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Review Article

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Glinus oppositifolius (L.) Aug. DC: A Repository of Medicinal Potentiality

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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 ethnobotanical 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; ethnobotanical 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 ethnobotanical pharmacopeia 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.

Ethnobotanical uses of *Glinus oppositifolius* by indigenous population and tribes across the world

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Traditional medicine and diet has 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. Combing through 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 Maldah 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 anti-microbial 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-methoxyacetophenone, 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-galacto pyranoside, isorhamnetin 3-O-β-D-xylopyranosyl-β-D-galactopyranoside, vitexin, and vicenin-2 [13, 28].

Among Triterpenoidal saponins, Spergulacin, spergulacin-A, glinoside 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, Stigmasterol [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.

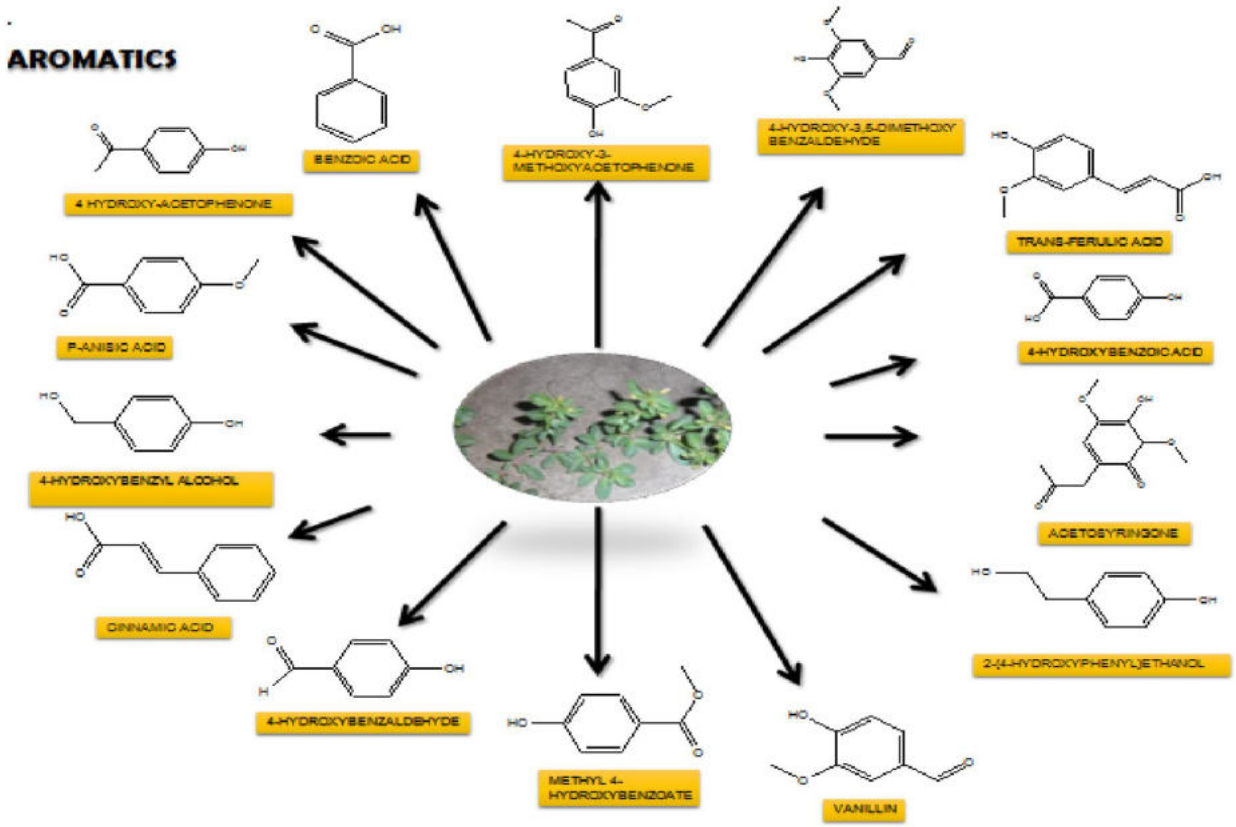

Figure 1. Different aromatic compounds extracted from *Glinus oppositifolius*.

