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A Review Paper on the Phytochemicals and Pharmacological Activity and Therapeutic Potential of *Dioscorea bulbifera roots*

Topinder Thakur[1*], Kiran Kumari[2], Abhishashi Sharma[3], Akanksha Sharma[4], Dr. Bhupendra Singh[5]

[1*] Student (Corresponding Author)
[2]Assistant Professor , M.Pharm Dept. of Pharmacognosy
[3]Assistant Professor, Dept. of Pharmacology
[4]Assistant Professor, M.Pharm Dept. of Pharmacognosy
[5]Professor, Dean of Pharmacy
Abhilashi University, Mandi, Himachal Pradesh, India

Abstract : *Dioscorea bulbifera L. (Dioscoreaceae) is extensively being used in African, Chinese and Indian traditional medicinal systems since ages. It is an ingredient in many herbal and Ayurvedic preparations that are used against various ailments. The current study is aimed to systematically review and document findings on ethnobotany, phytochemistry, pharmacology, nutritive value and toxicity of the herb. The study is intended to overcome the inconsistency between the traditional and pharmacological applications of the herb concerning its folkloric use and offer novel insights for future researchers. The literature was systematically collected from various offline and online sources using relevant keywords. Electronic databases including Google Scholar, PubMed, Science Direct, Springer Online, Research Gate, Scopus etc. were used to retrieve the relevant information. D. bulbifera L. is widespread in tropical and temperate regions of Asia, Africa and America. In traditional medicinal systems, it is used widely to cure sore throat, skin diseases, ulcers, boils, piles, pain, inflammation, dog bites, snake bites, food poisoning, asthma, cough, tuberculosis, cold, jaundice, malaria, typhoid of children, contraceptives, diabetes, ophthalmia, pink eye conjunctivitis etc. Among bioactive constituents, aglycone types of steroidal saponins dioscorin(e), dioscin(e), diosbulbin, and diosgenin possess significant biological activities. The chemical structures of the phytoconstituents presented in this review are drawn using ChemDraw Ultra software. The clinical studies included in this review have been performed to validate the folk usage of this herb. However, more studies are required to be done on scientific and clinical aspects to support its therapeutic applications. The updated information provided in this systematic review would open new perspectives for performing in-depth analysis of pharmacological research in future. The study would be useful for improving the clinical use of the herb and is surely going to bridge a gap between the traditional and modern use of scientific research for future researchers.*

Keywords: Ethnobotany, Phytochemistry, Pharmacology, Diosgenin, Saponins, Flavonoids

I. INTRODUCTION

Herbal medicines have played an important role in safeguarding health, preventing diseases, and ensuring the well-being of people since ages. They are preferably used in developing countries due to their rare or very less side effects and low cost as compared to the other conventional systems of medicine. As per a report of the World Health Organisation, 70 % of the world's population is dependent on traditional herbal care systems for curing various diseases and infections (World Health Organisation, 1999). The first report of Dioscorea bulbifera L. (Dioscoreaceae)

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in the world was recorded in the earliest known pharmacopoeia "Tang Bencao" (657-659 A.D.). It is most widely used in the African, Chinese and Indian systems of traditional medicine and is commonly known as air yam, aerial yam, bitter yam, cheeky yam, potato yam and parsnip yam. The diverse composition of the herb D. bulbifera L. makes it unique among 600 species of the family Dioscoreaceae. It is found in many regions of the world, which includes tropical region of Africa, Northern Australia, the Indian subcontinent, Florida of the United States, China, Cambodia, Thailand, Malaysia, and Laos (Coursey, 1967; Wilkin, 2001). D. bulbifera L. has served in traditional systems of medicine for ages due to the rich diversity of its phytochemicals. Ancient literature has reported the importance of its different parts, stem, tuber and leaves in traditional systems of medicine to treat several ailments such as cough, cold, dysentery, piles, ulcers, goitre, skin infections, orchitis, pharyngitis and cancer (Kundu et al., 2021). Additionally, it is also used to detoxify poison, clot blood to stop bleeding and is aphrodisiac. Roasted tubers of D. bulbifera L. are used to cure cough, dysentery, piles, ulcers, diabetics, leprosy and syphilis (Dutta, 2015). In sub-Saharan Africa, the tuber is eaten directly to cure cardiovascular * Corresponding author. disease (Odukoya et al., 2022). Meiteis, a dominant community of Manipur, a state in North-East India, utilises herbal medicines for curing various ailments closely related to their cultural and ritual practices. Examination of the ethnobotany of available plant species revealed that 96 % of the species were used as medicine (Khumbongmayum et al., 2005). The boiled tubers of D. bulbifera L. are consumed by local people to treat HIV patients in Uganda and raw bulbil is applied to cure ringworm in the Republic of Congo. Owing to its great traditional importance, it has gained prime attention of the scientific community to study it for remarkable scientific advancement in discovering new metabolites. In Chinese system of traditional medicine, it is used under the herbal name Huangdu and Huangyaozi and occurs naturally in the greater part of the Southern half of the country, namely, provinces of Henan,

