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Biological Potential and Phytopharmacological Screening of Gomphrena Species

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Abstract: The traditional system of medicine consists of large number of plants with various medicinal and pharmacological importance and hence considered as a priceless tank of new bioactive molecules. The *Amaranthaceae* family comprises of many species, which are used in nutrition and in traditional folk medicine for the treatment of several diseases such as infections, inflammation and fever. *Gomphrena* species found all over the world. It is commonly known as 'Bachelor's Button / Globe Amaranth' and has been recognized in different traditional system of medicines for the treatment of various diseases of human being. The phytoconstituents present in it are flavonoids, phytosterols, phenolics and terpenoids. The different parts of this plant are traditionally claimed to be used for the treatment of broad spectrum of ailment including baby gripe, oligouria, body sore, malaria, bacterial infections, jaundice, urinary problems, high cholesterol, cough, fever, diarrhea, liver disorders, kidney disorders and cooling. Due to changes in the lifestyle and associated decline of the use of plants, the ethnobotanical knowledge is continuing to decline. Hence further work to isolate and characterise the active compounds responsible for this activities in the plant is recommended.

Key words: *Gomphrena* · Phytochemistry · Pharmacology · Ethnobotany · Alkaloid · Flavanoid

INTRODUCTION

Medicinal plants have been playing a vital role on the health and healing of man since down of the human civilization. In spite of tremendous development in the field of allopathic medicines during the 20th century, plants still remain one of the major sources of drugs in modern as well as in traditional system of medicine [1, 2]. The green plants synthesise and they preserve a variety of biochemical products, many of which are extractable and used as a chemical feed stocks or as raw material for various scientific investigations. Many secondary metabolites of plant origin are commercially important and find use in a number of pharmaceutical compounds [3].

Nations with highly developed pharmaceutical industries are mainly interested in plants as a source of biologically active and medicinal important compounds which might be lead to discovery of new and better drugs with pharmacological potency [4]. The chemical constituents present in the herbal medicine or plants are the major part of the physiological functions of living flora and hence they are believed to have better compatibility with the human body.

Natural products from plants are a rich resource used for centuries to cure various ailments. The use of bioactive plant-derived compounds is on the rise, because the main preoccupation with the use of synthetic drugs is the side effects which can be even more dangerous than the diseases they claim to cure. In contrast, plant derived medicines are based upon the premise that they contain natural substances that can promote health, alleviate illness and proved to be safe, better patient tolerance, relatively less expensive and globally competitive. So, in respect of the healing power of plants and a return to natural remedies is an absolute requirement of our time [5, 6].

In this present review paper, an attempt has been made to summarize all the information so far available on the floristic composition, ethnobotanical practices on the edible and ornamental plant *Gomphrena* species. *Gomphrena* species is an edible, commercial ornamental and medicinal plant commonly known as Globe Amaranth or Bachelor Button, belongs to the family Amaranthaceae. It comprises approximately 120 species found in the America, Antartica and Indo-Malaysia. 46 species found in Brazil.

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The Amaranthaceae is a cosmopolian family which occurs at disturbed, arid or saline areas; one of the characteristics that ensure its survival in adverse environments is the operation of C4 pathway of photosynthesis [7]. It is erect or ascending herbs to 50cm. leaves spiral, deltoid to elliptic ovate. Inflorescence is axillary, slender, thyrsiform spike. Flowering mostly occurs in June to December. Globe amaranth [*Gomphrena globosa L.*] might be one of the plants that can use atmospheric sulfides for its growth [8, 9].

Taxonomy: The *Amaranthaceae* family, class Magnoliopsida and order Caryophyllales, was established by A. L. Jussieu in 1789 and includes approximately 176 genera and 2400 species [6]. The members of *Amaranthaceae* family are divided in four tribes: Celosieae, Achyrantheae, Braylineae and Gomphreneae. The species in Brazil are distributed in Celosieae, Achyrantheae and Gomphreneae tribes [10].

