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An Overview on Ethnopharmacology, Phytochemical and Pharmacology of *Eleusine indica*

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Many efforts have been made through publication of traditional studies on plants to increase the interest and improve on natural remedy since past few years. *Eleusine indica* is a diploid species of genus Eleusine belongs to family Poaceae. More than 20 diseases are traditionally treated by this plant around the different tropical and subtropical region of world. Phytochemically many inorganic and organic active constituents have been isolated from the plant. Many secondary metabolites has been isolated and identified such as vitexin, isovitexin, orientin, isoorientin, lutein, β-sitosterol, stigmasterol and derivatives of sterol glucosides belongs to categories of flavonoids, caretenoid and sterols. Plant possesses active constituents attributes several pharmacological actions like antimicrobial, anti-inflammatory, diuretic, anticonvulsant, antiobesity, anticancer, antihypertensive, antioxidant, hepatoprotective, *etc*. Further investigations are essential to fulfil many research gaps which were identified and still many bioactive constituents have to be discover in respect to traditional and pharmacological use.

Keywords: *Eleusine indica*, Diploid species, Poaceae, Weed, Goose grass, Glycosyl flavonoids.

INTRODUCTION

From prehistoric period many plants and herbs have been used as drugs for the treatment of diseases, ailments and to fulfil the basic need in the field of health sector for improvement of good health [1,2]. As per WHO, 2003 report more than 75% of world's population depends on traditional system of medicine for basic treatment [3-5]. Interest on the natural method of treatment has been increased day by day in the past few years [6]. Global efforts have been made to increase the interest on the natural therapy through publication of traditional methods used for the diseases and ailments [1].

Genus eleusine includes six diploid species, *Eleusine indica* is one of these [7]. It is an adventitious species belongs to family poaceae [8-12], commonly found in tropical and subtropical regions of the world [9,13,14] and grows mostly in open fields and grounds during rainy season [15,16]. In more than 40 countries, it is considered as a serious weed [15,17-19] and capable to resist herbicides [13,15,17-24] and environmental conditions [14]. It is an annual or short lived perennial tufted grass whose branches originated from the base, popularly known as goose grass. The ascending culms, 5 to 60 cm high, are sometimes compressed while the leaf blades are flat or sometimes folded, 15-30 cm long and 4-6 cm wide. *Eleusine indica* can produce more than 50,000 seeds and dispersed in soil easily [15,28,29]. *Eleusine indica* has been used in different areas or parts of world as food, fodder as a natural remedy for treatment of different diseases and ailments (Table-1). Traditionally more than 40 countries used *Eleusine indica* as diuretic, febrifuge, laxative, hepatoprotective and for other ailments.

Phytochemical constituents: Phytochemical examination is mandatory to explore medicinal components basis of herbal remedy. Many scholars have extensively studied on the phytochemical constituents of *Eleusine indica* and reported various inorganic and organic active constituents. *Eleusine indica* contains many minerals, which are essential for its growth and development [30]. For maintenance of physiological metabolic processes many major and minor elements are necessary [31], some of these essential minerals also affect the pharmacological activity of organic constituents [32]. Plant also contains hydrocyanic acid, which may attribute antiviral effect [33].

