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Arundo donax L.: An overview on its traditional and ethnomedicinal importance, phytochemistry and pharmacological aspects

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ABSTRACT

Arundo donax L. (Giant reed) is a grass species belong to Poaceae family with a myriad of uses such as traditional and ethnomedicinal values, bioenergy, and socio-economic importance. The plant is used in conventional medicine to treat various disorders related to skin, gastrointestinal, skeletal, menstrual problems, respiratory and urinary diseases. The present review summarises the scattered information on socio-economic importance, ethnomedicinal uses, phytochemistry and pharmacological aspects of this plant. We conducted a rigorous literature survey using databases such as Scopus, Science Direct, Web of Science, Google Scholar, and PubMed entering keywords like *A. donax*, Giant reed, and Spanish reed, etc. Phytochemical investigations have identified several alkaloids, terpenoids, sterols, phenolics, and lignin derivatives. The isolated phytoconstituents are reported to exhibit multiple pharmacological activities such as anti-bacterial, anti-oxidant, anti-proliferative, anti-spasmolytic, and also used to treat helminthic infestations in cattle. However, the scientific validity of traditional practices to cure various diseases has not been correctly evaluated yet. Therefore, it is recommended to further investigate the plant for clinical trials to unleash its therapeutic importance towards chemical characterisation for drug discovery and development in the pharmacological field.

Implication for health policy/practice/research/medical education:
This review article summarised the scattered information on socio-economic importance, ethnomedicinal uses, phytochemistry and pharmacological aspects of *Arundo donax*, which are the baseline information for future work and further exploration of the therapeutic potential of this plant.

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Introduction

Arundo donax L. (Giant reed) is a perennial and rhizomatous plant that belongs to the Poaceae family and one of the most widespread species of the genus *Arundo*. The plant is of general occurrence across the globe. It has been included amongst the worst invasive species of the world because it displaces the native flora and deteriorates the ecological state of lands wherever it grows (1). The plant also possesses several medicinal properties, and therefore, has traditionally been used by several ethnic groups across the world to cure various ailments. According to the World Health Organization (WHO), almost 80% of the world's population relies on indigenous medicinal plants to cure diseases (2,3). With the immense existing potential and rich knowledge about medicinal plants at the ethnic level, the ethnomedicinal system has reinforced the discovery of several therapeutically important drugs such as Quinine and Artemisinin from the Amazon and China, respectively (4). This traditional system of medicine has provided *A. donax* L. in Ayurvedic texts i.e., *Charak Saṁhitā, Suśruta Saṁhitā* and *Mādhava Chikitsā* for the treatment of urinary disorders such as *Mūtrakṛcchra*, in medical terminology called as Dysuria (5). A large group of people belonging to different ethnic groups and tribes uses this plant for treating fever, urinary disorders, bone fracture, menstrual disorders, and organ

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dysfunction in cattle (6).

In India, the plant is used in several traditional formulations as a vasopressor, uterine stimulator, hypotensive and antispasmodic agent (7). A decoction of its rhizome acts as an emollient, diuretic, galactagogue (for enhancing lactation) and menstrual stimulator (8).

Local Amchi people (herbalist) in the Kinnaur district of Himachal Pradesh use a decoction of the roots to cure cancer (9). In Chinese folk herbal medicine, the rhizome of Giant reed has been using to treat toothache, swollen gums, vomiting and knee osteoarthritis (10). In Manipur (north-eastern) India, the steam of boiled leaves is used to cure chronic haemorrhoids (11). Ethnic Albanian people in Italy use the internal stem membrane of this plant to arrest bleeding (12,13). The roots are diaphoretic, diuretic, emollient (14,15) and used by local peoples to treat cancer in Pakistan (16,17). Apart from this, the plant also possesses socio-economic importance as different ethnic groups use its strong stem and leaf to make rooftops, thatches, basket, and ropes (6). The stem is also used to make musical instruments and fishing nets (6,14). Phytochemical studies have revealed that the plant contains fatty acids, sterols, and secondary metabolites such as alkaloids (tryptamine, bufotenidine, gramine, and arundamine), terpenes, carotenoids and phenols (8).

Bioactive compounds are shown to have remarkable pharmacological properties such as anti-microbial, anti-oxidant, anti-pyretic (18) and anti-tumorous activities (19). Various types of tryptamines viz. N, N–dimethyltryptamine, 5–methoxy–N, N–dimethyltryptamine, bufotenine, etc., have been isolated from the rhizome, which possesses mild psychedelic effects (20,21). A lectin isolated from the rhizome of Giant reed is reported to have anti-tumorous properties (19). Despite having immense ethnomedicinal importance, there is a lack of systematic account of the literature on Giant reed. To the best of our knowledge, no review article published till date highlighting its ethnomedicinal values and therapeutic potential. Thus, the present study aimed to summarize the existing knowledge of ethnomedicinal uses, phytochemistry, and pharmacological aspects of *A. donax* L. This review hopefully will provide baseline information for other researchers who intend to work on this plant.

Methods

To get comprehensive and systematic information on its traditional and ethnomedicinal uses, as well as phytochemistry and pharmacological aspects of this plant, we carried out an extensive survey of literature through available search engines like Scopus, Web of Science, Science Direct, Google Scholar, and PubMed by using keywords such as *Arundo donax*, *Arundo benghalensis*, Giant reed, and Spanish reed. We found a total of 95 articles through a search made in the available databases. But we retained 82 articles for the preparation of the present review based on the suitability of the study. Chemical structures of the isolated phytoconstituents were drawn using software ChemDraw Pro 12.0 from Cambridgesoft. All figures were prepared through SigmaPlot 12.0 version software.

