

Verbena officinalis (Verbenaceae): Pharmacology, Toxicology and role in female health

Review Article

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Abstract

Verbena officinalis Linn (Verbenaceae), the common verbena or vervain, a traditional herb with immense cultural and medicinal significance in the European, Greek, American, Roman and Egyptian countries. Phytochemical analysis suggests the presence of iridoid glycosides, secoiridoid glycosides, phenylethanoid glycosides, flavones, pentacyclic triterpenoids, monoterpenes, sterols and their derivatives. Owing to the presence of these phytochemicals, wide range of pharmacological activities such as antibacterial, antiviral, antifungal, antidiarrheal, antitumour, antidepressant, anxiolytic, gastroprotective and hepatoprotective, etc are reported. Literature survey highlights the distinct role of *Verbena officinalis* in treating dysmenorrhoea, vaginitis, endometriosis, premenopausal night sweating, herbal tonic for pregnant women and lactating mothers and its use as emmenagogue. The review aims to promote studies on *Verbena officinalis* for its therapeutic role in female reproductive health and other ailments. The scientific databases used for compilation of the data were Google scholar, Pubmed the data made available specifically from 2010 to 2022.

Key Words: Ethnomedicine, Female health, Phytochemicals, Toxicity, *Verbena officinalis*, Verbenaceae.

Introduction

Needless to say, plants have immense medicinal properties and used in therapeutics since millennium. Traditional medicine systems, namely Ayurvedic, Unani, Siddha, Aromatherapy, Bach Flower remedies have been using medicinal plants extensively. Plant-based remedies are more acceptable in the public because of its likeliness to be safer than synthetic drugs (1). *Verbena officinalis* Linn, Verbenaceae is herbaceous perennial plant, with its origin in the Europe. *Verbena officinalis* has tiny purple flowers and slightly hairy, diamond shaped green, aromatic leaves. Verbena has been used since millennium in Traditional Chinese, American, European medicine systems. Phytoconstituents include iridoid glycosides, terpenoids, phenylethanoid glycosides and sterols. Pharmacological activities owing to the presence of phytoconstituents include anti-inflammatory, antinociceptive, neuroprotective, gastroprotective,

wound healing, anti-tumour, antimicrobial activities and many have been reported in scientific literature.

Aim

To promote studies on *Verbena officinalis* for its therapeutic role in female reproductive health and other ailments.

Objectives

- To promote studies on *Verbena officinalis* for its therapeutic role.
- To compile all database of *Verbena officinalis* and make it available to researchers to explore its therapeutic effects.

Vernacular names

Vervain, Bon Kariata, Herb of grace, pigeon's grass, Bhekpadee, Tharophijub, Pitta maree (2) L. – vervain Species: *V. officinalis* (3).

Geographical location

Verbena officinalis is found in the Asian, European, American continent as well as grown in China and Japan. In India, it is distributed in the north-eastern territory, mainly in Manipur, Assam, Meghalaya (4, 5, 6).

Cultivation and collection

The herb can be cultivated using seeds, root and stem cuttings. Seed propagation involves sowing seeds in late March. *Verbena officinalis* grows well in sandy

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soil with basic pH. Temperature requirement is 20°C to 30°C. Harvesting is done one month after the flowering season and the herb is dried at a temperature not exceeding 35°C. Water requirement is not abundant; it is quite stable in draught conditions (7). Aerial parts of *Verbena* are shown in Fig. 1.

Figure 1: Aerial parts of *V. officinalis*



Traditional uses

Chakpa community of Manipur used the decoction of *Verbena officinalis*, *Achyranthus aspera* and *Scutellaria discolor* along with honey to treat white discharge in women. *Verbena officinalis* aerial part extract was applied on body parts except head to cure viral fever in Manipur, India. In Tarai, Uttarakhand, crushed leaves of *V.officinalis* are applied topically on wounds, boils and cuts (8). In Europe, the decoction of *Verbena officinalis* along with *Tussilago farfara*, *Phytolacca americana*, *Mercurialis perennis*, *Daphne laureola*, and *Glycyrrhiza glabra* were used internally for treating swellings in throat and for corroding ulcers. Europeans used it for wounds due to snakes, spiders, dogs and for bladder stones. Europeans applied fresh juice/dried powdered herb with honey on chest for chest complaints. In China, verbena leaves were consumed raw to fortify bones and tendons. Americans used *Verbena officinalis* for depression and anxiety problems. In Italy, tea of *Verbena officinalis* was consumed for coughs and asthma (9,10).

