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Review Article

Plant Derived Novel Biomedicinal: Diosgenin

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ABSTRACT
Medicinal plants attain untapped prosperity of chemical compounds which make these plants as sources of useful biomedicinals. A biologically active steroidal phytochemical - Diosgenin is used as a preliminary intermediate for synthesis of steroidal compounds, oral contraceptives and sex hormones. On the basis of investigation it was revealed that diosgenin serves as a medicine useful for the treatment of different types of disorders in the future. In this current review, we have focused on the potential novel effects of diosgenin including chemistry, structure, its sources, uses, market demand, bioactive compounds derived from diosgenin and *in vitro* techniques for diosgenin production which could serve as a possible source for contribution in the modern system of herbal medicine.

Keywords: Biomedicinals, diosgenin, steroidal, *in vitro*, herbal medicine

INTRODUCTION

Plants have immense budding uses, especially as conventional medicine and pharmacopoeial drugs[1, 2]. Plant derived natural products include drugs such as alkaloids, colchicines, reserpine and steroids like diosgenin, digoxin and digitoxin. A diverse group of compounds widely distributed in the plant kingdom are saponins. A number of medicinally important steroids are synthesized from relatively cheap raw materials – sapogenins. These phytochemicals are consumer demand for natural products which are coupled with their physicochemical (surfactant) properties and mounting proof on their biological activity (such as anticancer and anticholesterol activity). This evidence has led to the emergence of saponins to exist as commercially noteworthy compounds with expanding applications in food, cosmetics, and pharmaceutical sectors. The structural diversity of sapogenins is reflected in their physicochemical and biological properties, which are exploited in a number of traditional and industrial applications [3]Research has established saponins as the active components in many herbal medicines[4]

Diosgenin, a steroidal sapogenin is a biologically active phytochemical responsible for various type of action in the plant including functional food[5]. In spite of the introduction of new precursors like solasodine, hecogenin and tigogenin for steroidal drug synthesis, diosgenin remains the major precursor. Biomedical study of bioactive biomedicals is a promising area of interest for the investigators throughout the world. One such novel bioactive compound is 'Diosgenin'., Although it is well known due to its versatility, but still it invites attention of researchers globally to explore its wide pharmacological activities . To the best of our knowledge, very little information is available on diosgenin as a novel bioactive biomedicinal. In this regard, the present investigation for the first time reviews to provide a comprehensive review of the novel effects of diosgenin including chemistry, structure, its sources, uses, market demand, bioactive compounds derived from diosgenin and *in vitro* techniques for diosgenin production that contributes its role as a beneficial phytochemical.

Background of Origin: A major bioactive constituent of various edible pulses and roots, well characterized in the seeds of fenugreek (*Trigonella foenum graecum* Linn) as well as in the root tubers of wild yams (*Dioscorea villosa* Linn) is diosgenin [6] Reference of diosgenin comes from the ethno botanical use of fenugreek seeds appears in the Egyptian Ebers papyrus (*c*. 1500 BC) as a medicine to induce childbirth. Greek physician *Hippocrates* (5th century BC) and *Dioscorides* (1st century AD) suggested its use in the treatment of gynaecological inflammation. Breakthrough of diosgenin has made it one of the most researched and studied herbal product [7]

Chemistry & Structure: Chemically diosgenin is a hydrolytic product of saponin – Dioscin. Structurally, diosgenin [(25*R*)-spirost-5-en-3b-ol] ($C_{27}H_{42}O_3$) is a spirostanol saponin with a molecular weight of 414.627. It consists of a hydrophilic sugar moiety linked to a hydrophobic steroid aglycone which belongs to triterpene group with a spiroketal side chain attached at positions 16 and 17 of the sterane along with double bond at 5-6. It has a hydroxyl group at 3rd position; hydroxyl groups are mostly found combined with sugars, making the compounds water soluble and highly saponaceous [8] (Figure 1).The chief active constituents of diosgenin are steroidal sapogenin constituting about 4 – 6 % and its glycosides smilagenin, epismilagenin and β – isomer yommogenin. It exists widely in the natural plant such as glucoside that is isolated from plants and is structurally similar to cholesterol.