Phytochemistry: The previous chemical studies with species of this genus were related to the isolation of hydrocarbons, alcohols, steroids, terpenoids, ecdysteroids, flavonoids and protoalkaloids. Despite of some phytochemical and biological activity studies have been performed in certain species, overall the genus *Gomphrena* still remains poorly studied [10].

Kingdom	Plantae
Subkingdom	Tracheobionta
Superdivision	Spermatophyta
Division	Magnoliophyta
Class	Magnoliopsida
Subclass	Caryophyllidae
Order	Caryophyllales
Family	Amaranthaceae
Genus	Gomphrena L.

Some species of *Amaranthaceae* have been studied seeking the characterization of inorganic elements and heavy metals in their tissues. Some of these works (Table 1) suggest that these vegetables can bioconcentrate inorganic elements and heavy metals. And using the X-ray fluorescence analysis, the results showed that several inorganic elements like Al, Si, P, S, Cl, K, Ca, Ti, Cr, Mn, Fe, Co, Ni, Cu, Zn, As, Br, Rb, Sr, Mo, Cd, Sn, Sb, Ba and Pb could be detected in the extracts and powder of species of Amaranthaceae [10].

Table 1: Inorganic elements detected in two *Amaranthaceae* species [10].

Species	Inorganic elements detected
Gomphrena glabrata [a]	P, S, Cl, K, Ca, Cr, Mn, Fe, Co, Ni, Cu, Zn, Br, Sr, Cd, Ba and Pb
Gomphrena globosa [d]	S, K, Ca, Sc, Ti, V, Mn, Fe, Co, Cu and Zn
Gomphrena globosa [b]	S, K, Ca, Fe, Co, Cu and Zn

Part used: whole plant[a], aerial part[b], roots[d] [P- phosphorus, S- sulphur, Cl- chlorine, K- potassium, Ca- calcium, Cr - chromium, Mn- manganese, Fe- Iron, Co- cobalt, Ni- Nickel, Cu- copper, Zn- Zinc, Br- bromine, Sr- strontium, Cd- cadmium, Ba- barium, Pb- Lead, Sc- scandium, Ti- Titanium, V-vanadium].

Table 2: Main biological activities reported for species from *Gomphrena* [10].

Species	Biological Activity
Gomphrena boliviana	Antimicrobial activity; Anticancer properties; Cytotoxic activity
Gomphrena celosioides	Antimicrobial activity (bacteria, Plasmodium falciparum); Anticancer properties; Analgesic activity
Gomphrena globosa	Antimicrobial activity ; Anticancer properties; Cytotoxic activity
Gomphrena haenkeana	Antimicrobial activity ; Anticancer properties; Cytotoxic activity
Gomphrena macrocephala	Molluscicidal (*Biomphalaria glabrata*) and cytotoxic against *Artemia salina*
Gomphrena martiana	Antimicrobial activity ; Anticancer properties; Cytotoxic activity
Gomphrena meyeniana	Antimicrobial activity ; Anticancer properties; Cytotoxic activity
Gomphrena perennis	Antimicrobial activity ; Anticancer properties; Cytotoxic activity
Gomphrena pulchella	Antimicrobial activity

Gomphrena species are employed in folk medicine for the treatment of several diseases and for their nutritive value. The species with biological activities (Table 2), including antimicrobial activity, used to treat gastrointestinal and respiratory disorders as well as infectious diseases were listed [10].

The phytochemical screening of *G. globosa* ethanol extracts [Gg-EE] detected the presence of saponins, alkaloids, reducing sugars and coumarins [11]. Dosumu *et al*. [12] Isolated the bioactive compounds like saponins, steroids, amino acids, non-reducing sugars, phenols and flavonoids from the methanol extract of *G. celosioides*. Hamiduzzaman and Azam [13] isolated three compounds stigmasterol [1], β-sitosterol [2] and isochavicinic acid [3, 16] from the crude methanol extract of whole plant of *Gomphrena globosa* by a combination of column chromatography and preparative thin layer chromatography over silica gel. The structures of these compounds were determined by H NMR spectroscopic (Fig. 1).