TABLE-1
TRADITIONAL USES OF *Eleusine indica*

Places	Beneficiary name	Local names	Part of plant used	Extracts or preparations	Folkloric uses	Ref.
Bangladesh	Kavirajes	Kachra	Roots	Marceration	Treatment for uterine prolapsed.	[34]
Brazil	Brazilian	Goose grass	Aerial parts	Infusion	Used for influenza and pneumonia treatment	[35]
Cambodia	Khmer	Smaochoeungtukke	Whole plant	Juice	Used for antipyretic and liver problems	[36]
Cameroona	Cameroonian	Ngongui (Bassa) Sargalde (Ewondo)	Whole plant	Extracts	Traditionally used for diarrhoea, dysentery, epilepsy, intestinal occlusion and solve infertility in females	[37]
China	Chinese	Long zhaoji	Whole plant	Decoction	Used for traumatic injury, rheumatism, ostealgia and infantile indigestion	[38,39]
Coastal Guyana	Guyanese	Goose foot grass	Whole plant	Decoction	Used as analgesic to relieve abdominal muscle strain, as tonic for bladder disorders, topically used as wound healer and astringent	[36]
Colombia	Colombians	Wire grass	Whole plant	Decoction	Traditionally used for diarrhoea, dysentery and convulsions.	[36]
India	Munda Tribe	Malkantari-Mundari	Root	Dried root	20 g root is crushed along with 10g *Zingiber officinale* and nine black pepper pieces; paste is divided into two equal parts, one part with a few drops of honey is administered orally and the other part is applied on the snake bitten area.	[40]
	Kaviraj	Kan Chulkani	Root	Decoction	Fresh root of *Eleusine indica* decoction mixed with sugar is traditionally used at morning in empty stomach to cure "Meho" [gonorrhoea]	[41]
Malaya	Mother woman	Rumputkekuasa	Fresh leave	Juice	Expel the placenta after birth of neonatal baby	[36]
Malaysia	Malaysian people	Sohinatad	Whole plant or root	Decoction	Used as diuretic, anti-helminthic, diaphoretic, febrifuge and for treating cough	[42,43]
Myanmar	Barmar	Sin-ngo-myet	Leaves	Powdered by grinding	For management of hypertension	[44]
Niger delta region	Ibibio	Gbegi	Leaves	Alcoholic extract	Used for malaria, diabetes and to cure some stomach problems. Used to treat convulsion in children, elder rheumatic pain and inflammation	[45,46]
Sablan, Benguet area	Ibalois	Jatjatan	Leaves	Decoction	Treatment of kidney diseases like nephrolithiasis, urolithiasis	[47]
Srilanka	Sinhala	Balathana	Whole plant or root	Powdered and heated with coconut and haldi	Used for recovery of bone fracture and to relieve muscle sprain with scraped coconut and processed Curcuma domestica	[48]
Sumatra	Sumatrian	Benda laut	Whole plant	Decoction	Traditionally used as anthelmintic	[36]
Suriago del sur Phillippines	Surigaonons	Bilabila	Leaves	Boil in water	Traditionally used as diuretic	[1]
Taiwan	Taiwanese	Wire grass	Whole plant	Alcoholic preparations	Treatment of liver diseases	[49]
Thailand	Thai people	Yaa teen-ka	Whole plant	Soaked and processed in alcohol	Traditionally used along with *Dactyloctenium aegyptium* for relieve of dysuria,fever,inflammation,jaundice and from toxins of scorpion & centipede	[50]
Trinidad and Tobago	Caribbean physicians	Dead man's grass	Root and leaves	Extracts	Used for urinary problems	[33]
Venezuela	Infants suffered from jaundice	Yard grass	Seed	Decoction	Used for black jaundice	[36]
Vietnam	Kinh people	Mantrau	Whole plant	Decoction	Used as diuretic, febrifuge and stomachic	[51]
West tropical Africa	Bakwiri people	Goose grass	Whole plant	Infusion	Used for haemoptysis	[36]

Various primary and secondary organic constituents such as amino acids, sugars, alkaloids, glycosides, tannins, flavonoids, triterpenoids, steroids, phenolic contents, *etc*. are present in *Eleusine indica*. Several secondary metabolites such as flavonoids such as vitexin, isovitexin, orientin and isoorientin; caretonoid like lutein; sterol such as β-sitosterol, stigmasterol; sterol glucosides 3-O-β-D-glucopyranosyl-β-sitosterol and 6-O-palmitoyl derivatives [35,51,52] have been isolated and identified from this plant.

