Pharmacogn J. 2025; 17(4): 520-530
A Multifaceted Journal in the field of Natural Products and Pharmacognosy
www.phcogj.com

Review Article

A Comprehensive Review on the Pharmacological Potential of *Dioscorea bulbifera* and its Potential Hepatotoxicity

Rudresh Adarkar[1], Chandrashekar K S[1]*, Vasudev Pai[1], Richard Lobo[1], Aswatharam H N, Vamshi Krishna Tippavajhala[2], Ullas Prakash D'Souza[3], Rajesh Kaverikana Shankara[3]

ABSTRACT

Dioscorea bulbifera, or the air potato has been studied and used in traditional medicine for centuries particularly in countries like China and India. It is loaded in different secondary metabolites such as steroidal saponins, flavonoids, diterpenoids, tannins, and carotenoids, which all play a major role in its pharmacological activities. Researchers have shown that it can be useful in the treatment of inflammation, microbial infections, oxidative stress, cancer, and liver diseases. even with these benefits there remains a shortage of clinical trials, toxicity assessment, and standardized extraction procedures to facilitate its application in herbal drug industry in a safe manner. One of the most striking features of *Dioscorea bulbifera* is its antimicrobial activity especially in the fight against antibiotic-resistant bacteria. also, studies done on anticancer activity are actively being conducted with some compounds being reported to induce apoptosis in cancer cells and suppress the growth of tumour. However, talking about its drawbacks some diterpenoid compounds such as diosbulbin A have been reported to show hepatotoxicity in humans and hence further studies are required to determine its safety for therapeutic purposes. The other significant challenge to developing this plant as a standard drug is its variability in chemical composition. The bioactive content is dependent on its cultivation, so it is quite a challenge to control for consistent potency. Sophisticated analytical methods such as HPLC and LC-MS could be utilized to overcome this and contemporary drug delivery systems like nano-formulations could enhance its absorption and bioavailability. Bringing together the ancient herbal knowledge and new scientific inquiry might reveal even greater therapeutic applications of the plant constituents. In the future the studies need to penetrate deeply into its safety, carry out extensive clinical trials, and explore sustainable mechanisms for mass-producing its major compounds. With additional studies, *Dioscorea bulbifera* could become a prominent natural medicine, providing solutions for numerous health conditions while maintaining its traditional medicinal significance.

Keywords: *Dioscorea bulbifera*, air potato, medicinal plants, bioactive compounds, antimicrobial, anticancer,

Rudresh Adarkar[1], Chandrashekar K S[1]*, Vasudev Pai[1], Richard Lobo[1], Aswatharam H N, Vamshi Krishna Tippavajhala[2], Ullas Prakash D'Souza[3], Rajesh Kaverikana Shankara[3]

[1]Department of Pharmacognosy, Manipal College of Pharmaceutical Sciences, Manipal Academy of Higher Education, Manipal-576104, Karnataka, INDIA.

[2]Department of Pharmaceutics, Manipal College of Pharmaceutical Sciences, Manipal Academy of Higher Education, Manipal-576104, Karnataka, INDIA.

[3]Department of Pharmacology, NGSM Institute of Pharmaceutical Sciences, NITTE (Deemed to be University, K S Hegde Medical Academy), Deralakatte, Mangaluru, Karnataka, INDIA – 575018.

Correspondence

K. S Chandrashekar

Department of Pharmacognosy, Manipal College of Pharmaceutical Sciences, Manipal Academy of Higher Education, Manipal-576104, Karnataka, INDIA.

E-mail: cks.bhat@manipal.edu

History

- Submission Date: 07-07-2025;
- Review completed: 12-08-2025;
- Accepted Date: 20-08-2025.

DOI : 10.5530/pj.2025.17.65

Article Available online

http://www.phcogj.com/v17/i4

INTRODUCTION

Man has relied on plants as long as human race traces back. Medicinal plants are the pioneer of the modern-day synthetic drugs. But the research gap in these so-called herbal drugs is so large that many pharmaceutical advances and ailments remedies are still under darkness the recent data from WHO shows that there around 21000 plant species are estimated for medicinal uses from which around 200-300 isolated compounds are used in our modern-day medicine. The world has about 374,000 known plant species according to Royal Botanic Gardens, Kew. Of these, only about 6% (21,000) are studied for medicinal use, leaving over 90% (350,000+) unexplored. So yes, it is not wrong to say there we are not even halfway there yet with all the modern research going on. technologies like AI & Omics Technologies use Computational biology and metabolomics to accelerate these drug discoveries. And yet still according to WHO worlds 80% of population is dependent on herbal drug.

Ethnopharmacology is another great method which has contributed to bringing these traditional folklore medications to light. ethnopharmacology revolves around traditional knowledge and practices observed across diversified cultures around the globe utilizing of medicinal plants. one such plant among them is *Dioscorea bulbifera* this plant is utilized in Chinese folklore medicine to cure various disease conditions *Dioscorea bulbifera*, commonly referred to as the air potato or bulbil-bearing yam, is a member of the Dioscoreaceae family with a history of being a traditional medicinal application across various cultures. The tubers and aerial bulbils of this plant have been widely utilized in folk medicine to address numerous health conditions. The growing acceptance of natural plant-based remedies has established medicinal plants as a crucial part of modern-day healthcare. In recent years, these botanical resources have played a significant role in the discovery and advancement of innovative therapeutic agents[1] bulbifera from Family Dioscoreaceae, commonly known as air yam or bitter yam, is a perennial climbing weed found in the tropical and subtropical areas of Asia and Africa. It is well known for its traditional uses for various ailments and its potential as a source of bioactive compounds. The distinctive or identifying feature of this plant is its large tuberous roots, which have been used as a staple food source and for medicinal applications, particularly in Southeast Asia. One of the unique properties of this species is its therapeutic properties, which have led to its increasing interest in modern pharmacognostics research.

Cite this article: Rudresh A, Chandrashekar K S, Vasudev P, Richard L, Aswatharam H N, Vamshi K T, Ullas P D'S, Rajesh K S. A Comprehensive Review on the Pharmacological Potential of *Dioscorea bulbifera* and its Potential Hepatotoxicity. Pharmacogn J. 2025;17(4): 520-530.

Dioscorea bulbifera has an abundance of many secondary metabolites, including alkaloids, flavonoids, saponins, glycosides, sterols, and essential oils, which yield to its divergent pharmacological activity. Among all the species, the most researched variety is D. bulbifera. This species has different chemical constituents, namely diosgenin, a steroidal saponin, and other sterol-containing compounds, which are believed to possess major therapeutic ability. Diosgenin particularly is known for its task as a precursor in the synthesis of many steroid hormones, making it a pivot in pharmacological study.

In the Chinese traditional medicine system, D. bulbifera has been used for years for its anti-inflammatory, analgesic, antidiabetic, antimicrobial, and anticancer activities. Various cultures around the world have engaged to treat various health conditions such as gastrointestinal disorders, wounds, infections, and reproductive health issues using the same. In the Indian traditional system of medicine, like Ayurveda, the tuber of D. bulbifera is used as a tonic, while in traditional Chinese medicine, it is believed to promote longevity and vitality

BIOLOGICAL SOURCE AND VERNACULAR NAMES

With 600 species, Dioscorea is one of the largest genera in the Dioscoreaceae family. It is primarily found in Asia, Africa, Central America, and South America's tropical and subtropical climates. Underground tubers or rhizomes of the Dioscorea species, usually referred to as yams worldwide, are a major food source for people living in tropical and subtropical areas with humid climates. It can grow in temperatures between 12°C and 38°C, although it grows best between 20°C and 30°C, reaching a length of roughly 10 meters. The simple, opposite, lobed, alternating leaves have a reticulate venation pattern and are around 20 cm long. The herbaceous stalks sprout from underground tubers[2]. It is fourth most consumed tuber crop after sweet potato, potato and cassava contributing about 10% of the world's root and tuber production[3-5].

CHEMICAL CONSTITUENTS

Research has shown that the concentration of phytoconstituents in Dioscorea bulbifera varies greatly depending on the country in which it is grown. These compounds include alkaloids, glycosides, proteins, fats, sterols, polyphenols, tannins, flavonoids, and saponins. The concentration of these compounds varies not only depending on the country of origin, but also on the life cycle of the entire plant. The concentration of alkaloids is higher in young tubers than in older, matured plants. Additionally, there are many inorganic compounds that are also reported to be present, such as iron (Fe), copper (Cu), zinc (Zn), manganese (Mn), cobalt (Co), vanadium (V), boron (B), chlorine (Cl), iodine (I), bromine (Br), and sodium (Na)[7-9]. In research that was conducted it was also reported that cooking the tubers changed the chemical constituent such that Uncooked tuber has higher moisture, ether extract, crude protein, and carbohydrate but lower ash and fiber than cooked tubers. Cooking increases moisture and carbohydrates while reducing other nutrients. uncooked tubers have higher carbohydrates (79.15-83.21%) and protein (9.27-5.55%) content than cooked tubers (78.82-82.26% and 5.95-3.41%), crashing white and water yams. Lipid content was found to be low but slightly higher than white yam fiber content significantly greater than polished rice and other root crops helping in better digestion. uncooked tubers were found to be richer in potassium and phosphorus,while cooked tubers had more calcium, magnesium, and sodium hence it was concluded that cooking reduced the mineral levels specifically magnesium in cooked tubers. Their high potassium-to-sodium ratio benefits hypertensive patients but is unsuitable for renal failure. Despite nutritional value, wild yams contain toxic anti-nutrients like alkaloids and saponins, requiring proper processing for safe consumption[6].