The ethyl acetate and methanol extracts of *Gomphrena celosioides* was phytochemically examined by Dosumu *et al.* [4] and revealed the presence of secondary metabolites. These metabolites include alkaloids, tannins, saponins, steroids, glycosides and reducing sugars. Babu *et al.* [17] isolated the compound oleuropein from *Gomphrena serrata* by subjecting it to exhaustive hot extraction with chloroform.

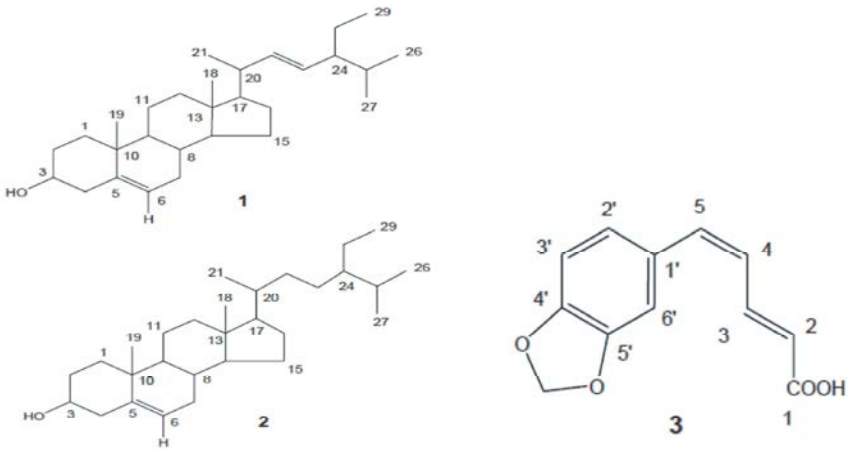
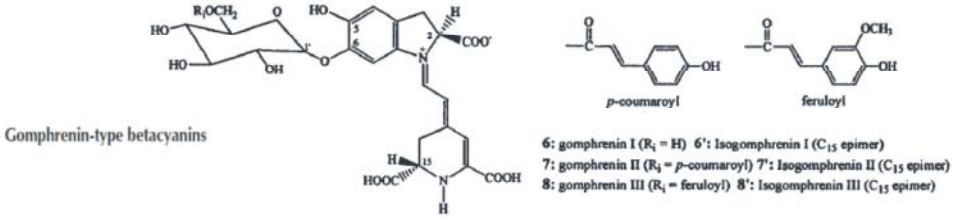


Fig. 1: Compounds extracted from *G. globosa.*



6	Gomphrenin I	32.83	540	551	*Gomphrena globosa*
6'	Isogomphrenin I	35.19	540	551	*Gomphrena globosa*
7	Gomphrenin II	58.34	310, 552	697	*Gomphrena globosa*
7'	Isogomphrenin II	61.58	310, 552	–	*Gomphrena globosa*
8	Gomphrenin III	59.10	322, 552	727	*Gomphrena globosa*
8'	Isogomphrenin III	63.59	324, 552	–	*Gomphrena globosa*

Fig. 2: Chemical structures and identification of Betalains [Betacyanins and Betaxanthins] from *G.globosa*.