Orientin: It is an aqueous soluble C-glycosyl flavonoid can be isolated and extracted from *Eleusine indica* by using any one polar solvent like methanol, ethanol or water [53]. Luteolin moiety is the core part [54-56], phenol groups are mostly present along with two ether and one ketone groups in the chemical structure of orientin. It contains C-glucopyranosyl residues [57]. Due to hydrophilic nature orientin poorly crosses blood brain barrier [58]. It has several therapeutically effects such as antioxidant, antiaging, antiviral, antibacterial, anti-inflammation, vasodilatation, cardioprotective, antiadipogenesis, radiation protective, antinociceptive, neuroprotective and antidepressant [53].

Isoorientin: It is the isoform of orientin and formerly known as homoorientin [57]. It is also a flavonoid C-glycoside phytochemically screened from *Eleusine indica*. Like orientin, it also contains luteolin nucleus [54-56] and the phenol groups are present at periphery. It contains C-glucopyranosyl ring and can be converted to orientin in hot dilute aqueous acid medium [57,58]. It has several pharmacological effects similar to that of orientin.

Vitexin: It is a type of C-glycosyl flavonoid and 8-C-glucosyl derivative of apigenin. Seven hydroxyl groups are present in a vitexin moiety with molecular weight 432.3775 g/mol. It has several biological effects such as antioxidant, anti-inflammation, antineoplastic, neuro protective effect, anxiolytic, anticonvulsant and antiepileptic antinociceptive, anti-hypoxia anti Alzheimer's disease and antidepressant effects [59]. Radical scavenging activity of vitexin mainly due to presence of A-ring [60]. Vitexin inhibits neutrophil migration so that influx of neutrophil blocked and helpful in treatment of lung inflammatory diseases such as influenza and pneumonia [35].

Isovitexin: It is a type of C-glycosyl flavonoid belongs to the category of flavones, an isoform of vitexin present in various plant parts as an active constituent. Like vitexin, it is also a derivative of apigenin namely apigenin 6-C-glucoside. Due to similar chemical structure to that of vitexin, it shows various similar therapeutic effects such as antioxidant, anti-inflammatory and antialzheimer's disease [59].

β-Sitosterol: Phuong *et al.* [51] isolated two derivatives of β-sitosterol namely 3-O-β-D-glucopyranosyl-β-sitosterol & 6′-O-palmitoyl-β-sitosterol. It is a plant sterol, isolated from aerial parts of *Eleusine indica*. It has a significant effect on lowering cholesterol level and reducing the enlarged prostate gland [61], β-sitosterol obtained from methanol extract by defatting with petroleum ether and acid hydrolysis with sulphuric acid along with *n*-propanol [51].

Stigmasterol: It is also called as stigmasterin or wulzen anti-stiffness factor [62]. It is a phytosterol present in many plants, plant derived preparations and extracted by means of a non-polar solvent like petroleum ether due its non-polar in nature. For the biosynthesis of steroids such as progesterone androgens, estrogens, corticosteroids, it is used as a precursor or intermediate [63]. It has several pharmacological effect such as antiosteoarthritic, antitumor, anti-hypercholestrolemic, hypoglycaemic, antimutagenic, antioxidant, CNS effects and anti-inflammatory [62].

Lutein: It is a xanthophyll carotenoid, stereo isomer of zeaxanthin found in many plant and animal tissues [64]. Macula and retina of eye in human enriched with lutein, which is essential for central vision and high visual potency [65]. Secondly in human, it is found in serum [66] and assumed that in plant, lutein is responsible for its antioxidant property and helps in screening of high frequent blue light [67].

Schaftoside: This is also a type of C-glycosyl flavonoid [apigenin glycoside] chemically known as 6-C-β-glucopyranosyl-8-C-α-arabino pyranosyl apigenin [35]. It produces wessely-moser isomer on acid hydrolysis [68] and extracted from infusion of aerial parts of *Eleusine indica* [35].