Anhui, Jiangsu, Fujian, Guangdong, Guangxi, Shaanxi, Gansu, Sichuan, Guizhou, Yunnan, and Tibet (Guan et al., 2017). The Chinese use this plant to treat hemoptysis, epistaxis, pharyngitis, goitre, pyogenic skin infections, scrofula, trauma, orchitis and cancer. Likewise, it is extensively used in the Indian traditional systems of medicine for curing various ailments (Bhat et al., 2019; 2022). Various ayurvedic preparations made from D. bulbifera L. include Ajamamsa Rasayanam, Narasimha Churna, Pancha Nimbadi Churna, Vastyamayantaka Ghrita, Varahytadighurdam (Galani and Patel, 2017). In India it is called Varahi kanda or Kadu Kanda, Ratalu in Hindi; Potato Yam or Air potato in English; Varahikanda, Aluka or Shukara in Sanskrit and has been reported from various areas of Jammu and Kashmir, Odisha (Kumar et al., 2017), Rajasthan (Choudhary et al., 2008), Maharashtra, Assam (Kala et al., 2005), Andhra Pradesh, Uttrakhand etc. There are almost 53 million tribal people, inhabiting the Indian subcontinent, constituting 7.7 % of India's population. They belong to over 550 tribal communities of 227 ethnic groups. These tribes have developed a great deal of knowledge over the potential use of plants including their products, over the period. Various researchers have reported the therapeutic potential of D. bulbifera L. in anthelmintic, anti-insecticidal, aphrodisiac, diuretic properties, curing piles, syphilis, dysentery, ulcers, inflammation, diabetes, gonorrhoea, leprosy, rheumatic arthritis, etc. that confirms the folkloric usages of the plant (Bhat et al., 2022; Okari et al., 2023; Sharma et al., 2023). The species-specific phytochemistry of D. bulbifera L. makes it special among 600 species of Dioscorea. Primary phytoconstituents of D. bulbifera L. include carbohydrates, fibre, lipids, protein and moisture whereas, the secondary phytoconstituents include steroids, flavonoids, triterpenes, fatty acids, phenols, anthraquinones, volatile oils and tannins (Table 2). The most important bioactive constituents of D. bulbifera L. are flavonoids, clerodane diterpenoids and a few steroidal saponins (Ikiriza et al., 2019; Sun et al., 2021). Among steroidal saponins, dioscorin(e), dioscin(e), diosbulbin, diosgenin have been reported to contribute towards its activity (Dweck, 2009). Also, diosgenin is used in pharmaceutical industries as precursors in the synthesis of sex hormones, cardiotonic glucosides, fertility control compounds, corticosteroids and anabolic agents (Ghosh et al., 2015). A review of the traditional uses, phytochemistry and biological activities of D. bulbifera L. can better guide its rational use. Previously, many workers have reviewed the work on the ethnopharmacological importance of D. bulbifera, but only a few have elaborated its phytocomposition, toxicity and therapeutic potential. In this paper, in depth review of the folk usage, phytochemicals, their structures, and therapeutic potential concerning its folkloric use of D. bulbifera L. has been done.

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Previous review conducted on D. bulbifera L. was aimed to systematically review and document findings on ethnobotany, pharmacology and conservation needs of the herb (Kundu et al., 2021). However, the detailed analysis of botanical aspects, ethnobotany, pharmacology, phytochemistry of D. bulbifera along with the detailed chemical structures of its phytoconstituents, nutritive value and hepatotoxicity has been included in the current study. Scientific literature reporting the toxic effects of D. bulbifera L. and its phytocomponents, their effect on the metabolic profile of specific tissues, identification of biomarkers and metabolic pathways using different analytical platforms has also been provided in this review. The information provided would be valuable for improving its clinical uses and the development of new pharmaceuticals. This review is aimed to serve as a reference for subsequent in-depth understanding and better exploitation of the herb D. bulbifera L. Thus, this review is going to bridge a gap by providing a comprehensive knowledge of botanical aspects, ethnobotany, phytochemistry, pharmacology, nutritive value and toxicity of the herb which is intended to overcome inconsistency between the traditional and pharmacological applications of the herb and offer novel insights for future researchers.

