

A review on phytochemistry, pharmacology and toxicology of *Euphorbia fusiformis*

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Received: 22.04.2026

Revised: 13.06.2026

Accepted: 15.06.2026

Doi: 10.68419/cb/v1i2/22-37

Euphorbia fusiformis Buch.-Ham. ex D. Don is distributed in India, Bangladesh and Nepal. Different parts of this ethnomedicinal herb are used by the Indian tribal groups like Santal, Bhil, Tharu, Bhagat, etc. for curing a number of diseases such as rheumatic pain, paralysis, poor lactation, fever, wounds, liver disorders, and others. The objective of this study is to review critically the pharmacological, phytochemical and toxicity profiles of this versatile medicinal species. For this review an extensive literature search has been done from January 2025 – January 2026 in authentic web-databases like Academia, ResearchGate, PubMed, Scopus, Elsevier, etc. using the key words *Euphorbia*, *Euphorbia fusiformis*, *Euphorbia acaulis* and the connector AND was typed for the following phrases: phytochemistry, pharmacology, toxicity. Detailed study of the downloaded literatures revealed that five chemical classes including diterpenoids, coumarins and steroids are the predominant phytochemical groups of this herb with potential of antimicrobial, analgesic, anti-inflammatory, hepatoprotective and many other bioactivities. The present study will help researchers to validate the ethnomedicinal claims of *E. fusiformis* by exploring the structure-bioactivity relationship of its many more chemical compounds.

Key words: *Euphorbia fusiformis*, Tribal medicine,
Phytochemistry, Bioactivity, Toxicity

Introduction

Medicinal properties of the *Euphorbia* species are known from 16th century onwards due to wide variety of bioactive chemicals present in the members of this genus [1]. In India, nearly 195 species of *Euphorbia* are reported of which some species have rich therapeutic values [2,3]. Various uses in traditional medicines and having an array of chemical groups, such as essential oils, sesquiterpenes, diterpenoids, steroids, flavonoids, coumarins, etc. made the genus *Euphorbia* very attractive to the scientists for undertaking many research programs including natural product discovery [4,5,6]. *Euphorbia fusiformis* Buch.-Ham. ex D. Don is one of such therapeutically important species found endemic to India, Bangladesh and Nepal (POWO). The researchers including ethnobotanists reported a

rich culture of uses of this rare plant species in curing different diseases and ailments among the 10 tribal communities from 11 states of India [7]. Up to date, a number of attempts have been made for scientific validation of some of the therapeutic uses of this ethnomedicinal herb through various modern investigational approaches including pharmacological screening in animal models, clinical and toxicological trials. In this article, we have made a thorough analysis of the published evidences on phytochemistry and various pharmacological aspects of this rare medicinal plant and highlighted some unexplored domains of research on it along with the explored targeted research areas. Studies on target identification, bioactivity prediction and mechanism of action are crucial in discovering effective drug molecules from natural products [8]. This is also

very important that this rare plant should come under conservation priority following in-situ and ex-situ methods to overcome its ecological threats in habitats and for getting smooth flow mass-scale production bioactive compounds out of it. Analysis on the conservation status along with ecological factors based on IUCN Red list criteria and Conservation Priority Index will also be good steps for its future conservation and to eliminate the possibility of wiping out the population of this species from natural habitats.

Materials and methods

Review methodology

Study design

This review was conducted following the guidelines of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) framework to ensure transparency, reproducibility, and rigor in the literature search and selection process.

Information sources and search strategy

A comprehensive and systematic literature search was performed across multiple peer-reviewed electronic databases, including PubMed/MEDLINE, Web of Science, Science Direct, Scopus, Google Scholar, and ResearchGate. Additionally, grey literature sources such as unpublished theses and dissertations were explored through institutional repositories and Academia.edu. All searches were conducted for literature published up to January 2026.

The search was carried out using predefined keywords and Boolean operators to maximize retrieval sensitivity. The following search string was applied:

("Euphorbia fusiformis" OR "Euphorbia acaulis") AND ("phytochemistry" OR "phytochemical constituents" OR "secondary metabolites") AND ("pharmacological activity" OR "biological activity" OR "medicinal properties") AND ("toxicity" OR "safety profile").

Euphorbia acaulis was included as a search term because it is a recognized taxonomic synonym of *Euphorbia fusiformis*, ensuring completeness of the literature retrieval.

Eligibility criteria

Inclusion criteria

Studies reporting phytochemical, pharmacological, or toxicological investigations of *Euphorbia fusiformis* or its synonym *Euphorbia acaulis* Articles published in peer-reviewed journals, books, or as thesis/dissertations. Studies published in the English language. Publications available up to December 2023. Both in vitro and in vivo experimental studies, ethnobotanical surveys, and review articles.

Exclusion criteria

Studies with no direct relevance to *Euphorbia fusiformis* or its pharmacological/phytochemical profile, Abstracts, conference proceedings, or editorials lacking sufficient methodological detail, Studies published in languages other than English without available translations.

Study selection process

The study selection was carried out in two sequential phases as recommended by PRISMA:

Screening Phase: Titles and abstracts of all retrieved records were independently screened for relevance based on the predefined eligibility criteria.

Eligibility Phase: Full texts of potentially eligible studies were retrieved and assessed in detail. Studies that did not meet the inclusion criteria upon full-text review were excluded, with reasons documented.

