Phytochemistry and Therapeutic Potential of Medicinal Plant: Dioscorea bulbifera

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Abstract

Dioscorea bulbifera is an immensely important medicinal plant which is extensively used in both Indian and Chinese system of traditional medicine. It is found in many parts of the world and has gained wide attention not only for health care but also as a food crop. It has attracted scientific interest owing to its numerous therapeutic applications in various pathophysiological conditions like ulcers, sores, wound, spasms, dysentery, diabetes and cancer. Spectacular success in extensive research particularly within last two decades has proven that these activities are attributed to its unique phytochemistry. Bioactive components from D. bulbifera have exhibited anti-oxidant, anti-inflammatory, antibacterial, plasmid curing, antidiabetic and anticancer activities. It has become a model system in nanobiotechnology as it harbours phytochemicals with reducing, capping and shape modulating efficiencies. Numerous studies, either separately or in association, have aimed to explain the chemical composition and mechanisms behind its pharmacognostic significance. Similarly, many reports have documented and validated the claimed traditional usage by providing a strong scientific rationale. However, there is no review published on its in vitro, in vivo and in silico applications along with detailed phytochemistry. In view of the background, this review elaborates the complete phytochemistry of D. bulbifera with therapeutic importance.

Keywords: Dioscorea bulbifera; Phytochemistry; Traditional medicine; Diabetes; Cancer; Nanoparticles

Introduction

Medicinal plants are rich source of diverse phytochemicals with multifaceted therapeutic potential [1]. Dioscorea bulbifera is one of the important medicinal plants among 600 species in the family Dioscoreaceae which has found its importance in traditional medicine throughout the world. Glycosides of its steroid sapogenins like diosgenin have gained attention as precursors in the synthesis of sex hormones, cardiactive glucosides, fertility control compounds, corticosteroids and anabolic agents [2]. In Bangladesh it is used for treatment of leprosy and tumours while in Chinese medicine as a remedy for sore throat and for struma [3-4]. Similarly, it is applied on cuts and sores as infusion in Zimbabwe, while for treatment of abscesses, boils and wound infections in Cameroon and Madagascar [5]. It has got its wide applications in piles, ulcers, pain and inflammation in Indian traditional medicine [6,7]. Ancient and modern literature on its medicinal use have indicated that its tubers have therapeutic benefits as purgative, anthelmintic, diuretic, deflattulent, rejuvenating tonic, aphrodisiac and can also be used for treatment in scrofula, haematological disorders, diabetic disorders, worm infestations, haemorrhoids, skin disorders, general debility as well as polyuria (Figure 1). Crushed tubers and decoction are emulsified into oil to treat infected ulcers and sinus [8,9]. It is profusely used in both Indian and Chinese traditional medicine to cure gastric cancer and carcinoma of rectum and goitre [10]. Similarly, its extracts are reported to be anti-hyperlipidemic, antitumor, antioxidant, anorexiant, analgesic, anti-inflammatory, plasmid curing, antidiabetic and anti-hyperglycemic [11-17]. Dried yam is known to dissolve toxins, cures carbuncles, scrofula and purulent infections. It is considered as remedy against dysentery and diarrhoea in addition to syphilis in Java and Brazil. Interestingly, it is used against dog bites, snake bites and food poisoning in China, in addition to hepatic fibrosis by protecting the liver [18] It is also reported to have remedial potential against conjunctivitis, leucoderma, dyspepsia, urinary discharges, jaundice, diabetes, asthma, bronchitis, strangay and vata biliousness [19]. More recently, we have shown that its unique phytochemistry enables it to synthesize both gold (AuNPs) and silver nanoparticles (AgNPs) [20,21]. In the recent past, D. bulbifera has emerged as a promising complementary and alternative source of traditional medicine attracting prime attention towards spectacular scientific advancement in exploration of new biomolecules.

However, there are no reviews on D. bulbifera which elaborates its phytochemistry providing a strong scientific rationale supporting its immense applications in therapy. Hereby, scientific literature to address this lacuna bridging the gap between traditional use and modern scientific research on the complex medicinal chemistry of D. bulbifera is of utmost importance for future researches. In view of this background, herein we present the first detailed review on phytochemistry and therapeutic potential of D. bulbifera (Table 1).

Phytochemicals from D. bulbifera

The phytochemical diversity of D. bulbifera exhibits pronounce variation according to its geographical location, parts of plant and the solvent for extraction used. Flavonoids are effectively extracted in ethyl acetate soluble fraction of 75 % ethanol extract of the rhizomes of Dioscorea bulbifera from China which consist of both flavonol aglycones, namely kaempferol-3,5-dimethyl ether, caryatin, (+)-catechin and flavonol glycosides, namely, quercetin-3-O-galactopyranoside, myricetin-3-O-galactopyranoside, myricetin-3-O-glucopyranoside [12]. 8-epidiosbulbin E acetate (EEA) was isolated from aqueous methanolic extract of bulbs from India [16], Diosbulbin B is a demethyl diterpenoid found as a main constituent of chloroform fraction (Figure 2) [22], 80 % ethanolic extract was reported for efficient.

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Figure 1: Therapeutic applications of *D. bulbifera*.

