**Abstract**

Plants have been used in the treatment of human diseases since centuries. Due to their medicinal values, more than 80% of the modern world population still rely on plants as their primary source of medicines. Traditional plant-based medicines are widespread in Asian countries like the Indian subcontinent, Bangladesh, China, Japan, Pakistan, Indonesia, Myanmar, and in the continent of Africa. Nowadays, plant-derived medicines are gaining wider acceptance even in developed countries of the Western world. More than 50% of all drugs currently in clinical use are of natural origin. Plants are therefore emerging as a novel source for drugs and opening up new vistas in drug therapy research. A bird’s eye view of the therapeutic potential of the angiospermic plant *Glinus oppositifolius* (L.) Aug. DC. (Family: Molluginaceae) has been presented in this review, along with the ethnomedical uses and scientific evidences presented in support of the traditional claims. Several pharmacologically active chemical compounds have been reported from the plant in recent years and the biological roles of those chemical compounds have been summarized. The anti-cancer effects shown by some of those phyto-constituents have also been elucidated. The novel chemical constituents reported from this plant may evoke further research on the plausible medicinal effects and the bio-safety standards of *Glinus oppositifolius*. 

**Keywords:** *Glinus oppositifolius*, pharmacological use; ethnomedical usage; bio-active compounds.

**Introduction**

Plants have been used to treat diseases since the dawn of civilization on earth. For thousands of years, medicinal plants have been the part and parcel for humankind for their healing abilities. Historical reports show that Shen Nung, an Emperor of ancient China around 2800 B.C. authorised the compilation of the first medicinal herbal literature, “*Pentsao*” [1, 2]. Plant-derived products have dominated the human pharmacopoeia for thousands of years in an almost unchallenged fashion [3]. Traditional medical practices are an important part of the primary healthcare system in the developing world [4]. According to World Health Organization (WHO) reports, more than 80% of the world’s population are dependent on plants for medicinal purposes. Traditional medicinal practices are widespread in Asian countries like India, Africa, Bangladesh, Japan and China and over the past decade they have gained widespread acceptance in first-world countries like USA. Often, whole plants have been used directly, or on occasions, plant constituents derived from a specific plant part have been used [5,6]. More than half of modern clinical drugs are natural product derived. Plants possess thousands of active chemical constituents which show various medicinal roles and they form an important part of drug-discovery programme. Hundreds of plants form the focus of laboratory studies every year for their medicinal roles. One such plant with a variety of medicinal roles is the subject of this review study. *Glinus oppositifolius* (L.) Aug. DC. (Molluginaceae) is a slender and much branched ascending annual herb growing up to 40 cm tall. The plant is commonly found in damp sandy areas or desiccated localities around ponds and lakes, and pans across South East Asian tropical and sub-tropical countries [7] at low elevations like India, Pakistan, Phillipines, Mali, Thailand, and China. The plant also grows in West Africa, from Senegal to South Nigeria. The plant is reportedly rich in macro and micronutrients and is widely used as a vegetable in Africa, India and the Phillipines. It is also widely used in traditional medicine and finds an important place in the ethnomedical Pharmacopoeia around these countries.

**Botanical information**

*Glinus oppositifolius* (L.) Aug. DC. is an annual, prostrate weed belonging to family Molluginaceae. They are diffuse or prostrate, glabrous herbs, and upto 50 cm long.