A total of 121 records were initially identified through the database search. After removal of duplicates and irrelevant records based on title and abstract screening, 72 articles were found eligible and included in the final review, comprising peer-reviewed journal articles and three unpublished thesis papers. An additional 12 references were consulted during the synthesis phase to provide contextual and background information. The study selection

process is summarized in the PRISMA flow diagram (Figure 1).

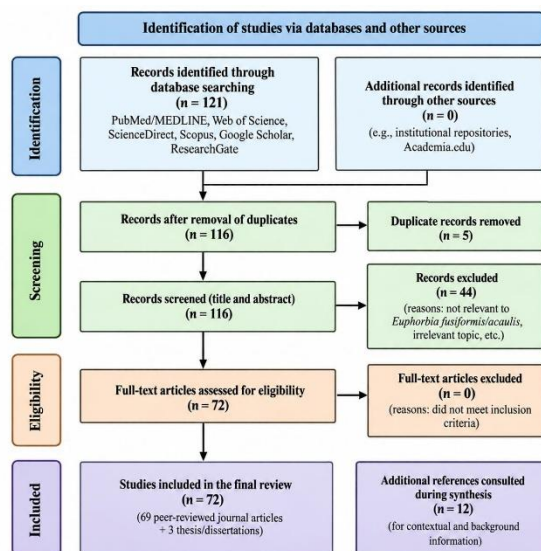


Figure 1. PRISMA flow diagram of the study selection process.

Data extraction

Data were extracted from the included studies using a standardized template covering: (i) study details (authors, year, country), (ii) plant part(s) investigated, (iii) extraction methods, (iv) identified phytochemical compounds, (v) pharmacological activities reported, and (vi) toxicity findings.

Quality assessment

The methodological quality of the included experimental studies was assessed based on clarity of study design, reproducibility of extraction and testing methods, and statistical reporting. Studies with insufficient methodological description were retained for qualitative synthesis but flagged accordingly.

Results and discussion

Medicinal uses

Tribes of Santal, Koya, Tharu, Bhagat, Meena, Bhil, etc. and some non-tribal people residing in different states all over India use root and leaves of this geophytic herb in the ethnomedicinal formulations for healing different types of

diseases and ailments like rheumatic pain, paralysis, poor lactation, fever, wounds, liver disorders, skin diseases, headache, antidote for poisonous bites, and in some veterinary medicines as well [3,7].

Phytochemistry

Investigation of phytochemical profile of any medicinal plant is very important for drug development and exploration of its pharmacological potential. Members of Euphorbiaceae are well known for their diverse chemical compounds especially for presence of numerous isoprenoid constituents. Many species of the genus *Euphorbia* have phytochemically characterized by presence of some major groups of secondary metabolites like, terpenoids, aromatics, alkaloids and phenolics. The chemicals of triterpene alcohols, sesquiterpenoids, phloracetophenones, cerebrosides, glycerols, steroids, and flavonoids are found in the latex of different species of *Euphorbia*. Many of such chemical compounds have already been identified as potent biomolecules with their varied pharmacological functions and have also exhibited the utility as chemotaxonomic markers in understanding of the systematics of the genus *Euphorbia* [9,10]. Polycyclic diterpenoids with a common 6/6/6-tricyclic ring are also found as major constituents in *Euphorbia* species. Occurrence of *ent*-atisanes in the species of *Euphorbia* is very rare and except *E. fidjiana*, it has so far been documented only in the root of *E. fusiformis* [11]. Preliminary phytochemical investigation on aqueous and methanol root extracts of *E. fusiformis* revealed presence of carbohydrates, flavonoids and steroids [12,13]. Phytochemical screening of the root stock of one variety of *E. fusiformis*, now established as a species *E. khandallensis*, also revealed the presence of different primary and secondary metabolites such as carbohydrates, alkaloids, vitamin C and E, flavonoids, phenols, glycosides, saponins and minerals like Fe, Zn, etc. [14]. Through chemical studies certain derivatives of ellagic acid, diterpenoids and *Ent*-atisane, compounds of coumarins and steroids have been reported from different solvent

extracts of the *E. fusiformis*. The chemical derivatives of Ent-atise group have been isolated by certain groups of workers from the root of this plant employing different solvents such as chloroform, hexane, chloromethylene and methanol in different concentrations [15,16]. Two chemical compounds namely Fern-7-en-3a'-ol, a triterpene and hexestrol, a sterol have been detected through GCMS analysis in the petroleum ether extract of *E. fusiformis* root [13]. Elemental analyses, detailed spectroscopic techniques such as UV-VIS, FTIR, NMR (¹H-NMR & ¹³C-NMR) and HRMS, and Single X-ray crystallographic studies are very helpful in elucidating structures of organic compounds. Chemical structures of some compounds isolated from the root of *E. fusiformis* have been determined using high resolution X-ray crystallography and NMR spectroscopy techniques [17,18,19]. Bindra et al. (1988) have isolated three compounds namely 3,3'-di-O-methyl ellagic acid 4'-rutinoside; 3,4,3'-tri-O-methyl ellagic acid 4'-rutinoside and 3,4,3'-tri-O-methyl ellagic acid, and characterised them using ¹H-NMR, ¹³C-NMR, MS, IR, UV data, but in this study single crystal X-Ray diffraction data was found absent. Suri et al. (1990) further reported a seco-artisane diterpene from this plant employing the NMR technique and single X-ray crystallography [16].