| Sr. No. | Phytochemicals       | Plant part | Country    | Reference/s |
|---------|----------------------|------------|------------|-------------|
| 1       | Diosbulbin A         | Tuber, leaf, stem | China | [23,4]       |
| 2       | Diosbulbin B         | Tuber, rhizome, Leaf, stem | China | [23,25,24, 12, 4] |
| 3       | Diosbulbin C         | Tuber, leaf, stem | China | [23,4]       |
| 4       | Diosbulbin D         | Tuber, leaf, stem | China, Bangladesh | [23,24,4,3] |
| 5       | Diosbulbin E         | Rhizome, leaf, stem | China | [25,4]       |
| 6       | Diosbulbin F         | Tuber, rhizome, leaf, stem | China | [23,25,4] |
| 7       | Diosbulbin G         | Tuber, rhizome, leaf, stem | China | [23,25,4] |
| 8       | Diosbulbin H         | Leaf, stem | NI | [4]          |
| 9       | Diosbulbin I         | Root tuber | China | [24]         |
| 10      | Diosbulbin J         | Root tuber | China | [24]         |
| 11      | Diosbulbin K         | Rhizome | China | [25]         |
| 12      | Diosbulbin L         | Rhizome | China | [25]         |
| 13      | Diosbulbin M         | Rhizome | China | [25]         |
| 14      | Diosbulbin N         | Tuber | China | [23]         |
| 15      | Diosbulbin O         | Tuber | China | [23]         |
| 16      | Diosbulbin P         | Tuber | China | [23]         |
| 17      | Bafoudiosbulbin A    | Bulbil, tuber | Cameroon | [28,29,30] |
| 18      | Bafoudiosbulbin B    | Bulbil, tuber | Cameroon | [28,29,30] |
| 19      | Bafoudiosbulbin C    | Bulbil, tuber | Cameroon | [28,30] |
| 20      | Bafoudiosbulbin F    | Bulbil | Cameroon | [28,30] |
| 21      | Bafoudiosbulbin G    | Bulbil | Cameroon | [28,30] |
| 22      | Diosbulbinsin A      | Rhizome | China | [26]         |
| 23      | Diosbulbinsin B      | Rhizome | China | [26]         |
| 24      | Diosbulbinsin C      | Rhizome | China | [26]         |
| 25      | Diosbulbinsin D      | Rhizome | China | [26]         |
| 26      | Diosbulbiside A      | Rhizome | China | [26]         |
| 27      | Diosbulbiside B      | Rhizome | China | [26]         |
| 28      | Diosbulbiside C      | Rhizome | China | [26]         |
| 29      | Dioscoreanoside A    | Flower | Cameroon | [32]         |
| 30      | Dioscoreanoside B    | Flower | Cameroon | [32]         |
| 31      | Dioscoreanoside C    | Flower | Cameroon | [32]         |
| 32      | Dioscoreanoside D    | Flower | Cameroon | [32]         |
| 33      | Dioscoreanoside E    | Flower | Cameroon | [32]         |
| 34      | Dioscoreanoside F    | Flower | Cameroon | [32]         |
| 35      | Dioscoreanoside G    | Flower | Cameroon | [32]         |
| 36      | Dioscoreanoside H    | Flower | Cameroon | [32]         |
| 37      | Dioscoreanoside I    | Flower | Cameroon | [32]         |
| 38      | Dioscoreanoside J    | Flower | Cameroon | [32]         |
| 39      | Dioscoreanoside K    | Flower | Cameroon | [32]         |
| 40      | Daucosterol          | Rhizome | China | [22]         |
| 41      | β-Sitosterol         | Rhizome, tuber | China, Cameroon | [22,29] |
| 42      | Palmitic acid        | Rhizome | China | [22]         |
| 43      | Succinic acid        | Rhizome | China | [22]         |
| 44      | Shikimic acid        | Rhizome | China | [22]         |
| 45      | 3, 5-dimethoxykaempferol | Rhizome | China | [22]         |
| 46      | 3, 5, 3′-trimethoxyquercetin | Rhizome | China | [22]         |
| 47      | Caryatin             | Rhizome | China | [22,12]      |
| 48      | (+)Catechin          | Rhizome | China | [33,22,12]  |
| 49      | Myricetin,           | Rhizome | China | [22,12,9]   |
| 50      | Myricetin-3-O-β-D-galactopyranoside, | Rhizome | China | [22]         |
| 51      | Myricetin-3-O-β-D-glucopyranoside | Rhizome | China | [22]         |
| 52      | Hyperoside           | Rhizome | China | [22]         |
53. Kaempferol  Rhizome, bulbil  China, Cameroon  [33,22,29]
54. Kaempferol-3-O-β-D-galactopyranoside  Rhizome  China  [22]
55. Kaempferol-3-O-β-D-glucopyranoside  Rhizome  China  [22]
56. Protocatechuic acid  Rhizome  China  [34,22]
57. Vanillic acid  Rhizome  China  [22,9]
58. Isovanillic acid  Rhizome  China  [22,9]
59. (+)-Epicatechin  Rhizome  China  [22,9]
60. Methyl-O-α-D-fructofuranoside  Rhizome  China  [22]
61. Butyl-O-α-D-fructofuranoside  Rhizome  China  [22]
62. Ethyl-O-β-D-fructopyranoside  Rhizome  China  [22]
63. Butyl-O-β-D-fructopyranoside  Rhizome  China  [22]
64. 3-Phenyl-2-propenyl-O-β-D-glucopyranoside  Rhizome  China  [22]
65. 2-(4-methoxyphenyl)-ethyl-O-β-D-glucopyranoside  Rhizome  China  [22]
66. Phenyl-methyl-O-β-D-glucopyranoside  Rhizome  China  [22]
67. Kaempferol-3,5-dimethyl ether  Rhizome  China  [12]
68. Quercetin-3-O-galactopyranoside  Tuber, rhizome  Cameroon, China  [29,12]
69. Myricetin-3-O-galactopyranoside  Rhizome  China  [12]
70. Myricetin-3-O-glucopyranoside  Rhizome  China  [12]
71. 8-epidiosbulbin E acetate  Bulb, tuber  India, Bangladesh  [16,3]
72. Demethyl batatasin IV  Tuber, bulbil  China, Nigeria  [24,31]
73. Diosbulbinoside D  Leaves, stem  Ni  [4]
74. Diosbulbinoside F  Leaves, stem  Ni  [4]
75. Diosbulbinoside G  Rhizome  China  [25]
76. C22 ω-hydroxy fatty acid  Tuber  China  [33]
77. 3-hydroxy-5-methoxybenzoic acid  Tuber  China  [33]
78. Batatasin III  Tuber  China  [33]
79. 1,6-dihydroxy-2,5,7-trimethoxyphenanthrene  Tuber  China  [33]
80. 2,4,6,7-tetrahydroxy-9,10-dihydrophenanthrene  Tuber  China  [33]
81. 2,5,2′,5′-tetrahydroxy-3′-methoxybenzyl  Tuber  China  [33]
82. Thunalbene  Tuber  China  [33]
83. 2,4-dimethoxyphenanthrene  Tuber  China  [33]
84. Flavanthinrin  Tuber  China  [33]
85. Isorhamnetin  Tuber  China  [33]
86. Quercitin  Tuber, China, Cameroon  [33,29]
87. 3,5,3′-trimethoxyquercetin  Tuber  China  [33]
88. (-)-epicatechin  Tuber  China  [33]
89. Isoquercitrin  Tuber  China  [33]
90. 2,7-dihydroxy-3,4,6-trimethoxyphenanthrene  Tuber  China  [33]
91. Diarylheptanone  Tuber  China  [33]
92. Pennogenin  Rhizome  China  [26]
93. Pennogenin-3-O-α-L-rhamnopyranosyl-(1→3)[α-L-rhamnopyranosyl-(1→2)]-β-D-glucopyranoside  Rhizome  China  [26]
94. Pennogenin-3-O-α-L-rhamnopyranosyl-(1→4)[α-L-rhamnopyranosyl-(1→2)]-β-D-glucopyranoside  Rhizome  China  [26]
95. 4-hydroxy-[2-trans,3′,7′-dimethyl-lodoca-2′,6′-dienyl]-6-methoxy acetoephone  Bulbs  India  [7]
96. 4,6-dihydroxy-2-O-[4′-hydroxybutyl]-acetoephone  Bulb  India  [7]
97. 2,7-dihydroxy-4-methoxyphenanthrene  Bulb, tuber  Cameroon  [28,29]
98. 3-O-α-L-rhamnopyranosyl-(1→3)-[α-L-rhamnopyranosyl-(1→2)]-β-D-glucopyranosyl-pennogenin (spiroconazol A)  Flower, tuber  Cameroon  [32,29,30]
99. Quercetin-3-O-β-D-glucopyranoside  Tuber  Cameroon  [29]
100. Diosgenin  Bulb, corn  India  [35,36]
101. Smilagenone  Corn  India  [36]
102. Epismilagenin  Corn  India  [36]
103. Pennogenin 3-O-α-L-rhamnopyranosyl-(1→4)-α-L-rhamnopyranosyl-(1→2)]-β-D-glucopyranoside  Flower  Cameroon  [32]
104. 26-O-β-D-glucopyranosyl-(25R)-5-en-furost-3β,17α,26-ol-26-O-β-D-glucopyranosyl-pennogenin (spiroconazol A)  Flower  Cameroon  [32]
105. 23β,27-dihydroxy-pennogenin 3-O-α-L-rhamnopyranosyl-(1→4)-α-L-rhamnopyranosyl-(1→2)]-β-D-glucopyranoside  Flower  Cameroon  [32]
106. Floriundasaponin B  Flower  Cameroon  [32]
107. Stigmasterol  Tuber  China  [24]
108. Lutein  Tuber  India  [27]
109. Neoxanthin  Tuber  India  [27]
110. Violaxanthin  Tuber  India  [27]
111. Zeaxanthin  Tuber  India  [27]
112. Auroxanthin  Tuber  India  [27]
113. Cryptoxanthin  Tuber  India  [27]
114. Tetracosanoic acid,  Tuber  Cameroon  [29]
115. 1-tetrasaoyloxy)-glycerol  Tuber  Cameroon  [29]
116. trans-tetracosenylerulate  Tuber  Cameroon  [29]
extraction of epicatechin, isovanillic acid, vanillic acid and myricetin [9]. Similarly, D. bulbifera from China contains diosbulbin A, B, C, D, E, F, G, H, I, J, K, L, M, N, O, P as major phytochemicals [4,23-25]. Steroidal sapogenins named diosbulbins A, B, C, D, spirostane glycosides named diosbulbisides A, B and cholestanol glycoside named diosbulbiside C were found to be predominant in 95 % ethanolic extract of rhizomes of China (Figure 3) [26] Carotenoids such as lutein, zeaxanthin, neoxanthins are also prevalent in D. bulbifera [27]. Methanolic extract of bulbils from Cameroon are found to be rich in clerodane diterpenoids, bafoudiosbulbins A, B, C, F and G (Figure 4) [28-30]. Phytoalexin called demethylbatatasin IV and norditerpenoid diosbulbin D were isolated from bulbils from Nigeria and tubers from Bangladesh, respectively (Figures 5 and 6) [3,31]. Flowers of D. bulbifera from Cameroon has wide range of steroidal saponins namely, dioscoreanosides A, B, C, D, E, F, G, H, I, J and K (Figure 7) [32].

