combination of polar and non-polar structural elements in their molecules explains their soap-like behavior in aqueous solutions.

Saponins are the important chemical compounds from tubers of this plant. They are used in the indigenous systems of medicine as a well known health tonic, aphrodisiac and galactagogue (Chopra *et al.*, 1956; Marais and Reilly, 1978; Nadkarni, 1996; Oudhia, 2001b). Pharmaceutical industries buy saponins in large quantities because of their use for the semi-synthesis of steroidal drugs for phyto-therapy and in cosmetic industry (Haque *et al.*, 2011; Ksouri *et al.*, 2011). They are believed to form the main constituents of many plant drugs and folk medicines responsible for numerous pharmacological properties (Marais and Reilly, 1978; Estrada *et al.*, 2000; Debnath *et al.*, 2006; Katoch *et al.*, 2010). Therefore, it is a category of phyto-nutrients (plant nutrients) found abundantly in many beans, and other plants such as Ginseng, Alfalfa, Yucca, Aloe, Quinoa seed and also in Safed Musli (Chopra *et al.*, 1956; Nadkarni, 1996). Saponins have a diverse range of properties from sweetness to bitterness (Grenby, 1991; Kitagawa, 2002; Heng *et al.*, 2006; Thakur *et al.*, 2009), foaming and emulsification (Price *et al.*, 1987), pharmacological and medicinal (Attele *et al.*, 1999; Debnath *et al.*, 2007; Rajeev *et al.*, 2012), haemolytic (Oda *et al.*, 2000; Sparg *et al.*, 2004), and antimicrobial, insecticidal, and molluscicidal activities (Sparg *et al.*, 2004; Sundaram *et al.*, 2011) and finds some place in beverages, confectionery and cosmetic industry

(Price *et al.*, 1987; Petit *et al.*, 1995; Uematsu *et al.*, 2000). (Fig. 1)

Saponins consist of a sugar moiety, usually containing glucose, galactose, glucuronic acid, xylose, rhamnose or methylpentose, glycosidically linked to a hydrophobic aglycone (sapogenin) which may be triterpenoid or steroid (Abe *et al.*, 1993; Haralampidis *et al.*, 2002); derived from the 30 carbon atoms containing precursor oxidosqualene (Haralampidis *et al.*, 2002).

The difference between the two classes lies in the fact that the steroidal saponins have three methyl groups removed (i.e. they are molecules with 27 C-atoms), whereas in the triterpenoid saponins all 30 C-atoms are retained. Saponins were classified into three classes, namely, the triterpenoid saponins, the spirostanol saponins and the furostanol saponins. However, due to secondary biotransformation such a classification emphasizes incidental structural elements and does not reflect the main biosynthetic pathways (Sparg *et al.*, 2004). There are some other classes of compounds that have been considered as saponins, such as the glyco steroid alkaloids (Haralampidis *et al.*, 2002). Baumann *et al.*, (2000) reported that saponins have hemolytic properties that generally are attributed to the interaction between the saponins and the sterols of the erythrocyte membrane. As a result erythrocyte membrane bursts, causing an increase in permeability and a loss of haemoglobin. A study was made to establish the relationship between the adjuvant and haemolytic activity of saponins derived and purified from 47 different food and medicinal plants. However, the results indicated that the adjuvant activity does not relate with haemolytic activity (Oda *et al.*, 2000). The toxicity towards cold-blooded species has lead to the use of saponin containing drugs to catch fish.

Saponins are also highly toxic to molluscs and have been investigated as molluscicides in the control of schistosomiasis (Sindambiwe *et al.*, 1998; Abdel-Gawad *et al.*, 1999). Itabashi *et al.*, (1999) isolated furcreastatin, a steroidal

saponin from ethanolic extract of the leaves of *Furcraea foetida* (L.) Haw (Agavaceae) and screened for its selective cytotoxicity towards mutant p53-expressing mouse fibroblasts.

Their finding suggests that saponins have weak toxicity if taken orally by warm-blooded species which is probably attributed to low absorption rates.

