Ethnopharmacological Potential and Medicinal Uses of Miracle Herb *Dioscorea* spp.

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**ABSTRACT**

*Dioscorea* a well-known source of Diosgenin-steroid raw material, is one of the oldest tuber crop cultivated or harvested from wild in the tropical region throughout the world and make up one of the chief food items for a number of tribal groups. In India there are about 50 species of *dioscorea*, mainly found in North-East region which is rich in tropical root and tuber crops. *Dioscorea* produces rhizomes or bulbils, which are having rich medicinal and economic value. The rhizomes are used for the treatment of different diseases like cardiovascular system disorders, central nervous system disorders, disease of bones and joint metabolic disorder, digestive disorders, sore throat for struma, diarrhea, irritability, abdominal pain, dysfunctional changes in the female reproductive system, skin diseases, oncology and immune deficiency and autoimmune diseases, anti-diabetes, neuroprotective used, decrease oxidative stress and many more disordered conditions. Diosgenin is a precursor for the chemical synthesis of drug like steroids and has a great importance for pharmaceutical industry. *Dioscorea* contains various bioactive chemical substances like diosgenin, corticosterone, and sigmasterol, which are of great market value. The current study is to appraise the medicinal properties, phytochemicals, and pharmacological activities of *Dioscorea*.

**Keywords:** *Dioscorea*, chemical constituents, pharmacological activities.

**INTRODUCTION**

*Dioscorea* species is a climber herb with rhizomatous rootstock. It belongs to the family Dioscoreaceae. The genus *Dioscorea* belongs to division Monocotyledon comprises 350-400 species. Dioscorea is spread all over the tropics and subtropical regions in the world, 96% production occur in Africa. Other production centers are South America, the Caribbean islands and also found in South East Asia [1]. *Dioscorea* is a perennial plant, growing up to 3m (10 ft) in height. Rhizomes are ligneous asymmetrical, alternately arranged. Leaves are simple, 5-11.5cm long, 4-10.5cm broad, triangular ovate, often heart-shaped, 7-9 nerved, long pointed, both sides smooth and glabrous, petiole slender, 5-10cm long. Male flowers in leaves axils, simple or sometimes branched, slender, flexible, 7.5-25cm long. Flowers tiny, seceded in clusters; stamens 6, anthers inferior. Female flowers stalk solitary, slender upto15cm long. Underground rhizomes of *Dioscorea* commonly known as wild yam. *Dioscorea* has been observed of very high importance in private agencies as well as pharmaceutical firms, and the plant is mainly collected in India along with Himalaya [2, 3]. *Dioscorea* is endangered in natural habitats due to illicit use, spread of cities, and over-use by local peoples for trading and domestic purposes [4]. The species (deltoidea) is mainly found in India, China, Nepal, Bhutan, Pakistan, Afghanistan and Vietnam. In India the plant species are mostly distributed in Kashmir to Assam at altitudes of 550-3100m [5]. In Indian Himalayan regions, it is found in Arunanchal Pradesh, Sikkim, Assam, Meghalaya, Jammu and Kashmir, Himanchal Pradesh, and Uttarakhand [1]. This plant is special because its rhizomes contain Diosgenin, which is a phytoestrogen that convert into the hormone progesterone. Diosgenin is a basis for anti-inertility drugs such as contraceptive pills, and sex hormones, such as testosterone and supplements are used by body builders to increase their testosterone levels and build muscle strength. *Dioscorea* tubers are straight and zinger like shaped. The tubers Of *Dioscorea* are use in the management of a number of diseases such as gastrointestinal disorders, sour throat from struma, diarrhea, irritability, abdominal pain, wounds, burns and anemia. The tubers are also supposed to possess activities like antimicrobial, antioxidant, stomachic and hypoglycemic activities [6]. Besides it, *Dioscorea* is used extensively in the treatment of dysentery, piles and chronic liver pain disease [7].
active en is used for the target drug delivery system. Diosgenin is also investigated to show. Regarding this.