**Ethnomedical uses of Glinus oppositifolius by indigenous population and tribes across the world**
Traditional medicine and diet have served mankind through the ages for the prevention and treatment of most chronic diseases. Chemical constituents present in *Glinus oppositifolius* are reported to be a good source of saponins, flavonoids, carbohydrates, polysaccharides, steroids, alkaloids and several other aromatic compounds. Combining the literature has shown that the plant has been traditionally used for various purposes since a long time. In Mali, hot water extract of aerial part has been traditionally used as a medicine to heal wounds, while decoction of aerial part has been known to possess an anti-malarial effect [8-13]. *Glinus* extracts are also used for relief from joint pain, inflammations, diarrhoea, intestinal parasites, fevers, boils and skin disorders [13, 14]. It is also used in treatment of jaundice [13, 15], and hepatitis [13, 16]. In India, *Glinus* has been used in traditional and herbal pharmacopeia as a stomachic, uterine stimulant, aperients, lochia, as treatment for earache [13, 17], and in dermatitis, itches and skin diseases [13, 18, 19]. Plant parts have been used to increase appetite, and as treatment for leucoderma, tonic for intestine and urinary infections [13, 20] and also for relieving fever, cough [13, 21] and liver problems. Whole plants or often plant parts have been used as diuretic, anthelmintic, expectorant [13, 22] and antipyretic [13, 23]. The Korku tribes of Amravati in Maharashtra use the whole plant as a vegetable [24]. In Tamil Nadu, the plant is considered an antiseptic and efficacious in suppressed lochia; it is mixed with castor oil and applied warm for earache. The plant juice is applied to itches and other skin diseases [25]. In Malda district of West Bengal, the root paste of this plant is given orally against white discharge and flower paste is mixed with wood paste of *Santalum album* and is used to treat dysentery [26]. The aboriginals from Gadchiroli District use the plant as vegetables [27]. Regular eating of the curry made from leaves of this plant is considered to have stimulatory action for liver [28]. In Thailand, aqueous whole plant extract of *Glinus* has been traditionally used as expectorant and antipyretic [13, 29]. In Bangladesh, *Glinus* extracts have been used traditionally for treatment of joint pain, inflammation, diarrhoea, fever, boils and skin disorders [13, 30, 31]. Folk medicinal practitioners [locally known in Bangladesh as Kavirajes or Vaidyas] and they use the leaves to keep the body cool and the leaves are also cooked and eaten [13, 32]. They also use the plant against gastrointestinal disorders (including dysentery, diarrhoea, indigestion, colic, acidity, constipation, bloating, lack of appetite, stomach ache) [13, 33]. In the Southern District Noakhali, whole plants are used to cure skin diseases, earache, indigestion, loss of appetite [34]. *G. oppositifolius* in Taiwan is used in treating inflammation with chronic illnesses, including cancer [13]. In the Philippines, it is reputed to exhibit anti-diabetes and antimicrobial properties [35].

### Chemicals constituents reported from *Glinus oppositifolius*

A huge number of chemical constituents have been reported from *Glinus oppositifolius*. The vast array of phyto-constituents present in *Glinus oppositifolius* can be broadly categorized into eight groups:

- **Aromatic compounds** [Figure. 1. Different aromatic compounds extracted from *Glinus oppositifolius*]. Flavonoid Glycosides, Acylamino derivatives and nucleosides [Figure. 2. Different flavonoid glycosides, acylamino derivatives and nucleotides extracted from *Glinus oppositifolius*], Triterpenoids and Triterpenoidal saponins [Figure. 3. Different triterpenoids and triterpenoidal saponins extracted from *Glinus oppositifolius*], Sterols and pectic polymers [11, 13] [Figure. 4. Different sterols extracted from *Glinus oppositifolius*].

The aromatic compounds reported from *Glinus oppositifolius* are benzoic acid, 4-hydroxybenzoic acid, 4-hydroxybenzaldehyde, 4-hydroxy-acetophenone, methyl 4-hydroxybenzoate, anisic acid, vanillin, 4-hydroxy-3-methoxycetophenone, acetosyringone, 4-hydroxy-3,5-dimethoxy benzaldehyde, 4-hydroxybenzyl alcohol, 2-(4-hydroxyphenyl) ethanol, cinnamic acid, trans-ferulic acid [13, 36].

The flavonoid glycosides which are reported to be present in *Glinus oppositifolius* are Kaempferol 3-O-galactopyranoside, isorhamnetin 3-O-β-D-xylpyranosyl-β-D-galactopyranoside, vitexin, and vicenin-2 [13, 28].