Phytoconstituents for medicinal uses secondary metabolites

Pharmacological actions of Dioscorea bulbifera

Antibacterial activity

The study by Victor Kuete et al. showed antibacterial action of Dioscorea bulbifera extracts fractions and isolated compounds against both strains Gram-positive and Gram-negative including the drug-resistant bacteria strains. methanolic and ethanolic extracts observed the most effective antibacterial potency, with MICs ranging from 8 to 64 µg/mL, indicating very high bacteriostatic effects. the derived isolated compounds diosbulbin A and other diterpenes showed antibacterial efficacy against specific bacterial strains such as Staphylococcus aureus and Escherichia coli. Similarly Sougata Ghosh et al. formulated silver nanoparticles (AgNPs) using Dioscorea bulbifera tuber extract and tested their antibacterial effects. In AgNPs it was observed that it show strong activity against both Gram-positive and Gram-negative bacteria including the drug-resistant strains. majorly when given in combination with antibiotics like ciprofloxacin and ampicillin, it significantly increased their effectiveness likely due to improvement in bacterial membrane disruption and drug uptake. This study highlights the potential of Dioscorea bulbifera-based AgNPs as natural enhancers for antimicrobial therapy[26]. Rémy Bertrand Teponno et al. found that Bafoudiosbulbins A and B, two natural compounds from Dioscorea bulbifera showed strong antibacterial activity against Salmonella, with MIC values between 4 and 16 µg/mL. Their activity was mainly due to the membrane disruption and metabolic interference making them suitable for fighting Salmonella infections naturally. In another study conducted by Rémy Bertrand Teponno et al. found that Bafoudiosbulbins A and B, two compounds from Dioscorea bulbifera inhibited Salmonella growth with MIC values between 4 and 16 µg/mL. Their antibacterial action likely comes from disrupting bacterial membranes and interfering with metabolism, suggesting they could be a natural way to help patients with Salmonella infections[27]. anti-bacterial resistance is a growing problem in todays world due to new and advanced strains of bacteria which makes it difficult for researchers to combat and meet the antibiotic demands of todays worlds in one study conducted by Varsha Shriram et al. it was noted that 8-epidiosbulbin E acetate compound found in Dioscorea bulbifera can be used to help antibiotic resistance in drug-resistant bacteria. alternatively of directly inhibiting bacterial growth it works by removing plasmids carrying resistance making antibiotics more effective. With MIC values ranging between 8 and 32 µg/mL, this compound shows a natural way to restore antibiotic sensitivity[28]. In another study which was focussed on peels of tubers it was seen by Omolade Mary Adeosun et al. that the antibacterial properties of Dioscorea bulbifera tuber and peel extracts against common pathogenic bacteria. The study found that both extracts exhibited broad-spectrum activity, with MIC values ranging from 10 to 100 µg/mL, and were effective against Staphylococcus aureus, Escherichia coli, and Pseudomonas aeruginosa(29). What makes this study different is that the comparative analysis of tuber and peel extracts showing that the peel extracts showed stronger antibacterial activity. This might suggests that antibacterial compounds are more concentrated in the peels the study also showed the presence of bioactive phytochemicals, reinforcing the tubers and peels' potential as natural antibacterial agents[30-35]

Antifungal activity

Adetoun Adeleye et al. found that dihydrodioscorine alkaloid extracted from a wild variety of Dioscorea bulbifera, has antifungal properties. This compound was helpfull against fungal strains like Candida albicans, Aspergillus niger, and Fusarium species with MIC values ranging from 5 to 25 µg/mL. What makes this study different is the

wild variety's enhanced antifungal activity compared to cultivated plants. This study also suggested that dihydrodioscorine could be a potential natural option for fighting fungal infections[36]. Another research also backed the data of phenanthrene derivatives found in Dioscorea spp Kum Eun-Joo et al. found that phenanthrene derivatives from the aerial parts of bulbils of Dioscorea batatas species have a very strong antifungal activity. These compounds exibited activity against fungal strains like Candida albicans and Aspergillus species, with MIC values between 10 and 40 μg/mL. The study suggested that these phenanthrene derivatives worked by disruption of fungal cells membranes suggesting their potential as natural treatments for fungal infections[37]. Also there was a study done on endophytic fungi found in Dioscorea bulbifera Kp S.et al. explored the antifungal properties of endophytic fungi found in Dioscorea bulbifera. They isolated nine fungal strains such as Aspergillus stellatus, Epicoccum nigrum, and Penicillium chrysogenum, and tested them against Candida albicans and Colletotrichum acutatum[38]. The study showed that the ethyl acetate extracts of these fungi had very strong antifungal effects with some of the fungal strains including Aspergillus stellatus and Epicoccum nigrum showing results stopping the growth of both pathogens[38-41].

Anticancer activity

Jun-Ming Wang et.al investigated the anticancer activity of Dioscorea bulbifera L. rhizome. In animal models, they found that tumour size and weight were decreased by the rhizome extract, exhibiting antitumor activity. The findings indicated that the extract functions by triggering cancer cell death, inhibiting the development of blood vessels to tumours, and enhancing the immune system to fight cancer. Significantly, the treatment was found to be nontoxic with no severe side effects. The research indicates the potential of the plant as a natural source of the development of new anticancer therapy, though more research is required to validate its efficacy in humans it was also mentioned that anticancer activity was dose dependent as it was observed at with 16 mg/kg sample of diosbulbin b it exhibited maximum anticancer activity by inhibiting the growth of tumour. Furthermore, research demonstrated that at anticancer-effect-producing doses, diosbulbin B of Dioscorea bulbifera rhizome did not affect serum markers for liver damage, such as ALT or AST. The low dosage levels which prevent liver toxicity may be one of the causes of the absence of liver damage by diosbulbin B. Thus, it can be said that diosbulbin could be utilized for clinical therapies at low concentrations provided the material is given in low amounts[42]. Another research by Huiyuan Gao et.al on Dioscorea bulbifera L. indicated its cancer-preventive activity. Researchers established that the ethyl acetate fraction of its rhizome extract were active in inhibiting tumour promotion in JB6 mouse epidermal cells. Key bioactive compounds like including diosbulbin B and several other flavonoids helped suppress oxidative stress, inflammation, and pro-tumor pathways like NF-κB and AP-1 while inducing apoptosis. Interestingly in this study it was observed that the flavonol aglycones were more potent than glycosides, and catechin outperformed epicatechin, highlighting the role of chemical structure in effectiveness. With low toxicity and strong antitumor properties this study gave insights about diosbulbin B along with flavonoids supressing cancer[43]. in another study conducted by Rashmi C et.al on Dioscorea bulbifera in breast cancer highlights diosbulbin B's binding affinity to estrogen, progesterone, Her2, and aromatase receptors. The hydroalcoholic extract reduced MDA-MB-231 cell viability in a time- and dose-dependent manner. It also lowered estrogen and progesterone levels in NMU-induced breast cancer, demonstrating its potential as a natural therapeutic agent. In major studies we found that diosbulbin b is main instigator compound in destroying cancer cells but its still controversial on what can the concentrated compound do to liver cells and its hepatotoxic drawbacks which will be discussed in article ahead[44]. Exploring more on cancer the most prevalent cancer in males' colorectal cancer with high fatality rate was also seen tackled by Dioscorea compounds in study by Ahmad Fadhlurrahman Ahmad Hidayat et.al on Dioscorea bulbifera (DBEAF fraction) in HCT116 colorectal carcinoma cells confirms its potent cytotoxicity (IC50: 37.91 ± 1.30 μg/mL). DBEAF induced apoptosis via mitochondrial depolarization, Bcl-2 regulation, caspase activation, PARP cleavage, and Fas-mediated death receptor signaling. It inhibited ERK1/2 while activating JNK, triggering both intrinsic and extrinsic apoptotic pathways. These findings highlight Dioscorea bulbifera as a promising candidate for colorectal cancer treatment. This study was particularly different because it gave the data about the whole extract and not just on isolated compound in another interesting study done by Hongxia Cui's investigated the combined effects of Dioscorea bulbifera polysaccharides (DBLP) and cyclophosphamide (CTX) in U14 cervical tumor-bearing mice. While CTX alone suppressed tumor growth (65.4% inhibition), DBLP alone also showed tumor inhibition (25.6% at 100 mg/kg, 37.6% at 150 mg/kg). The combination therapy further enhanced CTX's efficacy, increasing inhibition by 5.6% (100 mg/kg DBLP) and 9% (150 mg/kg DBLP). CTX-induced immunosuppression, oxidative stress, and organ toxicity were significantly attenuated by DBLP, which preserved thymus and spleen indices, regulated the CD4+/CD8+ T-cell ratio, and restored antioxidant enzyme activity. These findings suggested that DBLP can be used as adjuvant in chemotherapy[45]. In one study they explored another chemical constituent of diosbulbin family that is diosbulbin C Zhiyu Zhu et.al study explores Diosbulbin C, a diterpene lactone from Dioscorea bulbifera L., as a potential treatment for non-small cell lung cancer (NSCLC). Diosbulbin C significantly inhibits NSCLC cell proliferation by inducing G0/G1 phase cell cycle arrest, reducing clone formation, and suppressing DNA synthesis. Network pharmacology and molecular docking identified AKT1, DHFR, and TYMS as key targets. Diosbulbin C downregulates these molecules, disrupting cancer growth pathways. It also exhibits good drug-likeness, suggesting potential for drug development[46]. These findings highlight Diosbulbin C as a promising candidate for NSCLC therapy[47-55].