Phytochemistry

The various phytoconstituents isolated from different parts and extracts of *Verbena officinalis* are listed in Table 1.

Table 1. Phytoconstituents of *Verbena officinalis*

S.N.	Class of Phytoconstituents	Phytoconstituents	References
1	Iridoid glycosides Secoiridoid glycosides Phenylethanoid glycosides	Verbenalin 3,4-dihydroverbenalin Hastatoside 3-(5-(methoxycarbonyl)-2-oxo-2H-pyran-3-yl)butanoic acid, 7-hydroxydehydrohastatoside Verbenoside A Verbenoside B Verbacoside Isocverbacoside Capneoside-II Isocapneoside-II 4'''-acetyl-O-isoverbacoside 2'',4''-diacetyl-O- verbacoside, 3''',4'''-diacetyl-O-isoverbacoside, 4''',6''-diacetyl-O-betonyoside A 3''',4'''-diacetyl-Obetonyoside A.	Shu et al., (18) Xu et al., 2010 (19)
2	Flavones	Apigenin Luteolin	Zhang et al., 2011 (12)
3	Pentacyclic triterpenoids	Barbinervic acid Ursolic acid Oleanoic acid	Zhang et al., 2011 (12)
4	Sterols	β – sitosterol Daucosterol	Zhang et al., 2011 (12)
5	Terpenes	Citral α-Pinene β- Pinene Sabinene β- Phellandrene Limonene β- Caryophyllene	De martino et al., 2009 (20)

Iridoid glycosides

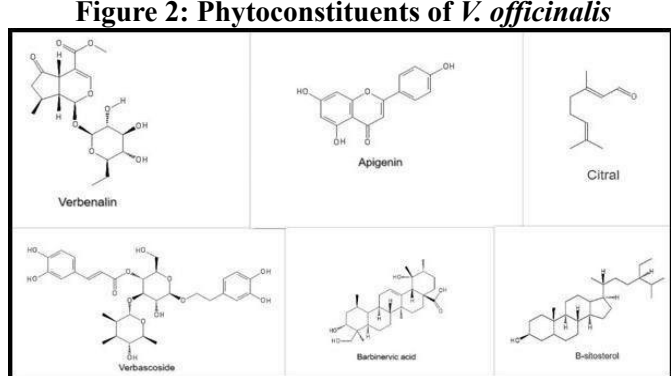
Iridoid glycosides isolated from aerial parts of *V. officinalis* include verbenalin, 3,4-dihydroverbenalin, hastatoside, aucubin (11,12). Two new iridoid glycosides, 3- (5- (methoxycarbonyl) - 2-oxo - 2H-pyran- 3- yl) butanoic acid, 7-hydroxyde hydrohastatoside were isolated (13). Xu *et al.* isolated secoiridoid glycosides, Verbenoside A and Verbenoside B (14).

Phenylpropanoid glycosides

Verbacoside, Isoverbacoside, leucoseptoside A, cistanoside D were isolated from methanolic extracts of microshoot cultures of *V. officinalis*. Quantitative analysis of verbacoside and isoverbacoside was done by ultra-high-performance liquid chromatography were found to be 4881.61 and 451.80 mg/100 g dry weight respectively (15).

Flavonoids

Flavonoids include luteolin, apigenin, scutellarein, pedalitin and derivatives. Scutellarein 7-digluconide, scutellarein 7-glucuronide, pedalitin 6-galactoside and scutellarein 7-glucoside were first isolated (16). Flavones isolated from plasma samples of Sprague Dawley rats after administration of hydroethanolic extract of *V. officinalis* using a validated LC-MS/MS method were determined as luteolin, kaempferol, apigenin, quercetol, isorhamnetin (17).



Reported pharmacological activities of *Verbena officinalis*

Anticonvulsant activity

Administration of dried methanolic extract of whole plant parts of *V. officinalis* prolonged onset of Pentylenetetrazole-induced general tonic-clonic, myoclonic seizures and reduces the duration of tonic-clonic seizures dose dependently in Swiss Albino mice. Verbenalin (iridoid glycoside) and safranal (benzyl alcohol) activate GABAA receptors producing anti-epileptic action (21).