From perusal of all these phytochemical studies, a list of twelve phytochemicals isolated from *E. fusiformis* root has been prepared and all twelve reported compounds are documented in a tabular form under five chemical classes, out of which three compounds are of ellagic acid, three are diterpenoid derivatives, three *Ent*-atise derivatives, two coumarins and one steroid (Table 1). Chemical structures with respective serial number of all the 12 compounds have been documented in Fig. 2. The numerals have also been referred against the name of each compound mentioned in the Table 1. Scientifically it has proved that the derivatives of ellagic acid, *Ent*-atise, diterpenoid, and compounds of coumarins, steroids have various biological roles like antioxidant, antiadipogenic activity of liver, cancer prevention in gastrointestinal tract and many others [19,20,21,22,23,24]. So, presence of different phytochemicals of these chemical classes provides the scientific rationales regarding the use of this medicinal herb in folk remedies and its corresponding biological activities. However, we believe, more systematic chemical investigation on this plant is still needed to explore complete chemical profiles of the leaf and root of this plant species for its thorough pharmacological validation.

Table-1: Table 1. List of the chemical compounds isolated from root of *Euphorbia fusiformis*

Chemical class of the compound	Compound name and its No.	Extractive and elution solvents used	References
Ellagic acid derivatives	3,3'-di-O-methyl ellagic acid -4'-rutinoside (1)	Root powder extracted in 50 % aqueous methanol and eluted it using chloroform-methanol (ratio 9:1; 17:3; 99:1)	[17]
	3,4,3'-tri-O-methyl ellagic acid- 4'-rutinoside (2)		
	3,4,3'-tri-O-methyl ellagic acid (3)		
Diterpenoid derivatives	(4R, 4aR)-4,4a-dihydroxy-3-hydroxymethyl-7,7,10a-trimethyl-2,4,4a,5,6,6a,7,8,9,10,10a,10b-dodeca hydrophenanthro [3,2-b]furan-2-one (4)	30 kg of powdered root extracted in 50 L of 5% aqueous acetone and eluted with n-hexane containing increasing proportions of ethyl acetate	[25]
	Caudicifolin (8)	Powdered root drug extracted with petrol (60-80°) and eluted using petrol-ethyl acetate mixtures (95:5) of increasing polarity employing column chromatography	[18]

Chemical class of the compound	Compound name and its No.	Extractive and elution solvents used	References
Coumarins	Euphol (9)	750 g of root powder extracted successively with <i>n</i> -hexane, ethyl acetate and methanol. The concentrated ethyl acetate extract (35 g) eluted successively with <i>n</i> -hexane and mixtures of ethyl acetate in <i>n</i> -hexane. The fractions eluted with 10% ethyl acetate in <i>n</i> -hexane yielded 450 mg of the compound in pure form	[25]
	Scoparone (10)	750 g of root powder extracted successively with <i>n</i> -hexane, ethyl acetate and methanol. The crude <i>n</i> -hexane extract (18 g) eluted successively with solvents <i>n</i> -hexane and mixtures of ethyl acetate in hexane. The fractions eluted in 2% ethyl acetate in <i>n</i> -hexane yielded 520 mg of the pure compound	
	Scopoletin (11)	750 g of root powder extracted successively with <i>n</i> -hexane, ethyl acetate and methanol. The fractions collected in 20% and 30% ethyl acetate in <i>n</i> -hexane and purified by eluting with chloroform and mixture of methanol in chloroform. The similar fractions collected in chloroform were combined and concentrated to get the compound of 125 mg	
	β –Sitosterol (12)	750 g of root powder extracted successively with <i>n</i> -hexane, ethyl acetate and methanol. The fractions collected in 20% and 30% ethyl acetate in <i>n</i> -hexane were combined and further purified by repeated column chromatography by eluting with chloroform and mixture of methanol in chloroform. The fractions collected in 1% methanol in chloroform that gave 35 mg of pure compound	
Steroid	β –Sitosterol (12)	750 g of root powder extracted successively with <i>n</i> -hexane and mixtures of ethyl acetate in hexane. The fractions collected in 5% ethyl acetate in hexane yielded 30 mg of the pure compound	
	<i>Ent</i> -3,4-seco-4,16α,17-trihydroxyatisan-3-oic acid (5)	Chloromethylene and methanol used in 9: 1 ratio for extraction and eluted with methanol by column chromatography	[15]
	<i>Ent</i> -atisane-3β,16α,17-triol (6)	Root powder extracted with methanol. Methanolic residue was partitioned in the dichloromethane and ethyl acetate solvents. The ethylacetate fraction was eluted with chloromethylene and methanol in 19:1 ratio using a column of silica gel	[15]
<i>Ent</i> -atisane derivatives	3-Oxoatisanane-16α, 17-diol (7)	Powdered plant sample extracted with <i>n</i> -hexane and eluted with increasing proportions of ethyl acetate in petroleum ether	