Anthelminthic activity

Helminthic disease conditions are result of parasitic worms and have been known to affect over a quarter of the world population predominantly increasing cases in developing countries with no proper access sanitation. These infections can be worsened to malnutrition, anaemia, and impaired cognitive development, especially in younger age groups. Dioscorea bulbifera with its bioactive compounds have shown very promising anti-parasitic properties making it a potential drug for combating helminthic diseases conditions. Helminth infections are prevalent in poor sanitation conditions Recent advances in helminth biology, including genomic studies, have identified new drug targets. Phytochemicals present in dioscorea bulbifera like diosbulbins and flavonoids show anthelmintic effects by destroying parasite metabolism and oxidative stress pathways. Research has shown its practicability in developing plant-based anthelmintic drugs making it a safer, cost-effective alternative to synthetic drugs while reducing drug resistance in helminthic infections. Ethnobotanical studies from Nigeria have shown us that Dioscorea bulbifera was traditionally used to treat parasitic infections potentially offering a natural alternative to combat resistance against synthetic anthelmintics. This study evaluated the methanolic extracts of D. bulbifera bulbils (flesh and peel) against Fasciola gigantica (liver fluke) and Pheretima posthuma (earthworm) at concentrations of 10–100 mg/mL. The peel extract has more potent activity inducing paralysis of worms in 5.6 min and death in 10 min at 100 mg/mL. The presence of phenolics like gallic acid and quercetin bioactive compounds may be responsible for the anthelmintic effects asking for further pharmacological investigation[56].

Antioxidant activity

Antioxidants are chemical compounds that will help our cells protect against damage that is caused by free radical damage. These free radicals are produced in the body due to byproducts of metabolism, pollution, UV radiation or stress. When these compounds accumulate in cells, they may cause oxidative stress which has been further linked to chronic conditions like cancer, heart disease, diabetes, and neurodegenerative conditions such as Alzheimer's. herbal antioxidants chemical compounds like polyphenols, flavonoids, and tannins play a important role in fighting against these free radical molecules. They may be used to help reduce inflammation, support the immune system, and slow down the aging process. Dioscorea bulbifera, used in traditional healing, has shown strong antioxidant properties making it a potentially a natural remedy for oxidative stress-related cell damage. The study conducted by Othuke Bensandy Odeghe et.al put light on the antioxidant related potential of Dioscorea bulbifera stem tuber confirming its bioactive properties relevant to traditional medicine. The methanolic extract exhibited free radical scavenging activity particularly against DPPH (69.39% inhibition), superoxide anion (52.86% inhibition), and nitric oxide radicals in a dose-dependent manner. Phytochemical analysis of drug showed the presence of phenolics (0.243 mg GAE), tannins (0.259 mg), flavonoids (0.060 mg QE), and flavanols (1.399 mg QE). The extract's activity was though slightly lower than standard antioxidants (ascorbic acid and quercetin) suggested therapeutic potential in oxidative stress-related diseases thus supporting its application in pharmaceuticals, nutraceuticals, and functional foods[57]. In a study that was conducted by M. Suriyavathana's the antioxidant potential of Dioscorea bulbifera was tested. using methanolic extracts standard antioxidant assays like DPPH, FRAP, and ABTS showed dose-dependent radical scavenging. The presence of phenolics, flavonoids, and tannins suggests its role in reducing oxidative stress in cells which has been linked to chronic diseases such as cancer, cardiovascular issues, and neurodegenerative disorders[58]. These results support the therapeutic value of D. bulbifera in preventing oxidative damage[59,60]

Antimalarial Potential

In today's world increasing cases of drug-resistant Plasmodium falciparum strains have emerged the search of new antimalarial agents derived from natural sources. A study done by Prapaporn Chaniad et al. investigated the antimalarial potential of compounds derived from Dioscorea bulbifera, showing that quercetin exhibited significant inhibition against both chloroquine-resistant (K1) and chloroquine-sensitive (3D7) strains. Molecular docking studies demonstrated very strong binding affinity of quercetin and other active compounds to Plasmodium falciparum lactate dehydrogenase (PfLDH), a important enzyme in parasite metabolism. The study also put light on low cytotoxicity of most compounds making them potential candidates for further drug development. These findings reinforce the traditional use of D. bulbifera in malaria treatment and provide valuable insights into its potential role in the discovery of novel antimalarial agents61.

Antidiabetic potential

Diabetes a chronic disease that affects millions globally affects quality of life and gets a person in constant fear Dioscorea bulbifera was observed to improve the profiles Zabeer et al. studied the antihyperglycemic and antidyslipidemic effects of the aqueous extract of Dioscorea bulbifera tubers (DBEA003) in glucose-primed and streptozotocin (STZ)-treated Wistar rats and high-fat diet-fed C57BL/6J mice. DBEA003 administered at 250, 500, and 1000 mg/kg for 3–7 weeks reduced blood glucose levels in diabetes induced rats and improved lipid profiles in dyslipidaemia mice. The extract also showed enhancement of body weight in severely diabetic rats and normalized serum glucose and lipid levels in high-fat diet-fed mice showing its potential in managing diabetes and dyslipidaemia. In another study done by Ghosh et al. investigated the antidiabetic potential of Dioscorea bulbifera, focusing on its ability to inhibit α-amylase and α-glucosidase which are said to be key enzymes in carbohydrate metabolism. The bulb extracts obtained through sequential and ethanol extraction showed powerful α-glucosidase inhibition, providing in vitro evidence of their potential to manage postprandial hyperglycaemia. This study highlights Dioscorea bulbifera as a promising natural therapeutic for type II diabetes but for its warranting further in vivo and clinical evaluation. Ghosh et al. also in another study studied the antidiabetic effects of Dioscorea bulbifera and its bioactive metabolite, diosgenin, as inhibitors of α-amylase and α-glucosidase. Ethyl acetate extract showed maximum enzyme inhibition (72.06% α-amylase, 82.64% α-glucosidase), GC-TOF-MS of which revealed maximum diosgenin content. Purified diosgenin compound showed uncompetitive inhibition decreasing the K_m and V_m, and fluorescence quenching experiments suggested evidence of binding to the enzyme. Molecular docking also demonstrated notable interaction with active site residues supporting that diosgenin might be a new lead compound for type II diabetes treatment needing further pharmacological investigation[62-64].

Anti-HIV potential (molecular docking)

Chaniad et al. studied the anti-HIV-1 integrase activity of compounds that were isolated from Dioscorea bulbils. Out of the seven compounds that were isolated from the ethyl acetate and water fractions myricetin was the compound which exhibited the strongest inhibition (IC_{50} = 3.15 mM). These compounds were followed by 2,4,6,7-tetrahydroxy-9,10-dihydrophenanthrene, quercetin-3-O-β-D-glucopyranoside, and quercetin-3-O-β-D-galactopyranoside. Molecular docking has revealed good interaction of these compounds with some key residues on the IN active site, such as Asp64, Thr66, and Glu152, which are important for the activity of the enzyme. This finding suggests *Dioscorea bulbifera*, and other natural sources could be a source for further anti-HIV therapeutic development, but in vitro and in vivo studies must be conducted[65].

Controversies regarding potential hepatotoxicity and ways to overcome them.

Clinical applications of Dioscorea bulbifera have been overshadowed by its hepatotoxicity drawbacks. More than 100 cases of liver injury have been documented as a result of D. bulbifera consumption in the past half-century witnessing the extent of this issue. The major malefactors of D. bulbifera hepatotoxicity are the Furano-diterpenoids, specifically diosbulbin B (DSB) and 8-epidiosbulbin E acetate (EEA). These compounds are bioactivated by cytochrome P450 enzymes, especially the P450 3A subfamily. Metabolism results in the generation of reactive intermediates, including cis-enedials, which covalently bind to nucleophilic functional groups on macromolecules such as proteins and DNA, leading to liver damage.

Observations have confirmed these undeniable findings. For example, mice injected with the ethyl acetate fraction of D. bulbifera rhizome showed elevated levels of serum biomarkers of liver injury like alanine transaminase (ALT) and aspartate transaminase (AST). Additionally, it was seen increased lipid peroxidation and decreased antioxidants like glutathione, along with reduced antioxidant defence-related enzymes, demonstrate that oxidative stress is a major factor in the hepatotoxic mechanism of D. bulbifera.

Given the hepatotoxic risks it is important to study methods to reduce or compleately mitigate the harmful effects of D. bulbifera Possible approaches for these include

Xiao-Rui Guan et al. carried out a systematic study on the bioactivity, toxicity, and mechanism of detoxification of D. bulbifera. They pointed

out that hepatotoxicity of the plant is due to some toxic molecules, mainly furanoditerpenoids diosbulbin B (DSB) and 8-epidiosbulbin E acetate (EEA). These molecules get activated metabolically in the liver by mainly being catalyzed by cytochrome P450 enzymes, thus giving rise to reactive intermediates. These intermediates have the capability to bind with essential biomolecules, like proteins and DNA, thus leading to liver injury[66].

Other studies by Hui Li and Ying Peng gave a more detailed description of how such toxic metabolites functioned. They discovered that DSB and EEA give rise to highly reactive intermediates such as cis-enedials, which disrupt the liver by breaking down cellular structures. This disruption of cells and oxidative stress are the foundation of the hepatotoxicity of D. bulbifera[67].

Interestingly, Junming Wang's research showed that susceptibility to liver damage depends on gender. Female mice, in comparison, suffered more damage to the liver. This can be explained in terms of enzymatic metabolism by their livers of poisonous compounds. This finding also suggests that inherent traits such as gender and gene pattern can make individuals increasingly susceptible to the toxic action of D. bulbifera[68].