Figure 1: Some common Dioscorea species. (1) Leaves of D. pentaphylla (2) D. bulbifera (3) D. puber (4) Unequal round winged shaped Seeds of Dioscorea deltoidea (5) Leaves of D. puber (6) Tuber of different Dioscorea spp. (7) D. oppositifolia Flowers, (8) D. hispida Flowers and (9) D. alata.

Chemical constituents

Dioscorea rhizomes contain 75% of starch. They are non-edible, due to their very bitter taste. The main constituents of dioscorea are diosgenin, a steroidal sapogenin (4 to 6%) and its glycosides, Smilagenin and β-sapogenin (yamogenin). Rhizomes also contain an enzyme sapogenase. Tubers are also rich in glycosides, and phenolic compounds. Diosgenin is the hydrolytic product of saponin-dioscin [6]. Dioscin is made of two molecules of L-rhamnose and one molecule of D. glucose. Gracilin comprises two molecules of D. glucose and one molecule of L-rhamnose [6]. Ozo. et al [10] in 1985 reported flavonoid constituents Cyanidin-3-glucoside and the procyanidin dimers B-1 and B-3 in Dioscorea alata L. A report shows that Dioscorea also contains dioscin which exhibit carbonic anhydrase and trypsin inhibition activities [11, 12]. Other studies report the presence of saponins, alkaldoids, flavonoids, tannin, and phenols in Dioscorea belaphylly [12]. Also Yoon et al [13] in 2008 reported Allantoin, in Dioscorea rhizomes.

Table 1: Common bioactive compounds present in Dioscorea species.

| Compounds     | Uses                        | Species                              |
|---------------|-----------------------------|--------------------------------------|
| Diosgenin [14] | Raw material for steroidal drugs | Dioscorea deltoidea Wall. ex Griseb. |
| Sapogenin [15] | Reduce inflammation          | Dioscorea sp.                        |
| Saponin [16]  | Skin disease                 | Dioscorea sp.                        |
| Cyanidin [11] | Reducing trypsin level       | Dioscorea sp.                        |
| Flavonoids [12] | Antioxidant and skin disease | Dioscorea belaphylly (Prain) Voigt ex Haines |
| Allantoin [17] | As detoxifying agent for ammonia | Dioscorea sp.                        |
| Dioscorine [18] | For Birth control            | Dioscorea bulbifera L.               |
| Ohenolic compounds [19] | Skin Disease               | Dioscorea pentaphylly L.             |

Pharmacological Activity

Anticancer Activity

The treatment of cancer from steroidal compounds is becoming an attractive choice for medicinal chemists and many active molecules have shown this activity [20, 21]. Diosgenin is also investigated to show chemopreventive/therapeutic effect against cancers of several organs, and this has established the high importance of this molecule as a potential antitumor agent [22, 23]. Diosgenin has been tested for anticancer activity in various tumoural cell lines and it was found that the anticancer activity depends on the cell type and on concentration. Thus, diosgenin has antiproliferative activity, for various cancers namely, in prostate cancer (PC-3 and DU-145 cells) [24]. (Colon carcinoma (HCT-116 and HT-29 cells), erythroleukaemia (HEL cells), squamous carcinoma (A431, Hep2, and RPMI 2650 cells), hepatocellular carcinoma (HepG2 and HCC cells) [21, 25, 26] gastric cancer (BGC-823 cells), lung cancer (A549 cells) [27] breast cancer (MCF-7), and human chronic myeloid leukaemia (CML) (K562 cells) [18]. Regarding mechanism of action, many studies report that diosgenin is associated with a change of several cell signalling events which are necessary for cell growth/proliferation, differentiation, epithelial-mesenchymal transition migration, and apoptosis, as well as oncogenesis and angiogenesis [30]. Within the various phases of tumorigenesis, Diosgenin is believed to induce apoptotic cell death in various stages of tumorigenesis and thus avoiding their malignant transformation [29, 32]. The antitumor effects of diosgenin have been demonstrated, to occur through p53 activation, immune-modulation, cell cycle arrest, modulation of caspase-3 activity, and activation of the transcription STAT3 signalling pathway [21, 23, 25]. Regarding this perspective, studies have revealed that diosgenin inhibits the production of osteosarcoma cells through the induction of apoptosis and cell cycle arrest in G1 phase [31] and also inhibits the spread of breast cancer cells (MCF-7 cells) by inducing the proapoptotic p53 protein and an improve in caspase-3 levels [21, 32]. Besides it, the propagation of PC-3 human prostate cancer cells is repressed by diosgenin in a depending on the dose. Diosgenin also shows antitmetastatic effect by decreasing the cell migration and incursion by diminishing matrix metalloproteinase expression [24]. Diosgenin is studied to have antioxidant activity, due to which it constitutes an interesting approach for lung cancer therapy [27, 33]. The diosgenin-induced apoptosis of human erythroleukaemia cell line was associated with increase in number of receptors of Cyclooxygenase-2 [34].