Fig. 1- Structure of Saponin

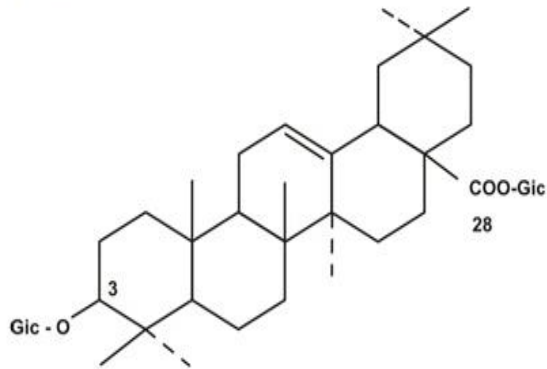
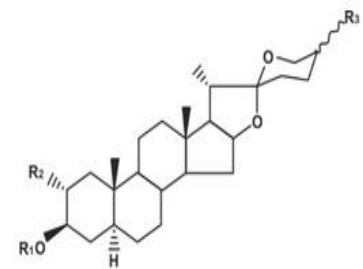
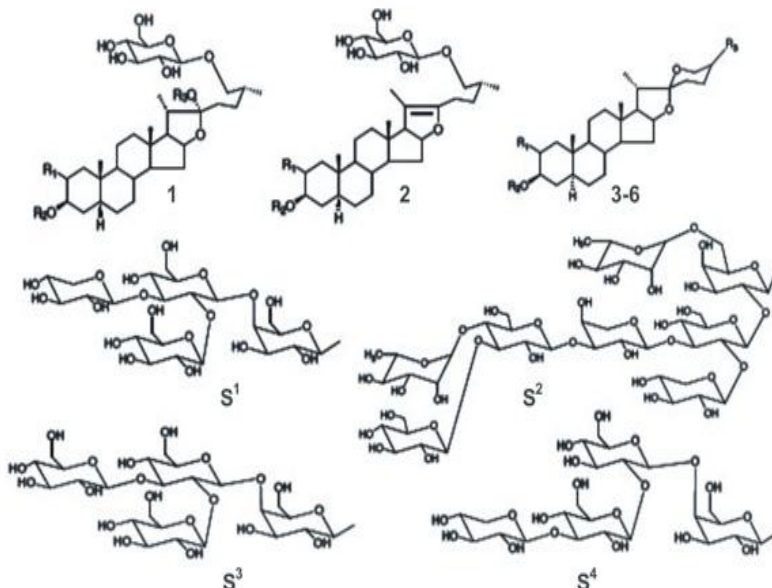


Fig. 2-A - Structure of Saponin of *Chlorophytum borivilianum*

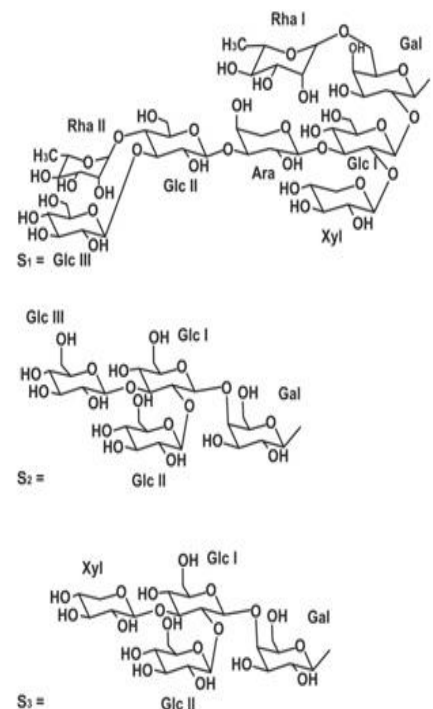


	R1	R2	R3
1	S1	H	eq Me
2	S1	H	exo CH2
3	S2	OH	exo CH2
4	S3	OH	exo CH2

Fig. 2-B - Structure of Saponin of *Chlorophytum borivilianum*



	1	2	3	4	5	6
R1	H	H	H	H	OH	H
R2	S ¹	S ¹	S ²	S ²	S ³	S ⁴
R3	CH ₃		CH ₃ (eq)	CH ₂	CH ₂	CH ₃ (ax)



The genus *Chlorophytum* includes 300 species, which are distributed throughout the tropical and subtropical parts of the world with 85% species reported from tropical and subtropical Africa. There are 17 species of *Chlorophytum* recorded in India out of these 11 species of *Chlorophytum* are found to be

growing in Maharashtra (Patil and Deokule, 2010). It is being widely cultivated in different parts of India on commercial basis. This review discusses about the major species of *Chlorophytum*, their major component saponins and their therapeutic values in Indian system of Medicine.