Fan Yang's second work studied saponins extracted from D. bulbifera and found that they are also causative factors in liver injury. The compounds are held to be responsible for dysfunctional mitochondria and resulting cell death through the oxidative stress mechanism. Meanwhile, Rong Tan and colleagues confirmed that DSB is the main factor for D. bulbifera's toxicity. Rong Tan's group discovered that the compound inappropriately cross-links proteins so that liver function may be severely impaired[68.69]. Quality Control & Standardization: Maintaining stringent controls to manage the levels of toxic substances, particularly DSB, in D. bulbifera products. Such regulation of the toxins through the maintenance of monitoring and control can limit the hazards of liver damage.

Detoxification Techniques: The creation of efficient processing techniques aimed at eliminating or inactivating harmful constituents without losing the beneficial components of the plant. Conventional preparation techniques like soaking and boiling can decrease toxicity.

Pharmacokinetic Adjustments: Exploring the co-administration of drugs that possess the potential to inhibit the activation of toxic compounds or increase their detoxification mechanisms. Through exploring the metabolic processes that are involved in toxicity, scientists can render D. bulbifera non-toxic for therapeutic applications.

Alternative Therapies: Investigating other medicinal herbs with similar benefits and lower toxicity levels is important. Studies into safer herbal alternatives can stem dependence on D. bulbifera and hold associated risks.

Diosbulbin A and diosbulbin B are furan-fused diterpenoids extracted from the rhizomes of Dioscorea bulbifera L. Although both have the same structure, diosbulbin B was reported to be hepatotoxic, but diosbulbin A is much less toxic.

The primary distinction between these compounds is their metabolic activation. Diosbulbin B is metabolically activated by cytochrome P450 enzymes of the CYP3A subfamily to produce reactive metabolites. These metabolites have the potential to bind covalently to cellular proteins and DNA, which results in hepatocellular injury. In particular, diosbulbin B's furan ring is metabolized to a highly reactive cis-enedial intermediate that can bind to nucleophilic sites on macromolecules, thereby initiating liver injury (Table 1).

On the contrary, diosbulbin A is not metabolized to the same extent to form reactive intermediates and hence is less hepatotoxic. The difference in metabolism by the metabolizing system accounts for the disparity in toxicity of the two molecules.

Table 1. Biological source of Dioscorea bulbifera

Kingdom	Plantae
Subkingdom	Viridaeplantae
Superdivision	Streptophyta
Division	Tracheophyta
Class	Mangoliopsida
Superorder	Lilianae
Order	Dioscoreales
Family	Dioscoreaceae
Genus	Discorea L
Species	Dioscorea bulbifera

Table 2. Common names of the plant/ Synonym

Language	Name(s)
Bengali	Ratalu, Ban Alu
English	Potato Yam, Air Potato
Gujarati	Dukkarkanda
Hindi	Varahi Kanda, Kadu Kanda, Ratalu
Kannada	Kuntagenasu
Konkani	Karamdo
Malayalam	Pannikizhangu, Kattukachil
Marathi	Manakund, Kadu-karanda, Varahi
Oriya	Pita Alu
Sanskrit	Varahikanda, Aluka, Shukara
Tamil	Kodikilanga, Kaattu-k-kaay-valli
Telugu	Adavi Dumpa

Understanding these metabolic pathways is significant in the assessment of the safety of Dioscorea bulbifera L. and its constituents, especially in view of the hepatotoxicity risk of diosbulbin B[70-72].

Regulatory Problems in Herbal Drugs

Herbal medicines have serious regulation issues all over the world because they have a unique position at the crossroads between dietary supplements and drugs. The main issues are:

Ambiguous Categorization: Many countries have serious difficulties in clearly classifying herbal products as either dietary supplements or drugs, thus making it more difficult to regulate them. For instance, in the United States, herbal products are generally being sold as dietary supplements, which are exempted from pre-market approval for safety or efficacy before they can be introduced to the market[73]. In contrast, in the European Union and most of the Asian countries, the same products become regulated under stricter controls reserved for medicinal products. There is no international standardized system for herbal medicine. While some countries have established national laws and regulations, others do not have complete legislative systems in place, which has led to inconsistency in standards in terms of quality, safety, and efficacy[74].

Quality Control: It is difficult to provide high-quality, pure, and consistent herbal product standards because they vary batch to batch and are prone to contamination with heavy metals, pesticides, or microbial impurities[75].

A number of reasons are responsible for the weak quality of the evidence base for most herbal medicines:

Lack of clinical evidence: The majority of investigations of herbal medicines are preclinical, i.e., laboratory or animal studies. There are few well-designed human randomized controlled trials (RCTs). Due to this absence, it's difficult to define some safety and efficacy profiles for the majority of herbal preparations[76,77].

Table 3. List of chemical constituents found in the plant with its pharmacological actions

Phytoconstituent Class	Specific Compounds	Pharmacological Uses	Reference
Steroidal Saponins	Dioscoreanoside A, B, C, D, E, F, G, H, I, J, K	Anti-inflammatory, anticancer, hepatoprotective, antioxidant	-7
Steroidal Sapogenins	Diosbulbisin A, B, C, D	Precursor for steroids, anti-inflammatory, antifungal	(8,9)
Spirostane Glycosides	Diosbulbisides A, B	Cardioprotective, antioxidant, anti-diabetic	(10,11)
Cholestane Glycosides	Diosbulbiside C	Cholesterol-lowering, antimicrobial	-12
Norclerodane Diterpenoids	Diosbulbin A, B, C, D, E, F, G, H, I, J, K, L, M, N, O, P	Hepatotoxic & hepatoprotective effects, anticancer, anti-inflammatory	-13
Clerodane Diterpenoids	Bafoudiosbulbin A, B, C, F, G	Antitumor, antibacterial	(13,14)
Flavonoid Derivatives	Quercetin, Isoquercitrin, Myricetin, Kaempferol, Hyperoside, Caryatin	Antioxidant, anti-inflammatory, neuroprotective, cardioprotective	-15
Phenanthrenes	2,7-Dihydroxy-4-methoxyphenanthrene, Diosbulbinone	Anti-inflammatory, antimicrobial, anticancer	-16
Carotenoids	Neoxanthin, Auroxanthin, Violaxanthin, Cryptoxanthine, Lutein, Zeaxanthin	Eye health, antioxidant, immunomodulatory	(17,18)
Volatile Oils	Vanillic acid, Isovanillic acid	Anti-inflammatory, antimicrobial, analgesic	(19,20)
Tannins	Catechin, Epicatechin, Protocatechuic acid	Antioxidant, antibacterial, anti-diabetic	-21
Phytosterols	Stigmasterol, β-Sitosterol, Daucosterol	Cholesterol-lowering, anti-inflammatory, anticancer	-22
Fatty Acids	Succinic acid, Shikimic acid, Palmitic acid, Behenic acid, etc.	Energy metabolism, anti-inflammatory, skin health	-23
Glycoside Derivatives	Pennogenin, Spiroconazol A, Diosbulbinoside D, F, G	Anti-inflammatory, neuroprotective, antimicrobial	(24,25)
Others	Batatasin III, Diarylheptanone, Allantoin, Tristin, Docosyl ferulate	Wound healing, anti-inflammatory, anticancer	(10,21)

Issues with the Methodology

Standardization issues are due to the inconsistency of herbal products, which make it difficult to prepare clinical trials to have dosing and active ingredient consistency between studies[78].

Designing herbal placebos poses significant challenges, as achieving identical appearance, aroma, and flavour to the actual product proves to be quite difficult[79,80].

Patient randomization and choice: Most of the studies lack adequate randomization and sample size, and the results are, therefore, not as statistically robust and reliable (Table 2).

Economic Aspects and Means: The clinical trials associated with herbal medicine are extremely expensive and tend not to be funded by the industry, particularly for simple or traditional preparations which are unpatentable[79].

The Significance of Good Manufacturing Practice (GMP) in Standardizing Herbs

In order to make herbal products safe, effective, and of good quality, GMP must be adhered to:

Standardization and Quality Control:

To minimize batch-to-batch variation and provide equal quantities of active ingredients, GMP standards recommend standard methods, strict quality control, and proper documentation (Table 3).

Major bioactive markers are determined and measured by methods like spectroscopy, GC, and HPLC, which help in keeping the product homogeneous.

Procurement of Raw Materials: GMP asserts that to prevent contamination and blending, raw herbal materials must be properly selected and authenticated.

Manufacturing Environment: Equipment should be designed and kept clean to prevent cross-contamination and ensure cleanliness in the manufacturing process.

Traceability and Documentation: Traceability and accountability rely on proper records of raw materials, manufacturing processes, quality control tests, and deviations.

Regulation Compliance: GMP compliance allows herbal manufacturers to abide by national and global regulations to safeguard consumer health[81]

Importance of Targeted Delivery Systems in the Context of *Dioscorea bulbifera*

Enhancing Efficacy:

Dioscorea bulbifera is rich in a broad range of bioactive phytochemicals—like flavonoids, saponins, and alkaloids having favorable pharmacological activities like anticancer, antimicrobial, and antioxidant effects. The clinical efficacy of these effects is compromised owing to poor absorption, high rate of metabolism, and low systemic bioavailability. Targeted delivery systems provide a means of overcoming these drawbacks by providing selective deposition of active ingredients at the desired site of action, thus improving the therapeutic response (Table 4).

