**Gymnanthemum coloratum**: Review of its Medicinal uses, Phytochemistry and Pharmacological Properties

Alfred Maroyi*

Department of Botany, University of Fort Hare, Private Bag X1314, Alice 5700, South Africa

Abstract: *Gymnanthemum coloratum* is a shrub or a small tree widely used as traditional medicine throughout its distributional range in tropical Africa. The current study is aimed at reviewing the phytochemistry, pharmacological properties and medicinal uses of *G. coloratum*. Literature on pharmacological properties, phytochemistry and medicinal uses of *G. coloratum* was obtained from numerous internet sources such as Scopus, Elsevier, Scifinder, Google Scholar, Pubmed, ScienceDirect, BMC and Web of Science. Other sources of information included pre-electronic sources such as journal articles, theses, book chapters, books and other scientific publications obtained from the university library. The articles published between 1964 and 2020 were used in this study. The current study showed that *G. coloratum* is used as an anthelmintic, and traditional medicine for reproductive problems, schistosomiasis, liver diseases, sexually transmitted infections, diabetes, sores and wounds, respiratory problems, malaria, skin diseases, fever and gastro-intestinal problems. Ethnopharmacological research identified flavonoids, lactones, amino acids, essential oils, alkaloids, anthocyanins, cardenolids, coumarins, flavonoids, glycosides, leucoanthocyanins, phenols, quinones, reducing sugars, saponins, steroids, tannins, terpenoids and triterpenes from the aerial parts, leaves, roots and stems of *G. coloratum*. The aerial parts, leaves, roots and whole plant parts of *G. coloratum* and compounds isolated from the species exhibited anthelmintic, antimicrobial, anti-inflammatoty, anti-sickling, insecticidal and larvicidal, antimalarial, antioxidant and anti-inflammatory activities. *Gymnanthemum coloratum* should be subjected to detailed phytochemical, pharmacological and toxicological evaluations aimed at correlating its medicinal uses with its phytochemistry and pharmacological activities.

Keywords: Asteraceae, Compositae, *Gymnanthemum coloratum*, indigenous knowledge, traditional medicine, *Vernonia colorata*.

INTRODUCTION

*Gymnanthemum coloratum* (Willd.) H. Rob. & B. Kahn is a shrub or a small tree belonging to the Asteraceae or Compositae family. The genus Gymnanthemum Cass. did not gain general acceptance and all species belonging to this genus were included in a broadly circumscribed genus Vernonia Schreb. [1], a genus that is now known to be restricted to North America [2,3]. Therefore, *G. coloratum* was later transferred to the genus Gymnanthemum, a genus characterized by a shrubby habit, epaleate receptacle with more or less obtuse involucral bracts, white to violet flowers and pinnately-veined leaves [1]. The genus name Gymnanthemum is derived from two Greek words, “gymnos” which means “naked” and “anthos” which means “flower” in reference to the lack of palease on the receptacle of Gymnanthemum species. The epithet “coloratum” is derived from the Latin word “colorata”, which means “colourful” in reference to whitish flowers [4]. The English common names of *G. coloratum* include “lowveld tree vernonia”, “lowveld bitter-tea”, “star-flowered bitter-tea”, “star-flowered vernonia” and “starry bitter tea”. The synonyms associated with the name *G. coloratum* include Baccharis senegalensis Pers., Decaneurum grande DC., D. senegalense (Pers.) DC., Eupatorium coloratum Willd., Gymnanthemum cupulare Cass., G. grande (DC.) Sch. Bip. ex Walp., G. querциfolium Steetz., G. senegalense (Pers.) Sch. Bip. ex Walp., Vernonia aldhbreensis Hemsl., V. ciiřifera S. Moore, V. colorata (Willd.) Drake, V. grandis (DC.) Humb., V. longipetiolata Muschl., V. oxyura O. Hoffm., V. polyura O. Hoffm. and V. senegalensis (Pers.) Less. [1,3,5].