Among Triterpenoidal saponins, Spergulacin, spergulacin-A, ginoside C, spergulin A, spergulin B [13, 18], spergulagenin-A, spergulagenin-B, spergulagenin-C, spergulagenin-D [13, 36], linoside A, glinoside B [13, 14] have been reported. Triterpenoids like squalene, oppositifolone and lutein [37] were reported to be also present in *Glinus oppositifolius*.

Two acylamino derivatives, L-(-)-(N-trans-cinnamoyl)-arginine [13, 28] and 132(R)-pheophytin a [13, 36] have also been reported from *Glinus*. Three steroid compounds—Spinasterol, β-sitosterol, Sigmasterol [13, 36] have been reported from *Glinus oppositifolius* as well as two novel pectic polymers [10, 13], GOA1 and GOA2, which have been successfully isolated and characterized.
Figure 1. Different aromatic compounds extracted from *Glinus oppositifolius*.

Figure 2. Different flavonoid glycosides, acylamino derivatives and nucleotides extracted from *Glinus oppositifolius*.
Figure 3. Different triterpenoids and triterpenoidal saponins extracted from *Glinus oppositifolius*.

Figure 4. Different sterols extracted from *Glinus oppositifolius.*
Pharmacological activities

With Crude Extracts

The crude extracts of *Glinus oppositifolius* were reported [13] to have some pharmacological activities [Figure 6. Different pharmacological activities of crude extracts and pure compounds isolated from *Glinus oppositifolius*] and the findings are discussed below:

**Figure 5.** Mode of action of Vicenin-2 and β-sitosterol isolated from *Glinus oppositifolius*.

**Figure 6.** Different pharmacological activities of crude extracts and pure compounds isolated from *Glinus oppositifolius*.
Cytotoxic activity of crude extract

Crude methanolic extract of 14 edible Bangladeshi vegetables (including *Glinus oppositifolius*) were prepared and their cytotoxic effect on brine shrimp was tested at different concentrations of 5 μg/mL, 10 μg/mL, 20 μg/mL and 50 μg/mL. *Glinus oppositifolius* extracts showed cytotoxicity [36] (Chen 2011). Another study on brine shrimp showed that after 24 hours of exposure, the LC50 and LC90 were found to be 8 μg/mL and 85.12 μg/mL (compared with standard vincristine sulphate) [38].

Crude methanolic and aqueous extracts showed no toxicity up to 4000 mg/kg as per the directive of European Economic Community and thus the LD50 dose was categorized as unclassified [EC Directive 83/467/EEC, 183] [20]. The crude ethanolic extract was shown to have no cytotoxic activity at 2000 mg/kg dosage when examined with the guidelines of Committee for the Purpose of Control and Supervision of Experimental Animals [21].

Crude methanolic extracts of different concentrations from 100 mg/kg to 2000 mg/kg showed no signs of toxicity up to 72 hours on female albino mice. The study was conducted as per OECD guidelines [22].

B. Toxic activity of crude extracts on organisms

On Fungi

Crude dichloromethane extract from whole *Glinus oppositifolius* was used to treat *Candida albicans* and then MTT assay was carried out. The study reported that the extract showed anti-fungal effects, evident from the clear spots on purple background [16].

On Microbes

Crude methanolic extract was tested against an array of microorganisms ranging from *Bacillus subtilis* to *Blastomyces dermatitidis* and *Candida albicans* and was reported to possess low to moderate amounts of inhibitory effect on the growth of the organisms. When tested with ethanolic extract, the treatment showed promise against *Salmonella typhi*, *Pseudomonas aeruginosa* and several other micro-organisms. Petroleum ether extract showed results against *Staphylococcus aureus*, *Pityrosporum ovale* and several other micro-organisms. All the extracts showed growth inhibitory effect against *Bacillus subtilis*. The minimum inhibitory concentrations (MIC) of the extracts against the microorganisms were also tested out, and petroleum ether, methanolic and ethanolic extracts showed significant MICs against *Bacillus subtilis*, *Escherichia coli* and *Trichophyton sp.* [39].