Vernacular names

In India, at the regional and state level, the plant is known by various vernacular names such as Giant reed, River reed, Wild cane, Spanish cane in English; Naal, Baranal, Narasal, Naade in Hindi; Kasa, Dhamana, Potagala, Sunyamadhya in Sanskrit; Noljora, Nol, Gabnol in Assamese; Caravanam, Mudampul, Nanalpul, Velam in Tamil, Yachi in local dialects of Arunachal Pradesh; Nolkhagra in Bengali; Yenthou in Manipuri; Nard, Naal, Narsaal, Naur in local dialects in Jammu; Ama in Malayalam; and Peepalu, Paatuveduru in Telegu. In Ayurveda (The traditional system of medicine in India), the plant is known by various names such as *Poṭgala, Śunayāmadhayā, Dhaman, Devanala.* In the Siddha (Tamil) system of medicine, it is known as Korukkai.

Botanical description and ecological distribution

It is one of the largest members of the genus (*Arundo*), which attains a luxurious growth with a height of 6-8 m (22). It has a very strong root architecture that penetrates deep into the soil and gives rise to fleshy tuberous rhizomes, which spreads horizontally and forms large thickets. Each stem is hollow, cane-like, divided into distinct nodes and internodes. Leaf-blades are large, somewhat bamboo-like, pale to blue-green, distichous, linear to lanceolate, rounded or cordate with a tuft of hairs at base, 30-60 cm long and 3-5 cm wide tightly clasped around the stem. The inflorescence is panicle-like 30-60 cm long with the onset of flowering from June-December (23).

It is thought to be native of South Asia (India, China, Bhutan, Afghanistan, Myanmar, and Thailand) and the Mediterranean region. It moderately grows in several climates across the world and, therefore, has become a naturalised invasive plant species in most of the countries of the European continent, South America, South Africa, Mexico, and the pacific islands (24). Giant reed commonly found along river beds, ditches, and roadsides reproduce through vegetative means by spreading its canes through floodwater and quickly encompass the entire landscape by outcompeting the native vegetation (1). In India, its distribution range generally varies from subtropical low lying Himalayan hills at 600 m to 2400 m. Morphological attributes and habitats of Giant reed are depicted in Figure 1.

Socio-economic importance

The Giant reed is a source of livelihood for people of the Meitei community in Manipur, North-East India.

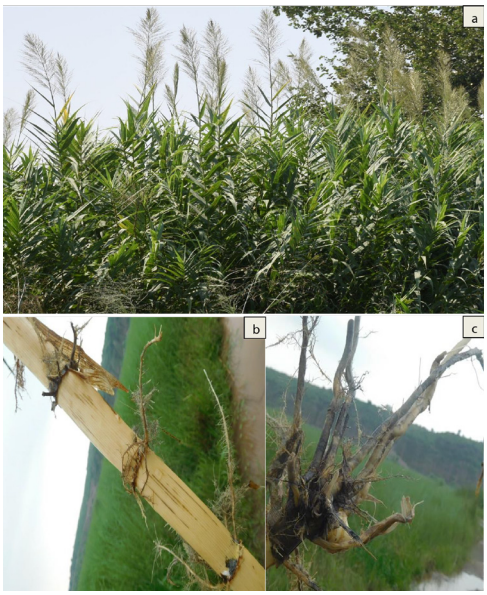

Figure 1. Morphological attributes of *Arundo donax* L. a) General appearance of the plant with leaves and inflorescence, b) Stem bearing roots at the node, c) Rhizome and cluster of roots.

The plant is commonly used in daily household stuff, life-fencing, soil binder, firewood, and cage for livestock rearing. Thrashing mat made from the stem of this plant costs around 2200-3000 ₹ per piece in the market of Manipur, India (6). Generally, the stem and leaves of the *A. donax* L. are used to make baskets, mats, ropes, and thatching of huts in Garhwal Himalaya (25). Terminal panicles of *A. donax* L. are also used to make brooms in other parts of India like Uttar Pradesh and Garhwal Himalaya (14,25). Local people from the Mishing tribe in Brahmaputra valley of Assam use the whole plant to keep their rice stock (26). Fumigants after burning of dried leaves of *A. donax* L. are used as mosquito repellents by tribals of Senapati district, Manipur (27).

The stem of the plant is used as a building material, fencing, and supporter for climbing crops and an important source of firewood for local people in Yangzhou, East China, and Manipur, India (6,28). The Tharu tribe of Katarniaghat Wildlife Sanctuary, Uttar Pradesh uses its stem to make fishing rods and walking sticks (14). It is also used in rituals, ceremonies for prayer to forefathers and deities (Apokpa Khurumba) by Chothe tribes in Manipur (29). The stem of Giant reed has been used for making musical instruments or woodwind such as flutes since ancient times (6,30). Besides, it is also used in the paper and pulp industry, source of fuel and phytoremediation of heavy metals (23). Various experimental studies have shown that the roots of this plant accumulate significant concentration of trace elements in sediments and water, and can be used as a promising tool for biomonitoring campaigns of wetlands (31).

