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A Review on the Chemical Constituents of Verbena Officinalis (L.Vervain) and therapeutic Importance of Common Vervain

[1]Riya Gautam, [2]Manpreet Kaur
[1]Student of pharmacy, [2]Assistant Professor (Pharmaceutical chemistry)
[1]Department of Pharmaceutical chemistry
[1]ASBASJSM College of Pharmacy, Bela Ropar (India)

Abstract : *Verbena officinalis*, commonly known as common vervain, is a medicinal plant species that is extensively distributed across the globe and is frequently utilized in the folk medicine practices of various countries, including traditional Chinese medicine. Since 2008, monographs on "*Verbenae herba*" have been incorporated into the European Pharmacopoeia, while the Chinese Pharmacopoeia has included it since 1995. This document outlines the botanical characteristics of this species and reviews the existing knowledge regarding its chemical composition, which predominantly consists of iridoids, phenylpropanoid glycosides, phenolic acids, flavanoids, terpenoids, and essential oils. A significant portion of this article is dedicated to summarizing traditional medicinal applications and professional pharmacological studies, both in vitro and in vivo that highlight new and significant uses, such as antioxidant, antimicrobial, anti-inflammatory, neuroprotective, anticancer, analgesic, and anticonvulsant properties of verbena herb extracts and their individual metabolites. Furthermore, this article emphasizes the application of V. officinalis in the food and cosmetics sectors, particularly due to its antioxidant, antibacterial, and anti-inflammatory effects, as well as the presence of essential oil with a pleasing fragrance profile. Additionally, this work discusses the current state of biotechnological research related to this species.

Keywords - Phenylpropanoid glycosides, Antioxidants, biotechnological research, Vervain

I. Introduction

Verbena officinalis L., or common vervain, is a notable medicinal plant within the Verbenaceae family, recognized for its established role in the medicinal practices of Europe, Asia, and North America. The raw material employed in both traditional and modern phytotherapy is the verbena herb, known scientifically as Verbenae herba. This species has a broad natural distribution, found in regions across Europe, the Americas, North and Central Africa, Asia, and Australia. V. officinalis predominantly inhabits temperate climate zones, with a significant occurrence in the Mediterranean region of Europe. It prefers dry soils that maintain moisture and is typically found in sunny locations. As a ruderal species, it flourishes in fields, on stony ground. V.officinalis is a species that is known by a variety of synonymous names. In Latin, it is referred to as Verbena sororia D. Don and V. spuria L. The common names for V. officinalis vary by country, including vervain, common verbena, official vervain, simpler's joy, turkey grass, and wild verbena in English. In France, it is called verveine officinale, while in Germany, it is known as echtes Eisenkraut. In Japan, it is referred to as kumatsuzura, and in Portugal and Brazil, it is called erva-de-ferro, ferra-ria, or planta-da-sorte. In Sweden, it is known as järnört, and in China, it is called ma bian cao.

The identification of V. officinalis primarily relies on morphological characteristics and phytochemical analyses. However, recognizing the species through morphological traits necessitates specialized expertise, especially when dealing with fragmented pharmaceutical raw materials. Phytochemical analysis poses challenges due to the significant variability in the chemical composition of the raw material, which is influenced by its origin. Presently, advanced methods utilizing genetic markers are available for the precise identification of the species. V. officinalis is a perennial herbaceous plant that typically reaches heights of 75 cm to 1 m. It features erect, woody stems that branch at the top and possess a quadrangular cross-section, covered in rough hairs. The upper leaves are sessile, serrated, and oppositely arranged, while the middle leaves are tripartite, and the lower leaves are petiolate and pinnate. In summer, this species produces small, pale lilac flowers that are grouped in spiky, loose top inflorescences, with some located in the leaf axils. Each flower has a small, nearly two-lipped corolla with a short, slightly curved tube that expands into a wreath. Inside the cup, which has four or five sharp serrations, lies an upper pistil with a chambered ovary. The number of stamens attached to the inside of a chamber can be 2, 4, or 5. The fruit is characterized as an elongated, ribbed schizocarp.