World Wide Market For Diosgenin: The current world demand for diosgenin is approximately between 50,000

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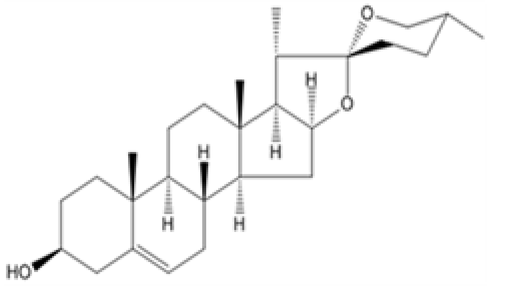

Fig 1: Structure of diosgenin

and 80,000 kg/annum. Out of the total steroid drug precursors, diosgenin accounts for 60% of the steroidal products of the world. Present world requirement of steroidal drugs for pharmaceuticals in terms of diosgenin is huge equivalent to about 10,000 tones of *Dioscorea* tubers per annum. It is estimated that about 60% of all steroidal drugs are derived from diosgenin. In India, commercial production of steroidal drugs by pharmaceutical industry is totally based on diosgenin which is about 450 tonnes[9]

Sources of Diosgenin: The richest source of diosgenin is *Dioscorea* species such as *Dioscorea nipponoca* Makino, *D .tokora, D .maxicana, D .spiculiflora, D .zingiberensis* (C.H.Wright), *D. villosa, D gracillima, D floribunda, D .compositae D.althaeoides, D.colletti.* In an extensive survey of nineteen different species of Indian *Dioscorea* plants Mirunalini and Shahira reported that *Dioscorea prazeri* (kokur torul) of Darjeeling and *Dioscorea deltoidea* (kins) of Kashmir are the rich sources of diosgenin.[10] While, Kambaska et al [11] investigated about twelve different species of *Dioscorea* found in different parts of Orissa. Other plant species containing diosgenin are *Smilax china* Linn, *Smilax bockii* Warb, *Solanum incanum*, *Solanum xanthocarpum, Aletris farinosa* and *Trigonella foenum* graecum *Trillium* [12, 13]. New Indian source for diosgenin are *Costus specious, Helicteres isora* [14 and 15]

Medicinal uses of diosgenin: Saponins have been successfully exploited in a number of commercial applications in food, cosmetics, agriculture and pharmaceutical sectors due to their diverse physicochemical and biological properties. Diosgenin is among the ten main important sources of steroids and is also the most often approved medicine of plant origin.

It plays an important role in cholesterol metabolism, variation in the lipoxygenase activity of human erythryoleukaemia cells responsible for morphological and biochemical variations in megakaryocyte cells [16]. Many health benefits are associated with diosgenin, for example, prevention against cardiovascular disease, colon cancer, and climacteric syndrome [17]. The aglycone is used for the industrial production of pharmaceutically important steroid drugs. The steroidal metabolite provides about 50 % of the raw material for the manufacture of oral contraceptives, sex hormones and other steroids and is a multibillion dollar industry [18]. Diosgenin is used to induce apoptosis in cancer cells and to reduce high blood pressure [19]. Recent studies have found that diosgenin has been used in traditional medicine as an antihypercholesterolemia, antihypertriacylglycerolimia, antidiabetic, antihyperglycemic agent and leukemia [20].Diosgenin has proved to be useful in the maintenance of healthy blood cholesterol levels along with the production of dehydroepiandrosterone Continued liberation of diosgenin has been able to significantly prevent bone loss to the same extent as that of estrogen [13]. The consumption of diosgenin has positive events on stress and inflammatory conditions [10]. Market trends showed increasing evidence of the use of natural ingredients for their biological activity and have increased the demand for saponins in recent years [21]. Due to their surface active properties, saponins are being utilized as natural surfactants in cleansing products as well as in cosmetics and in personal care sector such as shower gels, shampoos, foam baths, hair conditioners and lotions, liquid soaps, baby care products, mouth washes, and toothpastes [22]. Saponins and sapogenins are also marketed as bioactive ingredients in cosmetic formulations with claims to delay the aging process of the skin and prevent acne [23 and 24]. It has been used in traditional Chinese medicine for treatment of urethral and renal infections [12]. Diosgenin showed presumed ability to minimize post-menopausal symptoms [25]. Diosgenin is used as a good antispasmodic, that it can be used for cramps, coughs and for muscular spasms [10]

Bioactive Compounds Derived From Diosgenin: Plentiful bioactive compounds have been synthesized from diosgenin. A highly potent anticancer natural saponin, 22 – deoxy - OSW-1 and its analogue was synthesized by Jian et al by utilizing its intact skeleton [26]. This synthesized compound possessed 10-100 times more potent anticancer activity. From readily available diosgenin, Mickael et al [27] synthesized 16β-hydroxy-5α-cholestane-3, 6-dione, a metabolite derived from marine algae which is a potent oxysterol which exhibited a number of biological activities like inhibition of cellular proliferation and cytotoxicity associated with induction of apoptosis. Methyl protodioscin and polyhydroxysterol called Certonardosterol D2 as the potent anti - tumor agent has been synthesized stereo selectively from natural rich diosgenin [28 and 29]