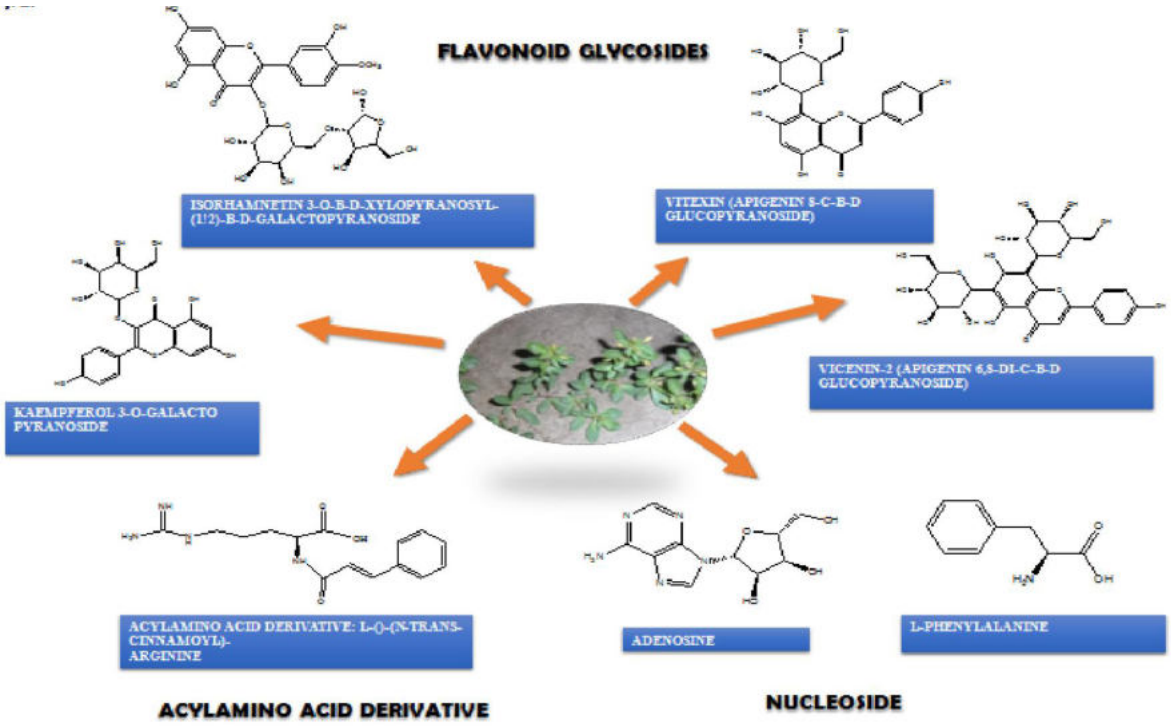

Figure 2. Different flavonoid glycosides, acylamino derivatives and nucleotides extracted from *Glinus oppositifolius*.

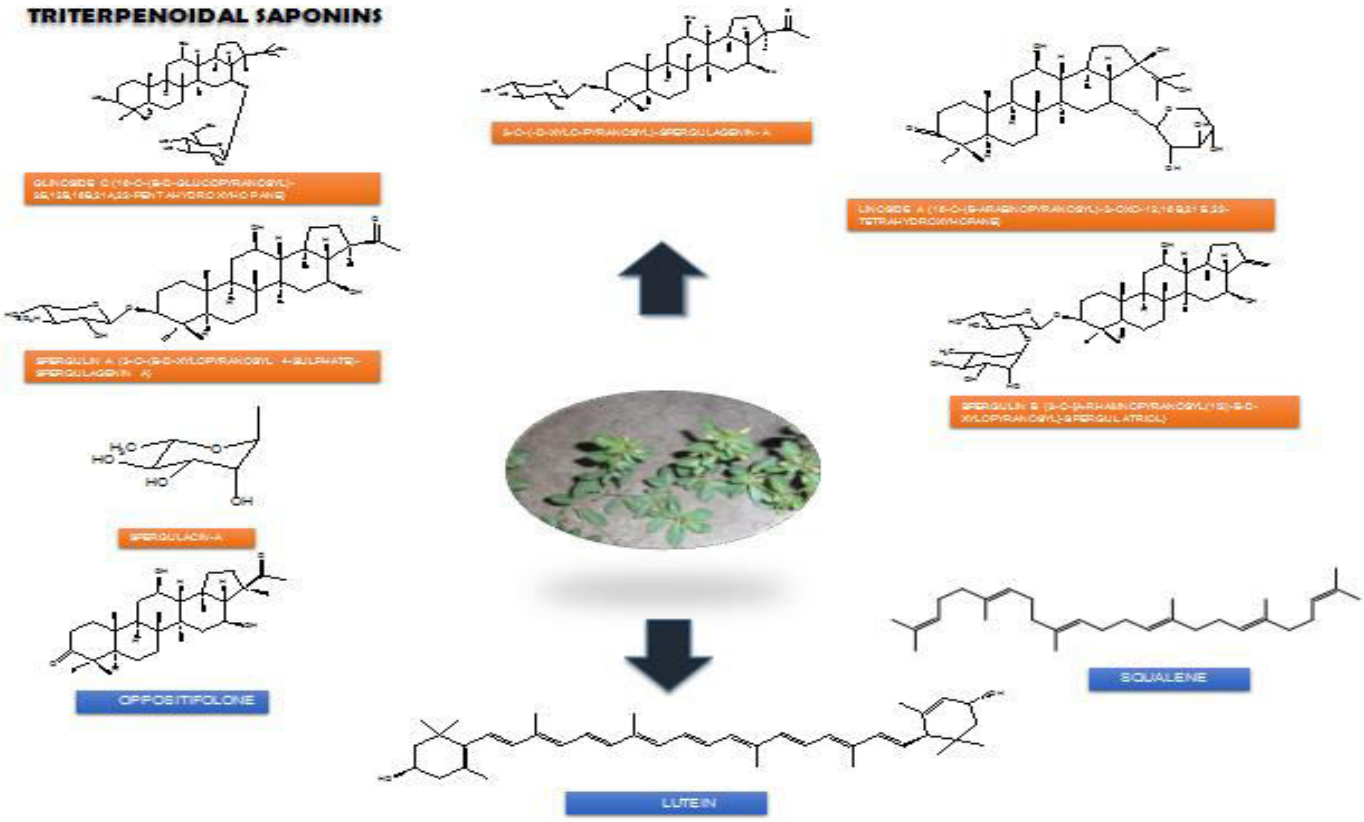

Figure 3. Different triterpenoids and triterpenoidal saponins extracted from *Glinus opposite*