Ethanolic extract of aerial parts of *V. officinalis* delayed onset and duration of seizure pentylenetetrazol (PTZ) model and reduced hind limb tonic extension in max electroshock (MES) induced seizures in mice. Anticonvulsant activity was due to increased GABA (γ -Amino butyric acid, inhibitory neurotransmitter) due to agonistic activity at benzodiazepine receptors and kappa

opioid receptor, this was confirmed by reversal of effects by flumazenil and naloxone (22).

Antidepressant activity

Aqueous extract of *V. officinalis* possessed antidepressant activity in Swiss albino mice. Shortened immobilisation time in forced swim test and Tail Suspension test alleviated depression. Molecular docking studies revealed verbenalin and verbacoside bound to Serotonin Reuptake Transporter (SERT), thus upregulating serotonin levels. Verbenalin and caffeic acid bound to Leucine Transporter (LeuT), proving its antidepressant effect (23). Methanolic extract of dried leaves of *V. officinalis* proved to be anti-depressant by reduces immobilization time in forced swim and tail suspension test and improved locomotor activity (24).

Antibacterial activity

Methanolic extract of aerial parts of *V. officinalis* supported antibacterial activity against *Listeria monocytogenes*, *Salmonella* DMS 560 (gram positive) and *Escherichia coli*, *Pseudomonas aeruginosa* (gram negative). Highest zone of inhibition was found to be for *Escherichia coli*. Polyphenolic compounds affect bacterial cell wall integrity and complex with membrane proteins and causes microbial death (25). In a study by Mengisteet *al.*, 80% methanol leaf extract showed potent antibacterial activity against *Staphylococcus aureus* and *Escherichia coli* (26).

Biomass generated by microshoot culture of *Verbena officinalis* had potent antioxidant and bacteriostatic and bactericidal activity against Gram positive bacteria, which could be attributed to the presence of phenolic acids and phenylpropanoid glycosides (15).

Biomaterial film made up of polyvinyl alcohol and *V. officinalis* ethanol extract had enhanced surface properties confirmed by profilometry and inhibited bacterial biofilms of *Staphylococcus aureus*, *Escherichia coli*, the polyvinyl-plant film was not cytotoxic to fibroblastic cells of rabbit (27).

Hepatoprotective activity

The herbal tea (aqueous) extracts of *V. officinalis* have protective effects in opposition to palmitic acid and acetaminophen induced hepatotoxicity in FL83B mouse hepatocytes. MTT assay supported improved hepatocellular viability after herbal tea treatment. Antioxidant phytoconstituents reversed the induced hepatotoxicity by combating toxic effects of free radicals (28).

Anti-inflammatory and analgesic activity

Methanolic leaf extracts and 3% cream formulated from the methanolic extract had anti-inflammatory effect on local inflammation induced by Carrageenan and antinociceptive effect was assessed by formalin in Wistar rats. Acute anti-inflammatory and analgesic activities were documented for occurrence of iridoid glycosides and flavonoids⁵. Anti-inflammatory activity against Xiaozhiling injection induced prostatitis mouse model was studied by Miao *et al* in-KM mice.

Verbenalin at 50 mg/kg, 100 mg/kg and 200 mg/kg ameliorated the histopathological changes due to prostate inflammation, improved the immune function and exhibited protective function (29).

In zymosan-induced leukotriene dependent hyperalgesia, BNO1016, a combined herbal dry hydroethanolic extract composed of *Verbena officinalis* along with gentian, primula, sorrel and elder flowers proved to have analgesic activity at a dose range of 15-500mg/kg, with dose effect up to 7 hours. Authors claimed that at 480mg dose of BNO1016, analgesic activity better than ibuprofen was observed in chronic rhinosinusitis conditions in this study on Wistar rats (30).

Neuroprotective effect

The aqueous extract of aerial parts of *V. officinalis* was evaluated for neuroprotective effect against beta amyloid peptide toxicity and dithiothreitol. Dose dependent attenuation in caspase-2 and caspase-3 mediated neuronal apoptosis due to reducing stress generated by beta amyloid peptide and dithiothreitol thus protected from progressive neuronal and neurites damage. Polysaccharides in the extract suppressed phosphorylation of reducing stress activated kinases, interferon-inducing protein kinase (PKR) and c-Jun N-terminal kinase (JNK) and pronounced application in Alzheimer's disease (31).