Medicinal Use

Goitre

Tubers of D. bulbifera are steeped in white wine for a week which is traditionally recommended as infused wine and taken daily to get benefits in treatment of goitre. Formulations have profound applications as clinical medicine to treat thyroid glands [9,18,25].

Respiratory disorders

Fresh tuber pieces are pounded with black pepper followed by mixing with curd is taken against cough and cold in India. Similarly, roasted, peeled and dried powder is known to cure respiratory problems when taken with honey. Bitter bulbils are useful against severe cough while edible normal tubers are used against asthmatic conditions. In China, it is considered as a styptic against lung bleeding and epistaxis [18].
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Figure 3: Clerodane diterpenoids isolated from D. bulbifera.

Figure 4: Steroidal sapogenins, spirostan glycosides and cholestan glycosides isolated from D. bulbifera.

Figure 5: Carotenoids isolated from D. bulbifera.
Figure 6: Steroidal saponins of dioscoreanosides series isolated from *D. bulbifera*.
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Eye disorder

*D. bulbifera* serves as a well-known opthalmic remedy. Purulent ophthalmia is treated with sap from stem as eye drops in Congo. Wakefulness is promoted in Ivory Coast by stillation of leaf sap into the eye. A potion made out of steamed leaf is used in east Africa for treating a type of conjunctivitis called „pink eye”[18].

Parasitic infections

*D. bulbifera* from Southwest Nigeria is reported to show anthelmintic activity as one of its significant ethnobotanical application when eaten after roasting. Scientific evidence to the fact was provided by a recent study confirming in vitro anthelmintic activity of methanol extracts of the flesh and peel of *D. bulbifera* bulbils. The extracts rich in phenolics (tannins, flavonoids), saponins as well as other secondary metabolites could efficiently show anthelmintic activity against *Pheritima posthuma* and *Fasciola gigantic*. Earthworms were paralysed in 5.6 min and death was observed in 10 min when treated with peel extract, while treatment with flesh extract showed paralysis in 8.4 min and death in 13.8 min at 100 mg/ml. Likewise, liverflukes were paralyzed after 10.2 min and died after 15.81 min at a concentration of 100 mg/ml of peel extract. The probable mechanism was explained to be the binding of phenolic and tannin compounds to glycoprotein present on the cuticle together with saponin mediated alteration of permeability and pore formation in the membrane of the parasite leading to paralysis and death [10].