***Chlorophytum borivilianum* Santapau & R. R. Fern.**

Chlorophytum borivilianum also known as *Safed Musli* is a traditional herbal plant with assorted Ayurvedic relevance. It has therapeutic application in Ayurvedic system of medicine (Purohit *et al.*, 1994). The species was first described from India in 1954 and reached rare status in nature due to over exploitation. The National Medicinal Plant Board (NMPB) of Government of India has recognized *Safed Musli* as sixth among the 28 selected priority medicinal plants to be protected and promoted. In India *C. borivilianum* is mainly distributed in Southern Rajasthan, North Gujarat and West Madhya Pradesh. The plants grow in a wide variety of places in nature, starting from open rocky places to shady and highly humus rich soil in the forest (Thakur *et al.*, 2009).

It is considered as an excellent herb to increase general body immunity. Its aphrodisiac properties have proved very much useful for the people suffering from Erectile Dysfunction and to increase male potency. It has spermatogenic property and helpful in curing impotency as they are rich in glycosides. Roots are widely used for various therapeutic applications in the Ayurvedic and Unani systems of medicine. It is known to cure many physical illness and weaknesses. It is also reported to cure diabetes, arthritis (Oudhia, 2001b). However, in recent years its effectiveness in increasing male potency has become very popular and is now considered as an alternative to ‘Viagra’ (Thakur *et al.*, 2009).

Saponins and therapeutic value of *C. borivilianum*

Among all the species of *Chlorophytum* present in India, *C. borivilianum* produces the maximum root tuber along with the highest saponin content (Attele *et al.*, 1999). Traditionally, roots of these species are reputed to possess various pharmacological utilities having saponins as one of the important phyto-chemical constituents (Marais and Reilly, 1978). Four new spirostane-type

saponins named borivilianosides E-H (1–4) were isolated from an ethanol extract of the roots of *C. borivilianum* together with two known steroidal saponins (5 and 6). The structures of 1–4 were elucidated using mainly 2D NMR spectroscopic techniques and mass spectrometry. The cytotoxicity of borivilianosides F (2), G (3), and H (4) and three known compounds were evaluated using two human colon cancer cell lines (HT-29 and HCT 116) (Acharya *et al.*, 2009). Compounds 1–4 had been isolated as white, amorphous powders. The sugars obtained by aqueous acid hydrolysis of each compound have been identified by comparison on TLC with authentic samples as glucose, galactose, xylose, arabinose, and rhamnose (in the case of 1 and 2), glucose and galactose (in the case of 3), and glucose, galactose, and xylose (in the case of 4) (Acharya *et al.*, 2009) [Fig 2(A, B)].

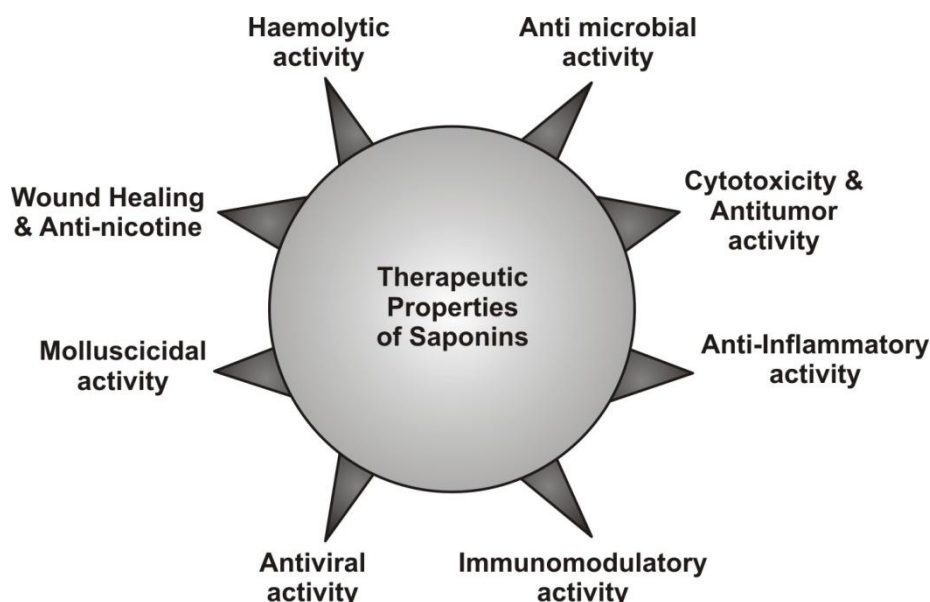
The plant yields a flavonone glycoside, which is a powerful uterine stimulant, steroidal saponins having muscle building properties and their structure is similar to male anabolic hormones testosterone. Roots of *Chlorophytum* contain 42% carbohydrate, 80–89% protein, 3–4% fiber and 2–17% saponin (Wagle *et al.*, 2000; Jat and Bordia, 2003). Apart from biologically effective steroidal and triterpenoidal saponins, sapogenins and fructans are reported to have prebiotic importance (Devon, 1975). The other phyto-constituents from the plant contain high quantities of simple sugars mainly sucrose, glucose, fructose, galactose, mannose and xylose (Sreevidya *et al.*, 2006). Proteins, phenolics, triterpenoids, gallo-tannins and mucilage have also been reported from *C. borivilianum* (Thakur and Dixit, 2005).