II. RESEARCH METHODOLOGY

The published literature on D. bulbifera L. was collected from various offline and online sources. Electronic databases including Google Scholar, PubMed, Science Direct, Scopus were used to collect information. Keywords like "Dioscorea bulbifera", "Ethnobotany", "Distribution", "Taxonomy", "Phytochemistry", "Hepatotoxicity", and "Pharmacology" were used to get relevant information. The articles available from 1911 to 2023 were employed for the current study. A total of 166 papers from 1911 to 2023 were included in our review that focus on distribution, morphology, ethnobotany, ethnopharmacology, phytochemistry, pharmacology, toxicity and nutritive value of D. bulbifera L. Majority (82 %) of the papers were focused on traditional importance, phytochemistry and pharmacology of the herb. The remaining scientific studies were found on its toxicity and nutritive value. D. bulbifera L. Research articles/reviews from nine countries viz., India, China, Nigeria, Cameroon, Thailand, Malaysia, Bangladesh, Australia and America have been considered in this review and the maximum number of research
articles have been published from China (68) followed by 55 from India. Among various research papers available on the studies involving ethnobotany, ethnopharmacological and pharmacological analysis of various tissues of D. bulbifera L., only those research papers have been incorporated in the manuscript where the extracts or phytochemicals with low doses have been used along with proper control (positive and negative) for assays. Moreover, assays have been included that have a direct connection with claimed traditional usages. Most of the assays included in the review involve in vivo studies rather than preliminary screening. The data has been taken from authentic sources where the information has been collected by interacting with the tribal/local communities using the herb.

III. CLASSIFICATION AND DISTRIBUTION KINGDOM: PLANTAE

Phylum: Tracheophyta
Order: Dioscoreales
Class: Monocotyledons
Family: Dioscoreaceae
Genus: Dioscorea
Species: bulbifera

The genus Dioscorea belongs to the monocotyledonous family Dioscoreaceae and order Dioscoriales (Coursey, 1967). The family Dioscoreaceae includes more than six hundred species which are widely distributed in the tropical and temperate regions of Asia, Africa, and America (Sautour et al., 2007; Kundu et al., 2021). The members belonging to the genus Dioscorea are one of the oldest tuber crops harvested from the wild throughout the world. Among six hundred species in the family Dioscoreaceae, Dioscorea bulbifera L. has wide therapeutic applications in traditional medicineall over the world. It is widely distributed in tropical and temperate regions of Asia, Africa and America. Apart from South East Asia, West Africa and South and Central America, it also grows in Australia, Louisiana, Texas,

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Hawaii, Puerto Rico, Polynesia, and Florida (Khare, 2007; Galani and Patel, 2017). In India, it is widely distributed in the warmer parts ascending to the Himalayan regions. Its cultivation is done in some regions of Africa and India. In India, it is cultivated in the Kumaon region and Western Himalayas (Kumar et al., 2017).