*Gymnanthemum coloratum* is an erect shrub or small tree up to 9 m in height [5,6]. The bark of *G. coloratum* is pale grey-brown in colour, rather rough when old and smaller branches are covered with velvety hairs. The leaves are leathery, elliptic to ovate in shape, dark green in colour and rather harshly hairy above, paler green with long dense woolly hairs below. The leaves have visible net-veins, tapering apex with tapering to slightly rounded base, markedly waxed, entire to very finely toothed margins. The flower heads occur in terminal dense heads, forming a wide branched panicle, which is white to off-white in colour and sweetly scented. The fruit is a slender nutlet, hairless, plumed with rough bristles. *Gymnanthemum coloratum* grows in open woodland, bushveld and

*Address correspondence to this author at the Department of Botany, University of Fort Hare, Private Bag X1314, Alice 5700, South Africa; Tel/Fax: 0027719600326; E-mail: amaroyi@u fh.ac.za*
grassland, at the base of kopjes, along streams, in riverine fringes, termite mounds, edges of vleis and pans. Gymnanthemum coloratum has been recorded in Angola, Benin, Botswana, Burkina Faso, Cameroon, Central African Republic, Comoros, Côte d’Ivoire, the Democratic Republic of Congo (DRC), Eswatini, Gabon, Gambia, Ghana, Guinea, Guinea-Bissau, Kenya, Mali, Mozambique, Nigeria, Senegal, Sierra Leone, Tanzania, Togo, Zambia and Zimbabwe at an altitude ranging from 20 m to 1540 m above sea level. Gymnanthemum coloratum is widely used as traditional medicine throughout its distributional range in tropical Africa with the roots sold as herbal medicines in informal herbal medicine markets for the treatment and management of parasitic diseases in humans in Mozambique [7]. Gymnanthemum coloratum is also collected from the wild as an edible leafy vegetable in Ghana and Nigeria [8,9]. It is, therefore, within this background that the current study was undertaken aimed at documenting the phytochemistry, pharmacological properties and medicinal uses of G. coloratum.

Medicinal uses

The bark, leaves, roots and whole plant parts of G. coloratum are widely used as an anthelmintic, and traditional medicine for reproductive problems, schistosomiasis, liver diseases, sexually transmitted infections, diabetes, sores and wounds, respiratory problems, malaria, skin diseases, fever and gastrointestinal problems (Table 1; Figure 1). Other minor medicinal applications of the species that are recorded in two countries and supported by at least two literature sources include the use of the species as an emetic [10,11], poison antidote [10-12] and herbal medicine for anaemia [11,12], epilepsy [8,10-12], heart failure [11,12], jaundice [11,12], pregnancy and labour [13,14], rheumatism [11,15-18] and tonsillitis [10-12].

Phytochemistry

Patel and Rawson [50] identified the compound vernonin and cardiac glycoside from the leaves, roots and stems of G. coloratum. Zdero et al. [51] isolated 19-hydroxyglaucolide A, 19-hydroxyvermodalin, vernodalin, isobutyrate, germacrene D, caryophyllene and lupeylacetate from the aerial parts of G. coloratum. Reid et al. [16] and Adu et al. [35] identified the compound vernodalin from the leaves of G. coloratum. Rabe et al. [29] identified sesquiterpene lactones such as vernolide, 11β,13-dihydroverno1ide and vernodalin from the leaves of G. coloratum. Ciocchi et al. [52] identified androst-8-en glycosides, stigmastane-type glycosides and stigmastane-type steroids from G. coloratum leaves. The major essential oils identified from G. coloratum leaves include 1-ethyl-2-methyl benzene (5.4%), 2,3-dihydroxypropyl ester (5.6%), p-xylene (8.2%), tetradecan-2-one (8.3%), hexadecan-2-one (8.6%), n-hexadecanoic acid (9.7%), hexahydrofarnesyl acetone (12.2%), 9-octadecenoic acid (12.9%), 13-docosenoic acid (13.9%), hexadecanoic acid (14.8%), 3,11-tetradecadien-1-ol (19.9%), 4-methyl-1-docene (24.1%) and cis-13-eicosenoic acid (36.6%) [9,53,54]. Other phytochemical compounds identified from the leaves of G. coloratum include alanine, alkaloids, anthocyanins, aspartic acid, cardenolids, coumarins, flavonoids, glutamic acid, glycine, glycosides, leucine, leucoanthocyanins, phenols, phenyl alanine, proline, phlobatannins, quinones, reducing sugars, resins, saponins, serine, steroids, tannins, terpenoids, threonine, triterpenes, tyrosine and valine [35,38,42,54-59]. Some of these phytochemical compounds identified from the species may be responsible for the biological activities of the species.