Minimizing Hepatotoxicity:

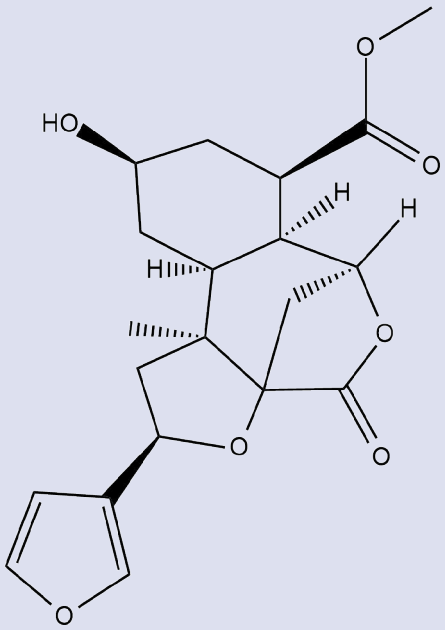
One of the main issues with D. bulbifera is the furanoditerpenoids (such as diosbulbin B), which are dose-dependent hepatotoxicants. With the use of targeted delivery systems, it could potentially lower systemic exposure and circumvent hepatic metabolism, thus lowering liver toxicity while maintaining pharmacological effects.

Breaking Biological Barriers

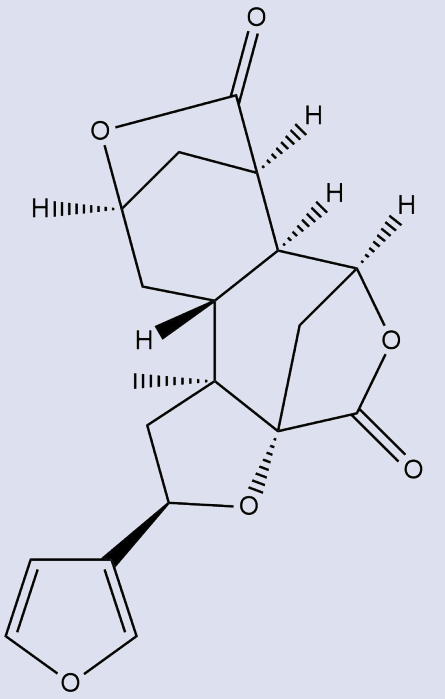
Some components of D. bulbifera could struggle to cross physiological barriers, including the gastrointestinal tract or blood-brain barrier, thus constraining their clinical potential. New delivery systems, particularly nanotechnology-based systems, can help carry drugs across such barriers, enhancing drug action and delivery.

Enhancing Consistency and Dosage Precision

Because of inconsistencies in plant cultivation, harvesting, and extraction, herbal products tend to be inconsistent in composition. Targeted delivery and encapsulation strategies can standardize the delivery of active ingredients to produce reproducible pharmacokinetics and therapeutic outcomes (Figure 1).



DIOSBULBIN A



DIOSBULBIN B

Figure 1. Structural differentiation of Diosbulbin A and Diosbulbin B

Examples of Targeted Delivery Methods Applicable to Dioscorea bulbifera

Nanoformulations: Nanoparticles, nanoemulsions, and liposomes have been investigated for phytochemical encapsulation. For D. bulbifera, these systems could enhance solubility, stability, and bioavailability, with hepatotoxicity reduction through controlled release. **Encapsulation in Biodegradable Polymers:** Methods such as polymeric micelles or hydrogels can offer sustained and localized release, beneficial for chronic diseases like cancer or inflammatory disorders.

Ligand-Targeted Delivery: Attachment of ligands (e.g., folate, antibodies, peptides) onto delivery carriers can target D. bulbifera phytoconstituents to specific organs such as tumors or sites of infection, possibly increasing therapeutic index and minimizing off-target effects.

Minimizing Hepatotoxicity: Delivery systems able to bypass hepatic flow or selectively target non-hepatic tissues could decrease risks related to toxic agents such as diosbulbin B. Improved Anticancer Potential: Various studies indicate anticancer activities of D. bulbifera extracts. Targeted delivery would improve drug accumulation in tumor tissues, increasing cytotoxicity while minimizing damage to normal tissues.

Increased Antimicrobial Efficacy: Drug formulations that facilitate localized delivery to infected tissues would enable sustained effective levels of antimicrobial agents, potentially combating resistant pathogens.

CONCLUSION

Dioscorea bulbifera or air potato or bulbil-producing yam has been used in medicine across many cultures for centuries, particularly in Chinese and Indian medicine. Dioscorea bulbifera is rich in phytochemicals such as steroidal saponins, flavonoids, diterpenoids, tannins, and carotenoids and has demonstrated an extensive range of pharmacological effects and is a prolific field of inquiry in contemporary pharmacognostic science. Several studies across history have established its medicinal activity, such as anti-inflammatory, antimicrobial, antioxidant, anticancer, and hepatoprotective activity. Notwithstanding these studies establishing the therapeutic application of Dioscorea bulbifera, much research gap remains to be bridged, particularly in clinical validation, toxicity evaluation, and standardization of bioactive fractions for pharmaceutical applications.

One of the most striking attributes of Dioscorea bulbifera is that it has a high secondary metabolite content, which is responsible for its extensive spectrum of pharmacological activities. The presence of steroidal saponins such as diosgenin and dioscoreanosides has made it a vital source for steroid hormone synthesis. These kinds of molecules are of great importance in anti-inflammatory and anticancer therapies and are lead molecule candidates for pharmacological discovery. Flavonoids such as quercetin, kaempferol, and myricetin are also responsible for its strong antioxidant and cardioprotective activity. Presence of diterpenoids such as norclerodane and clerodane derivatives is also responsible for its medicinal value, with studies proving antimicrobial, hepatoprotective, and cytotoxic activity.

The antimicrobial potential of the plant has been the area of focus, particularly in the case of antibiotic resistance. A number of studies have established that methanolic and ethanolic extracts of Dioscorea bulbifera have high antibacterial activity against Gram-positive and Gram-negative bacteria, including resistant species like Staphylococcus aureus and Escherichia coli. Interestingly, silver nanoparticles that has been synthesized through Dioscorea bulbifera extracts have been shown to exhibit better antibacterial activity when applied in combination with conventional antibiotics which gives the way for natural adjuvants in antimicrobial treatment. Phenanthrene derivatives

and diterpenoids of the plant have also been shown to exhibit high antibacterial and antifungal activity, further supporting its potential as a natural antimicrobial.

In addition to its antimicrobial effect, Dioscorea bulbifera also showed important anticancer activity. Its bioactive compounds, particularly steroidal saponins and diterpenoids, were reported to induce apoptosis and inhibit cancer cell proliferation in various models of cancers. Diosbulbin derivatives, for instance, showed cytotoxicity against hepatocellular cancer, leukemia, and breast cancer cells and thereby proved to be new anticancer drugs with potential. Some of the diterpenoid molecules, however, such as diosbulbin A, were reported to be hepatotoxic, a factor that qualifies them for safe therapeutic use. Additional research is therefore required to purify the useful molecules with low toxicity by structural modification and targeted drug delivery systems.

Despite promising pharmacology of Dioscorea bulbifera toxicology still remains major limitation. Various reports have shown hepatotoxicity and nephrotoxicity following chronic consumption of raw tubers. The toxicity is primarily attributed to the presence of certain diterpenoid compounds which induces oxidative stress and mitochondrial injury in hepatocytes. Detoxification by boiling or fermentation has been shown to reduce tuber toxicity, but these methods are not scientifically validated. Future research should be focussed on finding the precise mechanisms of toxicity, refining detoxification protocols and developing standardized extracts of improved safety profile.

Another critical area to be tackled is standardization and formulation of Dioscorea bulbifera extracts for pharmaceutical applications. While the medicinal activity of the plant has been well studied in vitro and in animal models, clinical trials are scarce. Phytochemical heterogeneity due to geographical and climatic differences is the cause of the problem in its standardization methods such as HPLC and LC-MS can help in accurate quantitative analysis of bioactive compounds of the drug allowing for uniform herbal formulation. Drug delivery systems such as nano-formulations and encapsulation processes can enhance the bioavailability and pharmacological activity of Dioscorea bulbifera-derived compounds making them suitable.

From an ethnobotanical perspective Dioscorea bulbifera continues to be a key plant in traditional medicine. Its ability to be used in Ayurvedic medicine in the treatment of gastrointestinal conditions, wound healing, and reproductive health confirms its traditional importance. However, with traditional medicine increasingly being integrated into modern healthcare models, it is essential to bridge traditional knowledge and scientific evidence. Ethnopharmacological investigations have the potential to provide information on the traditional use of Dioscorea bulbifera and guide future research toward the discovery of novel therapeutic applications. In the future, Dioscorea bulbifera's research agenda needs to address some important areas. First, strict toxicological assessment needs to be done to establish safe dosage levels and avoid potential side effects. Second, large-scale clinical trials need to be performed to establish its efficacy as a drug for certain diseases, including cancer, microbial infections, and inflammatory diseases. Third, advances in biotechnology, such as metabolic engineering and synthetic biology, can make the large-scale production of its bioactive compounds more feasible, weaning it from natural sources and making it sustainable. Fourth, multidisciplinary strategies combining pharmacology, nanotechnology, and bioinformatics can make the process of developing Dioscorea bulbifera-derived drugs more efficient, making it a useful addition to contemporary medicine.

In conclusion, Dioscorea bulbifera is a remarkable medicinal plant with vast therapeutic potential. Its dense array of bioactive compounds is the cause of its wide range of pharmacological activities, and as such it is a promising drug candidate for drug discovery and development. However, problems of toxicity, standardization, and clinical confirmation must be addressed to be able to fully harness its medicinal potential. With continued research work and innovation in phytopharmacology, Dioscorea bulbifera can be a key player in natural drug development, offering new solutions to global health problems while preserving the traditional wisdom of medicine.