Several medicinally important attributes have been assigned to the plant because of its multi-pharmacological aspect which includes aphrodisiac, immuno-modulatory, anti-diabetic, antioxidant, anti-stress, antimicrobial, anti-aging, antitumor and anti-inflammatory activities (Jat and Bordia, 2003) (Fig 3). Aqueous extract of dried roots of *C. borivilianum* displayed enhanced sexual

behaviour with increased potential of spermatogenesis in albino rats (Kenjale *et al.*, 2008). The plant has also been acclaimed for its anti-diabetic activity against streptozotocin induced diabetes (Mujeeb *et al.*, 2009). The anti-hyperglycemic activity of the aqueous extract of *C. borivillianum* roots was comparable with glibenclamide, a standard hypoglycemic drug (Govindarajan *et al.*, 2005a; 2005b). The herb is found to be significantly effective in ameliorating the lipid metabolism in hyper-cholesteremic animals and the presence of fructans are reported to be the major contributing factor in better management of hypercholestramia (Sreevidya

et al., 2006; Visavadiya and Narsimhacharya, 2007; Kenjale *et al.*, 2007; Deore and Khadabadi, 2009a). It also increased the HDL-cholesterol levels having a protective role in cardiovascular diseases (Deore and Khadabadi, 2009a; Loo *et al.*, 2005). Tuber extracts of *C. borivillianum* have been proved as anti-stress agent (Loo *et al.*, 2005; Mimaki *et al.*, 1996; Deore and Khadabadi, 2009b). Their study is based on the traditional claim of utilization of this herb against rheumatoid arthritis (Panda *et al.*, 2007). This activity could in part be attributed to the steroidal components in the plant.

Fig. 3- Therapeutic applications of Saponins



***Chlorophytum arundinaceum* Baker.**

Chlorophytum arundinaceum (Asparagaceae) a tuberous angiosperm, commonly also taken as ‘Safed Musli’ is indigenous to India and distributed in Eastern Himalayas, Eastern Ghats, Assam, Bihar and Andhra Pradesh. Due to excessive harvesting and poor ways of germination and vegetative propagation, this plant is now standing between one of the endangered species of *Chlorophytum* (Samantaray and Maiti, 2011). It is a plant of repute as its fasciculated roots are reported to be used as a tonic and

constitute an important ingredient of more than 20 Ayurvedic and Unani preparations with active constituents, especially steroidal sapogenins known to possess adaptogenic and aphrodisiac attributes. Owing to its therapeutic properties, it has been exclusively cannibalized from its wild habitats. According to one survey, the species has been placed in the endangered category in Eastern Ghats of India and figures prominently among the rare medicinal herbs of India (Panda *et al.*, 2007).

The major reported constituents in the roots of *C. arundinaceum* include 4 hydroxy-8, 11 oxidoheniconesol and pentacosanol,

docosanoic acid, pentacosonyl docosanoate, n-nonacosane, tetracosanoic acid, stigmasterol and stigmasterol β -d-glucopyranoside. Arundinoside A and B have also been reported as major glycosidic portions from *C. arundinaceum*. Presence of such constituents as straight chain alcohols with tetrahydrofuran moiety in saponin containing drugs are a rarity (Sreevidya *et al.*, 2003; Tandon and Shukla, 1995).