Basic characteristics of Verbena Species

The genus Verbena, which falls under the family Verbenaceae (subfamily Verbenae), is primarily represented by the species V. officinalis. There exists a degree of inconsistency in the scientific literature regarding the classification of genera and species within the Verbenaceae family. It is generally estimated that this family encompasses approximately 30 genera, including Aloysia, Citharexylum, Lantana, Lippia, Phyla, and Verbena, with the total number of species in the family reaching around 1100. This diverse family includes trees, shrubs, and herbaceous plants. The genus Verbena itself is reported to contain between 44 and 250 species, predominantly found in the Americas. Notably, two species, V. officinalis L. and Verbena supina L., are distributed across all continents. Among the commonly cultivated ornamental species are Verbena hastata L., Verbena bonariensis L., and Verbena × hybrida Groenl. & Rumplser, the latter being a hybrid of Verbena incisa Hook, Verbena peruviana (L.) Britto, Verbena phlogiflora Cham and Verbena teucroides.

Phytotherapy of Verbena officinalis

The vervain herb, scientifically referred to as Verbenae officinalis herba, has been utilized as a traditional medicinal ingredient for many years. Its formal acknowledgment in European medicine, however, is a more recent development. A monograph on "Verbena herb" was introduced in the European Pharmacopoeia (6th edition) in 2008. As per the guidelines established in the latest (10th) edition of the European Pharmacopoeia, this raw material is required to be standardized for verbenalin content, with a minimum threshold of 1.5% on a dry weight basis.

Furthermore, a monograph titled "Verbenae herba" was included in the Chinese Pharmacopoeia, specifically in its eighth edition published in 2005. Earlier, the British and German Pharmacopoeias had already incorporated monographs on the herb V. officinalis. This particular species has been recognized as a significant medicinal plant in the United States, with its description appearing in the Pharmacopoeia of the American Institute of Homeopathy from 1897. Notably, while the European Pharmacopoeia does not feature a monograph for V. officinalis, it does include one for another species of Verbena, namely "Verbenae citriodorae folium," which refers to the leaves of lemon verbena (Aloysia citriodora Palau; also known as Aloysia triphylla (L'Her.) Kuntze, among other synonyms). A. citriodora possesses a distinct chemical profile compared to V. officinalis and has a more limited natural habitat distribution. This shrub, native to South America, was introduced to Europe in the late 17th century and is commonly utilized in infusions for its antispasmodic, antipyretic, sedative, and digestive benefits. Research indicates that phenylpropanoids and their metabolites are the primary compounds that confer blood-cell protection against oxidative stress following the administration of L. citriodora in rat studies. Recent systematic investigations reveal that A. citriodora, unlike V. officinalis, belongs to a different subfamily within the Verbenaceae family, specifically the Lantanae subfamily.

V. officinalis herba is characterized by a diverse chemical composition. The key groups of secondary metabolites that contribute to the biological activity of this material include iridoid glycosides, which encompass verbenalin (verbenaloside), aucubin (verbenin), and hastatoside. Additionally, the herb contains phenylpropanoid glycosides and caffeic acid derivatives, such as verbascoside (acteoside), isoverbascoside (isoacteoside), and eukovoside. Moreover, various flavonoids have been identified in verbena herb extracts, including common plant compounds like kaempferol, luteolin, and apigenin, alongside specific flavonoids such as scutellarein and pedalitin. The herb also contains notable phenolic acids, including chlorogenic, ferulic, protocatechuic, rosmarinic, and dicaffeoylquinic acid derivatives. Analyses of phytochemicals indicate that the methanolic extracts obtained from the stems of V. officinalis are characterized by the presence of sterols, specifically α-sitosterol, β-sitosterol, and daucosterol. Additionally, the herb V. officinalis is found to contain a range of carbohydrates, including galacturonic acid, arabinose, galactose, rhamnose, xylose, mannose, and glucose, along with substantial amounts of vital bioelements such as potassium, phosphorus, calcium, magnesium, zinc, iron, manganese, and copper.