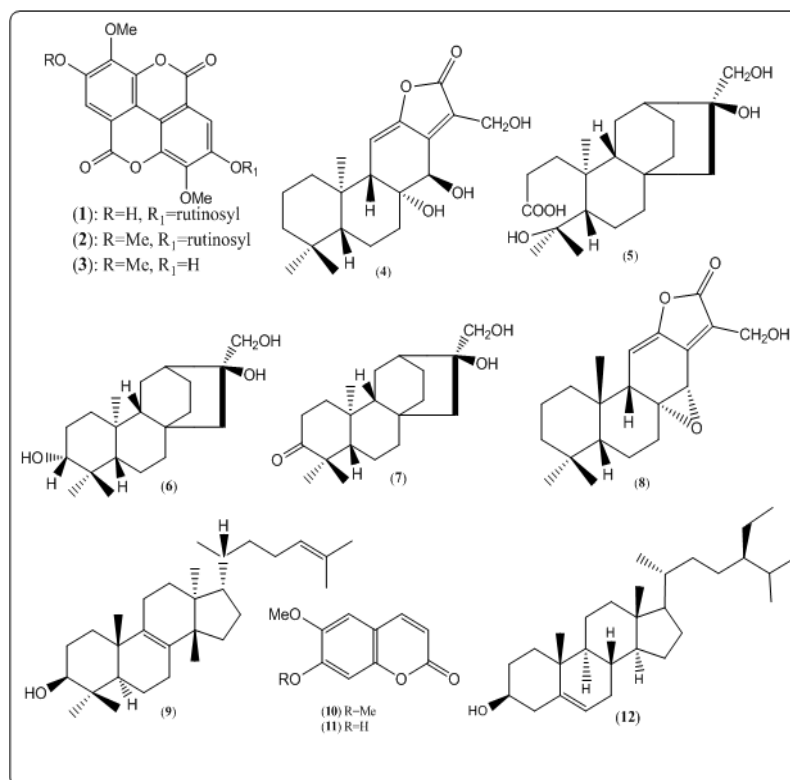


Fig 2. Structures of phytochemical constituents (1–12) isolated from *Euphorbia fusiformis*

Pharmacology

Pharmacological studies are one of the most desired scientific approaches for validation of the uses of medicinal plants. Among the medicinally potent angiosperm taxa, members of the family Euphorbiaceae as well as the genus *Euphorbia* are very important in terms of different pharmacological properties [3]. The biological activities exhibited by different species of *Euphorbia* include anti-proliferative, cytotoxic, DNA-damaging, antiviral, antimicrobial, anti-diarrheal, molluscicidal, anti-feeding, anti-inflammatory, antipyretic, analgesic and many others. [11]. Indigenous medicines coming from the knowledge of ethnic people are now a day playing most vital role in discovery of novel drugs from plants [27].

Biological actions of several species of *Euphorbia* have been executed taking clues from traditional medicines used by the folk people of different culture [28]. Scientific investigation and validation of different medicinal uses of *E. fusiformis* date back in 1970s [29]. Since then, the plant has been examined by many scientists for quite a good number of biological activities such as anti-eczema, anti-inflammatory, antimicrobial, antinociceptive, hepatoprotective, diuretics and many more. Various pharmacological actions of *E. fusiformis* along with justification of its ethnomedicinal uses are tabulated in Table 2. A precise discussion on the findings of pharmacological and biological activity studies performed by different workers on this herb is presented below.

Table-2: List of pharmacological studies on *Euphorbia fusiformis* along with justification of its ethnomedicinal uses

Pharmacological activity (References)	Animal model and other test organisms used	Administration of test drug and its effect	Justification of ethnomedicinal uses (References)
Anti-inflammatory [32]	Male albino rats and mice	Dried powdered rhizome extracted in n-hexane and 95% ethanol showed marked anti-inflammatory activity when administered orally and intra-peritoneally. The drug is potent against inflammations as much as a non-steroidal PNB (Peripheral Nerve Block) drug like Lidocaine.	Justifies the tribal claim on its uses in some skeleto-muscular problems like osteoarthritis, rheumatism and gout along with pain, swelling and stiffness in synovial joints [70,71]
Analgesic / Antinociceptive [12]	Wistar albino and Swiss albino mice	Aqueous extract of root powder exhibited potent analgesic property by inducing the paw licking response, writhing response and radiant heat test in mice.	Use of this herb in treatment of rheumatism, gout, pain, etc. in folk medicine is justified [49,71,72].
Diuretic [39]	Wistar albino rats	Powdered root drug significantly increase the excretion of urinary ions in dose dependent manner which is comparable to the diuretics like thiazide.	The study justifies the traditional claim regarding its use for treatment of urinary stones [39].
Gastro-intestinal motility [39]	Swiss albino mice	Administration of powdered root drug increases intestinal motility and quick excretion which is supposed to be due to presence of caudicifolin, methyllellagic acid and euphol in the root.	The study validates the use of its root as purgative drug which can enhance intestinal motility.
Hepato protective [50]	Male albino Wistar rats and Swiss albino mice	The ethanol extract of powdered root is effective in recovering liver function, to remove rifampicin induced toxicity, and therefore, biologically safe upon oral administration.	The tribal claim on use of tuber in liver disorders by the tribes of Chitteri hills of Tamil Nadu, India is validated [49].
Anti-eczema [29]	Human patients suffering from dry and wet eczema	Administration of root powder tablets (50mg) is found effective in curing 50 to 100% of male and female patients of eczema.	Efficacy of crude drug against eczema supports the tribal claim on treatment of various skin diseases including eczema [48,52].
Antibacterial [59]	Pathogenic Gram positive (<i>Bacillus subtilis</i> and <i>Staphylococcus aureus</i>) and Gram negative bacterial strains(<i>Escherichia coli</i> , <i>Klebsiella pneumoniae</i> , <i>Proteus vulgaris</i> , <i>Pseudomonas aeruginosa</i> , <i>Salmonella typhii</i> A and <i>Salmonella typhii</i> B)	Different solvent extracts (ethanol, acetone, methanol, chloroform and water) of leaf and root powder evaluated against pathogenic bacteria employing modified Disc diffusion and Agar well diffusion methods and exhibited distinct antibacterial action.	Results of these studies support the uses of this herb in traditional medicine to treat fever [73] and wound infection [49].
Anti fungal [57]	Pathogenic fungal strains (<i>Candida albicans</i> and <i>Cryptococcus neoformans</i> , <i>Aspergillus flavus</i> , <i>A. niger</i> , <i>A.fumigatus</i> , <i>A. erythrocephalus</i>)	Different solvent extracts of leaf and root powder (ethanol, acetone, methanol, chloroform, benzene, xylene, toluene, isopropyl alcohol, diethyl ether \dimethyl formamide and butanol) were tested against pathogenic fungi using modified Agar well diffusion method. Results revealed significant antifungal effect.	Root latex is effective against eczema [53]