Leaf extracts were tested out against several non-resistant and multi-drug resistant strains of *Escherichia coli*, *Pseudomonas aeruginosa*, *Staphylococcus aureus*, *Bacillus subtilis*, *Pseudomonas aeruginosa*, *Escherichia coli*, and *Aspergillus niger* and the extracts were reported to show potent antimicrobial effect, when compared against norfloxacin - a standard antimicrobial drug [21].

On Mollusc species

Crude extracts showed toxic effects on *Bulinus truncatus* and *Biomphalaria pfeifferi* [41].

On Helminths

Methanolic extracts were administered on *Pheretima posthuma* in a dose dependent manner and results showed that the shortest time of paralysis and death occurred at 20 mg/mL concentration. The activity was reported to be analogous to standard drug against Helminths-albendazole [23].

Against larval species

Dichloromethane and methanol extracts of the whole plants were prepared. The crude extracts were tested against two mosquito species - *Culex quinquefasciatus* and *Anopheles gambiae* larvae. The mosquito species tested showed complete mortality (100%) after 24 hours of treatment with the crude extract at a concentration of 500 mg/L [16].

Quantification of antioxidant capacity of crude extracts

Against a standard ascorbic acid IC50 of 14 μg/ml, crude ethanolic extract, petroleum ether extract and methanol extract of *Mollugo oppositifolius* exhibited an IC50 of 27 μg/ml, 28 μg/ml and 40 μg/ml respectively [39].

With crude ethanolic extracts, several radical scavenging assays like nitric oxide scavenging, superoxide anion scavenging, hydrogen peroxide scavenging and biochemical assays like total phenolic content, total flavonoid content were carried out. The reports showed that the free radicals scavenging ability of the extract was concentration dependent [17].

In a β-carotene linoleate model, crude methanol extracts were administered and it exhibited antioxidant activity [16]. Methanolic extract of leaves showed total flavonoid content to be 25.46 mg of crude extract per gram of quercetin equivalents and total antioxidant capacity to be 79.48 mg of crude extract per gram of ascorbic acid equivalents [31]. When the aqueous and crude methanolic extracts of whole plants were tested under Linoleic acid and DPPH models, the results showed that while the extracts possessed antioxidant activity, the methanolic extract was more potent in its effects [20].
Other pharmacological activities of crude extracts

Hepatoprotective activity

Ethanolic extract of the aerial parts of *Glinus oppositifolius* was used to carry out serum glutamate oxaloacetate transaminase (SGOT), serum glutamate pyruvate transaminase (SGPT), ALP, cholesterol and bilirubin assays and paracetamol was administered to induce increase in serum enzyme, bilirubin and cholesterol levels. Reports showed that treatment with 400 mg/kg dosage of crude ethanolic extract prevented the effect of paracetamol [18]. Carbon tetrachloride was used to induce to liver damage in rats and then they were treated with root methanolic extract of *Glinus oppositifolius*. The treatment was orally administered and the SGPT, SGOT, and bilirubin levels were tested. The results showed that the treatment with extract increased recovery from liver damage [18].

Anti-diarrhoeic activity

Methanol extracts and loperamide at the dosages of 500 mg/kg and 3 mg/kg respectively were used to treat diarrhoeic rats and experimental results showed that the total number of faeces and the number of diarrhoeic faeces were both reduced after treatment. The percentage inhibition of faecal count when compared to control came out to be 86% approximately for the methanolic extract [43].

Anti-depressant and anxiolysis activity

The effects of crude methanol extract of *Glinus oppositifolius* on the normal brain functioning of mice was studied. The study exhibited that oral administration of the ethanolic extracts induced anxiolytic effects. Results demonstrated that ethanol extract significantly ($p<0.01$) reduced locomotion of the animals both in hole cross and in open field tests. Ethanol extract decreased the falling latency of the animals from rotarod, significantly ($p<0.01$) with the doses of 100 and 200mg/kg. Diazepam was also seen to exhibit the same effects as ethanol extract in all the experiments. Ethanol extract also showed sedative effects on mice, which was proved by oral administration of the crude extract, where it enhanced the sleeping duration in a dose dependent manner [44].