ACKNOWLEDGEMENTS

Author Rudresh Adarkar is thankful to the Manipal Academy of Higher Education (MAHE) for providing Dr.T.M.A. Pai Doctoral Fellowship. The author also acknowledged with thanks to Manipal College of Pharmaceutical Sciences for providing facilities for this work.

REFERENCES

1. Sezer F, Deniz S, Sevim D, Chaachouay N, Zidane L. Plant-Derived Natural Products: A Source for Drug Discovery and Development. Drugs and Drug Candidates 2024, Vol 3, Pages 184-207 [Internet]. 2024 Feb 19 [cited 2025 Mar 21];3(1):184–207. Available from: https://www.mdpi.com/2813-2998/3/1/11/htm
2. Wang Z, Zhao S, Tao S, Hou G, Zhao F, Tan S, et al. Dioscorea spp.: Bioactive Compounds and Potential for the Treatment of Inflammatory and Metabolic Diseases. Molecules [Internet]. 2023 Mar 1 [cited 2025 Mar 21];28(6):2878. Available from: https://pmc.ncbi.nlm.nih.gov/articles/PMC10051580/
3. Kumar S, Das G, Shin HS, Patra JK. Dioscorea spp. (A Wild Edible Tuber): A Study on Its Ethnopharmacological Potential and Traditional Use by the Local People of Similipal Biosphere Reserve, India. Front Pharmacol [Internet]. 2017 Feb 14 [cited 2025 Mar 21];8(FEB):52. Available from: http://www.ncbi.nlm.nih.gov/pubmed/28261094
4. Epping J, Laibach N. An underutilized orphan tuber crop—Chinese yam : a review. Planta. 2020 Oct 1;252(4).
5. Padhan B, Panda D. Potential of Neglected and Underutilized Yams (Dioscorea spp.) for Improving Nutritional Security and Health Benefits. Front Pharmacol [Internet]. 2020 Apr 24 [cited 2025 Mar 21];11. Available from: https://pubmed.ncbi.nlm.nih.gov/32390842/
6. Nutritive and Anti-Nutritive Composition of the Wild (Inedible) Species of Dioscorea bulbifera (Potato Yam) and Dioscorea dumentorum (Bitter Yam) [Internet]. [cited 2025 Mar 21]. Available from: https://www.researchgate.net/publication/238115877_Nutritive_and_Anti-Nutritive_Composition_of_the_Wild_Inedible_Species_of_Dioscorea_bulbifera_Potato_Yam_and_Dioscorea_dumentorum_Bitter_Yam
7. Tapondjou leon. Steroidal saponins from the flowers of Dioscorea bulbifera var. sativa. Phytochemistry [Internet]. 2013 Jan 1 [cited 2025 Mar 22]; Available from: https://www.academia.edu/93853259/Steroidal_saponins_from_the_flowers_of_Dioscorea_bulbifera_var_sativa
8. Liu H, Chou GX, Wu T, Guo YL, Wang SC, Wang CH, et al. Steroidal sapogenins and glycosides from the rhizomes of Dioscorea bulbifera. J Nat Prod [Internet]. 2009 Nov 30 [cited 2025 Mar 22];72(11):1964–8. Available from: https://pubmed.ncbi.nlm.nih.gov/19842682/
9. Liu H, Chou GX, Wu T, Guo YL, Wang SC, Wang CH, et al. Steroidal sapogenins and glycosides from the rhizomes of Dioscorea bulbifera. J Nat Prod [Internet]. 2009 Nov 30 [cited 2025 Mar 22];72(11):1964–8. Available from: https://pubmed.ncbi.nlm.nih.gov/19842682/
10. Sharma S, Kaul S, Dhar MK. A systematic review on ethnobotany, phytochemistry and pharmacology of Dioscorea bulbifera L. (Dioscoreaceae). South African Journal of Botany. 2024 Jul 1;170:367–93.
11. Bailly C. A systematic review of spirostanol saponins and anticancer natural products isolated from Tacca plantaginea (Hance) Drenth. Phytochemistry. 2024 Dec 1;228:114252.

12. Liu XT, Wang ZZ, Xiao W, Zhao HW, Hu J, Yu B. Cholestane and spirostane glycosides from the rhizomes of Dioscorea septemloba. Phytochemistry. 2008 Apr;69(6):1411–8.
13. Liu H, Chou GX, Guo YL, Ji LL, Wang JM, Wang ZT. Norclerodane diterpenoids from rhizomes of Dioscorea bulbifera. Phytochemistry. 2010 Jul 1;71(10):1174–80.
14. Ida Y, Kubo S, Fujita M, Komori T, Kawasaki T. Furanoid-norditerpene aus Pflanzen der Familie Dioscoreaceae, V. Struktur der Diosbulbine-D, -E, -F, -G und -H. Justus Liebigs Ann Chem. 1978;1978(5):818–33.
15. Kuagny RBM, Saha BUF, Achu MBL, Kansci G, Medoua GN, Fokou E. Polyphenol and flavonoid contents, antioxidant activities and glycaemic index of Dioscorea spp and Coleus esculentus from Cameroon. Food Chemistry Advances. 2023 Dec 1;3:100500.
16. Kim M, Gu MJ, Lee JG, Chin J, Bae JS, Hahn D. Quantitative Analysis of Bioactive Phenanthrenes in Dioscorea batatas Decne Peel, a Discarded Biomass from Postharvest Processing. Antioxidants [Internet]. 2019 Nov 1 [cited 2025 Mar 22];8(11):541. Available from: https://pmc.ncbi.nlm.nih.gov/articles/PMC6912652/
17. Wang Z, Zhao S, Tao S, Hou G, Zhao F, Tan S, et al. Dioscorea spp.: Bioactive Compounds and Potential for the Treatment of Inflammatory and Metabolic Diseases. Molecules [Internet]. 2023 Mar 1 [cited 2025 Mar 22];28(6):2878. Available from: https://pmc.ncbi.nlm.nih.gov/articles/PMC10051580/
18. Identification and quantification of major carotenoids of deep yellow-fleshed yam (tropical Dioscorea dumetorum) [Internet]. [cited 2025 Mar 22]. Available from: https://www.researchgate.net/publication/286754659_Identification_and_quantification_of_major_carotenoids_of_deep_yellow-fleshed_yam_tropical_Dioscorea_dumetorum
19. Dan L. Analysis of Volatile Oils From the Fruits of Dioscorea nipponica Makino by GC-MS. Special Wild Economic Animal and Plant Research. 2011;
20. Miyazawa M, Shimamura H, Kameoka H. Volatile Components of the Rhizomes of Dioscorea japonica. Nat Prod Lett. 1997;9(4):245–8.
21. Odeghe OB, Adikwu E, Ojiego CC. Phytochemical and antioxidant assessments of Dioscorea bulbifera stem tuber. Biomedical and Biotechnology Research Journal [Internet]. 2020 Oct 1 [cited 2025 Mar 22];4(4):305–11. Available from: https://journals.lww.com/bbrj/fulltext/2020/04040/phytochemical_and_antioxidant_assessments_of.8.aspx
22. Sharma S, Kaul S, Dhar MK. A systematic review on ethnobotany, phytochemistry and pharmacology of Dioscorea bulbifera L. (Dioscoreaceae). South African Journal of Botany. 2024 Jul 1;170:367–93.
23. Fatty acid composition of Dioscorea spp a . | Download Scientific Diagram [Internet]. [cited 2025 Mar 22]. Available from: https://www.researchgate.net/figure/Fatty-acid-composition-of-Dioscorea-spp-a_tbl1_259533287
24. Yin J, Kouda K, Tezuka Y, Tran Q Le, Miyahara T, Chen Y, et al. Steroidal glycosides from the rhizomes of Dioscorea spongiosa. J Nat Prod. 2003 May 1;66(5):646–50.
25. Glycoside derivatives in D. bulbifera | Download Scientific Diagram [Internet]. [cited 2025 Mar 22]. Available from: https://www.researchgate.net/figure/Glycoside-derivatives-in-D-bulbifera_fig8_315835615
26. Kuete V, BetrandTeponno R, Mbaveng AT, Tapondjou LA, Meyer JJM, Barboni L, et al. Antibacterial activities of the extracts, fractions and compounds from Dioscorea bulbifera. BMC Complement Altern Med [Internet]. 2012 Nov 23 [cited 2025 Jul 10];12. Available from: https://pubmed.ncbi.nlm.nih.gov/23176193/
27. Teponno RB, Tapondjou AL, Gatsing D, Djoukeng JD, Abou-Mansour E, Tabacchi R, et al. Bafoudiosbulbins A, and B, two anti-salmonellal clerodane diterpenoids from Dioscorea bulbifera L. var sativa. Phytochemistry [Internet]. 2006 [cited 2025 Jul 10];67(17):1957–63. Available from: https://pubmed.ncbi.nlm.nih.gov/16876211/
28. Shriram V, Jahagirdar S, Latha C, Kumar V, Puranik V, Rojatkar S, et al. A potential plasmid-curing agent, 8-epidiosbulbin E acetate, from Dioscorea bulbifera L. against multidrug-resistant bacteria. Int J Antimicrob Agents [Internet]. 2008 Nov [cited 2025 Jul 10];32(5):405–10. Available from: https://pubmed.ncbi.nlm.nih.gov/18718743/
29. Mary Adeosun O, Juwon Arotupin D, Adebowale Toba O, Adewole Adebayo A. Antibacterial activities and phytochemical properties of extracts of Dioscorea bulbifera Linn (Air Potatoe) tubers and peels against some pathogenic bacteria. The Journal of Phytopharmacology [Internet]. 2016 [cited 2025 Jul 10];5(1):20–6. Available from: www.phytopharmajournal.com
30. Mary Adeosun O, Juwon Arotupin D, Adebowale Toba O, Adewole Adebayo A. Antibacterial activities and phytochemical properties of extracts of Dioscorea bulbifera Linn (Air Potatoe) tubers and peels against some pathogenic bacteria. The Journal of Phytopharmacology [Internet]. 2016 [cited 2025 Mar 21];5(1):20–6. Available from: www.phytopharmajournal.com
31. Shriram V, Jahagirdar S, Latha C, Kumar V, Puranik V, Rojatkar S, et al. A potential plasmid-curing agent, 8-epidiosbulbin E acetate, from Dioscorea bulbifera L. against multidrug-resistant bacteria. Int J Antimicrob Agents [Internet]. 2008 Nov [cited 2025 Mar 21];32(5):405–10. Available from: https://pubmed.ncbi.nlm.nih.gov/18718743/
32. Mohanty M, Choudhury R, Kumar S, Maggirwar R. PHYTOCHEMICAL SCREENING AND ANTIBACTERIAL ACTIVITY OF DIOSCOREA BULBIFERA L. FRUITS. Plant Arch [Internet]. 2021 Apr 30 [cited 2025 Mar 21];21(No 1). Available from: https://www.researchgate.net/publication/352181340_PHYTOCHEMICAL_SCREENING_AND_ANTIBACTERIAL_ACTIVITY_OF_DIOSCOREA_BULBIFERA_L_FRUITS
33. Teponno RB, Tapondjou AL, Gatsing D, Djoukeng JD, Abou-Mansour E, Tabacchi R, et al. Bafoudiosbulbins A, and B, two anti-salmonellal clerodane diterpenoids from Dioscorea bulbifera L. var sativa. Phytochemistry [Internet]. 2006 [cited 2025 Mar 21];67(17):1957–63. Available from: https://pubmed.ncbi.nlm.nih.gov/16876211/
34. S G, S P, M A, R K, S K, K P, et al. Synthesis of silver nanoparticles using Dioscorea bulbifera tuber extract and evaluation of its synergistic potential in combination with antimicrobial agents. Int J Nanomedicine [Internet]. 2012 Feb [cited 2025 Mar 21];7:483. Available from: https://pubmed.ncbi.nlm.nih.gov/22334779/
35. Kuete V, BetrandTeponno R, Mbaveng AT, Tapondjou LA, Meyer JJM, Barboni L, et al. Antibacterial activities of the extracts, fractions and compounds from Dioscorea bulbifera. BMC Complement Altern Med [Internet]. 2012 Nov 23 [cited 2025 Mar 21];12:228. Available from: https://pmc.ncbi.nlm.nih.gov/articles/PMC3528471/
36. Adeleye A, Ikotun T. Antifungal activity of dihydrodioscorine extracted from a wild variety of Dioscorea bulbifera L. J Basic Microbiol [Internet]. 1989 Jan 1 [cited 2025 Jul 10];29(5):265–7. Available from: /doi/pdf/10.1002/jobm.3620290504
37. Kum EJSJBHJSKHHY. Antifungal Activity of Phenanthrene Derivatives from Aerial Bulbils of Dioscorea batatas Decne. J Life Sci. 2006 Jul 31;16(4):647–52.
38. Kp S, Dv H, Sr K. Screening of Antifungal Activity of Endophytic Fungi From Dioscorea bulbifera. [cited 2025 Jul 10]; Available from: www.ijlsci.in
39. N. S, L. JM, S. VS, L. SG, G. SM, R. AP. Exploration of Endophytes from Tropical Tuber Crops against Colletotrichum gloeosporioides Causing Anthracnose in Greater Yam (Dioscorea alata L.) In Vitro. JOURNAL OF ROOT CROPS [Internet]. 2018 [cited 2025 Mar 21];44(2):32–43. Available from: https://journal.isrc.in/index.php/jrc/article/view/538