Pharmacological activity (References)	Animal model and other test organisms used	Administration of test drug and its effect	Justification of ethnomedicinal uses (References)
Anti fungal [26]	Fungal strains (<i>Aspergillus niger</i> and <i>Candida albicans</i>)	Root powder extracted in ethyl Acetate and n-hexane. Extracted compounds like caudicifolin, scoparone, scopoletin were applied against fungal strains using Agar well diffusion method and manifested distinct growth inhibitory effect on tested fungi.	Root extracts effectively cure various skin diseases [49,54]. Most of the tested fungi are the causal agents for a varied range of skin diseases.
Toxicity study [50,74]	Wistar albino rats	Oral administration of ethanolic extract of root powder up to the dose of 5000 mg/kg body weight showed no toxicity including nephrotoxic effect to the tested animals.	It justifies that consumption of this herbal drug is to be safe.
	Female Swiss albino mice	Root latex suspended in 0.5% w/v carboxy-methyl cellulose solution exhibited no toxicity in the studied mice at the highest dose of 2000 mg/kg body weight.	
Hypotensive [35]	Dogs, rats and mice	Freshly prepared euphol suspension from petroleum ether extract of root powder applied intravenously and intraperitoneally at the dose of 1.5 to 2 g/kg body weight showed relaxation of the peripheral vascular smooth muscle without affecting central nervous system.	The plant is used among the tribal people of Deogarh district of Odisha to treat the high blood pressure [75].
Antioxidant [26,63,69]	<i>In vitro</i> DPPH radical scavenging assay	n-hexane and ethyl acetate extracts of root drug and its isolated phytochemicals like caudicifolin extracted in ethyl acetate, showed very potent antioxidant activity.	These studies justify its use to treat fever, gout, arthritic pain, swelling and redness of joint, infections and wound [49,70,71,73] as such ailments are manifested due to prolong oxidative stresses and related inflammatory conditions.
	<i>In vitro</i> DPPH study	Powdered root extracted in acetone showed highest free radical scavenging activity as compared to ascorbic acid taken as standard.	
	<i>In vitro</i> DPPH radical, super oxide radical, nitric oxide radical, hydrogen peroxide radical scavenging activity and ferrous ion chelating potential	Acetone and methanol extracts of powdered leaf drug showed very good radical scavenging activities with a low IC ₅₀ value.	
Galactagogue [63]	Lactating Wistar rats	Alcoholic extract of the root powder was fed to the Wistar rats which manifested significant increase in yield of milk as determined by body weight, glycogen and protein, and serum prolactin hormone profile of blood.	The study supports traditional use of the root as galactagogue [3,49].

Anti-inflammatory activity

The characteristic expression of symptoms like pain, fever, redness due to induction of natural reactions with an infectious agent entered into our body, or due to some physical, chemical or traumatic damage is known as inflammation. Some species of the genus *Euphorbia* namely *E. nerifolia*, *E. hirta*, *E. heterophylla*, *E. tirucalli*

have become widely known to induce anti-inflammatory activities. Potential anti-inflammatory effects, for example, in *E. hirta*, *E. thymifolia* have been studied *in vitro* [30,31]. Singh et al. (1984) reported that the active principle euphol (a tetracyclic triterpene) of *E. fusiformis* and n-hexane fraction of its root extract exhibit potent anti-inflammatory

activities against carrageenan induced oedema and chronic arthritis in rats and mice which is equivalent to the anti-inflammatory activity shown by phenyl butazone, a standard anti-inflammatory drug [32]. It was found in some research that intravenous administration of euphol alone shows significant hypersensitive activity whereas anti-inflammatory activity of euphol was found once it is administered along with root extract of *E. fusiformis* intraperitoneally at the dose up to 100 mg/kg [32,33]. Further research on euphol is needed to evaluate its anti-inflammatory potential and also to nullify or subdue its hypersensitive activity.

Hypotensive effect

The blood pressure lowering ability of an agent is known as its hypotensive effect. Such effects of some plant-based diterpenoids like forskolin, stevioside, etc. have been recorded in earlier studies [34]. Similar kind of hypotensive role of euphol extracted from the root of *E. fusiformis* has been observed in anesthetized dogs, rats and mice. The euphol exhibited a marked hypotensive activity in the animal model through different autonomic responses in a dose selective way. It also produced a significant fall of blood pressure in anesthetized rats. In higher dose of euphol (500 -1000 mg/kg body weight), the coronary flow in heart is reduced by 10 - 25%. In a dose range of 1.25 to 10mg/kg body weight, the compound euphol showed 40—71.8 % ($ED_{50} = 2.18\text{mg/kg}$) hypotensive activity in dogs without any marked changes in respiration [35].