Saponins and therapeutic value of *C. arundinaceum*

Compounds isolated and identified from *C. arundinaceum* are; nonacosane, tetracosanoic, triacontanoc, 4-hydroxyl- 8, 11-oxidoheneicosanol and pentacosyl docosanoate 2, 2', 4, 4'-tetrahydrobibenzyl xyloside and tokorogenin based saponin arundinoside-A (Tandon and Shukla, 1997); four sapogenins - stigmasterol, tigogenin, neogitogenin, and tokorogenin (Tandon and Shukla, 1992) and glucopyranoside from the fruits of *C. arundinaceum* (Tandon and Shukla 1993) [Fig 4(A)]. However, no reports are available on the pharmacological assays of the compounds isolated.

The tuberous roots of the plant are specially used for the treatment of rheumatism, antiulcer activity and strengthening of the gastric mucosal barrier (Jackson *et al.*, 1999). Moreover, its active constituents' especially steroidal sapogenins are known to possess adoptogenic and aphrodisiac attributes (Chopra *et al.*, 1956). The root extract is considered as a potent antioxidant as it could render effective protection against the hemolysis and disruption and stress induced elevated plasma corticosterone (Ghosal, 2006).

Chlorophytum malayense Ridl.

Chlorophytum malayense is another important plant group evaluated extensively for various medicinal properties. Chromalosite A, isolated from this plant, is reported as a major cytotoxic agent and is being explored for its

potential as an anticancer agent. *Chlorophytum malayense* is also known as spider lily plant.

Saponins and therapeutic value of *C. malayense*

C. malayense Ridl. is indigenous to south-east Asia and south-west of Yunnan province of China. Four steroidal saponins (1–4) were isolated from *C. malayense* rhizome. These Four saponins, termed as chloromalosite A, B, C and D (1–4,) [Fig. 4(B)] have neohecofenin and neotigogenin as the aglycone moiety with various substitutions of sugar moiety. Chloromalosite - A, C and D belong to 25 (S) spirostane series, while Chloromalosite-B (4) is found to be furostane type. Chloromalosite A (1), isolated as colorless needles, is also the major saponin of *C. malayense* with 0.49% yield while yield of compound 2, 3, and 4 was 0.025, 0.074, and 0.018%, respectively (Qui *et al.*, 2000). In a bioassay guided fractionation, compound 1 showed broad cytotoxicity against various human cancer cell lines (Qui *et al.*, 2000). The ED₅₀ values varied from 1.4 to 5⁻¹ g/ml to different cell lines indicating moderate toxicity when compared to positive control colchicine and ellipticine; while, other compounds are still to be investigated for their pharmacological activity. A new steroidal saponin named as chloromalosite E having neohecofenin as aglycone (5) has been isolated (Yang and Yang, 2000). So far, activity of this compound has not been tested.

Chlorophytum comosum (Thunb.) Jacques

Chlorophytum comosum is another medicinal plant which has got maximum demand and commercial value today. This plant is one of the fast growing ever green plants of *Chlorophytum* species reaching up to 1–1.5 ft tall with a spread of 2 feet, popularly growing for its attractive foliage. Some other common names for the plant are “Ribbon plant or Spider plant”. The plant is native to South Africa having the tendency to grow in dry and humid conditions (Kaushik, 2005). It also produces branched stolons with small white flowers and baby plantlets. It has fleshy

tuberous roots that store reserve food. These spider plants are excellent house plants or indoor plants as they are not only easy-growing plants but have air purifying abilities by cleansing electronic air pollutants emitted by artificial lighting especially formaldehyde and carbon monoxide. They are ideally able to tolerate artificial lighting very well with air purifying abilities in office environment where electronic pollutants are emitted (Charlton, 1990).

Saponins and therapeutic value of *Chlorophytum comosum*

Seven anti-tumour promoter crude steroidal saponins have been isolated by silicagel, reverse phase RP18, and Diaion HP-20 chromatography and by partitioning of methanol extract with n-butanol from this species (Mimaki *et al.*, 1996). Compound 6–9 are known spirostanol saponins while compound 10, 11 and 12 are new spirostanol pentaglycosides embracing b-D-apiofuranose. The saponins of *C. comosum* are different from saponins of *C. malayense* having aglycone based on (25R)-Spirostan series as tigogenin, gitogenin and hecogenin, while saponins of *C. malayense* are based on (25S) spirostan series as neotigogenin and neo-hecogenin. The isolated saponins have been evaluated for *in vitro* anti tumor promoter activity by measurement of the inhibitory activity on TPA stimulated 32P-incorporation into phospholipids of HeLa cells. Compounds 7, 8, 10, 11 and 12 are found cytotoxic to HeLa cells at 50 µg/ml concentrations (Mimaki *et al.*, 1996) [Fig. 4(C)]. Compounds 6 and 9 exhibited 23.1% at 57.8% inhibition at 50 µg/ml without cytotoxicity towards HeLa cells. However, more investigations are required against various other human cancer cell lines (Ahmad and Basha, 2007).