Anti-inflammation and analgesic activity

Water and ethanol extracts of *Glinus oppositifolius* exhibited anti-inflammatory activity, and the extracts showed high potency in inflammatory paw oedema assay and constrictive abdominal response assays. The results exhibited that the ethanol extract was more potent in its anti-inflammatory capacity than the water extract. The extracts were reported to have a characteristic profile of non-steroidal anti-inflammatory drugs (NSAID) in their activity [45].

Anti-diabetogenic activity

Alloxan was used to induce diabetes in mice and *G. oppositifolius* was administered which exhibited decrease in blood glucose level compared with the control group. Doses of 200 mg/kg and 400 mg/kg showed a concentration-dependent glucose level lowering activity when compared to the control. The results were found to be statistically significant ($p<0.05-0.001$) [31]. The study was an effort to investigate the effect of different solvent extract of the *Glinus oppositifolius* on normal and streptozotocin-induced diabetic rats. In glucose tolerance test, the oral administration of methanolic extract of *Glinus oppositifolius* suppressed the increase in glucose level. The conclusion was that the methanolic extract of *Glinus oppositifolius* at a dosage of 500 mg/kg was anti hyperglycemic in streptozotocin-induced diabetic rats and oral glucose tolerant rats [46].

Ethanol extracts of the concentrations of 200 and 400 mg/kg of the aerial parts of *G. oppositifolius* produced significant decrease in the blood glucose level compared with the controls in alloxan-induced hyperglycemic, normoglycemic and oral glucose tolerance test in Wistar Albino rats and was comparable with the standard drug glibenclamide [2.5 mg/kg] [21].

Methanol extracts of the whole plant in single oral doses 200 and 400 mg/kg exhibited significant antihyperglycemic activity in glucose-overloaded hyperglycemic mice [20] and rats [22] compared to the standard drug metformin and glibenclamide, respectively.

Anti-hyperlipidemic activity

Crude methanolic and aqueous extracts of *Glinus oppositifolius* was used to orally treat diabetic rats and showed positive results when they were administered in dosages of 200 mg/kg and 400 mg/kg [20]. Crude methanolic extracts, when used to treat Triton induced diabetic rats showed that at dosages of 200 mg/kg and 400 mg/kg induced reduction of total cholesterol and triglycerides. It also showed antagonistic effects in two classes of lipoprotein, because while it reduced the low-density lipoprotein, it increased the high-density lipoproteins [22].

With pure compounds isolated from *Glinus oppositifolius*

Some pure compound fractions isolated from *Glinus oppositifolius* were reported [13] to have some pharmacological activities (Figure. 6.) and the findings are discussed as follows:

Antiplasmodial activity

Glinoside A and B fractions were separated from crude extract and were used to treat two strains of *Plasmodium falciparum*, one chloroquine-sensitive and another chloroquine-resistant. The results exhibited that Glinoside A and B had antiplasmodial activity against both the strains, 3D7 and W2, which are chloroquine sensitive and...
resistant, respectively. The evidence suggested that the fractions isolated had better activity than pure compound Glinoside A [13, 15].

**Immunomodulation activity**

From crude water of *Glinus oppositifolius* leaves and stems, pectin type polysaccharide fractions of GOA1 and GOA2 were isolated and tested for their activity towards various immune cells. The results exhibited that the polysaccharide fractions had immunomodulating properties. The polysaccharides, when administered in a dose-dependent manner, proliferated B cells, and induces chemotaxis of other cells like natural killer cells and T cells. The secretion of interleukin-1β was also induced by GOA1 fractions, and GOA2 exhibited potent induction activity on secretion of some cytokines involved in inflammatory response [10, 11].