Traditional and ethnomedicinal uses

Different parts of the plant, such as leaves, stem, roots, and rhizome are used in traditional and ethnic formulations to cure a broad spectrum of diseases (Table 1). The plant is well explored in folk medicines as a diuretic, emollient, and to treat skin disorders. An ancient Indian text (in Sushruta) states that if decoction of *Arundo donax* L.

Table 1. Ethnomedicinal uses of *Arundo donax* L.

Disease category	Disease	Part used	Mode of administration/use	References
Circulatory disorders	Haemostatic	Stem (Culm)	The dividing membrane of nodes or internal membrane of stem is used as a plaster for wounds to prevent infections and induce cicatrisation.	(12,13,33,34)
	Dropsy	Rhizome or roots		(38,39)
Dermatological disorders	Leprosy	Leaves and shoots		(40)
	Skin problems	Tender Shoot	The pounded new shoots applied to the affected area.	(41)
		Leaves and stem		(42)
	Eczema	Root	External application of root paste, about 20 g on affected area	(43)
	Condyloma	Roots and leaves		(17,39)
	Erysipelas			(36,44)
	Astringent	Whole plant		(45)
		Stem (culm)		(33)
Digestive disorders	Diarrhoea and dysentery	Whole plant		(45)
		Roots	Aqueous decoction of fresh root with adequate salt is given to cattle to cure dysentery by the Mundas	(46)
	Intestinal worms and typhoid	Stem	Fresh green shoots after mixing with honey are given to children	(47)
	Chronic haemorrhoids	Leaves	Leaf boiled in water and steam directed to the anal region	(11)

Table 1. Continued

Disease category	Disease	Part used	Mode of administration/use	References
Excretory problems	Diaphoresis	Roots		(14-15)
		Stem (culm)		(33-34)
Urinary disorders	Diuretic	Rhizome	Decoction	(48)
		Root		(14,15,49)
		Roots and Leaves		(17)
		Stem (culm)		(33,34)
Inflammatory	Fever	Leaves and shoots		(18,36,40,50)
	Headache	Root		(15,51)
	Headache	-		(52)
	Headache	Root and leaves		(17)
	Tonic, ulcer	-		(44)
	Otitis	Leaves	Vapours	(32,53)
Respiratory	Asthma	Stem	Tender shoot extract with honey is given orally	(54)
	Pertussis	Root sap	A little sugared glass of red sap (cut with sunset under the knot but left attached to the roots) is taken 3 times a day.	(37)
Skeletal	Bone dislocation	Root and stem	Powder with honey, splints	(55)
		Stem	Mash prepared after crushing the stem is directly applied for fracture-dislocation treatment	(56)
	Leg pain	Stem		(40)
Reproductive disorders	Menstrual disorders in cattle	Rhizome	Decoction of rhizome stimulates menstrual discharge in cattle	(8,48)
	Menolipsis in humans	Root	Aqueous decoction of fresh root (ca. 10 mL) with 7 long pepper (*Piper longum*) paste is given to women at early morning in empty stomach to cure menolipsis. The drug is given for successive 3 days just after completion of menstrual cycle by the Lodhas.	(46)
	Menstrual disorders	Rhizome	Decoction of rhizome is used to stimulate menstrual discharge (emmenagogue)	(57,58)
		Stem (Culm)	Emmenagogue	(33,34)
	Abortifacient	Root	Root decoction along with Jaggery is taken orally as an abortifacient.	(59)
	Antigalactagogue (diminish the secretion of milk)	Root		(14,39)
		Rhizome	Rhizome extract is used with black pepper	(60)
		Leaves		(53)
	Galactagogue (stimulate milk secretion)	Stem (culm)		(33,34)
Cancer		Roots and leaves		(17)
		Root and stem	Powder with honey	(55)
		Rhizome or rootstock	Decoction of rhizome in wine with honey	(39)

along with *Salix alba* L. is given, it can cure chronic fever (7). It has been widely used by local people of Sardinia, Italy for vulnerary (healing of wounds), emmenagogue (stimulation of menstrual discharge), galactagogue (promote lactation), haemostatic (arrest of bleeding), diuretic, diaphoretic, anti-inflammatory and anti-septic purposes (32-34).

Furthermore, about 100-250 g of fresh leaves of *Arundo donax* L. are given orally to cure worm infestation of cattle in the Jhang district, Pakistan (35). In Ayurvedic formulations, Trinpanchmula kwath Giant reed is used to treat fever, rabies, retention of urine, and erysipelas (36). Roots and rhizome are consumed in 56% of all ethnomedicinal practices, followed by stem (21%), leaves (17%), and whole plant (7%), as shown in Figure 2. Furthermore, the use of Giant reed to cure reproductive disorders is most cited (18.18%), followed by dermatological (14.28%) and inflammatory diseases (12.98%) (Figure 3). Out of all the documented ethnomedicinal uses, the plant has been extensively used as a diuretic, followed by emmenagogue, haemostatic, diaphoretic, and antipyretic agents.

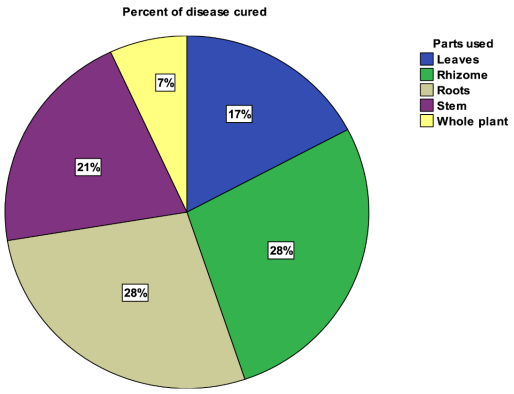

Figure 2. Pictorial representation of percent contribution of different plant parts to cure various diseases.