In Vitro Production of Diosgenin: *Dioscorea* species are traditionally dominant source of diosgenin and related steroidal saponins[9].However, overexploitation owing to wide-ranging damage to the plant-rich habitat due to degradation, agriculture encroachments, urbanization etc has led to the rapid depletion of these species. *Dioscorea deltoidea*, the richest source of diosgenin has subsequently become an endangered species; therefore the supply of diosgenin cannot currently satisfy the demands of the ever-growing steroid industry. Nevertheless, the annual production of diosgenin is 30 ton which is well short of required (150 ton) and therefore

relies on production of new plant species, new production methods, including biotechnological approaches are being researched for diosgenin production which emphasizes the need to enhance diosgenin production which can be used as an alternative source for the synthesis of steroids [2 and 30]. .This has prompted industries, as well as scientists to

Table 6: *In vitro* production of diosgenin in plant tissue cultures in different plant species

Plant Species	Culture	Reference
Costus specious	Rhizome, Embryo, callus, shoot and suspension.	Roy and Pal [34]; Bakruddin and Kumar[35] ; Punyarani and Sharma;[36] Singh et al;[37]
Dioscorea deltoidea	Callus, Suspension.	Mulabagal and Tsay;[30] Neumann et al; [38] Ashwani Kumar and Sopory; [39]
Dioscorea doryophora	Suspension.	Mulabagal and Tsay; [30]
Dioscorea zingiberensis	Suspension.	Peiqin Li et al; [40]
Dioscorea floribunda	Suspension.	Debjani and Bratati; [41] and Yanxin et al; [42]
D. alata	Nodal segments.	Das et al; [43]
D. japonica	Shoot tips.	Kadota and Niimi;[44]
D. bulifera	Nodal segments and bulbils.	Narula et al; [45]
Helicteres isora	Callus, Hairy root.	Deshpande and Bhalsing; [15] and Shriram and Shitole; [46]and Kumar et al;[47]
Solanum xanthocarpum	Callus, Hairy root.	Khatodia et al; [48]
Solanum surattense	Callus.	Solouki et al; [49]
Tribulus Terresteris	Callus, Somatic embryogenesis.	Nikam et al;[50]
Trigonella foenum graecum	Callus, Suspension and Hairy root.	Oncina et al;[51]Binesh and Gnanam;[52] Sharareh; [16] Ashwani Kumar;[53]

consider the possibilities of investigation into cell cultures as an alternative supply for the production of plant pharmaceuticals. Therefore, it is crucial to search new and alternative sources of diosgenin and to develop strategies for enhanced production without harming the plant species[31]. Production of important bioactive biomedicinals by plant tissue culture technology has been the ultimate goal of tissue culture research. A large number of diosgenin containing plant species have been produced in plant tissue cultures, as summarized in Table – 6. Advances in biotechnology particularly methods for culturing plant cell cultures, should provide new means for the commercial processing of even rare plants and the chemicals they provide. *In vitro* cell culture of medicinal plants with enriched bioactive principles and cell culture methodologies for selective metabolite production is found to be highly useful for commercial production of medicinally important biomedicinals[32 and 33]

CONCLUSION

Many medicinal plants constitute a rich source of bioactive chemicals which are predominantly free from the adverse effects and have excellent pharmacological actions due to their therapeutic activities[54]. Hence, they could lead to the progress of new classes of possibly safer agents for the treatment of disease. Many bioactive biomedicinals are constituents of very complicated biosynthetic networks. Large-scale production of biomedicinals is possible by creating proper reactor design together with the achievement of genetic engineering. An extensive survey of literature revealed that diosgenin forms an important basis for many pharmacologically and naturally occurring medicinally important bioactive chemicals. The review provides significant information regarding chemistry, structure, its sources, uses, market demand, bioactive compounds derived from diosgenin and *in vitro* techniques for diosgenin production which can be useful for the researcher who is interesting in exploring the hidden potential of diosgenin. The combined information summarized in the appraisal will act as an important segment for development of effective medicines. More research work is needed in order to explore its new areas of application.

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CONFLICT OF INTEREST

The authors declare that they have no conflict of interest.

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