C. comosum is traditionally known to be used against bronchitis; however, the active principle responsible for the cure of bronchitis is yet to be investigated. In China, these species has been traditionally used as a folk

medicine for cough, fracture, burns and treatment of bronchitis. There are only few reports on the biological behavior of *C. comosum* and its specific component so far (Matsushita *et al.*, 2005).

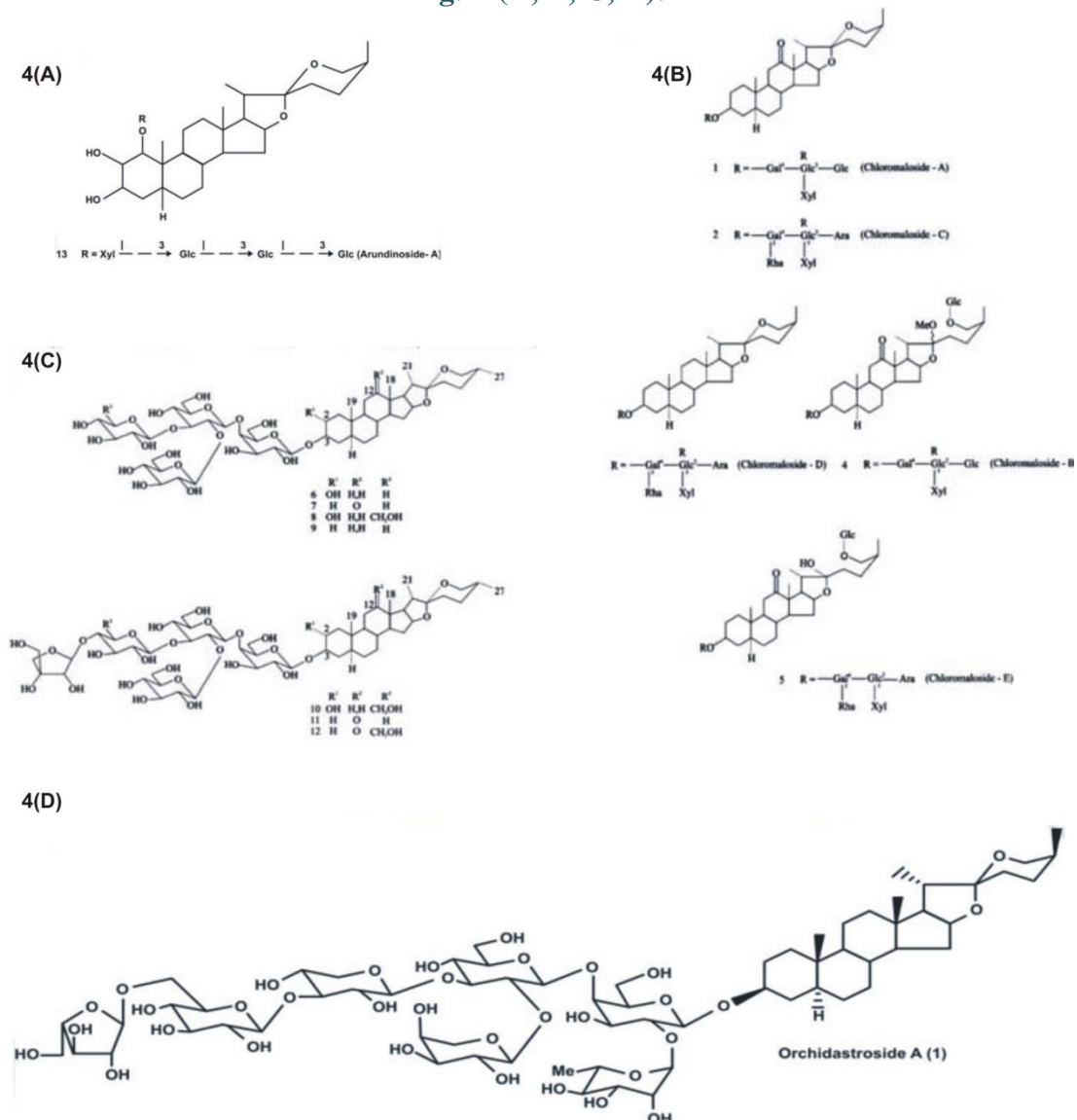
Chlorophytum orchidastrum Lindl.