40. Kum EJSJBHJSKHHY. Antifungal Activity of Phenanthrene Derivatives from Aerial Bulbils of Dioscorea batatas Decne. J Life Sci. 2006 Jul 31;16(4):647–52.

41. Adeleye A, Ikotun T. Antifungal activity of dihydrodioscorine extracted from a wild variety of Dioscorea bulbifera L. J Basic Microbiol [Internet]. 1989 Jan 1 [cited 2025 Mar 21];29(5):265–7. Available from: https://discovery.researcher.life/article/antifungal-activity-of-dihydrodioscorine-extracted-from-a-wild-variety-of-dioscorea-bulbifera-l/e5e651baef45322b95b1332d4a2eef24

42. Wang JM, Ji LL, Banford-White CJ, Wang ZY, Shen KK, Liu H, et al. Antitumor activity of Dioscorea bulbifera L. rhizome in vivo. Fitoterapia [Internet]. 2012 Mar [cited 2025 Jul 10];83(2):388–94. Available from: https://pubmed.ncbi.nlm.nih.gov/22178682/

43. Gao H, Kuroyanagi M, Wu L, Kawahara N, Yasuno T, Nakamura Y. Antitumor-promoting constituents from Dioscorea bulbifera L. in JB6 mouse epidermal cells. Biol Pharm Bull [Internet]. 2002 Sep [cited 2025 Jul 10];25(9):1241–3. Available from: https://pubmed.ncbi.nlm.nih.gov/12230129/

44. An RC, para, Tirgar PR. Investigation of Therapeutics Benefits of Dioscorea bulbifera in Breast Cancer. J Chem Pharm Res [Internet]. 2017 Jun 30 [cited 2025 Jul 10];9(6):313–26. Available from: https://www.jocpr.com/abstract/investigation-of-therapeutics-benefits-of-dioscorea-bulbifera-in-breast-cancer-8925.html

45. Ahmad Hidayat AF, Chan CK, Mohamad J, Abdul Kadir H. Dioscorea bulbifera induced apoptosis through inhibition of ERK 1/2 and activation of JNK signaling pathways in HCT116 human colorectal carcinoma cells. Biomedicine and Pharmacotherapy [Internet]. 2018 Aug 1 [cited 2025 Jul 10];104:806–16. Available from: https://pubmed.ncbi.nlm.nih.gov/29860114/

46. Zhu Z, Liu Y, Zeng J, Ren S, Wei L, Wang F, et al. Diosbulbin C, a novel active ingredient in Dioscorea bulbifera L. extract, inhibits lung cancer cell proliferation by inducing G0/G1 phase cell cycle arrest. BMC Complement Med Ther [Internet]. 2023 Dec 1 [cited 2025 Jul 10];23(1). Available from: https://pubmed.ncbi.nlm.nih.gov/38049779/

47. Zhu Z, Liu Y, Zeng J, Ren S, Wei L, Wang F, et al. Diosbulbin C, a novel active ingredient in Dioscorea bulbifera L. extract, inhibits lung cancer cell proliferation by inducing G0/G1 phase cell cycle arrest. BMC Complement Med Ther [Internet]. 2023 Dec 1 [cited 2025 Mar 21];23(1). Available from: https://pubmed.ncbi.nlm.nih.gov/38049779/

48. Zhao JQ, Zhou QQ, Sun Y, Yu T, Jiang Y, Li HJ. The anti-non-small cell lung cancer effect of Diosbulbin B: Targeting YY1 induced cell cycle arrest and apoptosis. Phytomedicine. 2024 Jul 25;130.

49. Cui H, Li T, Wang L, Su Y, Xian CJ. Dioscorea bulbifera polysaccharide and cyclophosphamide combination enhances anti-cervical cancer effect and attenuates immunosuppression and oxidative stress in mice. Sci Rep [Internet]. 2016 Jan 12 [cited 2025 Mar 21];5. Available from: https://pubmed.ncbi.nlm.nih.gov/26753518/

50. Ghosh S, Nitnavare R, Dewle A, Tomar GB, Chippalkatti R, More P, et al. Novel platinum-palladium bimetallic nanoparticles synthesized by Dioscorea bulbifera: anticancer and antioxidant activities. Int J Nanomedicine [Internet]. 2015 Dec 17 [cited 2025 Mar 21];10:7477–90. Available from: https://pubmed.ncbi.nlm.nih.gov/26719690/

51. Ahmad Hidayat AF, Chan CK, Mohamad J, Abdul Kadir H. Dioscorea bulbifera induced apoptosis through inhibition of ERK 1/2 and activation of JNK signaling pathways in HCT116 human colorectal carcinoma cells. Biomed Pharmacother [Internet]. 2018 Aug 1 [cited 2025 Mar 21];104:806–16. Available from: https://pubmed.ncbi.nlm.nih.gov/29860114/

52. Liu H, Chou GX, Wang JM, Ji LL, Wang ZT. Steroidal saponins from the rhizomes of Dioscorea bulbifera and their cytotoxic activity. Planta Med [Internet]. 2011 [cited 2025 Mar 21];77(8):845–8. Available from: https://pubmed.ncbi.nlm.nih.gov/21165820/

53. Anandpara RC, Tirgar PR. Investigation of Therapeutics Benefits of Dioscorea bulbifera in Breast Cancer. 2017;

54. Gao H, Kuroyanagi M, Wu L, Kawahara N, Yasuno T, Nakamura Y. Antitumor-promoting constituents from Dioscorea bulbifera L. in JB6 mouse epidermal cells. Biol Pharm Bull [Internet]. 2002 Sep [cited 2025 Mar 21];25(9):1241–3. Available from: https://pubmed.ncbi.nlm.nih.gov/12230129/