Diosgenin also shows antitmetastatic effects in human breast cancer by inhibiting the movement of human breast cancer MDA-MB-231 cells, by partially decreasing Vav2 protein activity [25]. It has been reported that diosgenin reduces the VEGF expression in PC-3 cells, depending on dose, signifying this steroid can inhibit angiogenesis by interfering with this factor [34]. All of the above stated studies have revealed considerably the potential use of diosgenin as a new therapeutic agent against various types of cancer. Therefore, efforts are being made to use the potential of diosgenin as individual drug and with some other bioactive compounds in regulating development and propagation of various types of human tumours and in the study of its potential mechanism of action. An example of this type, the combination of diosgenin and thymoquinone was found to have antiproliferative and apoptotic effects on squamous cell carcinoma (SCC), in a synergistic way, and thus, it could be a novel strategy for the development of potential antineoplastic therapies against squamous cell carcinoma [36]. Diosgenin with other potential drugs tamoxifen is used for the target drug delivery system enclosed in manganese ferrite nanocarriers for enhancing the bioavailability and as a therapeutic tool against breast cancer [37, 38]. Li et al [39] prepared and evaluated diosgenin-polystyrene glycol conjugates as a potential drug delivery system for cancer therapy.

Anti-Infectious Activity

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Diosgenin was also examined for its anti-microbial effects, namely, against fungi, bacteria, protozoa, and virus. As for the human pathogens like Candida albicans, C. glabrata, and C. tropicalis, this steroid show weak antimicrobial activity against all the tested organisms [40, 41]. In addition the above organisms, diosgenin also has little to no effect against the fungi like Aspergillus flavus, Aspergillus niger, Trichoderma harzianum, and Fusarium oxysporum. On contrary to this, the sapogenin showed considerable vulnerability against various Gram-positive (Bacillus subtilis, Bacillus cereus, Staphylococcus aureus, and Staphylococcus epidermidis) and many Gram-negative (Escherichia coli and Salmonella typhi) pathogens [42]. Besides, diosgenin has the antiamebic activity against Naegleria fowleri trichozoiites at the cellular and molecular levels. Furthermore, it is less toxic to mammalian cells at therapeutic levels than that of amphotericin B, which is currently used to treat N. fowleri infections [43]. In addition, diosgenin shown to be effective in some viral diseases. Diosgenin due to its antioxidant activity can be useful in HIV patients with dementia [44]. Moreover, the steroid exhibits antiviral activity against Hepatitis C Virus (HCV) in invitro studies. Diosgenin acts by reducing plasma cholesterol and HCV requires cholesterol for an efficient multiplication that is this shows antiviral effect [45].

Anti-Inflammatory and Immunological Activity

The anti-inflammatory activity of Diosgenin is known to show anti-inflammatory activity however, the mechanism of action is yet uncertain. D.H.Jung et al. [46] studied that a diminution in the production of several inflammatory mediators, including NO and interleukins 1 and 6, in murine macrophages which had been pretreated with diosgenin and stimulated with lipopolysaccharide/interferon-γ. Moreover, a study in mouse was carried out in which it was evidenced that diosgenin has an inhibitory effect on the production of superoxide generation in bone marrow activated neutrophils and it was observed that this steroid exhibits antiviral activity against Hepatitis C Virus (HCV) in invitro studies. Diosgenin acts by reducing plasma cholesterol and HCV requires cholesterol for an efficient multiplication that is this shows antiviral effect [45].