The herb V. officinalis is notable for its essential oil, which comprises approximately 40 different compounds, predominantly monoterpenoids such as citral, limonene, cineole, and carvone. The specific composition of the essential oil from V. officinalis is influenced by various factors, including environmental conditions, the chemotype of the plant, the type of plant material utilized, and the method of essential oil extraction. For instance, hydro distilled essential oil derived from fresh plants cultivated in Italy exhibited significant levels of citral (over 45%) and isobornyl formate (exceeding 40%). In contrast, steam-distilled essential oil from dried plants sourced from Morocco primarily contained spathulenol (greater than 10%), along with limonene and eucalyptol, each at 7.5%. Furthermore, the volatile fraction from dried V. officinalis collected in Algeria was characterized by high concentrations of limonene (over 17%), carvone (greater than 14%), citral (exceeding 14%), and caryophyllene oxide (more than 12%). Lastly, the volatile fraction extracted from the aerial parts of an intact V. officinalis plant gathered in Poland was predominantly composed of hexanoic acid (over 20%), linalool (greater than 8%), anethole (exceeding 5%), and carvone (more than 3%).

Therapeutic Importance

The extracts of V. officinalis herb have been utilized in traditional medicine for an extended period, particularly in European and North American practices, as well as in traditional Chinese medicine. The potential therapeutic uses of this herb, which have been established over centuries, are substantiated by contemporary scientific investigations into the chemical composition and efficacy of its active compounds. V. officinalis is recognized for its antimicrobial, secretolytic, and expectorant properties. It is commonly employed in the management of upper respiratory tract ailments, particularly in cases of throat and sinus inflammation, as well as conditions such as colds, fevers, chest tightness, bronchitis, asthma, whooping cough, and sinusitis. Additionally, extracts from the leaves of V. officinalis are known to assist in treating urinary tract issues, including urinary stones and infections, and exhibit diuretic effects. In women, this herb is utilized for menstrual irregularities, while in nursing mothers; it is known to promote lactation. Furthermore, V. officinalis has shown efficacy in addressing various nervous system disorders, including depression, insomnia, stress, anxiety, chronic fatigue syndrome, nervous exhaustion, sexual neurosis, and headaches. It is also applied in the treatment of digestive disorders such as abdominal colic, jaundice, gallbladder inflammation, diarrhea, dysentery, stomach pain, and intestinal parasites. Extracts from V. officinalis are employed to alleviate fever associated with colds and provide supportive treatment for malaria and rheumatism.

Anti-oxidant effect

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Anti-Inflammatory Effect

Researchers at the University of Pamplona in Spain conducted an investigation into the anti-inflammatory properties of an ointment containing 1 to 3% dry extract from the leaves of V. officinalis. The extract was prepared by macerating 50 grams of dried herb in 700 milliliters of 50% methanol. Following this process, the chlorophyll-free solution was evaporated under vacuum to yield a dry extract. The anti-inflammatory effects were assessed by measuring paw volume with a plethysmometer immediately after the injection of carrageenan and at intervals of 1, 2, 3, and 4 hours thereafter. Both oral and topical administration of V. officinalis extracts demonstrated an anti-inflammatory effect in the rat model.

Analgesic Effects

The analgesic effects were assessed in vivo by monitoring the frequency of paw licking episodes in rats following the application of ointments containing 1–3% verbena extract, 0.3 g of ointment base, or an ointment with 30% methyl salicylate, alongside the injection of 50 µL of a 2.5% formalin solution. Observations were conducted for duration of 60 minutes post-administration of formaldehyde. The results indicated a notable analgesic effect, as evidenced by a significant reduction in the number of licking episodes when compared to the control group.