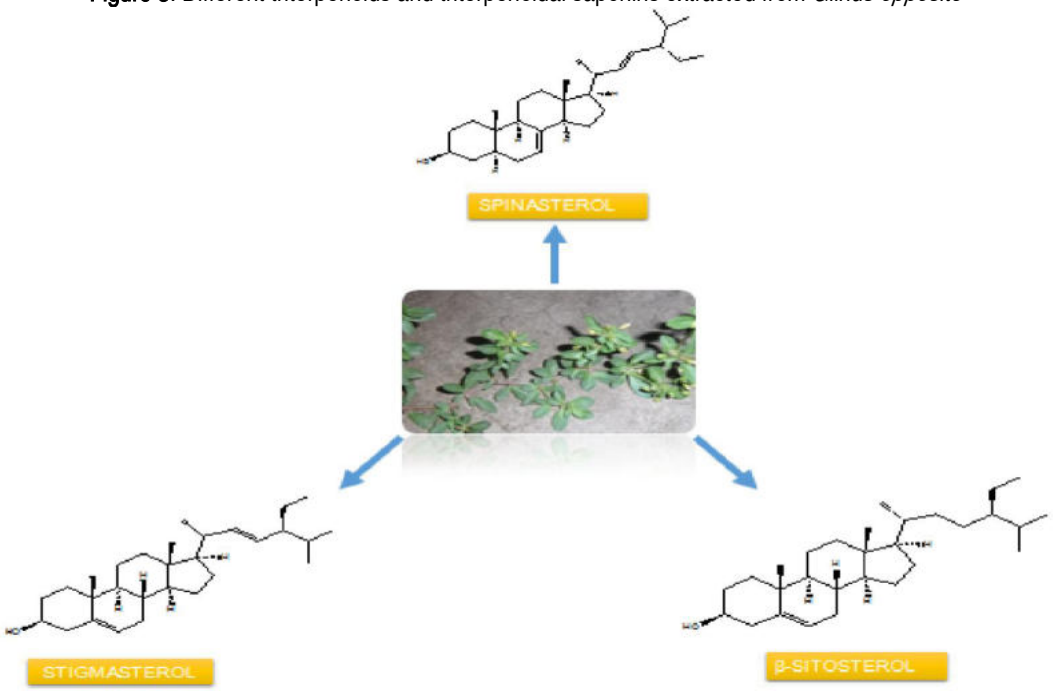

Figure 4. Different sterols extracted from *Glinus oppositifolius*.

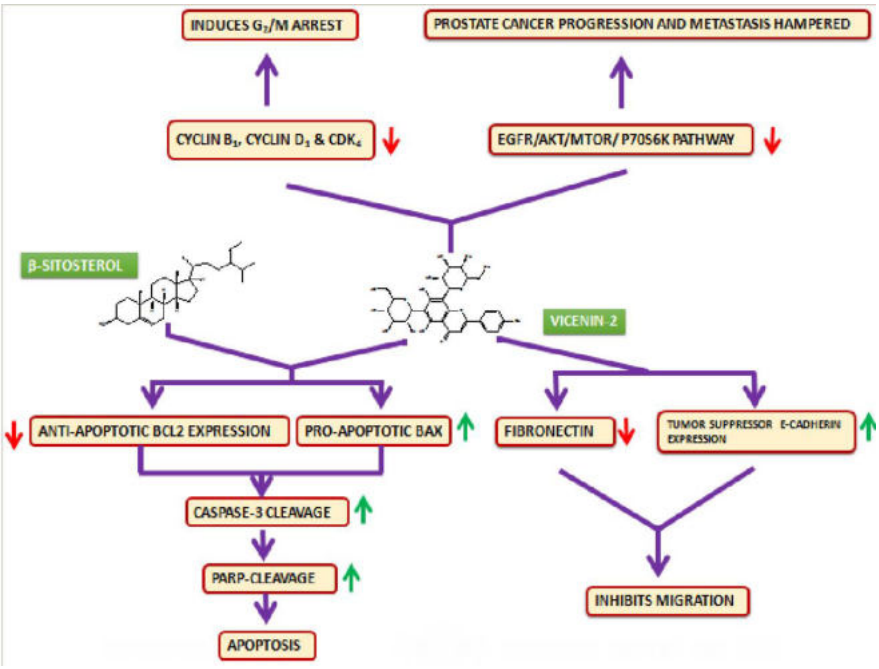

Figure 5. Mode of action of Vicenin-2 and β-sitosterol isolated from *Glinus oppositifolius*.

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:

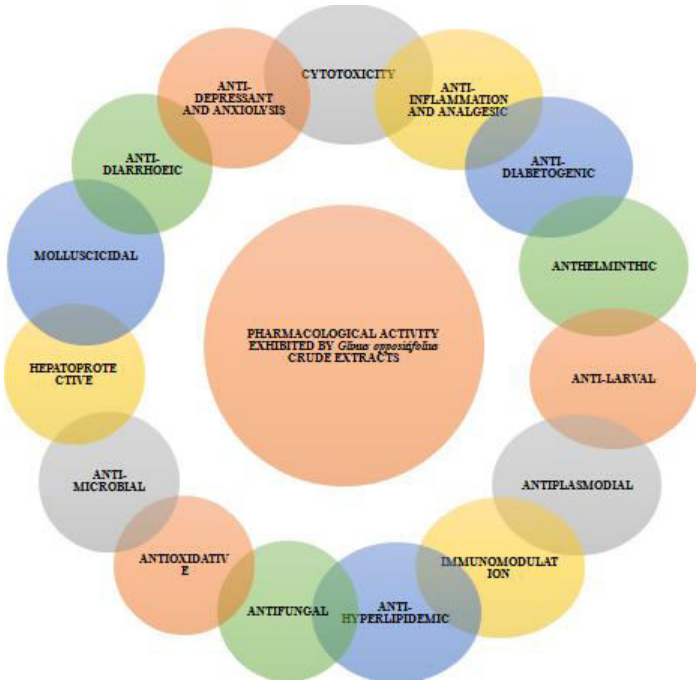

Figure 6. Different pharmacological activities of crude extracts and pure compounds isolated from *Glinus oppositifolius*.