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Effect on Cardiovascular System

Various studies indicated that, diosgenin has a considerable effect on lipid levels by reducing the level of total cholesterol (TC) in plasma and Low density lipoproteins (LDL) and increase the ratio of high density lipoproteins (HDL) to total cholesterol by decreasing cholesterol absorption and increasing cholesterol secretion [50]. Diosgenin is found to have concentration dependent vasorelaxation in superior mesenteric rings studied against phenylephrine as a standard. Diosgenin acts by increasing intracellular calcium concentrations in mesenteric endothelial cell loaded with FURA-2. Besides it, nitric oxide (NO) level is also increased by diosgenin [40]. Diosgenin was investigated for vasodilatory effect via porcine resistance left anterior descending coronary artery and it was found that diosgenin through protein kinase G signaling cascade and an opening of BK (Ca) channel of arterial smooth muscle cells caused an acute endothelium-independent coronary artery relaxation [61]. Diosgenin effects were examined in mouse by means of myography and confocal microscopy for contraction of smooth muscle cell and calcium signaling in isolated aorta. Diosgenin was also observed to have a potential therapeutic value for vascular disorders by inhibiting receptor-mediated calcium signals and smooth muscle contraction in the isolated aorta [54].

Effect on Blood System

Diosgenin was investigated to have anti-thrombosis effect in both invitro and in vivo studies by using thrombotic rat inferior vena cava and pulmonary thrombosis mice models, it resulted with repressed platelet accumulation, thrombosis and extended activated partial thromboplastin time (APTT), prothrombin time (PT) and thrombin time (TT) in the models depending on dose used. Anti-thrombotic effect of diosgenin is also demonstrated as it increases bleeding time and clotting time [63].

Effect on Central Nervous System

Effect of diosgenin on nervous system was investigated and is reported to have action on potential generation in human cortical neurons (HCN-1A) and big potassium (BK) channel activity improvement was also found. It also increased intracellular Ca2+ in human cortical neuronal-1A cells. HCN-1A cells contain alpha- subunit of BK (Ca) – channels seen by Western blotting technique. Therefore, diosgenin may have affect on the activity of cortical neurons by acting on these channels [64]. Further
a study, showed diosgenin significantly affect acetylcholinesterase (AchE) inhibitory activity [65].

**Effect on Reproductive System**

Diosgenin was investigated on ovariectomized rats and was found to show effect on the calpain isoform expression in ovariectomized rats. As compared to the normal controls expression of mu- or m-calpain was found to be reduced in the ovariectomized group [66]. Diosgenin was observed to considerably increase the mammary development scores, when studied for its effect on the growth of mammary epithelium for about fifteen days through factors of increase in DNA content, increase in number of ducts and appearance of terminal end buds. Diosgenin and estrogen when used concurrently, showed increase of estrogenic effect of diosgenin particularly at the higher dose level [67].

**Diosgenin as a raw material for steroid**

There is a three step efficient synthesis for the commercial production of 16-dehydropregnenolone acetate (16-DPA) which is a potent steroid drug intermediate obtained from diosgenin, in an overall yield of 60%. The steps are; acetylosis (isomerisation) of diosgenin to pseudodiogenin diacetate 4, Oxidation of pseudodiogenin diacetate 4 to Diosone 5, Hydrolytic degradation of Diosone 5 to 16-DPA 1 [68].