Pharmacology

Antidiabetic activity: Traditionally Ibibio's of Akwa Ibom state, Nigeria used leaf of *Eleusine indica* for the management of diabetes. Okokon *et al.* [46] studied the antidiabetic activity of 95% ethanol leaf extract of *Eleusine indica* and found dose dependent response on blood sugar level of alloxan induced diabetic albino wistar rats. The alleviated blood glucose level indicates presence of some antidiabetic agent in *Eleusine indica*. This antidiabetic agent may act by increasing the insulin level either increasing secretion from beta cells or its release from bound insulin [69] or by decreasing glucose production in liver [70] and insulin resistance [71].

Antiplasmodial activity: Ettenbong *et al.* [72] stated that *Eleusine indica* extract possesses antiplasmodial activity. Different extracts and fractions of whole plant was tested on infected albino mice for antimalarial activity. It is observed that ethyl acetate fraction shows significant antimalarial effect on infected albino mice [72]. In another study, Okokon *et al.* [46] reported that 95% ethanol leaf extract shows dose dependent chemosuppressive effect on *Plasmodium berghei.* The antiplasmodial activity may attribute to the presence of active secondary metabolites like alkaloids, flavonoids and terpenoids. The exact mechanism was not clear but the schizonticidal activity may be by inhibition of protein synthesis, which affect the survival of *Plasmodium berghei* [46].

Antiviral activity: Hamidi *et al.* [73] reported about screening of 61 medicinal plants for antiviral study. The macerated ethanolic leave extracts of *Alternanther asessilis*, *Blumea chinensis*, *Eleusine indica*, *Euphorbia hirta*, *Leea indica*, *Freycine tiamalaccensis* and *Solanum americanum* were found to be active in selectively inhibiting type-I herpes simplex virus [HSV-1] [73]. The antiviral effect may be due to presence of hydrocyanic acid in *Eleusine indica* [73,74]. Iberahim *et al.* [75] found that the aqueous extract have antiviral action against HSV-1, while the methanol extract have significant antiviral activity which may be attributed due to the presence of some

phenolic compounds. Tahir *et al.* [76] also reported that aqueous extract possesses antiviral effect against HSV-1.

Antileishmanial activity: Okokon *et al.* [77] reported the *in vitro* activity of ethanol leaf extract of *Eleusine indica* shows antileishmanial activity against promastigotes of *Leishmania major*. *Eleusine indica* possesses significant antileishmanial potency, which is incomparable with the standard drugs like pentamidine and amphotericin B as well as crude extract of *Hippocratea africana* [77].

Anticancer activity: Plants which are toxic to brine shrimp larvae, they might contain some anticancer agent [78]. Ogbole *et al.* [79] reported that *Eleusine indica* possesses significant anticancer effect using *in vitro* brine shrimp lethality assay (BLSA) method. Thirty one plant extracts were subjected to BLSA assay and found methanol extract of *Eleusine indica* have significant lethal effect on brine shrimp larvae than the standard drug cyclophosphamide [79]. Antiproliferative study of *Eleusine indica* was conducted by Hansakul *et al.* [50]. This activity was studied on hexane and butanol extracts of two grass species of poaceae family namely *Dactyloctenium aegyptium* [L.] and *Eleusine indica* [L.] Gaerth. Dose and time dependent lethal effect was found on the proliferative lung and cervical cancer cell lines.

Antibacterial activity: Ettenbong & Bassey [8] reported that *Eleusine indica* possesses antibacterial activity. *in vitro* activity was carried out on four bacterial cultures such as *Escherichia coli*, *Pseudomonas aeruginosa*, *Staphylococcus aureus* and *Bacillus subtilis* by agar diffusion method. Ethyl acetate extract showed a significant activity against all the studied bacterial strains. Chloroform extract also showed similar potency like ethyl acetate extract against *E. coli* and *P. aeruginosa*. Whole plant contains some alkaloids, flavonoids and tannins, which may be responsible for its antibacterial activity [8].