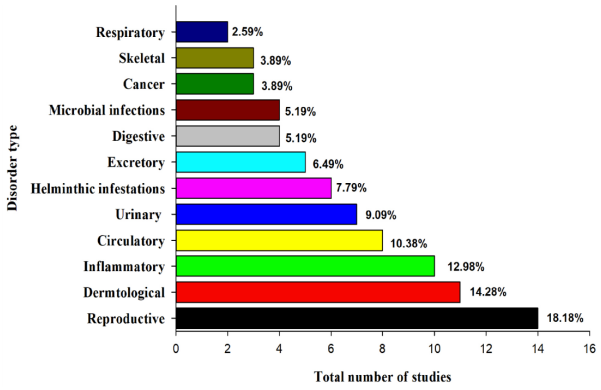

Figure 3. Category wise distribution of different studies as per their biological activities.

Phytochemical screening

The major classes of phytochemicals present in Giant reed are alkaloids, phenols, lignins, sterols, and triterpenoids (Table 2). The Giant reed is source of several classes of phytosterols as shown in Figure 4. The chief alkaloids isolated from the rhizome of Giant reed are bufotenine, dehydrobufotenine, bufotenidine, N, N-dimethyl-tryptamine, 5-methoxy-N- methyltryptamine, gramine, donaxine, donaxirine, donaxiridine, arundine, and ardine (8). Roots of the Giant reed yields major alkaloids such as arundaphine (61), arundinine (62), arundamine, arundanine, arundacine, arundarine, and arundavine (63,64) (Table 2). Recently a new bis-indole alkaloid named arundaline and four other known alkaloids i.e., N-acetyltryptamine, trans-N-(p-coumaroyl) serotonin, trans-N-feruloyl serotonin, and tuberosine B were extracted using 70% aqueous ethanol extract (10) (Figure 5). The latter four alkaloids were isolated for the first time from *Arundo donax* L. Besides, the leaves of Giant reed are reported to contain various pharmacologically active

Table 2. The list of reported phytoconstituents from *Arundo donax* L

Category	Source parts	Phytoconstituents	References
Alkaloids	Leaves	Donaxarine, gramine, donaxine, phenyl-β-naphthylamine, deoxyvasicinone, arundine, ardine, donaxarine, donaxanine, donaxaridine, donine	(8,63)
	Rhizome	Arundaline, arundalcohol, N-acetyltryptamine, trans-N-(p-coumaroyl) serotonin, trans-N-feruloylserotonin, tuberosine B	(10)
	Rhizome	Donasine	(18)
	Rhizome	N,N-dimethyl-tryptamine, 5-methoxy-N- methyltryptamine, bufotenine, dehydro-bufotenine, and bufotenidine	(8)
	Roots and rhizome	Arundaphine	(61)
	Epigeal and roots	Arundinine	(62)
	Roots	Arundamine, arundaline, arundanine, arundacine, arundarine, arundavine, arundafine, N-methyltetrahydro-β-carboline	(63,64)
	Leaves	Donaxine	(63)
	Flowers	Gramine, N,N-dimethyltryptamine, bufotenine, 5-methoxy-N-methyl-tryptamine, eleagnine	(66)
Sterols and triterpenes	Leaves	Campesterol, stigmasterol, stigmastanol, β-sitosterol, β-amyrin acetate, dihydrobrassicasterol, stigmasta-3,5-dien-7-one, stigmast-4-en-3-one, stigmasta-3,6-dione, Friedelin, α-amyrenone; β-amyrenone, cycloartenone	(65)
	Rhizome	Squalene	(67)
Phenolics	Rhizome	Xanthone, Xanthene	(67)
		Guaiacol, o-Cresol, m-Cresol, methyl-guaiacol, 4-methylguaiacol, 4-methylcatechol, 4-ethylguaiacol, 4-vinylguaiacol, 4-ethylcatechol, eugenol, 4-methylsyringol, E-isoeugenol, 4-ethylsyringol, Z-isoeugenol, 4-vinylsyringol, E-propenylsyringol, Z-syringylpropanol	(71)
Lignins	Stem and leaves	Guaiacyl, syringyl propane, p-hydroxyphenylpropane	(70)
Carotenoids		β-caroten, xanthophyll	(72)

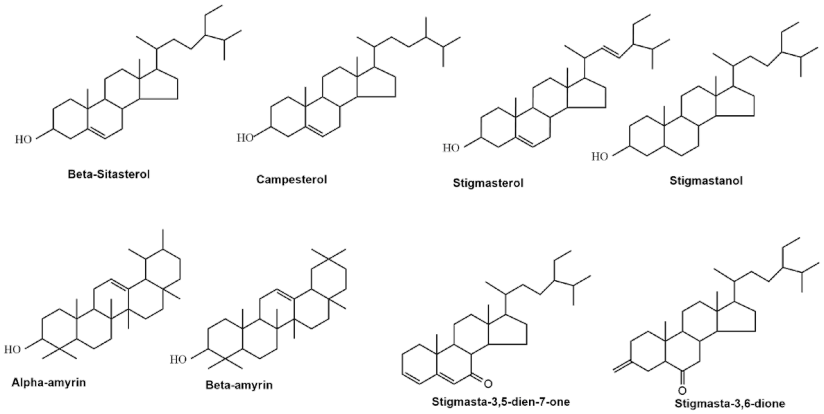

Figure 4. Chemical structure of some phytosterols isolated from Giant reed.