### Table 2: Ethnobotanical and medicinal uses of common Dioscorea species

| Botanical name                | Part of Plant | Ethno-botanical/medicinal use                                                                 |
|------------------------------|---------------|-----------------------------------------------------------------------------------------------|
| Dioscorea alata L.           | Tuber [69]    | Treatment of piles                                                                          |
|                              | Tuber [70]    | Reduce weakness                                                                             |
|                              | Tuber [71]    | Wormicide for stomach worms                                                                  |
| Dioscorea belophylla (Prain) Voigtex Haines | Tuber [72] | Taken with hot water is given for the treatment of fever, malaria, headache, and Dysentery |
| Dioscorea bulbifera L.       | Tuber [72]    | Appetizer.                                                                                  |
|                              | [74, 75, 76, 77] | Analgesic for labour pain, antacid, anti-inflammatory and for treating Dysmenorrheoa.         |
|                              | Leaves [78]   | Skin diseases.                                                                              |
|                              | Tubers [79]   | Analgesic for throat pain                                                                    |
|                              | Tubers [80]   | Antipyretic.                                                                                 |
|                              | Tubers [81]   | Treatment of boils and dysentery.                                                            |
|                              | Tubers [82]   | Antidiarrhoeal                                                                               |
|                              | Tubers [83]   | Cooling agent                                                                               |
|                              | Tubers [84]   | Treatment of skin infection                                                                  |
|                              | Tubers [85]   | Anticough and antiseptic                                                                     |
|                              | Tubers [86]   | Antaacid and ulcers treatment                                                                |
|                              | Stem [81]     | Antidandruff                                                                                |
|                              | Tubers [87]   | Taken with cow milk for the treatment of cough and Asthma.                                  |
|                              | Tubers [88]   | Treatment for typhoid when used with Curcuma aromatica                                       |
|                              | Tubers [89]   | Treat ulcer, piles, syphilis, and dysentery, and used to kill hair lice.                     |
|                              | Tubers [90]   | Used as contraceptive                                                                       |
|                              | Tubers [91]   | Treatment of abdominal pains. and ulcers                                                     |
|                              | Tubers [92]   | Used with salt to cure cough.                                                                |
| Dioscorea dumetorum (Kunth) Pax | Tuber [93] | Poison for arrow heads                                                                       |
| Botanical name               | Part of Plant  | Ethno-botanical/medicinal use                                                                 |
| Dioscorea esculenta (Lour.) Burkill | Tuber [94] | Used for treatment of jaundice                                                               |
|                              | Tuber [95]    | Analgesic for chest pain, anti-inflammatory                                                  |
|                              | Tuber [96]    | Treat boils, dysentery and swellings                                                         |
| Dioscorea hamiltonii Hook.f  | Tubers [97]   | Relieve stomach pain                                                                         |
|                              | Tubers [98]   | Appetizer                                                                                    |
|                              | Tubers [99]   | Refrigertant and Antidiarrhoeal                                                              |
| Dioscorea hirtiflora Benth   | Tubers [100]  | Used to cure gonorrhea                                                                       |
| Dioscorea hispida Dennst     | Tubers [101]  | Medicine for eyes                                                                            |
|                              | Tubers [102]  | Fish poison                                                                                  |
|                              | Tubers [103]  | Used to treat peeling out of skin                                                            |
|                              | Tubers [104]  | Antiemetic and purgative                                                                     |
|                              | Tubers [105]  | Used for healing wounds and injuries                                                          |
| Dioscorea kamoopenensis Kunth | Tuber [106] | Treatment of Rheumatoid arthritis                                                            |
| Dioscorea oppositifolia L.   | Tuber [107]   | Post pregnancy nutrition tonic                                                                |
|                              | Leaf [108]    | Taken with honey to increase sperm                                                            |

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CONCLUSION

The above study revealed that Dioscorea contains various phytochemicals such as Diosgenin, saponin, flavonoids, dioscorin and other important constituents. These chemicals have vast activities like anticancer, antimicrobial, cardiac activities, CNS effects and many more. For this reason, Dioscorea is a potential medicinal plant of interest in the treatment /prevention of several diseases. Diosgenin which is the most identified compound in Dioscorea species is a precursor of steroidal drugs as estrogen. Thus it can be said that Dioscorea is a packet which encloses medication for a number health conditions.

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