IV. MORPHOLOGY

D. bulbifera is a perennial, creeping and climbing vine with vigorously twinning (counter clockwise) non-spiny stem (Fig. 1). It may reach upto the height of 5 m in height with the support of trees and shrubs (Kumar et al., 2012) and possesses shallow-fibrous root system. The leaves are alternate or rarely opposite with heart-shape and a pointed tip; suborbicular or broadly ovate; apex acuminate or shortly caudate; base deeply cordate; membranous; 911 ribbed and 1015£7.510 cm (Kumar et al., 2013; Galani and Patel, 2017). Veins radiating out from a single point of origin (where the petiole attaches leaf) divide leaves longitudinally into lobes. Two types of storage organs: tuber and bulbils are present (Fig. 1). Beneath the ground, usually a single, sub-globose tuber without a defined stalk is present whereas round bulbils are formed in the leaf axils of the twining stem. A tuber gives rise to a new tuber and generally shrivels away with the induction of re-growth (Kumar et al., 2017). The conspicuous aerial tubers known as bulbils are comparatively smaller than underground tubers and specifically adapted for vegetative propagation. They are of various shapes and sizes; generally, round to globose in shape, and pale brown. Numerous and prominent, uniformly distributed warts/eye-bud structures can be seen on small bulbils but they become smooth when large. It has been found that in certain cultigens the tuber is suppressed in favour of large bulbils that contain all the reserve food. The formation of bulbils is accelerated by the short-day length. Once the winters are over, resprouting from bulbils and tubers occurs and gives rise to a new aerial stem. D. bulbifera is very fast growing; it can colonise an entire forest in one season by reproducing vegetatively by bulbils and tubers and sexually by seeds (Galani and Patel, 2017) However, the species mainly reproduces by aerial tubers (bulbils). Seeds are produced in winged fruit which is dispersed by wind and water (Kumar et al., 2017). Fruiting occurs from December onwards and fruits are quadrately oblong and winged. The oblong capsules possess three wings that turn green to brown upon maturation. The capsules are 12-30 mm in length and 10-15 mm in width. A single capsule may have one or more dark brown coloured seeds. Flowering occurs during late summer and early autumn (September-November). Since, the species is dioecious, male and female flowers are borne on two different plants.



Fig. 1. Dioscorea bulbifera L. and its parts[A] Stem[B] Leaf.

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The male flowers are tiny in size, fragrant, pale green arising from the axils of the leaf and smaller in size and are borne in elongated, slender, drooping clusters (with length of 613 cm). The individual flowers are borne on very short stalks and clusters are being produced in each of the upper leaf forks. Each flower has six cream or greenish-coloured petals and six stamens. The petals may turn purple to brown colour on aging. Similarly, female flowers are also borne in an elongated, slender, drooping clusters (with length of 630 cm). They also have six greenish-white petals, six stamens (partially-formed), and an ovary with a twolobed stigma on the top (https://weeds.brisbane.qld.gov.au/ weeds/aerial-yam; Galani and Patel, 2017; Kumar et al., 2017).

Ethnobotanical uses of D. bulbifera L.

Traditional medicinal plants have been used since ages to cure various diseases and ailments. Among six hundred species of the family Dioscoreacea, D. bulbifera has gained importance in traditional medicine all over the world (Ghosh et al., 2015). Its unique phytochemistry has made it an immensely important medicinal plant in the Indian and Chinese systems of traditional medicine (Dutta, 2015). Ancient literature has reported the importance of its different parts, stem, tuber and leaves in traditional medicinal systems. In the

Indian and Chinese systems of traditional medicine, it is used widely to cure sore throat, ulcers, boils, piles, pain, inflammation etc. Apart from this, anticancer, antihelminthic, and anti-worm properties have also been demonstrated (Ghosh et al., 2011a, 2015). Various reports have validated the claimed traditional importance of various tissues of D. bulbifera L. in curing various ailments. The updated details have also been depicted in the table (Table 1) as compared to the previous reviews. In Chinese traditional medicinal systems, it is used as a remedy for sore throat and hepatic fibrosis by protecting the liver. Also, it is very interesting to note that it is used against dog bites, snake bites and food poisoning (Williams, 2013). In Bangladesh, it is used traditionally for the treatment of leprosy and tumours. In Zimbabwe, it is applied on cuts and sores. People of Cameroon and Madagascar use it for treatment of abscesses, boils as well as wound infections (Ghosh et al., 2014). In Java and Brazil, dried tuber is considered a remedy against dysentery and diarrhoea in addition to syphilis. In Congo, the sap of the stem is used as eye drops to treat purulent ophthalmia whereas in the Ivory Coast wakefulness of the eye is promoted by the stillation of leaf sap into the eye. People of East Africa use a potion made out of steamed leaves to treat pink eye conjunctivitis (Williams, 2013). Since its tuber is a rich source of phytochemicals, it has profound therapeutic importance. The extracts or decoctions of tubers are used as formulations in traditional medicinal systems. Various researchers have well documented and validated the claimed traditional usage of the herb, thus, providing a strong scientific rationale (Dweck, 2000; Sautour et al., 2007; Ghosh et al., 2015; Kumar et al., 2017). Powder made from dried tuber is mixed with water to make a paste and applied on the skin to cure various skin diseases (Burkill, 1911; Abhyankar and Upadhyay, 2011). It is highly recommended for treating diabetic disorders and obesity. Scanty reports available on the potential use of its tubers in diabetes mellitus and dyslipidemia have been supported by the work conducted by Chandra et al. (2012), Ghosh et al. (2014). Choudhary et al. (2008) conducted an ethnobotanical survey on the medicinal plants of Rajasthan (India) and found that the tribals use either the single herb or its mixture with other herbs in curing asthma, cough, tuberculosis, cold, and other respiratory disorders. It has also been reported to be used as a contraceptive herb. Another survey was conducted to find out information regarding the uses of traditional medicinal plants by the tribals of the Cachar district (Assam, India). It was found that these tribals use D. bulbifera herb as a remedy against various ailments like cough, cold, jaundice, fever, malaria, diarrhoea, dysentery, skin, and sexual diseases