Pharmacological Properties of Gymnanthemum coloratum

The following biological activities have been reported from the aerial parts, leaves, roots and whole plant parts of G. coloratum and compounds isolated from the species: anthelmintic, antimicrobial, anti-Blastocystis, anti-inflammatory, antisickling, insecticidal and larvicidal, antiplasmodial, antimalarial, antioxidant, antiproliferative, anti-Toxoplasma, hypoglycaemic and antidiabetic and cytotoxicity activities.

Anthelmintic Activities

Morah et al. [9] evaluated the anthelmintic activities of 100 µg/ml, 50 µg/ml and 25 µg/ml essential oil isolated from G. coloratum leaves against Lumbricus terrestris. The mortality of worms after sixteen hours of exposure ranged from 26.7% to 100% at the evaluated concentrations [9].

Antimicrobial Activities

Kelmanson et al. [45] evaluated the antibacterial activities of methanol, ethyl acetate and water extracts of G. coloratum leaves, roots and stems against Bacillus subtilis, Escherichia coli, Klebsiella pneumoniae, Micrococcus luteus, Pseudomonas aeruginosa, Staphylococcus aureus and Staphylococcus epidermidis using the disc-diffusion assay and twofold serial dilution with neomycin (2.0 µg)
<table>
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<td>Poison antidote</td>
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<td>Reproductive problems (infertility, impotence, frigidity and painful uterus)</td>
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<td>Respiratory problems (cough, pneumonia and tuberculosis)</td>
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<td>Sexually transmitted infections (gonorrhoea and venereal diseases)</td>
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<td>Skin diseases (boils eczema, scabies)</td>
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<td>[8,10-12,16,25,27,29,30,33,35,45,46]</td>
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<td>Sores and wounds</td>
<td>Leaves and roots</td>
<td>Côte d’Ivoire, DRC, Ghana, Mali and Tanzania</td>
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<td>Tonic</td>
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<td>South Africa</td>
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<td>Tonsillitis</td>
<td>Bark, leaves and roots</td>
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<td>Ulcerative colitis</td>
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<td>Vertigo</td>
<td>Leaves and roots</td>
<td>Mozambique</td>
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as a positive control. The methanol and ethyl acetate extracts of the leaves exhibited activities against *Bacillus subtilis*, *Micrococcus luteus*, *Pseudomonas aeruginosa* and *Staphylococcus aureus* with minimum inhibitory concentration (MIC) values ranging from 0.5 mg/ml to 4.0 mg/ml [45]. Reid *et al.* [16] evaluated the antibacterial activities of hexane, ethyl acetate, water and ethanol extracts of *G. coloratum* leaves and the compound vernodalin isolated from the species against *Escherichia coli*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, *Bacillus subtilis*, *Micrococcus luteus*, *Staphylococcus aureus* and *Staphylococcus epidermidis* using the disc diffusion assay with neomycin as a positive control. *Micrococcus luteus*, *Klebsiella pneumoniae* and *Staphylococcus aureus* were inhibited by ethyl acetate extract while the MIC of vernodalin against *Staphylococcus aureus* was 100 µg/ml [16]. Rabe *et al.