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 ug/mL, 10 ug/mL, 20 ug/mL and 50 ug/mL. *Glinus oppositifolius*extracts showed cytotoxicity [36] (Chen 2011). Another study on brine shrimp showed that after 24 hours of exposure, the LC_{50} and LC_{90} 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 upto 4000 mg/kg as per the directive of European Economic Community and thus the LD_{50} 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 upto 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 dicholoromethane 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*. The extracts were reported to inhibit the growth of both types of strains tested [40].

Crude methanolic extracts were administered against several strains of *Bacillus subtilis, Staphylococcus aureus, 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

Dicholoromethane and methanol extracts of the whole plants were prepared. The crude extracts were tested against two mosquito species- *Culex quinquefasciatus* and *Anopheles gambiaelarvae*. 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].

Quantitation of antioxidant capacity of crude extracts

Against a standard ascorbic acid IC_{50} 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

Hepatoprotectiveactivity

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 [42].
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 lipoproteins, it increased the high-density lipoproteins [22].

With pure compounds isolated fromGlinus 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 fromGlinus 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 G_2arrest, 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]. T*rans*-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-1.Compounds Showing Pharmacokinetic Activity Against Cancer Cell Lines.

COMPOUND CLASS	NAME OF COMPOUND	CANCER TYPE AND CELL LINE	MODE OF ACTION	REFERENCE
AROMATIC COMPOUND	4-HYDROXYBENZOIC ACID	Prostrate cancer	Hsp90 chaperone activity	[47] (Seidel et al. 2016)
	TRANS-FERULIC ACID	Human lung cancer; cell line h1299.	Increase of intercellular ROS levels and promotes β-catenin instability	[48] (Fong et al. 2016)
		Colon cancer cells	Anti-proliferative effect	[49, 50] (Janicke et al. 2011; Jayaprakasam et al. 2006)
		Cervical cancer cells	Makes the cells more radiosensitive	[51] (Karthikeyan et al. 2011)
	VANILLIN OR 4-HYDROXY-3,5-DIMETHOXY BENZALDEHYDE OR SYRINGALDEHYE	Rat multiple organ carcinogenesis bioassay.	Decrease the number of small intestinal tumours	[52] (Akagi et al. 1995)
STEROIDS	**STIGMASTEROL**	Gastric cancer	-	[53] (De Stefani et al. 2000)
	SPINASTEROL	Breast cancer cell lines MCF-7, ZR-75-1, MDA-MB-231,SK-BR-3, and Hs578T.	Anti-proliferative effects	[54](Jeon et al. 2005)
		Anti-tumorigenic potential in Swiss	-	[55] (Villasenor & Domingo 2000)

		albino mice		
	β-SITOSTEROL	Breast cancer cells	Enhances tamoxifen effectiveness on cancer cells by tweaking ceramide metabolism regulation	[56] (Awad et al. 2008)
		Human Leukemic U937 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)
		Prostrate 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)
		Prostrate 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 COLO 320 DM	Dose-dependent growth inhibition and suppression of expression of beta-catenin and PCNA antigens	[62] (Baskar 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/Cip1and 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-	Increase of Fas levels and caspase-8 activity	[68] (Awad et al. 2003)

		231		
		Breast cancer cell line MCF-7 and MDA-MB-231	Stimulates serine palmitoyl transferase activity in both cells lines, and activates de novo ceramide synthesis, ceramide is pro-apoptotic signal	[56] (Awad et al. 2008)
FLAVONOID GLYCOSIDE	VITEXIN	MCF-7, T47D, MDA-MB-435s human breast cancer cells, Hela human cervical cancer cells, PC-3 prostate HepG2 liver cancer cells,	Caspase-dependent induction of apoptosis with cleavage in PARP protein, up-regulation of Bax, and down-regulation of Bcl-2.	[69] (Zhou et al. 2009)
	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-2.Compounds Showing Various Pharmacokinetic Activity

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

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 (Q_{max}) 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 Q_{max}. 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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References

[1]. Davies G. Time Tables of Medicine. Black Dog & Leventhal, New York. 2000.
[2]. Wang H, Khor TO, Shu L, Su ZY, Fuentes F, Lee JH, Kong ANT. Plants vs. cancer: a review on natural phytochemicals in preventing and treating cancers and their druggability. Anticancer Agents Med Chem. 2012; 12: 1281–1305.
[3]. Raskin I, Ripoll C. Can an apple a day keep the doctor away? Curr. Pharm. Des. 2004; 10: 3419–3429.
[4]. Sheldon JW, Balick MJ, Laird SA. Medicinal plants: can utilization and conservation coexist? Adv. Econ. Bot. 1997; 12.
[5]. Ishii R, Yoshikawa K, Minakata H, Komura H, Kada T. Specificities of Bio-antimutagens in Plant Kingdom. Agricultural and Biological Chemistry. 1984; 48: 2587–2591.
[6]. Hoyos LS, Au WW, Heo MY, Morris DL, Legator MS. Evaluation of the genotoxic effects of a folk medicine, *Petiveria alliacea* (Anamu). Mutat. Res. 1992; 280: 29–34.
[7]. Burkhill HM. The Useful Plants of West Tropical Africa, 1, second ed., Royal Botanical Gardens, Kew. 1985.