(Das et al., 2008). Bulbils of D. bulbifera have also been reported to cure typhoid in children (Jain et al., 2008; Ghosh et al., 2015). The Apatani tribe of Arunachal Pradesh (India) traditionally uses tuber for indigestion (Kala, 2005). Exploration of the ethnobotany of the plant species used by the tribal communities inhabiting hilly areas of tehsil Akole of Ahmednagar (Maharashtra, India) revealed the nutritional and pharmacological importance of D. bulbifera (Khyade et al., 2009). Meiteis, a dominant community of Manipur, a state in North-East India utilises herbal medicines for curing various ailments which is embedded in their cultural and ritual practices. Examination of the ethnobotany of available plant species revealed that 96 % of the species were used as medicine (Khumbongmayum et al., 2005). Local communities of Similipal Biosphere Reserve (SBR), Odhisa, India have been reported to utilise 89 tuberous plants for

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traditional uses which also include Dioscorea sp. Among locals, the tubers of Dioscorea were found to be of maximum use, because of their pharmacological and neutraceutical importance (Kumar et al., 2017). The use of Dioscorea sp. including D. bulbifera, tubers by the ethnic communities of Assam in the treatment of various diseases and as a source of food has also been reported (Dutta, 2015). The data available on the traditional importance of D. bulbifera L. depicts that this tuber crop is a sound reservoir of therapeutic values. Various documented medicinal folk uses of the plant presented in the review provide ample scope to explore its pharmacological values and sustainability. This knowledge is notably going to excite us for further exploration and scientific documentation of its bioactive compounds and their pharmacological activity for formulation of new drugs. Further, this valuable information can be used by students, practitioners and researchers who are keenly interested in the development, evaluation, and use of herbal medicines. Although various polyherbal formulations containing this plant are available in the market, hardly any information is available regarding their clinical study, standardisation method to avoid biological and geographical to some extent, further scientific and clinical evaluations are required to be done to provide good remedies and help mankind with various ailments.

Chemical constituents variation and detoxication techniques. Since the plant is pre-clinically evaluated

The rhizomes of Dioscorea are 75% starch. Their very bitter flavor renders them inedible. The primary components of dioscorea are the steroidal sapogenin diosgenin (4–6%) and its glycosides, βisomer yammogenin and smilagenin. The sapogenase enzyme is also found in rhizomes.

Additionally, tubers are abundant in phenolic compounds and glycosides. Saponin-dioscin hydrolyzes to produce diosgenin.(11) Cyanidin-3glucoside and the procyanidin dimers B-1 and B-3 were identified as flavonoid components in Dioscorea alata L. in 1985. According to a paper, dioscorins found in Dioscorea also have the ability to block trypsin and carbonic anahydrase. (12) According to other research, Dioscorea belophylla contains phenols, tannin, alkaloids, flavonoids, and saponins . Additionally, Yoon et al. discovered allantoin in Dioscorea rhizomes in 2008.(13)

Table 1: Common bioactive compounds present in Dioscorea species.

COMPOUNDS	USES	SPECIES
Sapogenin(14)	lessen inflammation	Dioscorea spp.
Saponin(15)	Skin disorders	Dioscorea spp.
Cyanidin(12)	lowering the trypsin level	Dioscorea spp.
Flavonoids (13)	Skin disorders and antioxidants	Dioscorea belophylla (Prain) Voigt ex Haines
Allantoin(16)	In order to detoxify ammonia	Dioscorea spp.
Dioscorine(17)	for contraception	Dioscorea bulbifera L.
Phenolic compounds(18)	Skin disorders	Dioscorea pentaphylla L.