Antihypertensive activity: According to *in vivo* study Desai *et al.* [80], *Eleusine indica* also possesses hypotensive activity. Antihypertensive effect was evaluated by *in vivo* tail-cuff model and adrenaline was used as hypertensive agent. Due to presence of some bioactive constituents like flavonoids, glycosides and phenolic compounds in ethanol, methanol and chloroform extracts of *Eleusine indica*, exhibits antihypertensive effect. In another study, Tutor & Hernandez [81] found that ethyl acetate fraction of methanol leaf extract of *Eleusine indica* possesses significant antihypertensive activity. The antihypertensive action is due to inhibition of angiotensin converting enzyme [ACE]. This *in vitro* study was followed to Elbl & Wagner ACE inhibition assay [82].

Antioxidant activity: The methanol extract of *Eleusine indica* possesses antioxidant potency. This was studied *in vitro* experiment by radical scavenging activity method using 2,2-diphenyl 2-picryl hydrazyl hydrate (DPPH) as the reactant with the antioxidant compound. Th assay of DPPH was find out by change in colour from deep violet to light yellow, which was monitored at 517 nm spectrophotometrically [83]. Sagnia *et al.* [84] also reported that extract of the *Eleusine indica* possesses antioxidant activity. Antioxidant activity was studied by chemiluminescence measurement against H_2O_2 as oxidant. From this report, antioxidant activity might be due to presence of some phenolic bioprinciples.

Hepatoprotective activity: Iqbal & Gnanaraj [42] that due to significant antioxidant activity, the plant also exhibit hepatoprotective effect on CCl_4 induced oxidative hepatic damage. Hepatoprotective activity may be due to the phenolic contents present in the aqueous extract of *Eleusine indica*.

Antiinflammatory activity: The anti-inflammatory activity of *Eleusine indica* was reported by Sagnia *et al.* [84]. The inhibition of cytokines like tumor necrosis factor-alpha [TNF-α] induced by lipopolysaccharide was measured in terms of anti-inflammatory activity [84].

Anticonvulsant activity: Ibibio tribes of Nigeria traditionally used *Eleusine indica* for anticonvulsant therapy. An *in vivo* study performed by Ettenbong & Nwafor [45] found that 70% ethanol extract of *Eleusine indica* exhibits significant antiepileptic potency. In this study, convulsion was induced by pentylene tetrazole [PTZ], aminophylline and isoniazid [INH] on adult albino mice separately. The extract was found to be more significant on PTZ and INH induced anticonvulsant model and compared with diazepam as standard drug. This indicates that the anticonvulsant action might be due to presence of some phytoprinciples like triterpene steroids and triterpene saponins in the extract of *Eleusine indica* and this seeks more investigations.

Diuretic activity: Traditionally many people of northern Surigao del sur, Philippines drinks *Eleusine indica* leaves extract three times per day as diuretic. Desai *et al.* [52] reported that *Eleusine indica* possesses strong diuretic activity. The ethanol extract exhibits more significant diuretic activity than methanol and chloroform extracts. Mechanism for diuretic effect of *Eleusine indica* may be due to blood flow or vasodilation or inhibition of tubular reabsorption. The diuretic effect may be due to presence of flavonoids, saponins or organic acids in *Eleusine indica*.

Antiurolithiatic activity: Nephrolithiasis or kidney stones is mainly occurred due to accumulation of certain metabolic byproducts like calcium oxalate and uric acid crystals in the kidney [85]. There is an increase in graph of nephrolithiasis prevalence rate around the world [86]. Amoah *et al.* [87] reported *in vivo* study of aqueous root extract of *Eleusine indica* exhibits significant antiurolithiatic property. Albino rats were subjected to nephrolithiasis by ethylene glycol induction. Root extract of *Eleusine indica* possesses some active constituents which inhibits nitrituria, proteinuria and oxaluria [87]. In another study, Desai *et al.* [52] confirmed that *Eleusine indica* possesses antiurolithiatic activity. The activity was conducted by *in vitro* calcium oxalate crystal assay method. The antiurolithiatic property was evaluated by calculating percentage dissolution of calcium oxalate crystal and found all extracts have more or less antiurolithiatic effect but ethanol extract exhibited more effect as compared to other solvent extracts.