[8]. Debes SC. Enmedisinplantefra Mali, *Glinus oppositifolius*, [Master's Thesis], School of Pharmacy, University of Oslo, Norway. 1998.

[9]. Diallo D, Hveem B, Mahmoud MA, Berge G, Paulsen BS, Maiga A. An Ethnobotanical Survey of Herbal Drugs of Gourma District, Mali. Pharmaceutical Biology. 1999; 37: 80–91.

[10]. Inngjerdingen KT, Debes SC, Inngjerdingen M, Hokputsa S, Harding SE, Rolstad B, Michaelsen TE, Diallo D, Paulsen BS. Bioactive pectic polysaccharides from *Glinus oppositifolius* (L.) Aug. DC., a Malian medicinal plant, isolation and partial characterization. J Ethnopharmacol. 2005; 101: 204–214.

[11]. Inngjerdingen KT, Kiyohara H, Matsumoto T, Petersen D, Michaelsen TE, Diallo D, Inngjerdingen M, Yamada H, Paulsen BS. An immunomodulating pectic polymer from *Glinus oppositifolius*. Phytochemistry. 2007; 68: 1046–1058.

[12]. Inngjerdingen KT, Patel TR, Chen X, Kenne L, Allen S, Morris GA, Harding SE, Matsumoto T, Diallo D, Yamada H, Michaelsen TE, Inngjerdingen M, Paulsen BS. Immunological and structural properties of a pectic polymer from *Glinus oppositifolius*. Glycobiology. 2007; 17: 1299–1310.

[13]. Sheu SY, Yao CH, Lei YC, Kuo TF. Recent progress in *Glinus oppositifolius* research. Pharm Biol. 2014; 52: 1079–1084.

[14]. Diallo D. Ethnopharmacological survey of medicinal plants in Mali and phytochemical study of four of them: *Glinus oppositifolius* (Aizoaceae), *Diospyros abyssinica* (Ebenaceae), *Entadaafricana* (Mimosaceae), *Trichilia emetic* (Meliaceae), These de Doctorat. Faculte des Sciences, Universite de Lausanne, Switzerland. 2000.

[15]. Traore F, Faure R, Ollivier E, Gasquet M, Azas N, Debrauwer L, Keita A, Timon-David P, Balansard G. Structure and antiprotozoal activity of triterpenoid saponins from *Glinus oppositifolius*. Planta Med. 2000; 66: 368–371.

[16]. Diallo D, Marston A, Terreaux C, Touré Y, Paulsen BS, Hostettmann K. Screening of Malian medicinal plants for antifungal, larvicidal, molluscicidal, antioxidant and radical scavenging activities. Phytother. Res. 2001; 15: 401–406.

[17]. Asok Kumar K, UmaMaheswari M, Sivashanmugam AT, Subhadra Devi V, Subhashini N, Ravi TK. Free radical scavenging and antioxidant activities of *Glinus oppositifolius* (carpet weed) using different in vitro assay systems. Pharmaceutical Biology. 2009; 47: 474–482.

[18]. Natarajan P, Thirupathi AT, Sekharan TR, Sundar AS, Arivukkarasu R, Ganesan M. Hepatoprotective effect of *Glinus oppositifolius* Linn. Research Journal of Pharmacology and Pharmacodynamics. 2010; 2: 289–292.

[19]. Kumar S, Pathania AS, Saxena AK, Vishwakarma RA, Ali A, Bhushan S. The anticancer potential of flavonoids isolated from the stem bark of *Erythrina suberosa* through induction of apoptosis and inhibition of STAT signaling pathway in human leukemia HL-60 cells. Chem. Biol. Interact. 2013; 205: 128–137.

[20]. Behera GM, Satish Kumar BN, Malay Baidya M, Panigrahi G. Antihyperglycemic, antihyperlipidemic and antioxidant activity of *Glinus oppositifolius* (L.) Aug. DC. DC. Pharmacologyonline. 2010; 3: 915–36.

[21]. Sahu SK, Das D, Tripathy NK. Evaluation of hypoglycemic activity of *Mollugo pentaphylla* and *Glinus oppositifolius* (L). Rasayan J Chem. 2012; 5: 57–62.

[22]. Panigrahi G, Mishra US, Mahapatra S. Hypoglycemic and hypolipidemic activities of methanol extract of *Glinus oppositifolius*. Int J Pharm. 2012; 2: 491–497.

[23]. Pattanayak S, Nayak SS, Dinda SC, Panda D, Kolhe DM. Antimicrobial and anthelmintic potential of *Glinus oppositifolius* (Linn.) family: Molluginaceae. Pharmacologyonline. 2011; 1: 165–9.

[24]. Jagtap SD, Deokule SS, Bhosle SV. Some unique ethnomedicinal uses of plants used by the Korku tribe of Amravati district of Maharashtra. India Journal of Ethnopharmacology. 2006; 107: 463–469.

[25]. Sekharan R, Jagadeesan M. An ethnobotanical survey of Javvadhu hills, Tamil Nadu. Ancient Science of Life. 1997; 16: 206-214.

[26]. Chowdhury M, Das AP. Inventory of some ethno-medicinal plants in wetland areas of Maldah district of West Bengal. Pleione. 2009; 3(1): 83-88.