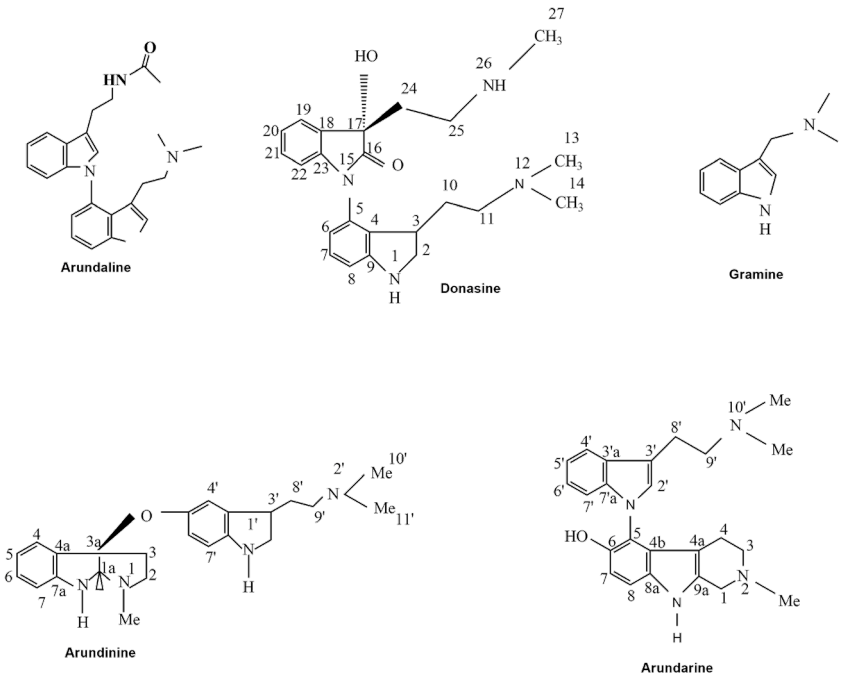

Figure 5. Chemical structure of some major alkaloids isolated from Giant reed.

terpenoids such as α-amyrenone, β-amyrenone, and cycloartenone (65) (Figure 6). Ghosal et al isolated several alkaloids such as gramine, N, N-dimethyltryptamine, bufotenine, 5-methoxy-N-methyltryptamine, and eleagnine from the flowers of *A. donax* L. (66).

From the gas chromatography-mass spectrometry (GC-MS) analysis of hexane, dichloromethane, ethyl acetate, and methanolic rhizomatous extracts, several phytoconstituents belonging to sterol groups, fatty acids, lipids, hydrocarbons, phenolics, terpenoids, xanthones, and xanthene were isolated (67). A study conducted by Coelho et al using the gas chromatography (GC) and GC-MS analysis identified a series of long-chain n-fatty acids, n-alkanes, n-aldehydes, n-alcohols, monoglycerides, free and esterified sterols, triterpenols, steryl glucosides, steroid hydrocarbons, as well as steroid and triterpenoid ketones (68). Shatalov and Pereira reported that the Giant reed stem (including both nodes and internodes) on a percent dry weight basis contained 21.12% lignin, 31.06% cellulose, and 30.26% hemicellulose (69). Giant reed lignin also constitutes a significant fraction (approximately (20%-25% by wt.) mainly composed of p-hydroxyphenyl (H), guaiacyl (G), and syringyl (S) phenylpropanoid units with a predominance of β-O-4 aryl ether linkages (~71%–82%), with the remaining part constituted by β-β, β-5, β-1, and α, β-diaryl ether linkages (70,71). However, the isolation and purification of lignin is a complicated process from any Poaceous plant owing to their strong association with cell wall carbohydrate polymers (71).

A recent phytochemical investigation, through acid

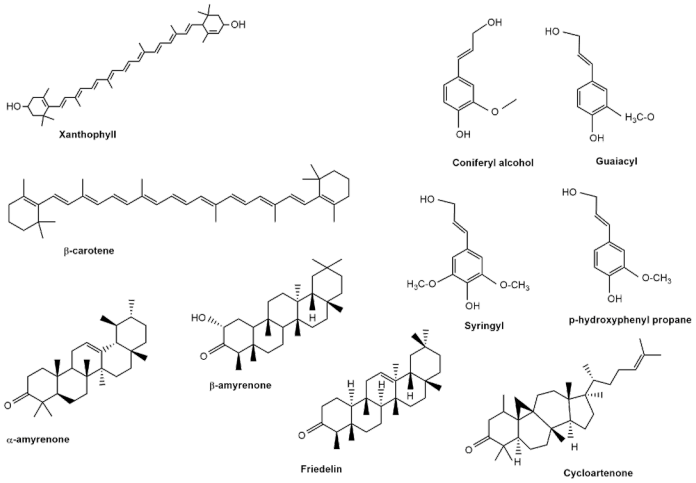

Figure 6. Chemical structure of some carotenoids, lignin, and terpenoids isolated from Giant reed.