Arginine-betaxanthin as a novel betaxanthin in *Gomphrena globosa* inflorescences was detected by Biswas *et al.* [18] and yellow Ulluco, which has not been reported so far as a pigment that occurs naturally and he performed characterization based on UV-Vis and mass spectrophotometry (Fig. 2). Corke *et al.* [19] identified the betacyanins for eight amaranthine-types, six gomphrenin types and two betanin-types from Amaranthaceae by HPLC characterization o f Reversed - Phase [RP] High-Performance Liquid Chromatography [HPLC]. *celosioides* extracts against organisms. The ethyl acetate and methanol extracts of the plant displayed inhibition activities on *Staphylococcus aureus, Bacillus subtilis, Pseudomonas aeruginosa, Escherichia coli and Salmonella typhi*. The methanol extract was active against *Candida albicans, Aspergillus niger* and *Trichophyton species* with diameter zones of inhibition between 14 and 20 mm. The fractionated methanol extract produced 3-[4-hydroxyphenyl] methylpropenoate with mild antimicrobial activity against the test microorganisms. The antihelmintic assay showed ethyl acetate and methanol extracts to be active *against Fasciola gigantica, Taenia solium and Pheretima pasthuma*. Ethyl acetate was the most toxic of the extracts causing paralysis of *Taenia solium* within 15 minutes and the death of *Fasciola gigantic* within 20 minutes of application. The brine shrimp assay gave an LC50 of 52.15 and 77.98 ìg/ml on hexane and methanol extracts respectively.

Ferreira *et al.* [20] found that the aerial parts contain sterol glucoside like Gomphsterol β- D-glucoside along with β - sitosterol, stigmasterol, campesterol, stigmasterol - β - glucoside, friedelin, 3 - epi - friedelinol, allantoin and chrysoeriol - 7 - O - β - D - glucoside, gomphrenoside, hopane - 7β - ol, β - sitosterol - 3-O-β - D- glucoside and 1 - triacontanol [31]. Betalain, betacyanin and flavones were also isolated from the whole plant [21] and the flowers [22]. Kuroda *et al.* [23] screened the phytochemical constituent of *Gomphrena macrocephala* and has resulted in the isolation of two new

oleananeglycosides (1 and 2) and a new taraxerane glycoside (3). The structures of 1-3 were determined as 11 α,12 α -epoxy-3 β -[[O-β-D-glucurono pyranosyl] oxy]olean -28,13-olide [1], 11 α,12 α -epoxy-3 β -[[O- β -D-galactopyranosyl-[1-->3]-O-[β -D-glucopyranosyl-[1-->2]]- β -D-glucuronopyranosyl]-oxy]olean-28,13-olide [2], and 11 α, 12 α -epoxy-3 β -[[O- β -D-glucurono pyranosyl] oxy]taraxer-14-en-28-oic acid β -D-glucopyranosyl ester (3), respectively, on the basis of their spectroscopic data and the results of hydrolysis.

Biological and Medicinal Uses of Genus *Gomphrena*: The leaves and flowers of *G. globosa* is a folk remedy for oliguria, heat and empacho, hypertension, antimicrobial, antioxidant [1], cough, diabetes, hypertension, kidney problems, hoarseness, cough, bronchitis and other respiratory diseases, mainly as expectorant, reproductive problems. It also has significant cytotoxic and estrogenic activity [13, 11, 16]. The different species of this genus also showed antibacterial, antimalarial, diuretic activities [24]. Besides as an ornamental plant *G.globosa* is also commonly used for the treatment of jaundice, high cholesterol and urinary problems in Latin America and Caribbean [25, 26]. Extracts of aerial parts of some species of the *Gomphrena* genus have the following biological activities reported: larvicide for *G. globosa*; antimicrobial for *G. martiana* and *G. boliviana*, antitumor to *G. martiana* and estrogenic to *G. demissa Mart*. *Gomphrena celosioides* is used in ethnomedical practice in Nigeria for treatment of various skin diseases, worms' infections and infectious diseases.

In South America, the plant is utilized as an abortifacient. A decoction of the whole plant and a related species *Gomphrena globosa* is applied to gangrenous wound. *G. martiana* [27] and *G. boliviana* are employed as antimicrobial agents by the natives [12]. *Gomphrena globosa* Linn is applied to gangrenous wounds [4]. As a treatment of body sore, the leaves are crushed as a paste which is applied to the affected part and covered with the leaf of the same plant [28]. A number of Brazilian *Gomphrena* species are employed in the treatment of bronchial asthma and fever and as an analgesic, tonic, or carminative. This species show antimalarial and diuretic activities [17]. *Gomphrena globosa* flowers contain betacyanins which have potential as food colorant, antioxidants and in prostate problems [29]. Ethnic tribes, farmers, fishers and hunters observe small size of lower leaves with dark colour of *G.globosa* to predict the weather forecasting which indicates the adverse weather condition (typhoon or flood) [30, 31].