Microarray gene expression analysis of Verbenalin treated human amnion epithelial cells downregulated the expression of epidermal growth factor (EGF) receptor (EGFR), and vascular endothelial growth factor B (VEGFB). Expression of neuregulin 1 (NRG1) was significantly upregulated, contributing to neurogenesis. Downregulated AD-associated genes include TMEM8A, USF2, PDZ and LIM domain 4 (PDLIM4), and TAF15 were observed. Pretreatment with 20 μ M of verbenalin for 24 h could significantly reduce the A β -induced cell death by upregulating NRG1 expression in amyloid β -induced human neuroblastoma SH-SY5Y cells, verbenalin could drastically reduce cell mortality, improve ATP levels, limit ROS formation and EGFR expression, and upregulate NRG1 expression (32).

Anti-diarrhoeal activity

Methanolic extracts of roots and leaves of *V. officinalis* were estimated for anti-diarrhoeal potential using castor oil induced diarrhoea model. The root extract significantly decreased the weight of fecal matter, frequency of defecation and intestinal secretions, evident from castor oil induced diarrhoeal model and entero-pooling model. Secondary metabolites in the extracts proved the anti-diarrhoeal effect (33).

Anti-hyperlipidemic activity

Crude methanolic extract of whole plant of *V. officinalis* possessed antihyperlipidemic potential against high fat diet (HFD) induced hyperlipidaemia in mice. Decrease in serum Triglycerides, Total cholesterol (TC), very low-density lipoprotein (VLDL) and low-

density lipoprotein (LDL) signaling increased β -oxidation and inhibition of pancreatic lipases. Inhibition of lipid peroxidation by polyphenols and increased glutathione peroxidase aided hepatocellular protection (34).

Antiproliferative effect

In vitro antiproliferative effect by MTT assay of extracts (aqueous, ethyl acetate, butanol) of aerial parts of *V. officinalis* on rat colonic epithelial cell line and HCT-116 human colon adenocarcinoma cell lines. Cytotoxicity on the cell lines was possibly due to presence of diacetyl phenyethanoids (35).

In vitro study by De martino et al of essential oil of *V. officinalis* and main component citral in the essential oil, on lymphocytes of normal, healthy subjects and chronic lymphocytic leukemia patients. Verbena essential oil and citral selectively induced proapoptosis in leukemic lymphocytes as a result of caspase-3 activation (20).

Au/CuO/ZnO nanoparticles formulated with aqueous extract of *V. officinalis* proved time and concentration dependent cytotoxicity in leukemic Jurkat cell lines assessed by MTT assay and Annexing V binding test. Lower percentage of cells in S phase and the G2/M phases and signs of caspase mediated late apoptosis due to terpenes supports anti-leukemic effect (36).

Antifungal activity

In vitro activity of methanolic leaf extract of *V. officinalis* on *Botrytis cinerea*, *Penicillium expansum*, *Alternaria alternat*, and *Rhizopus stolonifera* proved to be fungicidal against *P.expansum* and *R. stolonifer*. The caffeoyl derivatives (chlorogenic acid and verbacoside) in the methanolic extract rendered antifungal activity (37).

Antioxidant activity

Casanova et al, assessed the antioxidant activity of methanolic, ethyl acetate, chloroform extracts of leaves by DPPH (2,2'-diphenyl-1-picrylhydrazyl radical) scavenging assay. Methanolic extract owing to the presence of luteolin, apigenin and caffeoyl derivatives, verbacoside and chlorogenic acid, exhibited strong free radical scavenging activity than ethyl acetate and chloroform extract (37).

Chronic generalized gingivitis

Decoction of *V. officinalis* was evaluated for gingival inflammation and plaque formation in chronic generalized gingivitis patients. Diminished gingival inflammation and plaque formation due to inhibitory effect on growth of periodontopathic bacteria over the trial period was observed (38).

Anti-anxiety activity

The phytochemicals isolated from the ethyl acetate fraction of methanol extract of dried aerial parts of *V. officinalis*. Increased frequency and time of entry in open arms was evident in elevated plus maze model.

Flavonoids isolated were stated to have antianxiety activity (39).

Antileishmanial activity

Zinc nanoparticles formulated with aqueous extract of *V. officinalis* proved to be leishmanicidal against *Leishmania tropica*. The leishmanicidal activity was due to the nanosized delivery to leishmanial cells, induction of reactive oxygen species abating the metabolic activities and disruption of cell membrane leading to leakage of ions causing protozoal death (40).