Bacterial and fungal infections

*D. bulbifera* is known to be used for treatment of sexually transmitted diseases like gonorrhoea and syphilis in addition to sore throat in Chinese medicine. In Congo it is used against parasitic and fungal infections [18]. Its aqueous extract showed superior activity against *Escherichia coli* while ethanol extract was found to be potent against *Staphylococcus aureus* and *Candida albicans* [37]. Bacterial pathogens have posed a threat to the human health by developing multidrug resistance leading to re-emergence of diseases once controlled. Genetic determinants conferring resistance to one or more antibiotics are mostly located on plasmids which being extra chromosomal DNA, can be effectively transferred to other bacteria, co-existing in the same environment. This underlying mechanism for spread of antimicrobial resistance is an acute difficulty for treating infectious diseases which has led to the search of new drugs called plasmid-curing agents, although many of which such as acridine orange, ethidium bromide and sodium dodecyl sulphate, are toxic, mutagenic and carcinogenic. Hence, plasmid curing agents isolated from medicinal plants have gained more importance and are being investigated owing to their biocompatibility and minimum toxicity. Recently, norditerpene compound, 8-epidiosbulbin E acetate from *D. bulbifera* bulbs has exhibited significant broad spectrum potential to cure antibiotic resistance plasmids (R- plasmids) from clinical isolates although it showed low antimicrobial activity (MIC > 400 µg/mL) for all tested pathogens except *Escherichia coli* (pUC18) which showed an MIC = 200 µg/mL.
However, R-plasmids in clinical strains of Enterococcus faecalis, E. coli, Shigella sonnei, Pseudomonas aeruginosa and Bacillus subtilis were effectively cured. Plasmid curing by 8-epidiosbulbin E acetate resulted in effective reversal of bacterial resistance to multiple antibiotics in an E. coli strain that was resistant to gentamicin, kanamycin, neomycin, streptomycin, tetracycline, novobiocin, ciprofloxacin, cepofarzolane, oxacillin, ceftazidin, co-trimazine, imipenem, cefalexin, cefotaxime, oxytetracycline, cloxacinil, doxycycline, levofloxacin, ofloxacin, gatifloxacin, moxifloxacin, norfloxacin, cepirnome and cotrimoxazole. Further, S. sonnei was sensitised to ampicilin, gentamicin, tetracycline, novobioncin, ciprofloxacin, cepofarzolane, ceftazidin, oxacillin, ceftazidin, co - trimazine, imipenem, cefalexin, cefalaxin, cefotaxime, levofloxacin, ofloxacin, norfloxacin, and cepirnome as a result of 8-epidiosbulbin E acetate mediated plasmid curing. Vancomycin-resistant Enterococcus faecalis, resistant to roxithromycin, cloxacinil, cefalexin and clindamycin became sensitive to these antibiotics after plasmid curing by 8-epidiosbulbin E acetate. Similarly, reference R-plasmids such as RP4, RMs16, RIp64 and pU110 were also cured by 8-epidiosbulbin E acetate at curing efficiencies of 44%, 30%, 64% and 48%, respectively. Reduction of minimal inhibitory concentration (MIC) of antibiotics against MDR bacteria on curing of R-plasmid by 8-epidiosbulbin E acetate provided strong evidence for the novel mechanism behind the effective antibacterial treatment by D. bulbifera [16]. Additionally, vanillin acid and isovanillin acid have shown antibacterial activity [9]. In the western highlands of Cameroon, tubers of D. bulbifera are used against typhoid fever caused by Salmonella typhi and paratyphoid fever caused by Salmonella paratyphi A and Salmonella paratyphi B. Two clerdane diterpenoids, bafoudiosbulbins A and B were reported to have anti-bacterial activity when tested against Salmonella typhi, Salmonella paratyphi A, Salmonella paratyphi B, Pseudomonas aeruginosa, Escherichia coli, Klebsiella pneumoniae and Staphylococcus aureus by using both agar diffusion and broth dilution techniques. Both bafoudiosbulbins A and B exhibited bactericidal activity selectively against S. typhi, S. paratyphi A and S. paratyphi B [29]. Isolated bafoudiosbulbins B, C, F and G as well as crude ethyl acetate (EtOAc) extract (DBBI) and fractionated DBBI obtained from methanolic extract of bulbs from D. bulbifera L. var sativa from Babo village near Dschang (West region of Cameroon), showed growth inhibition in fifteen test strains (both clinical MDR and ATCC) of bacterial pathogens, namely, E. coli, E. aerogenes, K. pneumoniae, P. aeruginosa, M. smegmatis and M. tuberculosis. Selective inhibition of ATCC strain of E. coli, E. aerogenes, K. pneumoniae, M. smegmatis and M. tuberculosis as well as E. coli AG100A and M. tuberculosis MTCC2 by crude extracts can be considered as significant. Bafoudiosbulbin C was found to be active against M. smegmatis and M. tuberculosis ATCC and MTC2 strains at a value as low as 8 μg/mL. Inhibitory effect of the compounds isolated from D. bulbifera against MDR bacteria such as E. aerogenes EA289, CM64, K. pneumoniae KP63 and P. aeruginosa PA124 was better than that of standard antibiotic chloramphenicol in absence as well as in presence of efflux pump inhibitor, phenylalanine arginine β- naphthylamide [28].

Inflammation and pain

D. bulbifera is used to treat inflammation associated dispersal of “lumps”, hernia, sprain, injury, testicular inflammations, in China. Rheumatic pain and breast problems are relieved in Congo and Gabon, respectively by an ointment prepared by incorporation of bulbils into this plant. Inflammation and pain respectively by a folk remedy prepared by incorporation of bulbils into this plant [30]. Recent in vivo studies of aqueous and methanol extracts from bulbils of D. bulbifera var sativa confirmed potent antinociceptive effect. A dose dependent reduction in the acetic acid induced abdominal constriction was observed in white adult mice Mus musculus (weighing 25–30 g), on oral administration of aqueous and methanol extracts. Similarly, in case of formalin- induced paw licking test, intraplantar injection of formalin (2.5%) into the right hind paw of adult Wistar rats (weighing 180–200 g), generated a classical biphasic nociceptive response that was significantly inhibited by aqueous and methanol extracts as compared to indomethacin. These extracts also presented important anti-inflammatory effects on pressure induced pain sensitivity, acute oedema induced by carragenan, histamine, serotonin, formalin and chronic oedema induced by formalin [5]. Pronounced hypernociception induced by intraplantar injection of complete Freund’s adjuvant (CFA) in Swiss mice, could be countered significantly (61 % inhibition) owing to the antinociceptive effect of methanol extract of D. bulbifera (MEDB) administered orally. Hypersensitivity in mice due to neuropathic pain induced by partial ligation sciatic nerve (PLSN) was significantly reduced (38 %) followed by oral administration of MEDB. Similarly, the extract even reduced LPS and PGE2 induced mechanical hypernociception and further study helped in partial prediction that the antinociceptive activities of D. bulbifera both in inflammatory and neuropathic models of pain were attributed to its ability to activate the NO–cGMP–ATP -sensitive potassium channels pathway [15].