Literature Review

1. **Ghosh et al. (2015)** reported that Dioscorea bulbifera is a rich source of diosgenin which is an important precursor for steroidal hormones and corticosteroids.
2. **Sautour et al. (2007)** and Ikiriza et al. (2019) reported major bioactive constituents as flavonoids, clerodane diterpenoids and steroidal saponins including dioscin, diosbulbin and diosgenin.
3. **Kundu et al. (2021)** and Bhat et al. (2022) reviewed extensive traditional uses of stem, tuber and leaves for treatment of cough, piles, ulcer, dysentery, diabetes and cancer in Indian tribal systems.
4. **Galani and Patel (2017)** reported its importance in Ayurvedic formulations such as Ajamamsa Rasayanam and Narasimha Churna.
5. **Okari et al. (2023)** and Sharma et al. (2023) summarized pharmacological reports confirming anthelmintic,

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antidiabetic, anti-inflammatory, diuretic and anti-insecticidal activities.

6. **Dweck (2009)** emphasized the role of bioactive saponins and warned about toxicity of dioscorine and diosbulbin B which requires traditional detoxification processing before medicinal use.

Pharmacological Activity

Antidiabetic Activity - Potent alpha-glucosidase and alpha-amylase inhibition. Bulbil ethyl acetate fraction IC50 14.42 ug/mL better than acarbose. Mechanism via phenolics and saponins. Lowered blood glucose in STZ-induced diabetic rats at 200-400 mg/kg. High phenolic content
106.93 mg GAE/g responsible.

Analgesic, Anti-inflammatory, Antipyretic – Hydro methanolic extract 200-800 mg/kg showed significant analgesic activity in hot plate and tail flick, anti-inflammatory in carrageenan paw edema, antipyretic in yeast-induced pyrexia model in Wistar rats.

Antimicrobial & Wound Healing - Ethanolic tuber extract cream formulated. Showed strong antibacterial activity against S. aureus, P. acnes, E. coli, P.aeruginosa with ZOI 18-22 mm. Antifungal against Candida albicans. Promoted wound contraction.

Antitumor & Cytotoxic - Steroidal saponins and clerodane diterpenoids have anti-proliferative activity. Induced apoptosis, G2/M cell cycle arrest, ferroptosis in cancer cell lines via MAPK, PI3K/AKT, p53 pathways.

Anticancer - Papillary Thyroid Carcinoma - Molecular docking showed Diosbulbin B and diosgenin have binding affinity with PTC targets. Action via ferroptosis induction, PI3K/AKT pathway modulation.

Antioxidant Activity - Methanolic bulbil extract showed DPPH IC50 32.5 ug/mL, ABTS IC50
28.7 ug/mL, FRAP value high. Rich in flavonoids, phenolics. Nrf2 pathway activation. Reduced MDA, increased SOD, CAT, GSH.

Hepatotoxicity & Detoxification – Diosbulbin B-induced liver injury mechanism: CYP450 mediated activation, oxidative stress, NF-kB, NLRP3, ferroptosis. Paeoniflorin 60-120 mg/kg significantly reduced ALT, AST, protected liver. Traditional processing boiling, roasting reduces toxicity.

Immunomodulatory & Neuroprotective - Polysaccharides and saponins showed immunomodulatory via macrophage activation, IL-2, IFN-gamma upregulation. Diterpenoids showed neuroprotective by inhibiting neuroinflammation, improving memory.

Anti-arthritic & Anti-gout - Bulbil extract 100-400 mg/kg reduced uric acid levels, inhibited xanthine oxidase, reduced joint inflammation in gouty arthritis model via COX-2, LOX inhibition.

Cardioprotective & Antihyperlipidemic - Saponin rich fraction lowered total cholesterol, triglycerides, LDL, increased HDL in high-fat diet rats. Reduced cardiac markers CK-MB, LDH. Antioxidant effect on heart tissue.

Insecticidal & Pesticidal - Tuber powder and extracts showed larvicidal against Aedes aegypti, antifeedant against Spodoptera. Due to diosbulbin and saponins. LC50 45.2 ppm against mosquito larvae.

V. CONCLUSION

Dioscorea bulbifera has broad pharmacological activities: antidiabetic, anti-inflammatory, analgesic, antioxidant, antimicrobial, antitumor, immunomodulatory. Main constituents: diosgenin, diosbulbins, saponins, flavonoids, phenolics. Major limitation: dose-dependent hepatotoxicity. Future need: detoxified standardized extracts and clinical trials.

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