Anti-*Trichomonas vaginalis* activity

In a study by Brandelli et al, aqueous extract of leaves of *Verbena* sp. exhibited complete cytotoxicity against trichomoniasis causing protozoa *Trichomonas vaginalis* (41).

Antiviral activity

Computer-aided analysis of luteolin-7-galactoside of *V. officinalis* against multiple Severe Acute Respiratory Syndrome Corona Virus-2 (SARS-COV-2) targets, namely, papain-like protease, 3-chymotrypsin-like protease, RNA-dependent RNA polymerase, 2-O-methyltransferase, spike receptor-binding domain, human angiotensin-converting enzyme-2 (ACE-2), human type-II transmembrane serine protease (TMPRSS-2). Luteolin-7-galactoside bound significantly to ACE-2 and TMPRSS-2, with high binding energy. Thus, depicts application in prophylaxis of Covid-19(42).

Shufeng Jiedu capsule eight medicinal herbs, including *Bupleurum chinense*, *Fallopia japonica*, *Forsythia suspensa*, *Glycyrrhiza uralensis*, *Isatis indigotica*, *Patriniasca biosaefolia*, *Phragmites australis*, and *Verbena officinalis*. The phytoconstituents inhibited viral entry by blocking angiotensin-converting enzyme 2 (ACE2) and viral replication by inhibiting 3C-like protease and modulation of inflammatory pathways like IL-17, advanced glycationend-product (AGE)-advanced glycation end-product receptor (RAGE) and TNF signaling pathways (43).

Pericet *al*, assessed the action of herbal formulation, Sinulan forte tablet, containing *Andrographis paniculata*, leaf, *Sambucus nigra*, flower, *Verbascum thapsus*, flower, *Verbena officinalis*, herb and *Gentiana lutea*, root against acute rhinosinusitis. Alleviation in symptoms of nasal congestion, secretion, nasal mucosal edema, rhinorrhea, loss of smell sensation was observed (44).

Zhang *et al*, carried a clinical trial for the efficacy of Baidu Jieduan granules administered orally twice a day for 14 days against SARS COV2 infection and symptoms like fever, fatigue and cough. Expelling wind and dampness, draining heat and detoxifying the body, increasing blood circulation, alleviating cough, and lowering sputum production are the actions of *Verbena officinalis* in the formulation and can reduce dependence on antibiotics and glucocorticoids (45).

Anti-urolithiasis activity

Infusion of whole herb caused diuretic effect, enhanced urinary excretion of calcium, citrate, phosphate, creatinine and raised urinary pH after administration of the infusion in Wistar rats. Saponin components in *V. officinalis* serve as anti-adherent molecules on mucoproteins which aid crystallization and thus provide anti-kidney stone formation tendency (46).

Gastroprotective activity

Carbon dioxide extract, methanol and flavonoid enriched extract of aerial parts of *V. officinalis* had protective special effects against ethanol induced gastric damage. Phenylpropanoids, oleanoic acid, ursolic acid, beta-sitosterol proved to be anti-inflammatory. Antioxidant activity was due to flavonoids and polyphenols, these activities supported the gastroprotective activity (47).

Anti-tumour activity

Kou *et al*, studied the *in vivo* antitumour activity of aqueous extract of aerial parts of *V. officinalis* against H22 tumour bearing mice. High dose (40 mg/ kg) decreased the tumour weight and inhibited tumour growth rate comparable to cisplatin. *Verbena* extract did not affect humoral and cellular immune function as per footpad swelling (DTH) and serum hemolysin level tests (48).

Protective role against focal cerebral ischemia in rats:

Effect of verbenalin on focal cerebral ischemia reperfusion injury in KM rats was studied by Cao *et al*. Increment in the serum level of S100 β protein was investigated for implementation of cerebral ischemia reperfusion model in rats. Verbenalin, at doses 5 mg/kg, 10 mg/kg and 20 mg/kg significantly reduced S100 β protein, downregulated the expression of proapoptotic enzymes Bax, Caspase-3 and unregulated the expression of anti-apoptotic, Bcl-2 gene. Recovery was evident by improvement in morphological changes in the cerebral cortex tissue (49).

Moreover, Cornin, an iridoid glycoside derived from the fruits can increase proliferation, invasion, and lumen formation *in vitro*, resulting in angiogenesis. Cornin increased the proliferation of rat arterial smooth muscle cells (RASMC) and the expression of tissue homeostasis regulators like Wnt5a, β -catenin, cyclin D1 and angiopoietin-1, confirming that it can reduce BBB leakage, promote angiogenesis and functional recovery after stroke (50).