Diabetes and digestive problems

Traditional use of D. bulbifera is known to lower glycinemic index in Diabetes mellitus. Diosgenin has shown to ameliorate diabetic neuropathy [18]. A study carried out to evaluate aqueous extract of D. bulbifera tubers (DBEA003) for antihyperglycemic activity on streptozotocin (STZ) treated Wistar rats, provided scientific rationale behind the traditional use. A higher dose (1000 mg/kg p.o.) resulted in highly significant antihyperglycemic effect in glucose tolerance test bringing down the blood glucose level from 129±8.81 mg/dl (30 min) to 97±5.83 mg/dl (90 min). Remarkably, a long lasting glycemic control in diabetic condition was observed administration of DBEA003, which might be attributed due to its action at the tissue or receptor level [17]. However, the actual mechanism of action by which D. bulbifera exerts the antidiabetic effect was furnished in our previous report where we confirmed the inhibition of two key enzymes, α-amylase and α-glucosidase. Petroleum ether, ethyl acetate and methanol extracts of D. bulbifera bulbs were obtained by sequential hot Soxhlet extraction among which ethyl acetate extract showed most superior activity of 73.39 % against porcine pancreatic α-amylase. Strongest inhibition against α-glucosidase was found for ethyl acetate extract (99.6 %) of D. bulbifera bulb [38]. Similarly, even among cold extracts of bulbs of D. bulbifera, ethyl acetate extract showed highest inhibition up to 72.06 ± 0.51% and 82.64 ± 2.32% against α-amylase and α-glucosidase respectively. The bioactive principle was identified as diosgenin which in its isolated form showed superior α-amylase and α-glucosidase inhibition up to 70.94 ± 1.24% and 81.71 ± 3.39%, respectively. The mechanism was established to be uncompetitive mode of binding to α-amylase as confirmed by decrease in both Km and Vm values. Further, hydrogen bonding between carboxyl group of Asp300 and hydrophobic interactions between Tyr62, Trp58, Trp59, Val163, hydrophobic interactions between Tyr62, Trp58, Trp59, Val163, which might be attributed due to its action at the tissue or receptor level [17].
Oxidative stress and degenerative diseases

Free radicals are key mediators for emergence of disease, progression and its associated pathology including diabetes, cancer and even AIDS [39]. Antioxidants, namely, epicatechin, isovanillic acid, vanillic acid, myricetin are important bioactive principles in *D. bulbifera* that are responsible for protection against cardiovascular diseases and stypic activities [9]. Tubers of *D. bulbifera* collected from Nepal showing superior DPPH radical scavenging, ferrous ion chelating, reducing power, and total antioxidant activity contained high oxalic acid (67 ± 9 mg/100g), citric acid (282 ± 24 mg/100g), malic acid(266 ± 20 mg/100g), succinic acid(2510 ± 108 mg/100g) and olyphenols (166 ± 10 mg/100g). Thus the chemical constituents might be playing the key role behind its pronounced antioxidant activity [13]. *D. bulbifera* from Guangzhou of China showed the highest phenolic content (59.43 mg GAE/g), that further exhibited most superior antioxidant property in terms of ABTS’ radical scavenging activity (708.73 µmol Trolox/g) as well as ferric reducing antioxidant power (FRAP) assay (856.92 µmol Fe2+/g) [40]. Ethyl acetate fraction of hydro alcoholic extract of *D. bulbifera* from China, yielded a bibezyl compound, 2,5,2’,5’-tetrahydroxy-3-methoxybenzyl and diobulbinone A amongst which Trolox-equivalent antioxidant capacity of the new bibenzyl7 was found to be 0.52 ± 0.01 by FRAP at a concentration of 1 mM. Similarly it showed an ECV0 value of 2.57 ± 0.06 mM for DPPH radical scavenging. However, the new diarylethanone, diobulbinone A did not show significant antioxidant activity at the same concentration by either of the methods [33]. Dried bulbs of *D. bulbifera* from India were reduced to fine powder and extracted with 70% (v/v) ethanol in distilled water which was further sequentially extracted with petroleum ether, ethyl acetate and methanol. Among the extracts, methanolic extract with maximum phenolic content (145.44 ± 3.29 µg/mL) showed most superior antioxidant activity proved to be a function of phenolic content. Percentage scavenging activity of methanolic extract against DPPH, hydroxyl, superoxide anion radical and nitric oxide was found to be 84.94 ± 0.62 %, 76.11 ± 1.26 %, 59.75 ± 0.98 % and 57.59 ± 0.64 %, respectively. Simultaneously, it scavenged pulse radiolysis generated ABTS’ radical with a second order rate constant of 1.72×10⁴M⁻¹s⁻¹, respectively. Similarly, ethyl acetate extract also showed higher percent scavenging activity of free radicals owing to its high phenolic content (98 ± 1.17 µg/mL) and 94.05 % diosgenin [41]. *D. bulbifera* (DB) tubers obtained from Mumbai, India, were extracted using a Soxhlet-extractor by 70% ethanol. Sprague–Dawley male rats were administered with 1 mL of DB extract dissolved in water (150 mg kg⁻¹ of body weight) for 30 days, which resulted in significantly improved performance towards aortic flow (AF), left ventricular developed pressure (LVDP) and the first derivative of developed pressure (LVmax dp/dt) in DB treated hearts during post ischemic reperfusion. Additionally, marked reduction in myocardial infarct size (20 ± 2.64%) was observed in the treated group. Significant reduction of apoptotic cardiomyocytes (16.89 ± 1.7%) confirmed its anti-apoptotic activity. Increased Bcl2 expression and decreased Bax expression leading to reduction in Bax/Bcl2 ratio was evidenced. Further, upregulation of procaspase 3 and downregulation of cleaved caspase 3 coupled with prevention of loss of phase II enzyme HO-1 with proven cardioprotective ability considerably, provided a strong scientific rationale that *D. bulbifera* has the potential to ameliorate myocardial ischemia and reperfusion injury by improving ventricular function and inhibition of necrosis and apoptosis in cardiomyocytes [42].