[27]. Setiya AV, Narkhede SD, Dongarwar NM. Exploration and documentation of some wild edible plants used by the aboriginals from Gadchiroli District (MS) India. IARJSET. 2016; 3.

[28]. Pattanayak S, Mandal TK, Bandyopadhyay SK. Ethnomedicinal study of plants used for protection and stimulation of liver in Southern West Bengal, India. Exploratory Animal and Medical Research. 2016; 6: 164–178.

[29]. Sahakitpichan P, Disadee W, Ruchirawat S, Kanchanapoom T. L-(-)-(N-trans-cinnamoyl) arginine, an acylamino acid from *Glinus oppositifolius* (L.) Aug. DC. Molecules. 2010; 15: 6186–6192.

[30]. Hoque N, Habib MR, Imam MZ, Ahmed J, Rana MS. Analgesic and anti-inflammatory potential of methanolic extract of *Glinus oppositifolius* L. Aust J Basic & Appl. Sci. 2011; 5: 729-733.

[31]. Hoque N, Imam MZ, Akter S, Mazumder M, Hoque E, Hasan SM, Ahmed J, Rana M. Antioxidant and antihyperglycemic activities of methanolic extract of *Glinus oppositifolius* leaves. 2011; 01: 50-53.

[32]. Rahmatullah M, Haque MR, Islam SK, Jamal F, Bashar ABMA, Ahmed R, Ahmed I, Jahan R, Ahsan S, Chowdhury MH. A survey on the use of medicinal plants by folk medicinal practitioners in three areas of Pirojpur District, Bangladesh. American-Eurasian Journal of Sustainable Agriculture. 2010; 4: 247–259.

[33]. Mollik MAH, Hossan MS, Paul AK, Taufiq-Ur-Rahman M, Jahan R, Rahmatullah M. A Comparative Analysis of Medicinal Plants Used by Folk Medicinal Healers in Three

Districts of Bangladesh and Inquiry as to Mode of Selection of Medicinal Plants. Ethnobotany Research and Applications. 2010; 8: 195–218.
[34]. Bhowmik R, Saha MR, Rahman MA, Islam MAU. Ethnomedicinal Survey of Plants in the Southern District Noakhali, Bangladesh. Bangladesh Pharmaceutical Journal. 2015; 17: 205–214.
[35]. Ragasa CY, Cabrera EC, Torres OB, Buluran AI, Espineli DL, Raga DD, Shen CC. Chemical constituents and bioactivities of *Glinus oppositifolius*. Pharmacognosy Research. 2015; 7: 138.
[36]. Chen YH. Studies on the chemical constituents from *Glinus oppositifolius* (L.) Aug. DC [Master's thesis], China Medical University, Taichung City, Taiwan. 2011.
[37]. Ragasa CY, Espineli DL, Mandia EH, Don MJ, Shen CC. A new triterpene from *Glinus oppositifolius*. Chinese journal of natural medicines. 2012; 10: 284–286.
[38]. Ullah MO, Haque M, Urmi KF, Zulfiker AHM, Anita ES, Begum M, Hamid K. Anti-bacterial activity and brine shrimp lethality bioassay of methanolic extracts of fourteen different edible vegetables from Bangladesh. Asian Pac J Trop Biomed. 2013; 3: 1–7.
[39]. Islam MT, Khan MAA, Hossain JA, Barua J. Antioxidant, antimicrobial and cytotoxic bioassay of *Mollugo oppositifolius* L. International Journal of Green Pharmacy (IJGP). 2011; 5:141-144.
[40]. Martin-Puzon JJR, Valle DL, Rivera WL. TLC profiles and antibacterial activity of *Glinus oppositifolius* L. Aug. DC. (Molluginaceae) leaf and stem extracts against bacterial pathogens. Asian Pacific Journal of Tropical Disease. 2015; 5: 569–574.
[41]. Adenusi AA, Odaibo AB. Laboratory assessment of molluscicidal activity of crude aqueous and ethanolic extracts of *Dalbergia sissoo* plant parts against *Biomphalaria pfeifferi*. Travel Med Infect Dis. 2008; 6: 219–227.
[42]. Sahu SK, Das D, Tripathy NK. Hepatoprotective activity of aerial part of *Glinus oppositifolius* L. against Paracetamol-induced Hepatic Injury in Rats. Asian Journal of Pharmacy and Technology. 2012; 2: 154–156.