Anticonvulsant, anxiolytic, and sedative effects

The application of verbena in traditional medicine for the treatment of nervous system disorders has led researchers from Riphah International University in Islamabad, Pakistan, to investigate the anticonvulsant, anxiolytic, and sedative properties of V. officinalis. An extract from the V. officinalis herb was prepared by macerating the dried plant material in 70% methanol, followed by solvent evaporation under reduced pressure. This extract was then dissolved in an isotonic sodium chloride solution. Various experimental methods were employed to assess the effects of the verbena extract on the test subjects, including convulsions induced by pentetrazole (PTZ), elevated plus maze tests, light-dark box tests, open-field tests, thiopental-induced sleep tests, and acute toxicity assessments. The results confirmed the anticonvulsant, anxiolytic, and sedative effects of V. officinalis, revealing a dose-dependent delay in the onset of pentazocine-induced myoclonic and tonic-clonic seizures, as well as a reduction in the duration of tonic-clonic seizures. In the control group, which received only sodium chloride solution, the mortality rate was 100%. In contrast, the group administered a 100 mg/kg dose of the V. officinalis extract experienced a mortality rate of 75%, while doses ranging from 300 to 500 mg/kg body weight resulted in a mortality rate of 0%, comparable to that observed with a 1 mg/kg dose of diazepam. The open-field test indicated that administration of the extract at doses of 50, 100, and 300 mg/kg body weight significantly decreased the number of ambulations from 121.75 (control group) to 109.5, 106.5, and 74.25, respectively, and reduced rearing frequencies from 52.25 (control group) to 42.5, 39.5, and 24.25, respectively. Additionally, the extract increased the number of crossings in the central squares from 6.25 (control group) to 11.25, 15.0, and 10.75 for the respective doses of 50, 100, and 300 mg/kg body weight. The extract also influenced the onset time and duration of sleep, with the control group averaging a sleep onset after 3.53 minutes and duration of 8.25 minutes.

Sleep Promoting Effects

The conventional application of V. officinalis infusion for treating insomnia has been substantiated by scientific studies. In Japan, two research entities, the Central Research Institute of Mizkan Group Co., Ltd. in Handa, Aichi, and the Department of Molecular Behavioral Biology at the Osaka Bioscience Institute, investigated the impact of an aqueous extract from V. officinalis on sleep quality in a rat model. The study utilized not only the aerial parts of the plant during its flowering phase to create the extract but also included the entire plant, roots included. The compounds hastatoside, verbenalin, and verbascoside were isolated from the extract. The research examined both the extract's efficacy and the individual compounds by assessing the duration of the non-rapid eye movement (NREM) sleep phase, commonly referred to as deep sleep, through delta wave activity analysis using EEG-EMG. The brain wave frequencies measured were 0.5–30 Hz for EEG and 20–200 Hz for EMG. The V. officinalis extract and the isolated compounds were administered to the rats via direct stomach infusion for 30 minutes (between 8:00 p.m. and 8:30 p.m.) at a rate of 200 µL/min. The dosages were 9 g/kg BW for the verbena extract; 0.32, 0.48, and 0.64 mmol/kg for hastatoside; 0.32, 0.64, and 1.28 mmol/kg for verbenalin; and 0.64 and 1.28 mmol/kg BW for verbascoside. EEG-EMG recordings were conducted 24 hours post-administration of the extracts.

The extract of V. officinalis, when administered at the specified dosage, resulted in a 25.7% increase in NREM sleep duration over a continuous 12-hour period, in comparison to the control group. The frequency of NREM episodes rose from approximately 138 to 149, while the length of each episode increased from 1.2 minutes to 1.4 minutes. In contrast, hastatoside did not produce a significant change in NREM duration at a dosage of 0.32 mmol/kg BW; however, a dosage of 0.48 mmol/kg BW led to a 25% increase. The most pronounced effect was observed with a dosage of 0.64 mmol/kg (259 mg/kg BW), which initially decreased the overall NREM duration by 77% between 10:00 p.m. and 11:00 p.m., followed by an increase of 20% to 320% from 2:00 a.m. to 8:00 a.m. The average extension of the NREM phase during the period from 3:00 a.m. to 8:00 a.m. was 81%. Verbenalin did not influence the NREM duration at the lowest dosage tested, but a dosage of 0.64 mmol/kg BW resulted in a 27% increase in NREM sleep. The most significant effect occurred with a dosage of 1.28 mmol/kg BW (497 mg/kg BW), which initially reduced the NREM duration by 52% between 9:00 p.m. and 11:00 p.m., followed by a notable extension of 40% to 70% from 2:00 a.m. to 6:00 a.m. The average duration of the NREM phase from 4:00 a.m. to 8:00 a.m. was 42%. By the following day, the NREM duration returned to baseline levels.