catalysed hydrothermal conversion of lignocellulosic biomass to levulinic acid using advanced techniques like pyrolysis/gas chromatography/mass spectrometry (Py-GC/MS), thermogravimetric analysis/infrared spectroscopy (TGA/FTIR) and evolved gas analysis coupled with mass spectrometry (EGA-MS) revealed several lignin phenolic derivatives, such as guaiacol, o-cresol, m-cresol, methyl-guaiacol, 4-methylguaiacol, 4-methylcatechol, 4-ethylguaiacol, 4-vinylguaiacol, 4-ethylcatechol, eugenol, 4-methylsyringol, E-isoeugenol, 4-ethylsyringol, Z-isoeugenol, 4-vinylsyringol, E-propenylsyringol, Z-coniferyl alcohol, and syringylpropanol (71) (Figure 7). In a recent study, Sağir et al reported the concentration of soluble phenolics of 301 ± 0.14 mg/g fresh weight (FW) in both stem and leaves of Giant reed (72).

Pharmacological aspects

Anti-bacterial activity

Few studies have claimed scientific evidence for the anti-bacterial activity of Giant reed. Shirkani et al evaluated the anti-bacterial activity of aqueous and methanolic extract of stem node of Giant reed against bacterial strains; *Staphylococcus aureus*, *Micrococcus luteus*, *Klebsiella*, *Escherichia coli,* and *Pseudomonas aeruginosa*. The aqueous extract of the stem node exhibited anti-bacterial activity against methicillin-resistant *Staphylococcus aureus* at a concentration of 128 µg/mL (73). Moreover, in another study Sharma et al demonstrated that the methanolic root extract showed high efficacy against bacterial strains; *P. aeruginosa* with inhibition zone diameter (15.0 ± 2.8) followed by *Klebsiella pneumoniae* (14.0 ± 2.08) and *Streptococcus aureus* (14.0 ± 6.0) at an inhibitory concentration of 40.0 µg/mL. While in methanolic leaf extract, high efficacy was observed against *Streptococcus aureus* only, with maximum inhibition zone (7.3 ± 3.7) at the same concentration. However, a low activity was observed against *K. pneumoniae* (6.6 ± 3.5) at the same concentration (74).

In another study, Pansuksan et al observed that the dichloromethane (DCM) rhizome extract exhibited strong anti-bacterial activity against *Bacillus subtilis* and *Bacillus cereus* with inhibition zone 18.0 mm and 17.8 mm, respectively. However, hexane, ethyl acetate, and methanolic extract showed lower efficacy against *B.*

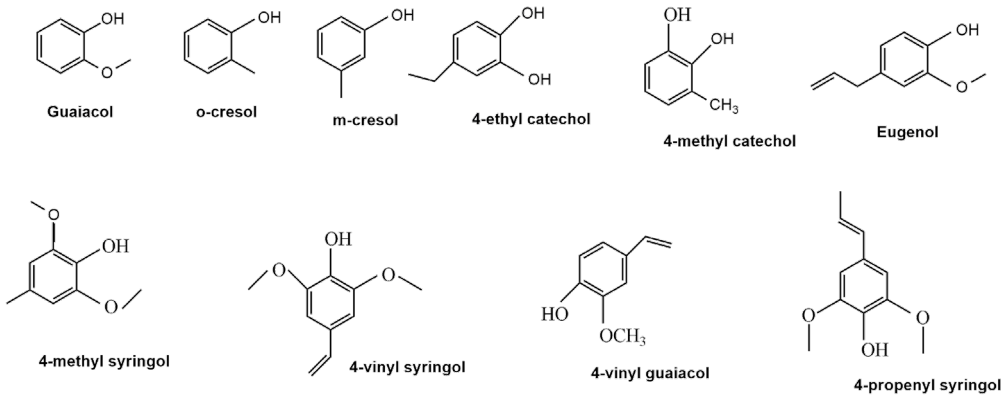

Figure 7. Chemical structure of some lignin pyrolysed phenolics isolated from Giant reed.

subtilis. No prohibitory effect was found against *E. coli*, *S. aureus,* and *Candida albicans* (67). The specific bioactive compounds responsible for anti-bacterial activities of Giant reed are not discussed in most of the studies. Therefore, future studies must focus on identifying the bioactive molecules and their mode of action. Furthermore, to elicit the anti-bacterial activities of Giant reed, more pathogenic strains are needed to be tested using different extraction solvents.

Anti-oxidant activity

In recent times much attention has been paid to natural anti-oxidants and their therapeutic potential for the cure of many complex disorders. The human body, due to metabolic and biochemical processes, produce several metabolic by-products called free radicals, which can damage cells, tissues, DNA, and promote aging. Anti-oxidants act as reducing agents that can quench the free radicals by donating hydrogen atoms and slow down the oxidation process, therefore protect cells and tissues from their deteriorating effects (4). A phytochemical investigation conducted by Sağir et al using leaf extract of the Giant reed reported a total anti-oxidant capacity of 3.4 ± 0.58 mg/g FW and total superoxide dismutase activity of 234.0 ± 74 units/g FW (72). The Giant reed is a rich source of secondary metabolites and derivatives of total phenols, non-tannic phenols, flavonoids, and tannins, which impart anti-oxidant properties (75). In another study, free radical scavenging activity of five percent aqueous extract of roots of Giant reed was investigated using 2,2-diphenyl-2-picrylhydrazyl (DPPH) and Phosphomolybdenum complex. The DPPH free radical scavenging activity was 399.10 µg/mL and 0.98 for phosphomolybdenum complex (76). Phenolic compounds contribute significantly to anti-oxidant activity, and it is well evidenced in Piluzza and Bullitta (75), where they found the total anti-oxidant activity of acetone leaf extract ranged 6.64±0.13 and 7.03±0.59 mmol/100 g/DW against DPPH and ABTS free radical ions. All of the above-cited anti-oxidant studies have been conducted using total anti-oxidant capacity, DPPH, and ABTS free radical scavenging assays *in vitro* conditions, which may or may not produce similar results *in vivo* conditions. Therefore, animal systems must be taken into consideration for free radical scavenging assays for the reliability of results.