Pharmacological Actions of *Gomphrena* Species

Anti-inflammation: Andrade *et al.* [8] determined the 24 phenolic compounds and eight betacyanins by HPLC-DAD in three different extracts of *G. globosa* inflorescences. The decoction presented the highest amount of phenolic compounds, kaempferol-3-O-[6-rhamnosyl] hexoside and kaempferol-3-O-hexoside being the main compounds. The rich betacyanins extract showed isogomphrenin III and gomphrenin III as major metabolites. The data provided the evidence that *G. globosa* inflorescences has the potential as a source of anti-inflammatory compounds, with relevance for the treatment of acute or chronic inflammatory conditions and health-promoting antioxidants for use by both food and pharmaceutical industries. *Gomphrena vaga* Mart. entire pant is used as anti-inflammatory of ovaries. And it is drunk "as water" until symptoms disappear. Its root is used as analgesic for toothache and leaves is used as an infusion against asthmas and allergies [15].

Antimicrobial, Antioxidant and Cytotoxic Activity: Hamiduzzaman and Azam [13] subjected the crude methanol extract and its hexane, carbon tetrachloride, chloroform and aqueous soluble fractions of *Gomphrena globosa* to antimicrobial, antioxidant [32] and brine shrimp lethality bioassays. Among all extractives the hexane soluble fraction exhibited the highest antioxidant activity having IC_{50} of 13.17±0.308 ìg/ml and the crude methanol extract showed significant antioxidant activity with IC_{50} of 20.35±0.360 ìg/ml. The chloroform soluble materials revealed significant cytotoxicity with IC_{50} of 0.331±0.029 ìg/ml. The carbon tetrachloride and chloroform soluble partitionates demonstrated mild to moderate antimicrobial activity with zone of inhibition 8±0.208 to 14±0.069 mm.

The methanolic extracts of leaf, stem and root of *G. celosioides* was investigated by Sharma and Vijayrergia [24] for anti-bacterial activity and was found to be most effective against the three tested bacteria [*Staphylococcus aureus, Pseudomonas aeruginosa* and *Escherichia coli*]. The stem and leaf extract were found to have maximum zone of inhibition against *Escherichia coli* with 15.5mm and 16mm, while the minimum zone of inhibition against *Staphylococcus aureus* was 10mm and 12.5 mm. The root extract was found maximum zone of inhibition against *Pseudomainas aeruginosa* with 12mm. The maximum activity index for the stem and leaf extracts was 1.19 and 1.23 for *Escherichia coli* and the root and leaf extracts showed minimum activity index of 0.72 against *Pseudomonas aeruginosa*. Abalaka and Damisa [14] carried out the antifungal activities for *Gomphrena*

celosiodes extracts at different concentrations on *Aspergillus niger, Candida albicans* and *Trichophyton rubrum*.

The methanol extract of *G. celosiodes* had a fungicidal effect on the selected fungal isolates at a concentration of 2000ìg/ml. The minimum inhibitory concentration [fungistatic] was ranged from 2000 ìg/ml to 1500 ìg/ml. The cytotoxic activity of 65 tested extracts was studied by Mahmoud *et al.*[33] from eight plant species [*Tabebuia heptaphylla [Vell.] Toledo, Bignoniaceae, Tapirira guianensis Aubl. Anacardiaceae, Myracrodruon urundeuva Allemão, Anacardiaceae, Schinus terebinthifolius Raddi, Anacardiaceae, Gomphrena elegans Mart. Amaranthaceae, Attalea phalerata Mart. ex Spreng. Arecaceae, Eugenia uniflora L. Myrtaceae and Annona dioica A. St.-Hil. Annonaceae*], *Gomphrena elegans* Mart. : n-hexane and n-butanol fraction of the leaves showed considerable activity.