**Tumor and cancer**

Aborigines from Tully district in North Queensland use a decoction of *D. bulbifera* against skin cancer [18]. Similarly it is also used in traditional Chinese medicine against cancer [25]. Phytochemicals present in extracts (75 % ethanol, v/v) of chopped rhizomes exhibited potent antitumor promoting properties. Among the flavonols, kaempferol-3,5-dimethyl ether (IC₅₀ = 0.64 µg/mL) exhibited strongest inhibition followed by carayatin (IC₅₀ = 3.0 µg/mL), myricetin (IC₅₀ = 3.7 µg/mL) and (+)-catechin (IC₅₀ = 13.1 µg/mL) against tumor promotion in JB6 (Cl 22 and Cl 41) cells induced by a promoter, 12-O-tetradecanoylphorbol-13-acetate (TPA). In contrast to aglycones, flavonol glycosides, quercetin-3-O-galactopyranoside, myricetin-3-O-galactopyranoside, myricetin-3-O-glucopyranoside showed a considerably reduced activity due to the presence of sugar moieties [12]. Diosbulbin B with demethyl diterpenoid skeleton, selectively inhibited solid sarcoma 180 tumor growth in mice significantly, compared to A375-S2, Hela, L929 and JB6 cells as reported in various studies [12,22]. The study was conducted by administration of diosbulbin B (0.2 mg/head/day), diosbulbin B (0.2 mg/head/day) and diosbulbin A 2-O-β-D-glucopyranoside (0.2 and 0.1 mg/head/day) by i.p. daily for 5 days to male ddY mice inoculated with total of 180 sarcoma cells. Sixteen days after inoculation, the tumors were removed and weighed which revealed that diosbulbin B resulted in reduction of tumor weight by 57.89 % while diosbulbin A reduced up to 50.19 % [4]. Further studies revealed moderate inhibitory effect of ethyl-O-β-D-fructopyranoside (IC₅₀ > 30 µg/mL) and butyl-O-β-D-fructopyranoside (IC₅₀ > 30 µg/mL) from *D. bulbifera* on JB6 neoplastic transformation [22]. In another study, norditerpene compound, 8-epidiosbulbin E acetate failed to show any cytotoxicity against variety of human cancer cells, namely MCF-7 (breast cancer), SiHa (cervical cancer) and A431 (epidermal carcinoma), ensuring its potential to be used in non-cancer drug discovery programmes [16]. Dried rhizomes of *D. bulbifera*, collected from Anhui Province of China containing pennogenin-3-O-α-L-rhamnopyranosyl-(1→3)-[α-L-rhamnopyranosyl-(1→2)]-β-D-glucopyranoside and pennogenin-3-O-α-L-rhamnopyranosyl-(1→4)-[α-L-rhamnopyranosyl-(1→2)]-β-D-glucopyranoside showed 99.1% and 92.6% inhibition against human hepatocarcinoma cells and Bel7402, respectively at a concentration of 10 µM. The compounds further, exhibited cell growth inhibition toward SMMC7721 human hepatocarcinoma carcinoma cells [26]. Diosbulbins N, O, P showed lower activity (IC₅₀ > 40µM) when tested against five cancer cell lines, namely, HL-60, SMMC7721, A549, MCF7 and SW480 for their cytotoxic activity [23]. Cytotoxicity studies on BCV364 cells (urinary bladder carcinoma cells), revealed that the isolated spirostanol derivatives, pennogenin 3-O-α-L-rhamnopyranosyl-(1→4)-[α-L-rhamnopyranosyl-(1→2)]-β-D-glucopyranoside (IC₅₀ = 8.5 µg/mL) and spirocanol A (IC₅₀ = 5.8 µg/mL) showed moderate inhibition due to membrane toxicity via LDH liberation. However, the furostanol derivative, 26-O-β-D-glucopyranosyl-(25R)-5-en-24-enoic acid (17α,22α,26-tetraol-3-O-α-L-rhamnopyranosyl-(1→4)-α-L-rhamnopyranosyl-(1→2)]-β-D-glucopyranoside (IC₅₀ = 14.3 µg/mL) also showed a moderate activity, but by a direct influence of the mitochondrial metabolism, without liberation of LDH [32].

**Synthesis of Nanoparticles**

In spite of having a treasure of diverse groups of phytochemicals, *D. bulbifera* was not explored in the field of nanobiotechnology, until recently. We had reported for the first time the potential of its tuber extract to synthesize AuNPs of exotic shapes, namely gold nanotriangles, nanoprism, nanotrapezoid and spheres in a range from 50 to 300 nm. Maximum synthesis of AuNPs was achieved at 50°C by complete reduction of 1 mM chloroauric acid at 90 mins which was found to be faster as compared to maximum synthesis of AuNPs after 5 h by Plumbago zeylanica root extract (PZRE) [20,43]. Rapid
reduction by *D. bulbifera* tuber extract (DBTE) might be due to its high total reducing sugar content (3.41 ± 0.15 mg/mL) and high flavonoid content (4 ± 0.12 mg/mL) while PZRE contained 1.25 ± 0.04 mg/mL and 0.95 ± 0.05 mg/mL of total reducing sugar and total flavonoids, respectively. Further, the aqueous tuber extract synthesized anisotropic AgNPs in the form of rare nanotriangles, nanorods, spheres and hexagons in the size range of 8–20 nm at 50°C with 0.7 mM AgNO₃ solution in 5 h. Bioreduced AgNPs possessed potent antibacterial activity against both Gram-negative bacteria, namely *Acinetobacter baumannii*, *Enterobacter cloacae*, *Escherichia coli*, *Haemophilus influenzae*, *Klebsiella pneumonia* *Neisseria mucosa*, *Proteus mirabilis*, *Pseudomonas aeruginosa*, *Salmonella typhi*, *Serratia odorifera*, *Vibrio parahaemolyticus* and Gram-positive bacteria, namely, *Bacillus subtilis*, *Psenbacillus koreensis* and *Staphylococcus aureus*. A selective synergistic activity was observed where β-lactam, piperacillin exhibited 3.6 fold increase while macrolide, erythromycin showed 3 fold increase in potency against multidrug-resistant *A. baumannii* when combined with AgNPs. Likewise, a combination of AgNPs with chloramphenicol and vancomycin against *P. aeruginosa* resulted in 4.9-fold and 4.2-fold increase in zone diameter, respectively. 11.8-fold increase in zone diameter of streptomycin in combination with AgNPs against *E. coli* was found to be most significant. The unique phytochemistry of *D. bulbifera* with both reducing agents like ascorbic acid, citric acid and phenolics along with starch as capping agent and saponins helped in reduction, stabilization and shape evolution of nanoparticles [21].