Anti-algal and anti-fungal properties

Bloom forming algae (algal blooms) may pose a severe threat to water bodies, and underlying aquatic life primarily promotes fish mortality due to depletion of dissolved oxygen in the water and releasing harmful toxins (28). Therefore, the use of allelochemicals from aquatic plants to control algal blooms is a hot topic of research. A study conducted by Hong et al reported that methanolic shoot extract of Giant reed inhibited the growth of bloom-forming cyanobacterium *Microcystis aeruginosa* (77). They fractioned the methanolic extract into acidic and neutral fractions, of which the neutral fraction had higher inhibitory growth than the acidic fraction. They accredited it to the presence of allelochemical gramine and proved to be one of the most effective anti-algal compounds known in aquatic plants.

Other allelochemicals isolated from methanolic shoot extract of Giant reed were 3-methyl-indole (Skatone), 2,4,6-trimethyl-benzonitrile, and 6,10, 14-trimethyl-2-pentadecanone (also called Phytone), 3,7,11,15-tetramethyl-2-hexadecan-1-ol (phytol), and 4,8,12,16-tetramethyl heptadecan-4-olide, which speculated to possess anti-algal properties (78). Pyrolytic vinegar or bio-oil from Giant reed is shown to have algicidal properties and inhibit red tide dinoflagellate *Karenia brevis,* which may cause neurotoxic poisoning to the marine organisms. The pyrolytic vinegar was predominantly composed of acetic acid, phenol, aldehyde, ketones, and ester, which could render anti-algal properties (28). In another study, it was found that a neutral fraction of methanolic extract of Giant reed was able to suppress the growth of harmful golden alga *Prymnesium parvum* and the maximum algicidal activity was observed at 50 mg/L (79). Likewise in the case of *Microcystis aeruginosa*, gramine was proved to be the most potent growth suppressing compound in golden alga as well. Another indole compound skatole was also found to suppress the growth of golden alga; however, its algicidal activity was less potent than gramine. Since synthetic anti-algal compounds are toxic to aquatic life and suppress the growth of non-harmful algae as well, therefore, the algicidal activity of giant reed extract proved to be a promising tool for control of harmful algal blooms in water bodies. Gramine is also reported to suppress the growth of freshwater algae *Desmodesmus armatus* (80) and marine *Chattonella marina* (81). Information about the antifungal activity of *Arundo donax* L. is very sparse in the literature. However, its efficacy has been reported against few basidiomycetes i.e., *Trametes versicolor, Coniophora puteana, Gloeophyllum trabeum*, and *Postia placenta* (22).

Anti-parasitic and anthelmintic uses

Badar et al studied the anti-parasitic and anthelmintic potential of Giant reed leaves. Crude aqueous methanolic extract of leaves was used to study *in vitro* (adult motility assay and egg hatch test) and *in vivo* (faecal egg count reduction test) anthelmintic activity against *Haemonchus contortus*. In adult motility assay, 56.7% mortality of *H. contortus* was observed by 10 hours post-exposure with the extract at 50 mg/mL. In egg hatch test, *A. donax* L. exhibited ovicidal activity with LC_{50} = 200.1 µg/mL; whereas, crude powder of *A. donax* resulted in 50.5% reduction in egg per gram of faeces in sheep, naturally infected with gastrointestinal nematodes (36). Anthelmintic activity of giant reed was also observed against cattle worms, such as

Ascaris sp., *Oesophagostomum* sp., and *Paramphistomum* sp. (82,83). In Sardinia, Italy, the leaves of Giant reed are used to cure coughs and intestinal worms in horses (33,75).

Anti-cancerous properties

People in Calabria, Southern Italy, use a mixture of *Arundo donax* L. with *Spartium junceum* L. and *Cynodon dactylon* L. (Pers.) to treat tumors (the type of tumor is not specified) (84). Roots and leaves of Giant reed are used to treat cancer by local people in Bahawalpur, Pakistan (17). Root and stem powder with honey is given to cure cancer in Muzaffarabad, Pakistan (55). All the reports of anti-cancerous uses of this plant are restricted to the ethnic and local level. There is no scientific validation of the anti-cancerous properties of this plant so far. Although in 2005, a specific lectin named N-acetyl-D-glucosamine isolated from the rhizome of Giant reed was found to possess anti-proliferative properties towards human cancer cell lines and mitogenic towards human peripheral blood mononuclear cells (19). Of the several human cancer cell lines studied, the lectin at the highest concentration of 50 µg/mL showed the maximum effect of 62% against ovarian cell line (OVCAR-5) followed by SKN-N-MC (CNS), Hep-2 (Liver), SW-620 (Colon), and SK-N-SH (CNS) cell lines, with 59%, 53%, 51% and 45% growth inhibition, respectively.