Antinociceptive activity

Antinociception is the body's response to potentially toxic stimuli like harmful chemicals (e.g., benzene, formalin), mechanical injury (e.g., cutting, crushing), or adverse temperatures (heat and cold) by the sensory nervous system. Many medicinal species of Euphorbiaceae are well known for their antinociceptive role [11,36]. The methanolic extracts of some members of *Euphorbia* such as *E. thymifolia*, *E. milli* have exhibited significant antinociceptive activities [37,38]. Likewise, aqueous extracts of root powder of *E. fusiformis* exhibited marked analgesic activity which indicates its rationale

for use in rheumatism in folk medicine. The results of this study indicate that the root possesses potent analgesic property. The analgesic effect of *E. fusiformis* has been recorded when Swiss albino mice and Wistar strain albino rats are orally administered with root extract of it. The analgesic effect has been recorded for 30 min by counting the writhing syndrome, a response to pain induced in the test animals after injection of acetic acid. The root extract manifested similar kind of analgesic effect like that of a standard drug indomethacin at higher dose level by significantly inhibiting the formalin induced paw licking responses [12].

Diuretic property

The substance that promotes diuresis or urine secretion is called a diuretic. Diuretic property in the plants of Euphorbiaceae family is quite well known [11]. Ashok et al. (2011b) for the first time proved that root powder of *E. fusiformis* possess a significant diuretic activity. Oral application of powdered root showed marked increase in urinary electrolyte excretion along with significant increase in urine volume in albino rats as compared to the control set of rats. Researchers of this study suggested that presence of certain chemical components namely caudicifolin, methyl ellagic acid and euphol might contribute to the diuretic property of the tested root drug. Such phytochemicals may act by decreasing re-absorption of Na ion in the distal convoluted tubule, inhibiting the Na/Cl co-transporters on luminal membrane and increase loss of K ion in the collecting duct of kidney [39]. These mentioned compounds and also other compounds isolated from root of this plant should be thoroughly studied to elucidate their diuretic properties.

Intestinal motility

Intestinal motility is involved in movement of food particles from mouth through the gastrointestinal tract followed by colonic transit. Gut motility is controlled by many factors such as enteric nerves, smooth muscle cells, interstitial cells, hormones and certain stimuli from gut bacteria and their metabolites [40]. This process influences several of the metabolic activities of our body by maintaining energy homeostasis

through nutrient absorption and excretion [41]. The effect of enhanced intestinal motility helps in digestion, controls diarrhoea and reduces the risk of several metabolic disorders specially obesity and diabetes [42]. Role of phytochemicals extracted from medicinal plants is very well documented in curing different gastrointestinal problems [43]. The effect of *E. fusiformis* root powder on intestinal transit has been studied in Swiss albino mice by Ashok et al. (2012). The test drug enhanced the motility of intestine at a higher dose without exerting any toxicity to the albino mice [44]. For instance, a significant decrease in the duration needed for the release of kaolin was observed in the 40 % kaolin (aluminium silicate) administered albino mice which were treated with high dose of root drug. Ashok and other researchers predicted that phytochemicals like caudicifolin, methyl ellagic acid and euphol of the root drug are possibly responsible for intestinal motility enhancing activity. Such promising effects of *E. fusiformis* drug elucidate its future application in development of medicine against a number of gastrointestinal problems employing its main bioactive compounds such as euphol, methylellagic acid, caudicifolin, and others.

Hepatoprotective function

Traditional herbal medicine does have a significant role in alleviating the hepatic damages caused by the viral and microbial infections or by some toxic agents [45,46]. Hepatoprotective activity of plant drugs obtained from many members of the genus *Euphorbia* is very well known [31,47,48]. *E. fusiformis* is one of such important herbal drugs used in folk medicine in treatment of liver problems [49]. The rifampicin induced hepatic damage was recovered by oral administration of ethanolic extract of *E. fusiformis* tuber in the albino rats and albino mice at a lower (125 mg/kg) to higher dose (500 mg/kg) [50]. Prior administration of ethanolic plant extract significantly normalizes the elevated levels of some biochemical parameters in blood generally manifested in hepatic dysfunction like, serum glutamate oxaloacetate transaminase, glutamate pyruvate transaminase, gamma glutamyl

transpeptidase, alkaline phosphatase, bilirubin and protein. Moreover, the same plant extract has significantly restored the liver weight, reduced the necrosis and degeneration of bile capillaries.

Anti-eczema property

Traditional plant-based remedies are very commonly practiced in India for curing skin diseases. Many plant species belonging to the Lamiaceae, Leguminosae, Euphorbiaceae and other families are regularly used in traditional medicine for treatment of skin diseases [51,52]. The crude drug of *E. fusiformis* is used as a cure for different types of skin diseases including eczema [53,54,55]. The anti-eczema property of this medicinal herb has been experimentally proved by Agrawal et al. (1971) [29]. In this study, a clinical trial has been performed with 38 eczema patients (26 men and 12 women) by oral administration of 50mg root powder to each patient for 2-6 weeks to cure acute wet and dry eczema. Very promising results have been obtained from this experiment where almost every patient was cured from eczema or started recovering the diseased condition significantly. The results of this study highlight that the root drug of *E. fusiformis* has the potential for curing the eczema of skin.