55. Wang JM, Ji LL, Banford-White CJ, Wang ZY, Shen KK, Liu H, et al. Antitumor activity of Dioscorea bulbifera L. rhizome in vivo. Fitoterapia [Internet]. 2012 Mar [cited 2025 Mar 21];83(2):388–94. Available from: https://pubmed.ncbi.nlm.nih.gov/22178682/

56. Adeniran AA, Sonibare MA. Journal of Pharmacognosy and Phytotherapy In vitro potential anthelmintic activity of bulbils of Dioscorea bulbifera L. on earthworms and liverflukes. 2013 [cited 2025 Mar 21];5(12):196–203. Available from: http://www.academicjournals.org/JPP

57. Odeghe OB, Adikwu E, Ojiego CC. Phytochemical and antioxidant assessments of Dioscorea bulbifera stem tuber. Biomedical and Biotechnology Research Journal [Internet]. 2020 Oct 1 [cited 2025 Jul 10];4(4):305–11. Available from: https://journals.lww.com/bbrj/fulltext/2020/04040/phytochemical_and_antioxidant_assessments_of.8.aspx

58. "Formulation of antibacterial ointment from Dioscorea Bulbifera." 2024 [cited 2025 Jul 10]; Available from: www.ijnti.org

59. Odeghe OB, Adikwu E, Ojiego CC. Phytochemical and antioxidant assessments of Dioscorea bulbifera stem tuber. Biomedical and Biotechnology Research Journal [Internet]. 2020 Oct 1 [cited 2025 Mar 21];4(4):305–11. Available from: https://journals.lww.com/bbrj/fulltext/2020/04040/phytochemical_and_antioxidant_assessments_of.8.aspx

60. Suriyavathana M, Indupriya S. Screening of antioxidant potentials in Dioscorea bulbifera. 2011;

61. Chaniad P, Mungthin M, Payaka A, Viriyavejakul P, Punsawad C. Antimalarial properties and molecular docking analysis of compounds from Dioscorea bulbifera L. as new antimalarial agent candidates. BMC Complement Med Ther [Internet]. 2021 Dec 1 [cited 2025 Mar 21];21(1):1–10. Available from: https://bmccomplementmedtherapies.biomedcentral.com/articles/10.1186/s12906-021-03317-y

62. Antihyperglycemic and antidyslipidemic activity of aqueous extract of Dioscorea bulbifera tubers [Internet]. [cited 2025 Mar 21]. Available from: https://www.researchgate.net/publication/239570766_Antihyperglycemic_and_antidyslipidemic_activity_of_aqueous_extract_of_Dioscorea_bulbifera_tubers

63. Chopade BA, Ghosh S, Ahire M, Patil S, Jabgunde A, Bhat Dusane M, et al. Antidiabetic Activity of Gnidia glauca and Dioscorea bulbifera: Potent Amylase and Glucosidase Inhibitors. Evid Based Complement Alternat Med [Internet]. 2012 [cited 2025 Mar 21];2012. Available from: https://pubmed.ncbi.nlm.nih.gov/21785651/

64. Ghosh S, More P, Derle A, Patil AB, Markad P, Asok A, et al. Diosgenin from Dioscorea bulbifera: Novel Hit for Treatment of Type II Diabetes Mellitus with Inhibitory Activity against α-Amylase and α-Glucosidase. PLoS One [Internet]. 2014 Sep 12 [cited 2025 Mar 21];9(9):e106039. Available from: https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0106039

65. Chaniad P, Wattanapiromsakul C, Pianwanit S, Tewtrakul S. Anti-HIV-1 integrase compounds from Dioscorea bulbifera and molecular docking study. Pharm Biol [Internet]. 2016 Jun 2 [cited 2025 Mar 21];54(6):1077–85. Available from: https://www.tandfonline.com/doi/abs/10.3109/13880209.2015.1103272

66. Guan XR, Zhu L, Xiao ZG, Zhang YL, Chen HB, Yi T. Bioactivity, toxicity and detoxification assessment of Dioscorea bulbifera L.: a comprehensive review. Phytochemistry Reviews [Internet]. 2017 Jun 1 [cited 2025 Mar 21];16(3):573–601. Available from: https://link.springer.com/article/10.1007/s11101-017-9505-5

67. Li H, Peng Y, Zheng J. Dioscorea bulbifera L.-induced hepatotoxicity and involvement of metabolic activation of furanoterpenoids. Drug Metab Rev [Internet]. 2020 Oct 1 [cited 2025 Mar 21];52(4):568–84. Available from: https://www.tandfonline.com/doi/abs/10.1080/03602532.2020.1800724

68. Wang J, Liang Q, Ji L, Liu H, Wang C, Wang Z. Gender-related difference in liver injury induced by Dioscorea bulbifera L. rhizome in mice. Hum Exp Toxicol [Internet]. 2011 Sep [cited 2025 Mar 21];30(9):1333–41. Available from: https://journals.sagepub.com/doi/full/10.1177/0960327110389926

69. Tan R, Hu Z, Zhou M, Liu Y, Wang Y, Zou Y, et al. Diosbulbin B: An important component responsible for hepatotoxicity and protein covalent binding induced by Dioscorea bulbifera L. Phytomedicine [Internet]. 2022 Jul 20 [cited 2025 Mar 21];102. Available from: https://pubmed.ncbi.nlm.nih.gov/35660353/

70. Tan R, Hu Z, Zhou M, Liu Y, Wang Y, Zou Y, et al. Diosbulbin B: An important component responsible for hepatotoxicity and protein covalent binding induced by Dioscorea bulbifera L. Phytomedicine. 2022 Jul 20;102:154174.

71. Li W, Lin D, Gao H, Xu Y, Meng D, Smith CV, et al. Metabolic activation of furan moiety makes Diosbulbin B hepatotoxic. Arch Toxicol [Internet]. 2016 Apr 1 [cited 2025 Mar 22];90(4):863–72. Available from: https://link.springer.com/article/10.1007/s00204-015-1495-8

72. Tan R, Hu Z, Zhou M, Liu Y, Wang Y, Zou Y, et al. Diosbulbin B: An important component responsible for hepatotoxicity and protein covalent binding induced by Dioscorea bulbifera L. Phytomedicine. 2022 Jul 20;102:154174.

73. Dubale S, Usure RE, Mekasha YT, Hasen G, Hafiz F, Kebebe D, et al. Traditional herbal medicine legislative and regulatory framework: a cross-sectional quantitative study and archival review perspectives. Front Pharmacol. 2025 Jan 30;16:1475297.

74. Rousseaux CG, Schachter H. Regulatory Issues Concerning the Safety, Efficacy and Quality of Herbal Remedies. Birth Defects Res B Dev Reprod Toxicol [Internet]. 2003 Dec [cited 2025 Jul 9];68(6):505–10. Available from: https://pubmed.ncbi.nlm.nih.gov/14745988/

75. Wang H, Chen Y, Wang L, Liu Q, Yang S, Wang C. Advancing herbal medicine: enhancing product quality and safety through robust quality control practices. Front Pharmacol [Internet]. 2023 [cited 2025 Jul 9];14:1265178. Available from: https://pmc.ncbi.nlm.nih.gov/articles/PMC10561302/

76. Parveen A, Parveen B, Parveen R, Ahmad S. Challenges and guidelines for clinical trial of herbal drugs. J Pharm Bioallied Sci [Internet]. 2015 Oct 1 [cited 2025 Jul 9];7(4):329. Available from: https://pmc.ncbi.nlm.nih.gov/articles/PMC4678978/

77. Uehleke B. Herbal Medicine: No Research To Evaluate Clinical Evidence. Int J Complement Altern Med [Internet]. 2017 Apr 12 [cited 2025 Jul 9];Volume 6(Issue 3):254–5. Available from: https://medcraveonline.com/IJCAM/IJCAM-06-00190.php

78. Sharma AK, Kumar R, Mishra A, Gupta R. Problems associated with clinical trials of Ayurvedic medicines. Revista Brasileira de Farmacognosia [Internet]. 2010 [cited 2025 Jul 9];20(2):276–81. Available from: https://www.scielo.br/j/rbfar/a/rjVhRWbrhCdRVnYhqBhFtwp/

79. Ramandeep K, Vikas G, Francis CA, Parveen B. Scope and Bottlenecks in Clinical Trials of Herbal Drugs - Present Scenario. Journal of Pharmaceutical Research [Internet]. 2015 Jan 1 [cited 2025 Jul 9];14(1):26–32. Available from: https://jopcr.com/articles/scope-and-bottlenecks-in-clinical-trials-of-herbal-drugs—present-scenario

80. Parveen A, Parveen B, Parveen R, Ahmad S. Challenges and guidelines for clinical trial of herbal drugs. J Pharm Bioallied Sci [Internet]. 2015 Oct 1 [cited 2025 Jul 9];7(4):329. Available from: https://pmc.ncbi.nlm.nih.gov/articles/PMC4678978/

81. WHO guidelines on good manufacturing practices (GMP) for herbal medicines.

Cite this article: Rudresh A, Chandrashekar K S, Vasudev P, Richard L, Aswatharam H N, Vamshi K T, Ullas P D'S, Rajesh K S. A Comprehensive Review on the Pharmacological Potential of *Dioscorea bulbifera* and its Potential Hepatotoxicity. Pharmacogn J. 2025;17(4): 520-530.