The plant *Chlorophytum orchidastrum* can generally be seen growing on the mountain grassy slopes in India especially in the rainy season. As, like other *Chlorophytum* species, this plant also grows gaining its nutrition by tuberous roots. The tuberous roots are long, slender 15–34 cm long and each about 1 cm in diameter. This plant can be distinguished from other spider plants because of its different flower spike producing many fertile seeds. *C. orchidastrum* is found to have various nutritional properties along with immuno enhancing and hepato-protective properties (Nergard *et al.*, 2004; Patil and Deokule, 2010).

Saponins and therapeutic value of *Chlorophytum orchidastrum*

Six new spirostane-type saponins (1–6), named orchidastrosides A–F, and chloromaloside D were isolated from an ethanol extract of the roots of *Chlorophytum orchidastrum*. The saponins have neotigogenin or neogitogenin as the aglycon and oligosaccharidic chains possessing seven to nine sugar units. Their structures were elucidated mainly by 2D NMR spectroscopic analyses COSY (Correlation spectroscopy), TOCSY (Total correlation spectroscopy), NOESY (Nuclear overhauser effect spectroscopy), HSQC (Heteronuclear single-quantum correlation spectroscopy), HMBC (Heteronuclear multi-bond correlation spectroscopy) and FABMS (Fast atom bombardment mass spectroscopy) and HRESIMS (High resolution electron spray ionization mass spectroscopy) [Fig. 4(D)]. Compounds 1–6 were tested for cytotoxicity against two human colon cancer cell lines, HCT 116 and HT-29 (Acharya *et al.*, 2010).

Fig. 4-(A, B, C, D):



Saponins from different species of *Chlorophytum* (A) Structure of saponin from *C. arundinaceum*, (B) Structure of saponin from *C. malayense*, (C) Structure of saponin from *C. comosum*, (D) Structure of saponin from *C. orchidastrum*

CONCLUSION AND FUTURE PROSPECTS

Chlorophytum species grows wild in thick forests and are traditional medicinal plants. Because of its significant medicinal properties, some varieties got maximum demand and commercial value which is increasing day by day. There are around 256 varieties of *Chlorophytum* in the world; in India we have around 17 of them, of which, *C. borivilianum* has got a good market all over the world, especially in the Gulf countries and the West. Presently production is not even 5% of the

estimated demand because of its use in more than a hundred Ayurvedic, Allopathic, Homoeopathic and Unani medical preparations. Due to its vast demand its retail price in India is 1500 INR per Kg. or (US\$ 30) which is very high if compared to other plants with medical applications (Garima and Shruthi, 2012). The work on production of secondary metabolites and their pharmacological investigations should be on momentum by the pharmaceuticals and nutraceuticals sectors on *C. borivilianum* which can play a vital role in human welfare.

Saponins are found in wide varieties of foods such as asparagus, beans, blackberries, peas, potatoes, sugar beet and tea etc. The isolation, purification and formulations of the phytochemicals of this plant viz. steroidal saponins, β -sitosterol, stigmasterol and hecogenin, fructans and fructooligosaccharides which is reported for various therapeutic applications, viz. aphrodisiac, adaptogen, antidiabetic, antimicrobials, anti-inflammatory effective against lipid metabolism, analgesic etc, definitely provide effective drugs against these destructive diseases. Eventhough, a number of pharmacological studies have been performed, the phyto-chemistry of the tuber and leaf is not clearly understood. Similarly a major limitation in this species appears to be a poor knowledge about various physiological

and biochemical processes. Saponin from *Chlorophytum* is a hidden gift from nature which is now proving its efficacy and potential as a miracle herb for biopharmaceutical and neutraceutical attention for human welfare. It appears that there are still a number of biologically active compounds to be explored in this genus and the future research may be oriented in that direction along with evaluation of the remedial properties.

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