Antifungal activity

Antimicrobial activity of the herbal drugs used in ethnomedicine is very well known and it includes inhibitory activities against both fungi and bacteria. Antifungal studies on different parts of *Euphorbia fusiformis* against some pathogenic fungi have been carried out by different workers [56,57,26]. The research work done by Natarajan and his co-workers (2007) reported potent growth inhibitory effects of root extracts of *E. fusiformis* against *Candida albicans* and *Cryptococcus neoformans*, the causative fungal agents of human candidiasis and cryptococcosis, respectively. They observed maximum inhibition zone in acetone extract followed by ethanol, chloroform and methanol extracts of the root [56]. Ramachandran and Natarajan (2009) evaluated the antifungal activity of *Euphorbia fusiformis* leaf against 4 aflatoxin producing fungi (*Aspergillus flavus*, *A.*

niger, *A. fumigatus*, *A. erythrocephalus*) and one other mold i.e., *Fusarium* sp. using disc diffusion assay. Among the different extractive solvents, isopropyl alcohol and xylene solvent extracts exhibited much efficacy against all the tested fungi [57]. Whereas the study performed by Devendar et al. (2014) highlighted that ethyl acetate extract of the root part of this *Euphorbia* species potentially restricted the growth of pathogenic fungi namely *C. albicans* and *A. niger* [26]. The promising results of these studies might be helpful in systematic antifungal investigation towards natural product development in future.

Antibacterial activities

Antibacterial activity of different medicinal plants has been elucidated by scientists all over the world. These studies will be promising to generate very effective anti-infective therapeutic drugs from plants by the pharmaceutical industries [58]. *E. fusiformis* has so far been used in traditional medicine to cure fever, infections and intestinal disorders, etc. A group of researchers reported potential antimicrobial activity of root and leaves of this herb against some Gram negative (*Escherichia coli*, *Klebsiella pneumoniae*, *Proteus vulgaris*, *Pseudomonas aeruginosa*, *Salmonella typhii* A and *Salmonella typhii* B) and Gram positive (*Bacillus subtilis* and *Staphylococcus aureus*) pathogenic bacterial strains using disc diffusion and agar well diffusion methods [56]. The acetone and methanol-based leaf extracts revealed potent antibacterial activities against all tested microorganisms. In this study, the antimicrobial activity of the root extract was more prominent than the activity of leaf extract against most of the microorganisms except *Bacillus subtilis*. Later on, Ramachandran et al. (2008) reported the growth inhibitory activities of combined extracts from leaves and rootstocks (1:1 ratio) of *E. fusiformis* against some human pathogenic bacterial strains (4 Gram negative strains namely, *S. typhii* A & B, *P. aeruginosa* and *K. pneumonia* and 2 Gram negative strains namely, *B. subtilis* and *S. aureus*) [59]. Acetone and methanol extracts exhibited most significant antibacterial properties against all the tested

pathogens. The antibacterial activity of silver nanoparticles (AgNP's) found in leaf extract of *Euphorbia fusiformis* is an interesting finding [60]. Mondal 2020, investigated the antimicrobial activities of methanolic root extracts using Agar Well Diffusion method and it was found effective against the growth of *B. subtilis*, *P. aeruginosa* and *S. aureus* whereas, petroleum ether extract of it exhibited growth inhibitory effect on *E. coli*, *P. aeruginosa* and *S. aureus* significantly [13]. Presence of fernane type triterpenoids and sterols in the root extracts might be the cause of microbial growth inhibitory property of this plant as such groups of triterpenoids have established as effective antimicrobial agents by many studies [61].

Poor lactation

Several reports are there in Indian ethnomedicine database which document *E. fusiformis* as an effective galactagogue used for rectifying the poor lactation in humans and veterinary animals [62,3]. Manna et al. (2013) validated the galactagogue property of this plant in lactating Wistar rats by oral administration of ethanolic root extract with the dose range between 250 and 500 mg/kg [63]. The results showed a dose dependent increase in milk secretion in tested rats. After treatment with the plant extract, the serum prolactin level, propagation of acini and lobuloalveolar size in the mammary gland have been increased considerably in the rats which is very supporting towards the efficacy of this plant drug as galactagogue. Though, the compounds present in *E. fusiformis* root and their exact mechanism responsible for enhanced secretion of milk is still not validated. Pharmacological evidences from different researches elucidated that increase in lactation is promoted by different plant based active compounds (sitosterols, stigmasterols, etc.) which can regulate the activities of or act as hormones like prolactin, estrogen, progesterone, etc. to stimulate the milk production and its secretion in mammals [64,65].

Antioxidant efficacy

Natural antioxidants including diterpenoid compounds are very common in plants including

species of the genus *Euphorbia* [66,67]. Some studies in some *Euphorbia* species confirm the antioxidant activities of β -sitosterol and euphol [68]. Devendar et al. (2014) studied the antioxidant activities of different solvent extracts of this plant as well as some chemical compounds present in this drug plant [26]. Among the extracts, ethyl acetate extract has been found most potential with IC_{50} value of $2.781 \mu\text{g/ml}$ and amongst compounds studied caudicifolin, a diterpenoid derivative, exhibited very prospective antioxidant activity with $3.25 \mu\text{g/ml}$ of IC_{50} value, as the activities in both cases are very close to the IC_{50} of standard Ascorbic acid (IC_{50} $2.26 \mu\text{g/ml}$). Among the other isolated compounds, beta-sitosterol and euphol were found less potent in DPPH radical scavenging assay. Another similar kind of study has been performed by Kamalanathan et al. (2015) with leaf extract of *E. fusiformis* employing the DPPH, superoxide, nitric oxide and hydrogen peroxide radical scavenging assays [69]. Very good activity was observed in acetone extract of leaf in the DPPH and hydrogen peroxide scavenging assays with IC_{50} values of $15 \mu\text{g/ml}$ and $42 \mu\text{g/ml}$, respectively. Whereas methanolic extract of the plant showed inhibition of nitric oxide, superoxide and hydrogen peroxide radicals scavenging activities.