Further studies are required to unravel the molecular mechanisms for the anti-proliferative properties of this plant. Therefore, traditional formulations and medicinal plants used for the ethnic cure of diseases must be screened pharmaceutically to pass ethnic knowledge to the modern system of medicine for the betterment of humankind.

Effect on skeletal and smooth muscle

Defatted ethanolic extract from rhizome of Giant reed is proved to hypotensive and antispasmodic against histamine, serotonin, and acetylcholine-induced spasms. Several pharmacological aspects of rhizomatous alkaloid bufotenidine have been studied on smooth muscles such as the intestinal loop of guinea pig, dog's intestine, the uterus of albino rats and guinea pigs, and dog's tracheal chain (8). A muscular spasm was observed after injection of alkaloid, and repeated doses followed tachyphylaxis in dog's intestine. In the isolated loop of the intestine, the alkaloid initially relaxes the muscle but when administered in doses above 20 mg/kg it alters the spasmodic effects of histamine, acetylcholine.

A muscular spasm was observed in isolated guinea pig uterus and rat uterus at an initial concentration of alkaloid (20 µg/mL and 10 µg/mL, respectively). However, at higher doses, the drug blocked acetylcholine-induced spasm. This might be the reason behind the stimulatory action of rhizome extract against menstrual discharge in traditional formulations (8). In contrast, there was no effect of alkaloid's higher doses on dog's tracheal chain, nor it influenced the acetylcholine-induced spasm. Surprisingly, there was no such kind of study conducted on human beings yet.

Toxicological aspects

The first toxicological report about Giant reed was published in 1969, where a rhizomatous extract was reported to be toxic towards albino mice and rats (8). The chief alkaloid responsible for toxicity was bufotenidine. When the alkaloid was administered to albino mice and rats at a dose of 10 mg/kg, the sudden death of all five mice and ataxia in all ten rats was observed. Besides, the alkaloid produced head drop followed by death in rabbits in 5-6 mg/kg dose given against 0.3-0.5 mg/kg dose of alkaloid d-tubocurarine. The alkaloid bufotenidine acts as a neuromuscular blocking agent, which is mainly a toad poison. However, no toxicological aspects of Giant reed have been studied concerning human beings so far.

Other uses

Ethanolic rhizome extract from Giant reed has antipyretic properties due to the prevalence of bis-tryptamine alkaloid donasine (18). A significant reduction in the rat anal temperature was observed in donasine infused rats. Bioactive compounds in Giant reed are reported to show antifeedant activity against cotton boll weevil (*Anthonomus grand*). The strong inhibitory effect against cotton boll weevil is due to the presence of alkaloid N-(4'-bromophenyl) 2,2-diphenylacetanilide in *A. donax* L. (85).

The Giant reed is a rich source of indole bases (gramine, N, N dimethyltryptamine, 5-methoxy-N-methyltryptamine, 5-methoxy-N,N-dimethyltryptamine, bufotenine, bufotenidine, dehydrobufotenine, Nb-Methyltetrahydroharman) and tetrahydro-p-carbolines. These alkaloids at low concentrations produce fine tremors, salivation, and hypermotility in mice and rats. However, a higher dose of alkaloids resulted in jumping movements, rapid tapping of the forelimbs, and paralysis of hindlimbs, convulsions, and respiratory arrest and completely antagonised the pre-treatment effect of the drug chlorpromazine (20). Therefore, the psychedelic effects of indole compounds and other phytoconstituents from giant reed should be screened at broad-spectrum while considering humans as well.

Conclusion

The present study summarised information about ethnomedicinal values, isolated chief phytoconstituents, and pharmacological aspects such as anti-bacterial, anti-oxidant, anti-proliferative, anthelmintic, and toxicological properties. Although all components of the plant are used to cure health ailments, chiefly rhizomes and roots find their mention across all formulations. In traditional healthcare practices, the plant has been extensively used

in the treatment of skin disorders, urinary diseases, menstrual problems, diarrhoea, respiratory problems, and complex diseases such as cancer. However, the mode of consumption and administration is not mentioned in several studies. The scientific plausibility of cured ailments is also lacking. Yet, the plant has invaded several parts of Africa, America, and Mexico and has acquired the status of the worst invasive weed. Nonetheless, in European countries and the Indian subcontinent, the plant has been used in rural areas as a source of livelihood, medicines, substitute of firewood for locals. Therefore, further cultivation of Giant reed is recommended to generate income and livelihood resources for the local communities. Future ethnobotanical studies must focus on validating the reliability of formulations and modes of administration. Apart from this, the plant must be screened pharmaceutically for the isolation of bioactive molecules and the development of drug discovery and therapeutic potential.

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Authors' contribution

All authors have equally contributed to data acquisition, analysis, and interpretation. PK and ANS conceived the idea. PK chiefly designed the manuscript, prepared figures, arrange tables, and draw chemical structures. GK helped in drawing chemical structures. SS, AS and RK also helped in the preparation of the manuscript and gave critical suggestions. ANS supervised the whole process and approved the final version of the manuscript.

Conflict of interests

The authors declare no conflict of interests.

Ethical considerations

All ethical issues have been carefully observed by authors.

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