Verbascoside did not demonstrate any notable effects, even at the maximum dosage administered. In contrast, hastatoside and verbenalin exhibited properties akin to benzodiazepines by prolonging the duration of the NREM phase; however, unlike these medications, they did not negatively impact the activity of delta waves in the brains of the rats examined. The adverse effects observed included agitation and diarrhea lasting up to two hours following the administration of the solutions. It was indicated that hastatoside and verbenalin are compounds with potential applicability in the treatment of sleep disorders, although further investigation is warranted.

Neuroprotective effects

Research conducted at the University of Hong Kong (China) has revealed the neuroprotective properties of extracts from V. officinalis. The investigations were performed in vitro using neurons derived from the cerebral cortex of rats. The cultured neurons were exposed to an aqueous extract of the plant, followed by treatment with various toxins, including β-amyloid25–35 (25 µM for 24 hours), tunicamycin (1 µg/mL for 16 hours), dithiothreitol (0.5 and 1.0 mM for 16 hours), hydrogen peroxide (50 µM for 16 hours), and ultraviolet radiation (32 kJ/cm² for 2 hours). After treatment, the cells were rinsed with fresh medium. The resulting cell lysates underwent a caspase activity assay, while cytotoxicity was assessed by measuring the levels of lactate dehydrogenase (LD) in the collected media. The findings indicated that a verbena herb extract at a concentration of 100 µg/mL decreased the mortality of nerve cells subjected to β-amyloid (Aβ) by 9.1% and dithiothreitol by 9.8% (0.5 mM DTT) and 29.6% (1.0 mM DTT). However, the extract did not confer protection against tunicamycin, hydrogen peroxide, and ultraviolet radiation, suggesting a limited efficacy of the extract against agents that directly damage DNA.

Colorimetric assays for caspase-3-like and caspase-2-like activities were employed to evaluate the impact of a verbena extract at concentrations ranging from 25 to 150 µg/mL .The cleavage of DEVD and VDVAD induced by Aβ highlighted the toxic effects associated with Aβ. Notably, the extract from V. officinalis demonstrated a significant reduction in Aβ-induced activity at a concentration of 75 mg/mL, achieving a 1.4-fold decrease compared to control conditions. This effect was observed to be dose-dependent. The findings suggest that V. officinalis extracts may hold potential for the prevention of neurodegenerative disorders, particularly Alzheimer's disease.

Anti-depressant effects

The antidepressant properties of 50% water-methanol extracts derived from the leaves of V. officinalis have been investigated. Collaborative research conducted by the Hygia Institute of Pharmaceutical Education and Research and Integral University Lucknow assessed the impact of V. officinalis extracts on mouse behavior. The subjects were categorized into four groups: a control group receiving a saline solution, a reference group administered imipramine (15 mg/kg BW), and two experimental groups receiving the extract at dosages of 100 and 200 mg/kg BW. The treatments were administered over a period of seven days. Depressive behaviors were evaluated using three distinct tests: the tail suspension test (TST), the forced swim test (FST), and the spontaneous locomotor activity test (SLMA). In the TST, a significant decrease in immobility duration was noted, with reductions of 53 seconds for the 100 mg/kg BW group and 73 seconds for the 200 mg/kg BW group compared to the control. The FST results showed reductions of 36 seconds and 46 seconds, respectively. However, the SLMA test yielded similar results across all groups. Additionally, the researchers assessed the toxicity of the extract by administering a dose of 2000 mg/kg BW, which did not result in any fatalities among the test subjects. The findings from the TST and FST tests demonstrated a significant and dose-dependent decline in passive posture relative to the control group, although this decline was not as substantial as that found in the reference group. While V. officinalis extracts have been shown to possess antidepressant activity in animal models, the specific mechanism behind this effect remains unknown and calls for further exploration.