Pomilio *et al.* [34] determined the antimicrobial activity of extracts and constituents of *Gomphrena martiana* [35] and *Gomphrena boliviana* [Amaranthaceae] in order to identify the compounds responsible for the folk-medicinal use of these plants. Each extract was evaluated against 20 microorganisms, including Gram-positive and Gram-negative bacteria, spore-forming Gram-positive bacteria, an acid-fast bacterium, a fungus and two yeasts. Fractionation of each with petroleum ether [PE] extract yielded five 5, 6, 7-trisubstituted flavones that were separately tested showing highest activity against *M. phlei* with minimum inhibitory concentration of 15, 20 and 75 mg/ml, approaching that of commercial bactericides.

Natural Blood Coagulant: The leaves of *G. globosa* act as a natural blood coagulatory. It stops bleeding due to cut injury is of immense importance among the ethnic people. The ethanolic extract of four medicinal plants *Polygonum microcephalum, Moringa oleifera, Croton tiglium* and *Gomphrena globosa* were examined for antioxidant activity, phenol and flavonoid content. Total phenol and flavonoid content and DPPH radical scavenging activity of the extracts were spectrophotometrically determined. The antioxidant activity was found to be higher in *Polygonum microcephalum, Moringa oleifera and Gomphrena globosa* [1].

Cardiovascular Effects: *Gomphrena globosa* is used in the treatment of high blood pressure. It promoted a hypotensive activity by significant reduction in arterial blood pressure without change in heart rate, confirming the therapeutic use as antihypertensive for this plant [11, 15]. They also prepared the ethanol extract from leaves of *G. globosa L*. by maceration and analyzed the phytochemical screening and biological assays. The phytochemical screening detected the presence of saponins, alkaloids, reducing sugars and coumarins.

Cooling and Cough: In Trinidad, the flowers of *Gomphrena* are boiled to make a tea which is used for baby gripe, oliguria, cough, diabetes and cooling.

Food Colourant: The fresh crude extract samples *Gomphrena globosa* without any purification was used by Corke *et al.* [19] for MALDI-QIT-TOF MS analysis using 2, 5-dihydroxybenzoic acid as a matrix. Fourteen free and acylated betacyanins, belonging to amaranthin-type, betanin-type and gomphrenin-type betacyanins, respectively, were identified. Lans [29] confirmed that *Gomphrena globosa* flowers contain betacyanins which have potential as food colorants and antioxidants.

Anti-Microbial Activity: Dias *et al.* [6] screened the ethanolic extract and pure compounds of *Gomphrena celosioides* for antimicrobial activity by Kirby-Bauer method. Quantitative determination of 4-hydroxy-3-methoxy-benzoic acid in stems, leaves, flowers and roots was established by TLC-densitometry. Their results showed significant activity against *Staphylococcus aureus* and *Salmonella typhi.* Dosumu *et al.* [4] found that ethyl acetate and methanol extracts of *G. celosioides* exhibited anthelmintic activities against *Pheretimia pasthuma, Fasciola gigantica* and *Taenia solium*. Higher anthelminthic and antibacterial activities were displayed in ethylacetate extract. Methanol extract exhibited pronounced antifungal activity. Preliminary phytochemical analysis of the extracts indicated the presence of steroids, glycosides, alkaloids, saponins and tannins.

The ethyl acetate and methanol extracts of *G. celosioides* was tested by Dosumu *et al.*[12] which showed inhibition activities on *Staphylococcus aureus, Bacillus subtilis, Pseudomonas aeruginosa, Escherichia coli* and *Salmonella typhi*. Methanol extract was active against *Candida albicans, Aspergillus niger* and *Trichophyton species* with diameter zones of inhibition between 14 and 20 mm.