Toxicology

In recent times, a number of toxic principles have been documented from some medicinal plants as studies in animal model have also shown adverse effects of plant drugs to different organs and multiple systems. In toxicity study, there are three recommended levels of dose as proposed in OECD Test guideline 408(1998). A dose of 1000 mg/kg body weight/day, which is the high dose limit and doses of 500 and 250 mg/kg body weight /day are selected as medium and low doses, respectively. It was reported that consumption of plant parts of certain *Euphorbia* species may cause health hazards [76]. Experimental evidences also suggested that drugs obtained from *E. fusiformis* are safe to prescribe among the patients. The first report on its non-toxic nature has been made by Anusuya

et al. in 2010. In this investigation, the acute and sub-chronic toxicity have been examined by determining histological profiles of liver and kidney in experimental mice and rats [50]. A dose ranges from 125 to 5000 mg/kg was found non-toxic in case of oral route consumption of plant as no significant changes noticed in the studied animals in terms of their body weight, temperature, food intake, general behavior, histological, hematological and biochemical parameters. The ethanolic root extract of *E. fusiformis* has also been investigated for its toxicity assessment by Manna et al. (2013) and they found no toxicity up to the maximum dose of 2000 mg/kg body weight on histological as well as blood parameters in the Wistar rats [63]. These successful toxicological studies ensure the safety of use of this plant drug in different forms and doses for treatment of diseases ailments. Recently Ozarde and Choudhari (2022) reported that latex of *E. fusiformis* is safe at the dose of 2000 mg/kg body weight in fasted mice [64]. The female mice of up to 35g body weight were feed in oral route with this dose of latex (up to 2g/kg body weight) and observed for 14 days round the clock for several clinical signs of toxicity such as diarrhoea, increased salivation, lethargy, changes in skin fur, eyes and mucous membranes, sleep behaviour and locomotion. No such symptoms of toxicity were observed in this study, thus crude drug of *E. fusiformis* was proved as safe for oral administration and therefore, it is placed in Category 5 proposed in the Globally Harmonized System for hazards.

Conclusion

Euphorbia fusiformis possesses a mosaic of varied chemical and pharmacological attributes. The plant is used by the Indian people of various culture and traditions for a wide range of therapeutic purposes. Reported phytochemical studies elucidate a rich stock of chemicals including many potent bioactive molecules present in this species of *Euphorbia*. Such chemical profile of the plant correlates its effectiveness in curing various human and veterinary diseases. Considering the medicinal importance of this species in Indian traditional

medicine and some relevant pharmacological validation of its ethnomedicinal uses, it is now clearly understood that *E. fusiformis* is a very prospective candidate for development of natural products through systematic investigations in the lines of phytochemistry and pharmacology.

Compelling evidence is that the extracts of this medicinal herb passed some toxicity tests in animal model as well which indicates the safety of its crude drugs used traditionally in Indian ethnomedicine. Still a thorough investigation of *E. fusiformis* root and leaf employing the *in vitro*, acute and chronic toxicity protocols is seriously needed to ensure its safety for human as well domesticated animal consumption.

Considering its rarity and present threat status, we feel that there is a need of conservation of this species through mass propagation by different biotechnological approaches including tissue culture technique. *In vitro* conservation of seeds of this plant will be a good approach for future restoration and *in-situ* and *ex-situ* conservations of this plant.

The plant has various medicinal values due to presence of large number of secondary metabolites. Root stock and cell suspension culture of *E. fusiformis* can be employed to increase yield of secondary metabolites. In addition, metabolic engineering techniques can be used in regulation or modifying common precursors, enzymes, regulatory proteins in different metabolic pathways to amplify the synthesis of valuable phytochemicals. Such investigation will be helpful for large scale production of plant metabolites out of this herb.

There is a genuine problem in proper identification exclusively depending upon the morphological attributes of *E. fusiformis* as certain range of morphological plasticity is evident among the populations collected from various habitats of certain Indian states. In this context, present review highlights a scope for investigating the detailed chemical profiles of such geographical populations of *E. fusiformis* to facilitate their exact identity through chemotaxonomical approach. Such sort of

chemical studies may also be very useful to determine the chemotypes of this *Euphorbia* species from its different population accessions. The chemotypes, if identified in this species, may be the instrumental in metabolomics research for synthesis and production of novel secondary metabolites through plant biotechnological approaches.

Finally, experimental research on animal models is necessary to ensure the efficacy of the studied phytocompounds. This could lead to the development of highly targeted therapies against various diseases.

Acknowledgement: We are thankful to Dr Asrafi Khatun, Principal, M.U.C. Women's College, Purba Bardhaman, West Bengal for allowing access to necessary laboratory, library and internet facilities of the college. We are also grateful to Prof. Dr Chowdhury Habibur Rahaman has critically revised the manuscript and for giving his precious inputs.

Author contributions: Swarnendu Mondal conceptualized, designed and wrote the present work; Arkendu Bhattacharya wrote the manuscript and helped in compilation of data. All authors have read and agreed to the final version of the manuscript.

Conflicts of interest: The authors report no conflicts of interest in this work.

Funding: This research received no external funding.

Data availability statement: All data are contained within the article.

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