**Pharmacological activities of pure compounds (reported from *Glinus oppositifolius*) studied in other systems**

Several compounds reportedly present in *Glinus oppositifolius* have been the subject of separate studies against cancer cell lines in various models and also have shown effective results against several other diseases. The sources of the chemical compounds were either synthetic, or from a plant other than *Glinus oppositifolius*. Several chemical compounds like benzoic acid [47], trans-ferulic acid [48-51], vanillin [52], stigmasterol [53], spinasterol [54, 55], β-sitosterol [56-68], vitexin [69], vicenin [70], kaempferol [71] showed anti-cancer effects against breast cancer cell lines, prostate cancer cell lines, colon cancer cell lines, stomach cancer cell lines, leukaemia (Table 1). β-sitosterol acts through down-regulation of Bcl-2 and upregulation of Bax, thereby causing caspase 3 cleavage and PARP cleavage and thereby causes apoptosis (Figure 5.). Vicenin-2 regulates cyclin expression and induces G2 arrest, downregulates the Akt/mTOR signalling pathways and thus interferes with cell proliferation. It also interacts with fibronectin and E-cadherin and prevents cell migration [Figure 5.]. Mode of action of Vicenin-2 and β-sitosterol isolated from *Glinus oppositifolius*. Among the chemical compounds mentioned, some have other biological roles too (Table 2). 2,2-(hydroxypropanamido) benzoic acid has been reported to show anti-thrombosis effects [72]. Trans-ferulic acid showed effect against inflammation and nephrotoxicity [73, 74] and hepatotoxicity in male Wistar rats [75]. It is effective against oxidative damage [76-78] and protects DNA from chemical induced damage [79, 80].Vanillin reportedly shows anti-mutagenic activity in damaged cells [81]. Stigmasterol was found to possess larvicidal activity [82].

<table>
<thead>
<tr>
<th>COMPOUND CLASS</th>
<th>NAME OF COMPOUND OF</th>
<th>CANCER TYPE AND CELL LINE</th>
<th>MODE OF ACTION</th>
<th>REFERENCE</th>
</tr>
</thead>
<tbody>
<tr>
<td>AROMATIC COMPOUND</td>
<td>4-HYDROXYBENZOIC ACID</td>
<td>Prostate cancer</td>
<td>Hsp90 chaperone activity</td>
<td>[47] (Seidel et al. 2016)</td>
</tr>
<tr>
<td>STERIODS</td>
<td>STIGMASTEROL</td>
<td>Gastric cancer</td>
<td>-</td>
<td>[53] (De Stefani et al. 2000)</td>
</tr>
<tr>
<td></td>
<td>SPINASTEROL</td>
<td>Breast cancer cell lines MCF-7, ZR-75-1, MDA-MB-231,SK-BR-3, and Hs578T.</td>
<td>Anti-proliferative effects</td>
<td>[54] (Jeon et al. 2005)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Anti-tumorigenic potential in Swiss</td>
<td>-</td>
<td>[55] (Villasenor &amp; Domingo 2000)</td>
</tr>
</tbody>
</table>

**Table-1. Compounds Showing Pharmacokinetic Activity Against Cancer Cell Lines.**
| β-SITOSTEROL | albinio mice | Enhances tamoxifen effectiveness on cancer cells by tweaking ceramide metabolism regulation | [56] (Awad et al. 2008) |
| Human Leukemic U937 cells | Breast cancer cells | Induced cytotoxicity and apoptosis by concentration dependent activation of caspase 3 and induction of Bax/Bcl-2 ratio | [57] (Park et al. 2007) |
| Stomach cancer | - | | [53] (De Stefani et al. 2000) |
| Stomach cancer cell line SGC-7901 | Apoptosis may be due to decrease of the bcl-2/bax ratio and DNA damage | [58] (Zhao et al. 2009) |
| Prostate cancer cell line PC-3 | Inhibition of cell growth and cell cycle arrest at different stages due to ROS and prostaglandin production | [59] (Awad et al. 2005) |
| Colon cancer cell line HT116 | induction of caspase-3 and caspase-9, decreased expression of Bcl-2 increase of Bax proteinrelease of cytochrome c | [60] (Choi et al. 2003) |
| Prostate cancer cell line LNCaP | Increase in apoptosis mediated by activation of the sphingomyelin cycle, and there is an increase in ceramide production | [61] (Awad et al. 1998) |
| Colon cancer cell line HT-29 | Increase of ceramide production | [61] (Awad et al. 1998) |
| Colon cancer cell line HT-29 | Inhibition of cell growth | [63] (Awad et al. 1996) |
| Cervical cancer cell line SiHa | Inhibition of cellular proliferation by inhibition of microtubule associated protein 2 and tubulin alpha and subsequent mitotic arrest | [64] (Wu et al. 2006) |
| Breast cancer cell line MDA-MB-231 | Synergistic action with TRAIL | [65] (Park et al. 2008) |
| Breast cancer cell line MDA-MB-231, Lung cancer cell line A549 and Skin cancer cell line A431 | Dose-dependent cell growth inhibition, decrease in CDK4 and cyclin D1, increase in p21/Cip1 and p27/Kip1 protein levels, increased Bax/Bcl-2 protein ratio | [66] (Vundru et al. 68) |
| Breast cancer cell line MDA-MB-231 | Inhibition of cancer cell growth and increase in apoptosis | [67] (Awad et al. 2007) |
| Breast cancer cell line MDA-MB-231 | Increases in the activities of caspases 8 and 9, and caspase 3, thus inducing both intrinsic and extrinsic pathways | [68] (Awad et al. 2003) |
| Breast cancer cell line MCF-7 and MDA-MB-231 | Increase of Fas levels and caspase-8 activity | [68] (Awad et al. 2003) |