**Toxicity and Detoxification**

Roots of *D. bulbifera* from China are reported as toxic, thereby might have achieved limited focus on its use in traditional medicine. Dioscin and diosbulbin B, derived from *D. bulbifera* roots (Huang-yao-zí) are responsible for liver toxicities, nausea, abdominal pain, coma and even death. Oral administration of decoction (400 g/kg) in male Sprague–Dawley rats for 72 h, exhibited elevated levels of taurocholate, creatinine, betaine, dimethylglycine (DMG), acetate and glycine. On the contrary, a reduction in the levels of succinate, 2-oxoglutarate, citrate, hippurate and urea was observed. Marked increase in the organ coefficients of liver and kidney of rats was noticed on exposure to Huang-yao-zi. Histopathological alterations of liver included diffuse hepatocyte degeneration, apoptosis, necrosis in addition to ballooning degeneration of hepatocytes and vascular congestion of hepatic sinusoid and portal areas. Impairment of mitochondrial energy metabolism indicated by reduction in citrate, 2-oxoglutarate and succinate levels coupled with inhibition of ornithine cycle and urea production confirmed oxidative injury of hepatic mitochondria leading to inhibition of ATP formation resulting in further inhibition of hippurate synthesis. Similarly, elevation in taurocholate levels due to glutathione depletion also indicated oxidative hepatic damage [44]. Another study, revealed that ethyl acetate fraction (EF) of hydroalcoholic extract of *D. bulbifera* rhizome from China exhibited dose dependent hepatotoxicity in ICR male and female mice when administered consecutively for fourteen days. Maximum elevation in levels of biomarkers of liver injury, namely, alanine transaminase (ALT) and aspartate transaminase (AST) were observed at a highest dose of 480 mg/kg. Reduction in the levels of glutathione-related enzymes including superoxide dismutase (SOD), glutathione peroxidase (GPx), glutathione-S-transferase (GST), glutathione reductase (GR) and glutamate-cysteine ligase (GCL) of hepatic tissues of EF treated mice indicated oxidative stress mediated liver injury in mice [45]. Hepatotoxicity against normal human liver cell line L-02 was reported by diosbulbin D isolated from the rhizome of *D. bulbifera* from China. A time and dose dependent manner of reduction in cell viability was shown by the benzene fraction, highest being 4.32% ± 1.87 at a dose of 800 µg/mL. Annexin V and propidium iodide assay, Hoechst 33258 staining and the occurrence of a sub-G1 peak indicated diosbulbin D mediated apoptosis induction which was further confirmed to be caspase 3 dependent [46].

Traditional food processing techniques were scientifically validated as most efficient for removal of bitter and toxic compounds from *D. bulbifera* tubers collected by aboriginal people from two locations in northeast Arnhem Land, NT, Australia. Bitterness due to presence of saponins and sapogenins in Central American, South African and Indian species, tannins and polyphenols in Indo-Chinese varieties and furanoid nortiterpenes (diosbulbins) mostly in China, can be effectively removed by the traditional techniques like leaching, thereby, rendering palatability to the processed sliced tubers, otherwise described as "cheeky", meaning bitter or poisonous in aboriginal English. Treatment practices varying from baking, followed by overnight leaching of the sliced tubers for 12 h in running water, resulted in reduction of major bitter and toxic compound, diosbulbin D (0.07 mg/g) decreasing it to a very low level under the taste threshold rendering the final food palatable [47].

**Conclusions**

Since ancient times, *D. bulbifera* is being used in different parts of the world as traditional medicine against several diseases. Numerous studies on its therapeutic potential are accomplished, as it is considered to be a natural treasure of bioactive principles which can be used for production of new medicines with higher efficacy and biocompatibility with least side effects. Recent researches are continuously adding up new attributes to its pre-existing wide spectrum therapeutic window. As detailed in this review, the comprehensive classical compilation of promising medicinal applications, *in-vitro* and *in-vivo* studies on *D. bulbifera* will enable to search for the untapped pool of novel lead compounds. Further intensive study on isolation and identification of novel compounds with antiviral and antibiofilm properties can broaden its horizon against infectious diseases. Similarly, this review will encourage the screening of more compounds from different groups for plasmid curing efficacy and even for synthesis of novel multifunctional nanomedicine by conjugating with nanocarriers towards rational drug designing and targeted drug delivery. Simultaneously, more scientific experimentation can be initiated with different parts of *D. bulbifera* as well as its isolated phytochemicals to generate evidences supporting its traditional applications, deciphering the underlying mechanism and searching for its utility as nutraceuticals.

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**References**

1. Saravanan M, Ignacimuthu S (2015) Hypocholesterolemic effect of Indian medicinal plants - A review. Med Chem 5: 040-049.
2. Baija YPS (1999) Dioscorea balanciana Kosanin and D. caulicacca Lipsky: In vitro culture and production of diosgenin. In: Biotechnology in agriculture and forestry 43Medicinal and Aromatic Plants XI. Springer, Berlin Heidelberg, New York, 85-102.
3. Murray RDH, Jorge ZD, Khan NH, Shahjahan M, Qasiduddin M (1984) Diosbubin d and 8-epidiosbulbin e acetate, norclerodane diterpenoids from Dioscorea bulbifera tubers. Phytochemistry: 23: 623–625.
4. Komori T (1997) Glycosides from Dioscorea bulbifera. Toxicon 35: 1531-1536.
5. Mbitamcha M, Kamyani A, Teponno RB, Tapondjou AL, Walcho P, et al. (2011) Analgesic and Anti-Inflammatory Properties of Extracts from the Bulbil
of Dioscorea bulbifera L. var sativa (Dioscoreaceae) in Mice and Rats. Evid Based Complement Alternat Med 2011.

6. Lather A, Gupta V, Garg S, Singh A, Sachdeva K (2011) Pharmacological potential of the plants used in treatment of piles - A review. J Natura Concinitia 2: 255-265.

7. Gupta D, Singh J (1989) p-Hydroxyacetophenone derivatives from Dioscorea bulbifera. Phytochemistry 28: 947–949.

8. Subasini U, Thenmozhi S, Sathymurthy D, Vetriselvan S, Rajamanickam GV, et al. (2013) Pharmacognostic and phytochemical investigations of Dioscorea bulbifera L. Int J Pharm Life Sci 4: 2693-2700.

9. Tang Z, Zhou Y, Zeng Y, Zang S, He P, et al. (2006) Capillary electrophoresis of the active ingredients of Dioscorea bulbifera L. and its medicinal preparations. Chromatographia 63: 617-622.

10. Adeniran AA, Sonibare MA (2013) In vitro potential anthelmintic activity of bulbs of Dioscorea bulbifera L. on earthworms and liverflukes. J Pharmcogn Phytother 5: 196-203.

11. McKoy ML, Omoruyi F, Simon O, Asemota H (2003) Investigation of the effects of a sapogenin-rich preparation from a Jamaican yam (Dioscorea sp.) on blood cholesterol levels in rats. Proc West Pharmacol Soc 46: 156–159.

12. Gao H, Kuroyanagi M, Wu L, Kawahara N, Yasuno T, et al. (2002) Antitumor-promoting constituents from Dioscorea bulbifera L. in JB6 mouse epithelial cells. Biol Pharm Bull 25: 1241-1243.