Tyrosinase Inhibitory activity

Capetti *et al* identified α and β -pinene, sabinene, limonene, citronellal, neral, geranial, β -myrcene, as the major components of essential oil in *V. officinalis* by GC-MS analysis. *In vitro* Tyrosinase Inhibitory Assay supported β -myrcene, citral and citronellal inhibited mushroom tyrosinase and could interfere with the melanin biosynthetic pathway by downregulating tyrosinase enzyme and *V. officinalis* could be used in treating hyperpigmentation (51).

Table 2 : The pharmacological activities exhibited by various parts of *V. officinalis*

Pharmacological actions	Part used	Extract	Mechanism of Action	References
Anticonvulsant	Whole plant, Aerial parts	Methanol Ethanol	Activation of GABA _A receptors by verbenin and safranal. Increased GABA agonistic activity at benzodiazepine and kappa opioid receptor.	2,122
Antidepressant	Leaves	Ethanol	Binding of verbacoside to Serotonin Reuptake Transporter (SERT), and Verbenalin and caffeic acid bound to Leucine Transporter (LeuT)	23
Antibacterial	Aerial parts	Methanol	Complexation with membrane proteins and disruption of cell wall integrity of bacteria	25
Neuroprotective	Aerial parts	Aqueous	Attenuation in caspase-2 and 3 mediated neuronal apoptosis, suppression of phosphorylation of reducing stress activated kinases, PKR AND JNK	31
Anti-diarrhoeal	Roots and leaves	Methanol	Decreased intestinal secretion due to reduced Nitric oxide by terpenoids and flavonoids. Astringent property of tannins.	33
Antihyperlipidemic	Whole plant part	Methanol	Inhibition of lipid peroxidation by polyphenols and increased glutathione peroxidase aided hepatocellular protection.	34
Antiproliferative	Aerial, Whole plant	Aqueous, Ethyl acetate, Butanol Essential oil and citral Aqueous in Au/CuO/ZnO nanoparticles	Cytotoxicity due to diacetyl phenyethanoids Induction of proapoptosis in leukemic lymphocytes as a result of caspase-3 activation. Caspase mediated late apoptosis due to terpenes in leukemic Jurkat cell lines	20, 35, 36
Antioxidant	Leaf	Methanol, Ethyl acetate, Chloroform	Luteolin, Apigenin, Verbacoside and chlorogenic acid exhibited strong free radical scavenging activity.	37
Antileishmanial	Whole plant	Aqueous extract in zinc nanoparticles	Disturbed metabolic activities and interference of cell membrane causes leakage of ions	40
Antiviral	Whole plant	Methanol	Luteolin-7-galactoside bound significantly to ACE-2 and TMPRSS-2 with high binding energy on SARS-COV-2 targets	42-45
Anti-urolithiasis	Whole plant	Infusion	Saponins serve as anti-adherent on mucoproteins inhibit crystallisation and kidney stone formation	46
Gastroprotective	Aerial part	Methanol, Carbon dioxide, Flavonoid	Combined anti-inflammatory due to Phenylpropanoids, oleonic acid, ursolic acid and beta-sitosterol and antioxidant flavonoids, polyphenols support gastroprotective activity.	47

***V. officinalis* in Female Health**

Ease in premenopausal night sweating

Deficiency of oestrogen in the body during premenopausal phase of a woman's life, causes intervals of extreme sweating and cold, damp feeling at night, which is intensified by presence of xenoestrogens from plastics, chemicals (perchlorate, polychlorinated biphenyls, triclosan, vinyls and phthalates) accumulated in the body. Coadministration of *Actaea racemosa* (source of phytoestrogens) and *V. officinalis* (nervine tonic) as a tincture alleviates the symptoms as the phytoconstituents in verbena can bind to estrogen-progesterone receptor (52). Galactagogue activity *V. officinalis* is administered by lactating mothers for increasing milk quantity. Its oxytocic and prolactin elevating effect attributes to the galactagogue activity (53).

Role in endometriosis

Endometriosis is a painful, chronic inflammatory condition. *Verbena* spp, have shown to prohibit the phagocytosis of granulocytes and thus

reduce inflammatory progression. Furthermore, stimulation of the secretion of luteinizing hormone and follicle stimulating hormone and inhibition of human chronic gonadotropin, has proved it to be a useful herb against endometriosis (54).