Breast cancer cell line MCF-7 and MDA-MB-231 stimulates serine palmitoyl transferase activity in both cell lines, and activates de novo ceramide synthesis, ceramide is pro-apoptotic signal [56] (Awad et al. 2008).

**FLAVONOIDS**

**VITEXIN**


**VICENIN**

- Prostate Cancer
  - Inhibits angiogenesis, migration and induces G2/M arrest, inhibits EGFR/Akt/mTOR/p70S6K pathway and induces apoptosis. [70] (Nagaprashantha et al. 2011)

**KAEMPFEROL**

- Breast cancer MCF-7 cells
  - Inhibited cell proliferation by showing an anti-oestrogenic activity [71] (Kim et al. 2016)

<table>
<thead>
<tr>
<th>COMPOUND CLASS</th>
<th>NAME OF COMPOUND</th>
<th>MEDICINAL ROLE</th>
<th>REFERENCE</th>
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<tbody>
<tr>
<td>AROMATIC COMPOUND</td>
<td>2-(2-HYDROXYPROPANAMIDO) BENZOIC ACID</td>
<td>Anti-platelet aggregation and anti-thrombosis</td>
<td>[72] (Zhang et al. 2017)</td>
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<tr>
<td></td>
<td>TRANS-FERULIC ACID</td>
<td>Ameliorated ionizing radiation-induced inflammation and glycerol-induced nephrotoxicity</td>
<td>[73, 74] (Das et al. 2014; Manikandan et al. 2014)</td>
</tr>
<tr>
<td></td>
<td>Modulated fluoride-induced oxidative hepatotoxicity in male Wistar rats</td>
<td>[75] (Panneerselvam et al. 2013)</td>
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<td></td>
<td>Water-soluble trans-FA sugar esters protected normal rat erythrocytes against peroxyl radical 2,2'-azobis-2-amidinopropane dihydrochloride (AAPH)-induced oxidative damage.</td>
<td>[76] (Yuan et al. 2005)</td>
<td></td>
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<tr>
<td></td>
<td>Exhibited protective capacity against oxidative damage caused by diabetes</td>
<td>[77, 78] (Roy et al. 2013; Ramar et al. 2012)</td>
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<td></td>
<td>Exerted protective effects against chemical induced DNA strand breaks</td>
<td>[79, 80] (Stagos et al. 2005; Tanaka et al. 1993)</td>
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<td></td>
<td>VANILLIN OR 4-HYDROXY-3,5-DIMETHOXY BENZALDEHYDE OR SYRINGALDEHYE</td>
<td>Exerts antimutagenic activity in damaged cells by promoting recombination and rejoining of DNA at homologous sites</td>
<td>[81] (Tamai et al. 1992)</td>
</tr>
<tr>
<td>STEROIDS</td>
<td>STIGMASTEROL</td>
<td>Larvicidal and repellent activity by acetylcholinesterase property</td>
<td>[82] (Gade et al. 2017)</td>
</tr>
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</table>