13. Bhandari MR, Kawabata J (2004) Organic acid, phenolic content and antioxidant activity of wild yam (Dioscorea spp.) tubers of Nepal. Food Chem 88: 163–168.

14. Jindal MN, Kelkar VV, Doctor RB (1969) The anorexient activity of Kalool-kund (Dioscorea bulbifera Linn.), methylphenidate and cocaine in rats: a preliminary study. Indian J Med Res 57: 1075-1080.

15. Nguelfack TB, Dutra RC, Paszcuk AF, Andrade EL, Tapondjou LA, et al. (2010) Anticotoxic activities of the methanol extract of the bulbs of Dioscorea bulbifera L. var sativa in mice is dependent of NO-cGMP-ATP-sensitive-K(+) channel activation. J Ethnopharmacol 128: 567-574.

16. Shiriam V, Jahagirdar S, Latha C, Kumar V, Puranik V, et al. (2008) A potential plasmid-curing agent, 8-epi-pseudobolin E acetate, from Dioscorea bulbifera L. against multidrug-resistant bacteria. Int J Antimicrob Agents 32: 405-410.

17. Ahmed Z, Chishti MZ, John RK, Bhagat A, Gupta KK, et al. (2009) Antihyperglycemic and antidyslipidemic activity of aqueous extract of D. bulbifera tubers. Diabetologia Croatica 38: 63–72.

18. Williams C (2013) Medicinal plants in Australia volume 4: an antipodean apothecary, Rosenberg Publishing Science 552: 437-444.

19. Panduraju T, Bitra VR, Vemula SK, Reddy P, Reddy V (2010) Wound healing activity of Dioscorea bulbifera lin. J Pharm Res 3: 3138-3139.

20. Ghosh S, Derle A, Ahire M, More P, Jagtap S, et al. (2013) Phytochemical analysis and free radical scavenging activity of medicinal plants Gnidia glauca and Dioscorea bulbifera: Potent Amylase and Glucosidase Inhibitors. Evid Based Complement Alternat Med 2012: 929051.

21. Okigbo R N, Arnaquasi CL, Amadi JE, Ukpai UJ (2009) Potential inhibitory effects of some African tuberous plant extracts on Escherichia coli, Staphylococcus aureus and Candida albicans. Int J Integrat Biol 6: 91-98.

22. Ghosh S, Ahire M, Patil S, Jagbunde A, Bhat Dusane M, et al. (2012) Antidiabetic Activity of Gnidia glauca and Dioscorea bulbifera: Potent Amylase and Glucosidase Inhibitors. Evid Based Complement Alternat Med 2012: 929051.

23. Salunke GR, Ghosh S, Kumar RJS, Khade V, Vashisth P, et al. (2014) Rapid efficient synthesis and characterization of silver, gold, and bimetallic nanoparticles from the medicinal plant Plumbago zeylanica and their application in biofilm control. Int J Nanomedicine 9: 2635–2653.

24. Liu Y, Huang R, Liu L, Peng J, Xiao B, et al. (2010) Total phenolic contents and antioxidant capacities of selected chinese medicinal plants. Int J Mol Med 26: 2362-2372.

25. Ghosh S, Derle A, Ahire M, More P, Jagtap S, et al. (2013) Phytochemical analysis and free radical scavenging activity of medicinal plants Gnidia glauca and Dioscorea bulbifera. PLoS One 8: e82529.

26. Vasanthi HR, Mukherjee S, Ray D, Pandian Jayachandran KS, Lekki I, et al. (2010) Protective role of air potato (Dioscorea bulbifera) of yam family in myocardial ischemic reperfusion injury. Food Junct 1: 278-283.

27. Webster J, Beck W, Ternai B (1984) Toxicity and bitterness in Australian and New Zealand medicinal plants. Vol 1 TERI Press, India 85-88.

28. Kuate V, Betrandteponno R, Mbaveng AT, Taponjou LA, Meyer JJ, et al. (2012) Antibacterial activities of the extracts, fractions and compounds from Dioscorea bulbifera. BMC Complement Altern Med 12: 228.

29. Teponno RB, Taponjou DL, Gating D, Djoukeng JD, Abou-Mansour E, et al. (2006) Bafoudiosbulbins A and B, two anti-salmonellal clerodane diterpenoids from Dioscorea bulbifera L. var sativa. Phytochemistry 67: 1957-1963.

30. Teponno RB, Taponjou DL, Gating D, Djoukeng JD, Abou-Mansour E, et al. (2006) Bafoudiosbulbins A and B, two anti-salmonellal clerodane diterpenoids from Dioscorea bulbifera L. var sativa. Phytochemistry 67: 1957-1963.

31. Adesanya SA, Ogundana SK, Roberts MF (1989) Dihydrodistilbene phytotoxins from Dioscorea bulbifera and D. dumetorum. Phytochemistry 28: 713-774.

32. Taponjou LA, Jenett-Siems K, Bottger S, Melzig MF (2013) Steroidal saponins from the flowers of Dioscorea bulbifera var. sativa. Phytochemistry 95: 341-350.

33. Liu H, Tsim KW, Chou GX, Wang JM, Ji LL, et al. (2011) Phenolic compounds from the rhizomes of Dioscorea bulbifera. Chem Biodivers 8: 2110-2116.

34. Wang G, Lin B, Liu J, Wang G, Wang F, et al. (2009) [Chemical constituents from tubers of Dioscorea bulbifera]. Zhongguo Zhong Yao Za Zhi 34: 1679-1682.

35. Ghosh S, More P, Derle A, Patil AB, Markad P, et al. (2014) Diosgenin from Dioscorea bulbifera: novel hit for treatment of type II diabetes mellitus with inhibitory activity against α-amyrase and α-glucosidase. PLoS One 9: e106039.

36. Das A (2008) Agro-techniques of selected medicinal plants. Vol 1 TERI PRESS, India 85-88.

37. Okigbo R N, Arnaquasi CL, Amadi JE, Ukpai UJ (2009) Potential inhibitory effects of some African tuberous plant extracts on Escherichia coli, Staphylococcus aureus and Candida albicans. Int J Integrat Biol 6: 91-98.

38. Das A (2008) Agro-techniques of selected medicinal plants. Vol 1 TERI PRESS, India 85-88.

39. Webster J, Beck W, Ternai B (1984) Toxicity and bitterness in Australian and New Zealand medicinal plants. Vol 1 TERI Press, India 85-88.

40. Das A (2008) Agro-techniques of selected medicinal plants. Vol 1 TERI PRESS, India 85-88.