* [29] evaluated the antibacterial activities of the compounds vernolide, 11β,13-dihydrovernolide and vernodalin isolated from the leaves of *G. coloratum* against *Staphylococcus aureus*, *Bacillus subtilis*, *Escherichia coli* and *Klebsiella pneumoniae* using the micro-dilution technique with neomycin as a positive control. The compounds exhibited activities with the MIC values ranging from 0.1 mg/ml to >8.0 mg/ml [29]. Stafford *et al.* [60] evaluated the antibacterial activities of ethanol extracts of *G. coloratum* leaves against *Bacillus subtilis*, *Staphylococcus aureus*, *Escherichia coli* and *Klebsiella pneumoniae* using the micro plate method. The extract exhibited activities with the MIC values ranging from 0.8 mg/ml to 1.6 mg/ml [60]. Adebayo *et al.* [56] evaluated the antibacterial activities of aqueous and ethanol extracts from the leaves of *G. coloratum* against *Escherichia coli*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa* and *Staphylococcus aureus* using agar diffusion and the dilution methods with chloramphenicol as a positive control. The extracts exhibited activities with zone of inhibition ranging from 5.0 mm to 24.0 mm and the MIC values ranging from 4.0 mg/ml to 6.0 mg/ml [56]. Guenne *et al.* [57] evaluated the antibacterial activities of dichloromethane, ethyl acetate and butanol extracts of *G. coloratum* leaves against *Escherichia coli*, *Vibrio cholerae*, *Salmonella typhimurium*, *Bacillus cereus*, *Escherichia coli*, *Proteus mirabilis*, *Shigella dysenteriae* and *Staphylococcus aureus* using agar diffusion method and serial dilution technique. The extracts exhibited activities with the zone of inhibition ranging from 6.0 mm to 34.0 mm and the MIC values ranging from 2.5 mg/mL to >20.0 mg/mL [57]. Julien *et al.* [58] evaluated the antibacterial activities of ethyl acetate extract of *G. coloratum* leaves against *Staphylococcus aureus* and *Pseudomonas aeruginosa* using agar diffusion method and serial dilution technique. The extract exhibited activities against *Staphylococcus aureus* and *Pseudomonas aeruginosa* with the zone of inhibition of 13.0 mm and 11.0 mm and the MIC values of 3.1 mg/mL and 3.1 mg/mL, respectively [58]. Adebayo *et al.* [8] evaluated the antibacterial activities of crude, aqueous, petroleum ether, chloroform and diethyl ether leaf extracts of *G. coloratum* against *Staphylococcus aureus*, *Pseudomonas aeruginosa*, *Escherichia coli*, *Klebsiella pneumoniae* and *Salmonella typhi* using the agar-well diffusion methods. The aqueous and crude extracts exhibited activities against *Staphylococcus aureus* with MIC values ranging from 5.0 mg/ml to 7.5 mg/ml [8]. Bongo *et al.* [59] evaluated the antibacterial activities of petroleum ether, ethyl acetate and methanol extracts of the leaves of *G. coloratum* against *Escherichia coli* and *Staphylococcus aureus* using the microdilution method.
Only *Staphylococcus aureus* was sensitive to the extract exhibiting MIC value of ≤ 250.0 µg/mL [59]. Adu *et al.* [35] evaluated the antibacterial activities of the compound vernolide isolated from the leaves of *G. coloratum* against *Escherichia coli*, *Staphylococcus aureus* and *Enterococcus faecalis* using the micro broth dilution assay. The compound showed activities against *Escherichia coli*, *Staphylococcus aureus* and *Enterococcus faecalis* with MIC values ranging from 0.3 mg/ml to 0.4 mg/ml [35]. Morah *et al.* [9] evaluated the antimicrobial activities of essential oil isolated from *G. coloratum* leaves against *Candida albicans*, *Rhizopus nigricans*, *Streptococcus faecalis*, *Staphylococcus aureus*, *Pseudomonas aeruginosa* and *Salmonella typhi* using the agar disc diffusion and the dilution methods. The essential oil exhibited activities with zones of inhibition ranging from 8.0 mm to 20.0 mm while MIC values ranging from 0.8 µg/ml to 3.1 µg/ml [9].