Clinical trials of compounds reported to be present in Glinus oppositifolius

Clinical trials were done for the following bio-active compound: β-sitosterol:

The study was designed to conduct a systematic review of the efficacy of β-sitosterol in subjects with benign prostatic hyperplasia (BPH). The study consisted of four trials comprising a total of 519 men, all of whom had BPH. The study was double-blind and lasted 4-26 weeks. Three trials used non-glucosidic β-sitosterols and one trial used a preparation that contained only β-sitosterol-β-d-glucoside. Compared with placebo, β-sitosterol improved urinary symptom...
scores and flow measures. For the two studies reporting the International Prostate Symptom Score (IPSS), the weighted mean difference against placebo was -4.9 IPSS points (95% confidence interval -6.3 to -3.5). The weighted mean difference for peak urinary flow rate was 3.91 mL/s (95% confidence interval 0.91 to 6.90, four studies) and for residual volume the weighted mean difference was -28.62 mL (95% confidence interval -41.42 to -15.83, four studies). β-sitosterol did not reduce prostate size. The trial using pure β-sitosterol-β-d-glucoside showed no improvement in urinary flow measures. Withdrawal rates for men assigned to β-sitosterol and placebo were 7.8% and 8.0% (not significant). The study concluded that although β-sitosterol improved urological symptoms and flow measures, the study was limited by short treatment duration and lack of standardized β-sitosterol preparations [83].

The trial was repeated again in the year 2000 by the same group of researchers and they found that 100% β-sitosterol-β-d-glucoside exhibited an improvement in the urinary flow measures [84]. At 18 months after enrolment in the 6-month multicentre double-blind placebo-controlled clinical trial with β-sitosterol (reported in the above paragraphs), the patients were re-evaluated using the modified Boyarsky score, the International Prostate Symptom Score and quality-of-life index, the maximum urinary flow rate (Qmax) and postvoid residual urine volume (PVR). This was an open extension of the original trial, and the condition was that after 6 months of treatment with β-sitosterol or administration of placebo (depending on which group the patients fell into), the patients were free to choose their further treatment for BPH. Patients were examined and 117 patients were eligible for analysis during the follow-up. Of the group, 38 patients who continued β-sitosterol treatment had stable values for all outcome variables between the end of the double-blind study and after 18 months of follow-up. The 41 patients choosing no further therapy had slightly worse symptom scores and PVR, but no changes in Qmax. Of the former placebo group, 27 patients who started β-sitosterol after the double-blind trial improved to the same extent as the treated group for all outcome variables. The 18 patients choosing no further therapy showed no signs of improvement [85].

Concluding remarks and future directions

The current review strives to offer an overall overview of the literature regarding phytochemical, traditional use and pharmacological activities of the angiosperm Glinus oppositifolius, which establishes that the studied plant is a treasure trove of bioactive compounds and the chemical constituents are therefore worthy of further study. The literature might be helpful to interested researchers, who are intending to investigate the plant in the near future to separate, isolate and identify the phytochemicals responsible for the disease curing properties of the plant, and also pharmaceutical companies which rely on natural products for preparing evidence based formulations. Some of the crude extracts show particular promise in curing common ailments, and the pure fractions isolated from the plant show truly novel immunomodulating activities, which needs to be further studied by researchers in near future for an avenue into drug discovery programme. It is evident from the review that some of the chemicals compounds reported to be present in Glinus oppositifolius have exhibited potent anti-cancer effects in other studies, however in those studies, the research groups worked with compounds which were obtained from different plant sources or bought commercially. Thus, it opens up an avenue of research into the isolation and testing of anti-cancer efficacy of bio-active compounds from Glinus. Nevertheless, more detailed study and clinical evaluations are needed to conclusively establish the efficacy, usefulness and safety standards for using this plant for medicinal purposes.

Conflict of Interest

The authors report no conflict of interest.

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