Cardiovascular effects

V. officinalis is characterized by its high concentrations of potassium, phosphorus, calcium, and magnesium. Conversely, its sodium levels are comparatively low, especially in relation to potassium. This favorable low sodium-to-potassium ratio is beneficial for those suffering from cardiovascular issues when consuming products made from V. officinalis.

Antiproliferative and anticancer effect

At the University of Salerno's Faculty of Pharmaceutical Sciences in Italy, a study has been undertaken to explore the cytotoxic effects of V. officinalis essential oil and citral, its principal component, particularly regarding their apoptotic impact on chronic lymphocytic leukemia. The research was conducted in vitro using cells derived from patients with untreated lymphocytic leukemia. The apoptotic cells were identified using the CD19-APC-Cy7 antibody and quantified through flow cytometry. Assessments were made at intervals of 4, 8, and 24 hours post-treatment with the oil and citral. The highest percentage of CD19-positive cells was recorded in the samples incubated for 8 hours, with the control sample showing about 7%, while the oil and citral treatments resulted in 68.2% and 65.9%, respectively. The results indicate a strong cytotoxic effect of both the oil and citral on tumor cells; however, further investigation is required to fully understand the mechanisms involved.

Scientific investigations conducted at the Medical University of Henan in China have validated the cytotoxic properties of the V. officinalis herb against liver cancer cells. The study involved 50 mice that were subcutaneously injected in a paw with H22 mice ascite hepatoma cell line tumor cells. Following a 24-hour period post-injection, the mice were categorized into five distinct groups: a control group, three groups receiving dry extracts of V. officinalis at dosages of 10, 20, and 40 g/kg body weight, and a group administered cisplatin at a dosage of 1 mg/kg body weight. Each mouse was monitored for weight, behavior, activity levels, and food consumption. The antitumor efficacy was evaluated by measuring the tumor inhibition rate in relation to tumor and body weight. Additionally, assessments of paw swelling post-immunization with sheep's blood and hemolysin levels in the serum of the mice provided insights into the extract's effects on the immune system. Changes in body weight and spleen index, defined as the ratio of spleen weight to body weight, were also recorded. All experimental groups exhibited an increase in body weight, although these increases were less pronounced compared to the model group, with a general negative correlation observed with dosage. While the spleen indices for the groups treated with 20 and 40 g/kg body weight showed increases relative to the model group, the differences were not statistically significant, indicating that the extract did not have a notable impact on the spleen index. An increase in body weight was observed across all experimental groups. However, these increases were less pronounced when compared to the model group, and the extent of the increase generally exhibited a negative correlation with the dosage administered. In comparison to the model group, the spleen indices for the groups receiving 20 and 40 g/kg BW showed an increase, although the differences were not statistically significant, indicating that the tested extract did not have a meaningful impact on the spleen index. A correlation was established between the reduction in tumor mass and the dosage of the extract given. The tumor inhibition rates were recorded at 15.71%, 28.20%, and 38.78% for the low, medium, and high dosages of verbena extract, respectively. In contrast, cisplatin at a dosage of 1 mg/kg BW achieved an inhibition rate of 42.94%. Evaluations of footpad swelling and hemolysin levels indicated that the extract, at the administered doses, did not significantly alter immune system functionality.