Relief in dysmenorrhea

Pain during menstruation accompanied by vomiting and diarrhoea is dysmenorrhoea. Traditional Chinese medicine (TCM) terms congestive dysmenorrhoea as blood accumulation in the uterus during menstruation and interruption of normal blood flow within the uterus causing intense pain. TCM suggests use of herbs such as *Verbena officinalis*, *Taraxacum officinalis*, *Achillea millefolium* aiding adequate blood supply to pelvic region, reducing prostaglandin synthesis and are liver tonics (55).

Herbal tonic in Obstetrics

Traditional Chinese Medicine prescribes use of an infusion of Raspberry, Stinging nettles and *V. officinalis* (1 part) in the second trimester of pregnancy.

It is a nervine tonic, has antispasmodic action, which aids relaxation and calms the woman. Iridoid glycosides present enhance digestion and absorption of nutrients due to activation of parasympathetic activity. An ancient herbal elixir containing *V. officinalis* (0.5 part) called cordial elixir (3-5 ml daily) is administered in the third trimester until delivery for supporting contractility of uterus during labour, softening of cervix and minimizing postpartum haemorrhage (56).

Antimicrobial against microbes causing vaginitis

Ethanol extract of *V. officinalis* at 50, 100, 200 mg/ml presented antibacterial action against *Gardnerella vaginalis*, the etiological agent causing vaginitis. A combination of the *V. officinalis*, *Malva sylvestris* and *Ageratum conyzoides* ethanolic extracts at 50, 100, 200 mg/ml also inhibited *G. vaginalis* growth. Microdilution technique was used to measure minimum inhibitory concentration which was found to the lowest for *Ageratum conyzoides* followed by *V. officinalis* and then the combination (57).

Reported toxicology of *V. officinalis*

In vitro Ames mutagenicity assay supported significant mutagenicity of aqueous extract of *V. officinalis* in *Salmonella typhimurium* strains TA100 and TA98. According to previous studies using Ames assay, apigenin and luteolin can cause mutations. *In vivo* genotoxicity was assessed with rat bone marrow micronucleus assay. *In vivo* studies revealed no significant genotoxic effects of extract in rats, which was evident from reduction in the ratio of polychromatic to normochromatic erythrocytes (58). Administration of aqueous extract of *V. officinalis* in pregnant Sprague Dawley rats (dams) during organogenesis, caused no severe maternal toxicity except weight loss, decreased gravid uterus and ovarian weight, decreased number of corpus luteum, increase in pre or post-implantation loss especially in 3000 mg/kg treated dams was evident, affecting maternal reproductive health. The adverse effects on foetal growth of 2000mg/kg and 3000 mg/kg treated dams include decreased foetal weights, decreased head cranium, crown-rump and tail lengths, skeletal deformities. 2000 mg/kg and 3000 mg/kg doses had potential teratogenic effects, possibly due to apigenin and luteolin (59). Moreover, the use of ShufengJiedu capsules, a traditional Chinese medicine containing *Verbena officinalis* has been contraindicated in early pregnancy, as it is considered as a uterine stimulant and in lactating women. MHRA yellow card system pharmacovigilance data has been documented with occurrence of gastrointestinal adverse effects after *Verbena officinalis* consumption (60).

Enhanced ethanol induced hepatotoxicity treated with *Verbena officinalis* herbal tea as observed in FL83B hepatocytes. Metabolic activation of the cytochrome P450 enzymes inducing hepatocellular damage contributes to hepatotoxicity and it is advisable to avoid intermittent consumption of *Verbena officinalis* herbal tea and alcohol (28).

Conclusion

V. officinalis, an herb of tremendous cultural and ethnomedicinal importance, from its involvement in magic and purification remedies to its use in conditions like urolithiasis, anxiety, swelling in throat, chest pain, rheumatism, many of which are substantiated by pharmacological studies. *V. officinalis* also finds distinct role in gynaecology and obstetrics and can be involved in treatment of dysmenorrhoea, endometriosis, postpartum depression, hypolactemia in breast feeding women and as herbal tonic. The possible *in vivo* teratogenic effects of *V. officinalis* at higher concentrations and also its use as a galactagogue, is intriguing and needs attention in future. Moreover, toxicological studies carried out also mention its cautious use by pregnant women due to risk of prenatal toxicity.

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Conflict of Interest

All the authors declare that there are no any conflicts of interest with this data.

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