[43]. Pattanayak S, Nayak SS, Dinda SC, Panda D. Preliminary anti-diarrhoeal activity of aerial parts of *Glinus oppositifolius* (L.) in rodents. Recent Advances in Pharmaceutical Science Research. 2012; 1: 50-57.
[44]. Moniruzzaman M, Sharoti Bhattacharjee P, Rahman Pretty M, Sarwar Hossain M. Sedative and Anxiolytic-Like Actions of Ethanol Extract of Leaves of *Glinus oppositifolius* (Linn.) Aug. DC. Evidence-Based Complementary and Alternative Medicine. 2016.
[45]. Vasincu A, Miron A, Bild V. Preliminary research concerning antinociceptive and anti-inflammatory effects of two extracts from *Glinus oppositifolius* (L.) Aug. DC. Rev Med ChirSoc Med Nat Iasi. 2014; 118: 866–872.
[46]. Pattanayak S, Padmalatha K. Anti Diabetic Activity of aerial parts of *Glinus opposi-tifolius* L, against glucose overloaded and streptozoto-cin-induced Diabetes in Albino Rats. Int J. Nat. Prod Mar Bio. 2015; 1: 29-34.
[47]. Seidel C, Schnekenburger M, Mazumder A, Teiten MH, Kirsch G, Dicato M, Diederich M. 4-Hydroxybenzoic acid derivatives as HDAC6-specific inhibitors modulating microtubular structure and HSP90 chaperone activity against prostate cancer. Biochem. Pharmacol. 2016; 99: 31–52.
[48]. Fong Y, Tang CC, Hu HT, Fang HY, Chen BH, Wu CY, Yuan SS, Wang HMD, YC. Chen, Teng YN, Fong CCC. Inhibitory effect of trans-ferulic acid on proliferation and migration of human lung cancer cells accompanied with increased endogenous reactive oxygen species and β-catenin instability. Chin Med. 2016; 11: 45–45.
[49]. Janicke B, Hegardt C, Krogh M, Onning G, Akesson B, Cirenajwis HM, Oredsson SM. The antiproliferative effect of dietary fiber phenolic compounds ferulic acid and p-coumaric acid on the cell cycle of Caco-2 cells. Nutr Cancer. 2011; 63: 611–622.
[50]. Jayaprakasam B, Vanisree M, Zhang Y, Dewitt DL, Nair MG. Impact of alkyl esters of caffeic and ferulic acids on tumor cell proliferation, cyclooxygenase enzyme, and lipid peroxidation. J. Agric. Food Chem. 2006; 54: 5375–5381.
[51]. Karthikeyan S, Kanimozhi G, Prasad NR, Mahalakshmi R. Radiosensitizing effect of ferulic acid on human cervical carcinoma cells in vitro. Toxicol In Vitro. 2011; 25: 1366–1375.
[52]. Akagi K, Hirose M, Hoshiya T, Mizoguchi Y, Ito N, Shirai T. Modulating effects of ellagic acid, vanillin and quercetin in a rat medium term multi-organ carcinogenesis model. Cancer Lett. 1995; 94: 113–121.
[53]. De Stefani E, Boffetta P, Ronco AL, Brennan P, Deneo-Pellegrini H, Carzoglio JC, Mendilaharsu M. Plant sterols and risk of stomach cancer: a case-control study in Uruguay. Nutr Cancer. 2000; 37: 140–144.
[54]. Jeon GC, Park MS, Yoon DY, Shin CH, Sin HS, Um SJ. Antitumor activity of spinasterol isolated from Pueraria roots. Exp. Mol. Med. 2005; 37: 111–120.
[55]. Villaseñor IM, Domingo AP. Anticarcinogenicity potential of spinasterol isolated from squash flowers. Teratog, Carcinog. Mutagen. 2000; 20: 99–105.
[56]. Awad AB, Barta SL, Fink CS, Bradford PG. beta-Sitosterol enhances tamoxifen effectiveness on breast cancer cells by affecting ceramide metabolism. MolNutr Food Res. 2008; 52: 419–426.
[57]. Park C, Moon DO, Rhu CH, Choi BT, Lee WH, Kim GY, Choi YH. Beta-sitosterol induces anti-proliferation and apoptosis in human leukemic U937 cells through activation of caspase-3 and induction of Bax/Bcl-2 ratio. Biol. Pharm. Bull. 2007; 30: 1317–1323.
[58]. Zhao Y, Chang SKC, Qu G, Li T, Cui H. Beta-sitosterol inhibits cell growth and induces apoptosis in SGC-7901 human stomach cancer cells. J. Agric. Food Chem. 2009; 57: 5211–5218.