**Anti-Blastocystis Activities**

Christensen *et al.* [71] evaluated the anti-Blastocystis activities of ethanol extracts of folium, flos and radix of *G. coloratum* against Blastocystis spp. (subtype 4) using an anti-Blastocystis activity assay with metronidazole as a positive control. The extracts exhibited activities with half maximal inhibitory concentration (IC$_{50}$) value of 117.9 µg/mL [71].

**Anti-Inflammatory Activities**

Stafford *et al.* [70] evaluated the anti-inflammatory activities of aqueous and ethanol extracts of *G. coloratum* leaves using the cyclooxygenase (COX-1) inhibition assay. The COX-1 inhibition exhibited by aqueous and ethanol extract was 38.0% and 100.0%, respectively [70]. Cioffi *et al.* [52] evaluated the anti-inflammatory activities of the chloroform: methanol (9:1) extract of the *G. coloratum* leaves which exhibited activities using a carrageenan-induced rat paw assay. Cioffi *et al.* [52] also evaluated the anti-inflammatory activities of the compounds androst-8-en glycosides, stigmastane-type glycosides and stigmastane-type steroids from *G. coloratum* leaves using the carrageenan-induced rat paw assay, and the compounds were either inactive or exhibited weak activities [52].

**Anti-Sickling Activities**

Bongo *et al.* [59] evaluated the anti-sickling activities of petroleum ether, ethyl acetate and methanol extracts of the leaves of *G. coloratum* using the Emmel test. The extracts showed anti-sickling activities with a normalization rate of between 10.0% and 50.0% [59].

**Insecticidal and Larvicidal Activities**

Morah *et al.* [9] evaluated the insecticidal and larvicidal activities of essential oil isolated from *G. coloratum* leaves against adult and larvae of *Anopheles mosquitoes*. The essential oil exhibited activities with the median lethal concentration (LC$_{50}$) values of 75.0 µg/ml and 50.0 µg/ml after sixteen hours of exposure for the larvae and adult mosquitoes, respectively [9].

**Antiplasmodial Activities**

Benoit *et al.* [62] and Benoît-Vical *et al.* [63] evaluated the antiplasmodial activities of the aqueous extract of leaves and stems of *G. coloratum* against two strains of *Plasmodium falciparum*, FcB 1-Colombia (chloroquine-resistant) and F32-Tanzania (chloroquine-sensitive) using the parasite $^3$H-hypoxanthine incorporation assay with chloroquine as a positive control. The extract exhibited activities with the IC$_{50}$ values ranging from 2.4 mg/L to 7.8 mg/L [62,63]. Kraft *et al.* [64] evaluated the antiplasmodial activities of petrol ether: ethyl acetate (1:1) extracts of the aerial parts of *G. coloratum* and the compounds 11β,13-dihydrovernoladin, vernodalol, 11β,13-dihydrovernonolide and 11β,13,17,18-tetrahydrovernonolide isolated from the aerial parts of the species using the $[^3]$H hypoxanthine incorporation assay against the chloroquine sensitive and chloroquine-resistant strains of *Plasmodium falciparum*. The extracts and compounds exhibited activities with the IC$_{50}$ values ranging from 1.1 µg/mL to 4.8 µg/mL [64]. Clarkson *et al.* [65] evaluated antiplasmodial activities of aqueous, dichloromethane, and dichloromethane: methanol (1:1) extracts of leaves and twigs of *G. coloratum* against *Plasmodium falciparum* using the parasite lactate dehydrogenase (pLDH) assay. Both the dichloromethane: methanol (1:1) extracts of the leaves and twigs showed activities with the IC$_{50}$ values of 4.7 µg/ml and 14.1 µg/ml, respectively [65]. Ménan *et al.* [66] evaluated the antiplasmodial activities of water, ethanol and pentane extracts of the leaves of *G. coloratum* against two strains of *Plasmodium falciparum*, FcM29-Cameroon (chloroquine-resistant) and a Nigerian chloroquine-sensitive strain, with chloroquine as a positive control. The extracts exhibited activities with the IC$_{50}$ values ranging from 10.0 µg/ml to 102.0 µg/ml in comparison to IC$_{50}$ values of 0.03 µg/ml to 0.04 µg/ml exhibited by the positive control [66]. Chukwujekwu *et al.* [67] evaluated the antiplasmodial activities of the compounds vernolide and vernodal from the
leaves of *G. coloratum* against a chloroquine-sensitive strain of *Plasmodium falciparum* (D10), using the parasite lactate dehydrogenase (pLDH) with chloroquine as a positive control. The compounds vernolide and vernodalin exhibited activities with the IC$_{50}$ values of 1.9 µg/ml and 0.5 µg/ml, respectively, against the IC$_{50}$ value of 7.6 ng/ml exhibited by the positive control [67]. Idris *et al.* [54] evaluated antiplasmodial activities of methanol extracts of the leaves of *G. coloratum* against *Plasmodium bergeri* at 200, 400 and 600 mg/kg body weight with chloroquine as a positive control. The extract exhibited dose-dependent activities, reducing parasitemia by 81.8%, 80.9% and 83.2% for 200, 400 and 600 mg/kg body weight groups, respectively, compared to 100% inhibition exhibited by the positive control [54].