Anti-Cancer Agent: The phytochemical analysis of chloroform extract of *Gomphrena serrata* was studied by Babu *et al.* [17] and reported the presence of carbohydrates, glycosides, aminoacids, phytosterols,

flavonoids, phenolics and terpenoids. They isolated the compound oleuropein from *Gomphrena serrata*. The development of novel oleuropein as an anti cancer agents and in-silico docking or computational studies are in progress.

Latha *et al.* [37] performed a study to investigate the anticancer activity of chloroform extract of aerial parts of *Gomphrena globosa* against Ehrlich Ascites Carcinoma [EAC] induced solid tumor. This study showed that, the extract was non-toxic up to 2000 mg / kg body wt. The histological study indicated that the damaged tissue was recovered by extract and solid tumor volume was reduced significantly. Thus, the findings revealed a significant anti-cancer activity of the extract

Reproductive Problems: *Gomphrena globosa* are used for prostate and reproductive problems [29]. The root decoction of *Gomphrena demissa* Mart. in a liter of water is used for the treatment of female sterility, amenorrhea, inflammations and ovarian diseases [15].

Organic Sulfur Fertilizer: Wang *et al.* [38] explored that *G. globosa* absorb atmospheric sulfides, which may be of great importance for ameliorating the environment and for farming as a green organic sulphur fertilizer used to balance insufficient soil sulphur content for intensive cultivation in China; H_2S and mainly SO_2 are emitted to air as a result of the rapid industrialized and economic development.

Urinary Problems: A non-experimental validation was conducted by Lans [26] on the plants used for urinary problems and diabetes mellitus. The *G.globosa* plant is used for hypertension, jaundice that may be safe. [39] Conducted the survey of ethnomedicinal plants in the muzaffarnagar district of Uttarpradesh to assess the potentiality of plant resources. The study revealed that 15 plant species belonging to 13 families are used as anti-urolithiatic agents in local remedies. *G.celosioides* Mart. is most effective and commonly used in treatment of urinary tract and kidney stones.

Anti-Malarial Activity: *Gomphrena arborescens* Mart. leaves, flowers and tuberous root is used as anti-malarial activity which is introduced by Brazilian priests that learned it from Indians [40].

Analgesic Activity: Hamiduzzaman [41] investigated the central and pheripheral analgesic activity of *Gomphrena globosa* for the wound healing activity to the tribal people of Bangladesh. The fractions like n-hexane soluble fraction, carbon tetrachloride soluble fraction, chloroform soluble fraction, aqueous soluble fraction were investigated for analgesic activity. The crude methanolic extract and n-hexane soluble fraction have significant analgesic activity at 400mg/kg dose. The central analgesic activity was highest after 30 minutes. After 60 minutes there was no central analgesic activity in the plant extracts.

The anti-inflammatory and analgesic properties of aqueous leaf extracts of *Gomphrena celosioides* and *Momordica charanti*a in rats and mice were reported by Oladele *et al.* [42]. The result of the study revealed that the leaf extracts of the two plants possess anti-inflammatory property as they were found to significantly [$p<0.05$] inhibit oedema induced by carrageenan in the rat paws. The results of the study suggest the anti-inflammatory and analgesic effects of the aqueous leaf extracts of the two plants.

Concluding Remarks: The studies on *Gomphrena* species elaborate the biological and medicinal applications in various ways from the ancient time have been discussed in the present review. It has been used throughout India not only as an ornamental source but also as a natural remedy for treatment of kidney failure and reproductive problems, cough, etc. On the basis of the above biological screenings and folk medicinal uses it can be concluded that this plant has significant medicinal properties and hence it can be carried out to isolate and characterise the active compounds responsible for this activities in the plant is recommended. The present knowledge on medicinal uses of plants needs scientific investigation to confirm their medicinal values.

Competing Interests: This review article has no competing interests.

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