[59]. Awad AB, Burr AT, Fink CS. Effect of resveratrol and beta-sitosterol in combination on reactive oxygen species and prostaglandin release by PC-3 cells. Prostaglandins Leukot. Essent. Fatty Acids. 2005;72:219–226.
[60]. Choi YH, Kong KR, Kim YA, Jung KO, Kil JH, Rhee SH, Park KY. Induction of Bax and activation of caspases during beta-sitosterol-mediated apoptosis in human colon cancer cells. Int. J. Oncol. 2003; 23: 1657–1662.
[61]. Awad AB, von Holtz RL, Cone JP, Fink CS, Chen YC. Beta-Sitosterol inhibits growth of HT 29 human colon cancer cells by activating the sphingomyelin cycle. Anticancer Res. 1998; 18: 471–473.
[62]. Baskar AA, Ignacimuthu S, Paulraj GM, Al Numair KS. Chemopreventive potential of beta Sitosterol in experimental colon cancer model--an in vitro and In vivo study. BMC Complement Altern Med. 2010; 10: 24.
[63]. Awad AB, Chen YC, Fink CS, Hennessey T. beta-Sitosterol inhibits HT-29 human colon cancer cell growth and alters membrane lipids. Anticancer Res. 1996; 16: 2797–2804.
[64]. Wu C, Chen F, Rushing JW, Wang X, Kim HJ, Huang G, Haley-Zitlin V, He G. Antiproliferative activities of parthenolide and golden feverfew extract against three human cancer cell lines. J Med Food. 2006; 9: 55–61.
[65]. Park C, Moon D, Ryu C, Choi B, Lee W, Kim G, Choi Y. Beta-sitosterol sensitizes MDA-MB-231 cells to TRAIL-induced apoptosis. Acta. Pharmacol. Sin. 2008; 29: 341–348.
[66]. Vundru SS, Kale RK, Singh RP. β-Sitosterol induces G1 arrest and causes depolarization of mitochondrial membrane potential in breast carcinoma MDA-MB-231 cells. BMC Complement Altern Med. 2013; 13: 280.
[67]. Awad AB, Chinnam M, Fink CS, Bradford PG. beta-Sitosterol activates Fas signaling in human breast cancer cells. Phytomedicine. 2007; 14: 747–754.
[68]. Awad AB, Roy R, Fink CS. Beta-sitosterol, a plant sterol, induces apoptosis and activates key caspases in MDA-MB-231 human breast cancer cells. Oncol. Rep. 2003; 10: 497–500.
[69]. Zhou Y, Liu YE, Cao J, Zeng G, Shen C, Li Y, Zhou M, Chen Y, Pu W, Potters L, Shi YE. Vitexins, nature-derived lignan compounds, induce apoptosis and suppress tumor growth. Clin. Cancer Res. 2009; 15: 5161–5169.
[70]. Nagaprashantha LD, Vatsyayan R, Singhal J, Fast S, Roby R, Awasthi S, Singhal SS. Anticancer effects of novel flavonoid vicenin-2 as a single agent and in synergistic combination with docetaxel in prostate cancer. Biochem. Pharmacol. 2011; 82: 1100–1109.
[71]. Kim SH, Hwang KA, Choi KC. Treatment with kaempferol suppresses breast cancer cell growth caused by estrogen and triclosan in cellular and xenograft breast cancer models. J. Nutr. Biochem. 2016; 28: 70–82.
[72]. Zhang Q, Wang D, Zhang M, Zhao Y, Yu Z. Studies on New Activities of Enantiomers of 2-(2 Hydroxypropanamido) Benzoic Acid: Antiplatelet Aggregation and Antithrombosis. PLOS ONE. 2017; 12: e0170334.
[73]. Das U, Manna K, Sinha M, Datta S, Das DK, Chakraborty A, Ghosh M, Saha KD, Dey S. Role of ferulic acid in the amelioration of ionizing radiation induced inflammation: a murine model. PLoS ONE. 2014; 9: e97599.
[74]. Manikandan R, Beulaja M, Thiagarajan R, Pandi M, Arulvasu C, Prabhu NM, Saravanan R, Esakkirajan M, Palanisamy S, Dhanasekaran G, Nisha RG, Devi K, Latha M. Ameliorative effect of ferulic acid against renal injuries mediated by nuclear factor-kappaB during glycerol-induced nephrotoxicity in Wistar rats. Ren Fail. 2014; 36: 154–165.
[75]. Panneerselvam L, Subbiah K, Arumugam A, Senapathy JG. Ferulic acid modulates fluoride induced oxidative hepatotoxicity in male Wistar rats. Biol Trace Elem Res. 2013; 151: 85–91.
[76]. Yuan X, Wang J, Yao H. Antioxidant activity of feruloylated oligosaccharides from wheat bran. Food Chemistry. 2005; 90: 759–764.
[77]. Roy S, Metya SK, Sannigrahi S, Rahaman N, Ahmed F. Treatment with ferulic acid to rats with streptozotocin-induced diabetes: effects on oxidative stress, pro-inflammatory cytokines, and apoptosis in the pancreatic β cell. Endocrine. 2013; 44: 369–379.
[78]. Ramar M, Manikandan B, Raman T, Priyadarsini A, Palanisamy S, Velayudam M, Munusamy A, MarimuthuPrabhu N, Vaseeharan B. Protective effect of ferulic acid and resveratrol against alloxan-induced diabetes in mice. Eur. J. Pharmacol. 2012; 690: 226–235.
[79]. Stagos D, Kazantzoglou G, Magiatis P, Mitaku S, Anagnostopoulos K, Kouretas D. Effects of plant phenolics and grape extracts from Greek varieties of Vitis vinifera on Mitomycin C and topoisomerase I-induced nicking of DNA. Int. J. Mol. Med. 2005; 15: 1013–1022.
[80]. Tanaka T, Kojima T, Kawamori T, Wang A, Suzui M, Okamoto K, Mori H. Inhibition of 4 nitroquinoline-1-oxide-induced rat tongue carcinogenesis by the naturally occurring plant phenolics caffeic, ellagic, chlorogenic and ferulic acids. Carcinogenesis. 1993;14: 1321–1325.
[81]. Tamai K, Tezuka H, Kuroda Y. Different modifications by vanillin in cytotoxicity and genetic changes induced by EMS and H2O2 in cultured Chinese hamster cells. Mutation Research/Fundamental and Molecular Mechanisms of Mutagenesis. 1992; 268: 231–237.
[82]. Gade S, Rajamanikyam M, Vadlapudi V, Nukala KM, Aluvala R, Giddigari C, Karanam NJ, Barua NC, Pandey R, Upadhyayula VSV, Sripadi P, Amanchy R, Upadhyayula SM. Acetylcholinesterase inhibitory activity of stigmasterol & hexacosanol is responsible for larvicidal and repellent properties of *Chromolaena odorata*. Biochim. Biophys. Acta. 2017; 1861: 541–550.
[83]. Wilt T, Ishani A, MacDonald R, Stark G, Mulrow C, Lau J. Beta-sitosterols for

benign prostatic hyperplasia. Cochrane Database Syst Rev. CD001043. 2000.
[84]. Wilt TJ, MacDonald R, Ishani A. beta-sitosterol for the treatment of benign prostatic hyperplasia: a systematic review. BJU Int. 1999; 83: 976–983.
[85]. Berges RR, Kassen A, Senge T. Treatment of symptomatic benign prostatic hyperplasia with beta-sitosterol: an 18-month follow-up. BJU Int. 2000; 85: 842–846.