**Antimalarial Activities**

Kaou *et al.* [31] evaluated the antimalarial activities of dichloromethane, methanol and methanol: water (1:1) extracts of *G. coloratum* aerial parts and roots using culture-adapted reference strain of *Plasmodium falciparum* type W2 resistant to chloroquine, pyrimethamine and proguanil. The dichloromethane extracts of roots and aerial parts were the most active with the IC$_{50}$ values of 3.0 µg/ml and 6.0 µg/ml, respectively [31].

**Antioxidant Activities**

Guenne *et al.* [55] evaluated the antioxidant activities of methanol extracts of *G. coloratum* leaves using 2, 2'-diphenyl-1 picrylhydrazyl (DPPH) free radical scavenging, 2,2'-azinobis (3 ethylbenzothiazoline-6-sulphonate (ABTS) and ferric reducing antioxidant power (FRAP) assays with quercetin as a positive control. The extract exhibited activities with the IC$_{50}$ value of 14.0 µg/ml in DPPH, 54.4 µmol/g in ABTS and ferric ion reduction of 0.6 mmol AAE/g [55].

**Antiproliferative Activities**

Kaou *et al.* [31] evaluated the antiproliferative activities of dichloromethane, methanol and methanol: water (1:1) extracts of *G. coloratum* aerial parts on human monocytic THP1 cells in an *in vitro* toxicity assay. The dichloromethane extract was the most active with the IC$_{50}$ value of 10.0 µg/ml [31].

**Anti-Toxoplasma Activities**

Benoit-Vical *et al.* [63] evaluated the anti-Toxoplasma activities of the aqueous extract of leaves and stems of *G. coloratum* on Toxoplasma gondii in an *in vitro* assay assessed on MRC5 tissue cultures and quantified by enzyme-linked immunoassay. The extract exhibited activities with IC$_{50}$ values ranging from 17.0 mg/L to 18.0 mg/L [63].

**Hypoglycaemic and Antidiabetic Activities**

Sy *et al.* [68] evaluated the hypoglycaemic and antidiabetic activities of the aqueous extract of the leaves of *G. coloratum* in normoglycaemic and alloxan-induced diabetic rats in comparison to glibenclamide antidiabetic activities. The extract at 300 mg/kg, per os induced hypoglycaemic effect in normoglycaemic rats. In alloxan-induced diabetic rats, the extract at 300 mg/kg, per os decreased the blood glucose level. Therefore, the extract exhibited hypoglycaemic and antidiabetic activities in normoglycaemic and alloxan-induced diabetic rats [68]. Sy *et al.* [22] evaluated the hypoglycaemic and antidiabetic activities of acetone and hexanic extracts of the leaves of *G. coloratum* in normoglycaemic and alloxan-induced diabetic rats. The acetonic extract at 100 mg/kg, per os induced a reduction of blood glucose in normoglycaemic rats while the hexanic extract increased the glycaemia in normoglycaemic rats. Therefore, the acetonic extract possesses both hypoglycaemic and antidiabetic activities in normoglycaemic and alloxan-induced diabetic rats [22].

**Cytotoxicity Activities**

Ménan *et al.* [66] evaluated the cytotoxicity activities of water, ethanol and pentane extracts of the leaves of *G. coloratum* against melanoma cells (A375) by estimating the cell growth using the [3H]-hypoxanthine incorporation assay after 24 hours and 72 hours of incubation. The extracts exhibited activities with the IC$_{50}$ values ranging from 30.0 µg/ml to 150.0 µg/ml [66]. Chukwujekwu *et al.* [67] evaluated the cytotoxicity activities of the compounds vernolide and vernodalin isolated from the leaves of *G. coloratum* using the 3-(4,5-dimethylthiazol-2-yl)-2-5-diphenyltetrazolium bromide (MTT) colorimetric assay with emetine as a positive control. The compounds vernolide and vernodalin exhibited activities with the IC$_{50}$ values of 1.8 µg/ml and 1.5 µg/ml, respectively, against the IC$_{50}$ value of 0.08 µg/ml exhibited by the positive control [67].

**CONCLUSION**

The present review summarizes the medicinal uses, phytochemistry and pharmacological properties of *G.
**CONFLICT OF INTEREST**

The author declares no conflict of interest.

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Gymnanthemum coloratum


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