Antiobesity activity: Antiobesity activity of *Eleusine indica* was studied by Ong *et al.* [88] and reported that lutein is the active constituents present in hexane extract of *Eleusine indica*. It shows maximum inhibitory activity against porcine pancreatic lipase. Porcine pancreatic lipase is the enzyme

increases the human dietary fat and inhibition of this enzyme can be assayed by *in vitro* method [89]. Ong *et al.* [88] followed this method with slight modification found that *Eleusine indica* possesses significant antiobesity activity.

Conclusion

This study enumerates the knowledge on ethnobotanical, traditional uses, phytochemistry and pharmacological effects of *E. indica* which has been used as ailment, food, fodder and biomedicine in ancient and modern India. Based on this review information many bioactive principles have been isolated from *Eleusine indica*. However, still many research gaps exist in the scientific studies on *Eleusine indica* and suggests that should have priority for further investigations. Firstly, anticancer or antiproliferative activity of *Eleusine indica* seeks further clinical study and phytochemical investigations. Secondly, based on the available insufficient phytochemical studies, the more research is necessary about the isolation, identification and characterization of secondary metabolites responsible for the antiplasmodial activity. Thirdly, ethanol leaf extract possesses antileishmanial activity, which requires further study to isolate the active principal ingradient present in it. Fourthly, *Eleusine indica* different extracts seems to possess antihypertensive effect. It revealed that ethanol and methanol extract shows significant antihypertensive effect and chloroform extract shows less significant effect. This needs further phytochemical as well as pharmacological investigations on the extracts of *E. indica*. The mechanism need to be confirmed through *in vivo* study. Fifthly, antiepileptic potentials need further study to investigate the specific active constituents present in the ethanol extract of *Eleusine indica* and need to prove its exact anticonvulsant mechanism. Sixthly, antiobesity activity of *Eleusine indica* is due to the phytoactive moiety lutein but it requires further *in vivo* study to confirm and subjected to clinical trials. Seventhly, phytoactive principle of *Eleusine indica* attributes diuretic and antiurolithiatic activities. This needs phytochemical isolation, structural elucidation and identification of diuretic and antiurolithiatic drug with mechanism of action. Eighthly, the hypoglycaemic activity was studied only in ethanol extract of leaf. This seeks further study on other extracts like hexane, chloroform, ethyl acetate, methanol, *etc*. and other plant parts. Antidiabetic agents may be isolated from the *Eleusine indica* but may require further phytochemical and pharmacological investigations. Ninthly, aqueous and methanol extract mainly possesses antiviral action against HSV-1. Still lots of the investigation recommends further finding in the field of isolation, characterization and identification of antiviral agent from the extract of *Eleusine indica*, which may comprehend the antiviral action of the plant. Tenthly, *Eleusine indica* contains some active phenolic components which may have antioxidant activity. The antioxidant activity limited to the *in vitro* pharmacological experiments so requires *in vivo* studies and further phytochemical investigations. Hepatoprotective effect will be evaluated with phytochemical investigation. Anti-inflammatory activity was *in vitro* studied which needs clinical study and the bioactive constituent responsible for inhibition of cytokines *i.e.* TNF-α have to be isolated and identified. From the phytochemical investigation it is clear that the plant possesses many secondary metabolites but many active constituents activity and its mechanism of action are still in dark so further studies are necessary to evaluate the medicinal value of these active constituents. Traditional uses of *Eleusine indica* has been investigated but some of these still now has not covered like antivenom, infertility, antigonorrhoea, anthelmintic, antihaemoptysis, laxative, *etc*.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interests regarding the publication of this article.

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