Acceleration of wound healing

A collaborative research effort involving scientific institutions from Italy, specifically the Universities of Bologna and Parma, alongside the University of Innsbruck in Austria, investigated the impact of V. officinalis on wound healing in rat models. The study evaluated gels infused with one of three distinct types of V. officinalis extracts: a methanolic extract (VoME), a flavonoidsrich extract (VoFE), and an extract obtained through carbon dioxide extraction (VoCO2). Under anesthesia, the rats underwent a surgical procedure where a 1.5 cm incision was made into the adipose tissue. Following this, the wound area was treated with 0.5 mL of gel containing 20 mg of the respective extract and subsequently covered with an occlusive dressing. The healing process was monitored at 24 and 48 hours post-treatment. Observations at the 24-hour mark included the length, color, and overall appearance of the wound. The evaluation of cicatrization at 48 hours involved examining tissue morphology, including vascular caliber and leukocyte presence. Results indicated that after 24 hours, the rats treated with the VoCO2 extract exhibited a greater degree of cicatrization. Histological analysis at 48 hours revealed the most pronounced wound reduction in the group receiving the VoFE treatment. Additionally, the VoME extract demonstrated a significant decrease in tissue damage, characterized by the emergence of new fibrous tissue, when compared to the control group. These findings provide compelling evidence that the topical application of V. officinalis extracts substantially enhances wound healing.

Gastroprotective properties

Alongside the research aimed at promoting wound healing, the collaborating units undertook an investigation into the gastroprotective effects of VoFE and $VoCO_2$ extracts, administered at doses of 100 and 200 mg/kg body weight. Misoprostol was utilized as a reference treatment at a dosage of 100 µg/kg body weight. Thirty minutes post-administration of the extracts and misoprostol, 96% ethanol was applied as a damaging agent. After an additional two hours, the animals were sacrificed, and their stomachs were examined to assess the lesion index and measure gastric secretion, including volume and pH. All extracts exhibited gastroprotective effects, with $VoCO_2$ showing the most pronounced efficacy. The ulcer scores significantly decreased following the administration of the extracts at both 100 and 200 mg/kg (1.83 and 1.33 for VoME, 1.38 and 1.00 for $VoCO_2$, and 1.62 and 1.12 for VoFE, respectively) compared to the control group (3.50). However, the reduction was less than that observed in the misoprostol group.

Prevention against the spread of dangerous insect-borne diseases

Mosquitoes serve as vectors for the transmission of severe infectious diseases, including malaria, dengue fever, and filariasis. To mitigate the risk of an epidemic, it is crucial to decrease insect populations. Traditionally, toxic pesticides have been employed for this purpose, although they pose risks to both human and animal health. In an effort to discover safer alternatives, researchers at the University of Bab-Ezzouar in Algeria have demonstrated that oil extracted from the leaves of V. officinalis is lethal to aquatic mosquito larvae (Culex pipiens). The study involved testing oil concentrations ranging from 1 to 500 mg/L dissolved in water. Mortality rates were assessed after 3, 6, 12, and 24 hours of exposure. After 24 hours, concentrations of 100 and 500 mg/L resulted in larvicidal effects of 43% and 100%, respectively. These findings may be significant for the development and formulation of new, effective insecticides. The combination product may lead to disturbances in the digestive system and, in some cases, result in allergic skin reactions. It is advised that vegetarians and vegans refrain from consuming vervain during meals. According to Mills and Bone, phenylpropanoids can hinder the absorption of non-haem iron, and vervain is included among the herbs that may pose a risk in this regard. A study conducted in Morocco utilizing an in vitro digestion model indicated that vervain reduced the absorption of non-haemeiron, despite containing only one-third the amount of polyphenols found in tea. This study aimed to assess the impact of consuming tea, vervain, or mint teas on women who are weaning their infants, thus necessitating further validation. There is insufficient reliable data regarding the safety of V. officinalis for pregnant or breastfeeding women. Multiple sources recommend against the use of this herb during pregnancy and it has been explored in China as a potential agent for inducing early pregnancy termination.

The toxicity of vervain extracts has been evaluated in various in vivo animal studies. In the research conducted by Jawaid et al., which focused on the antidepressant properties of V. officinalis leaf extracts, the researchers assessed the toxicity of the extract. They determined that the toxic dose for mice was 2 g/kg body weight, a level that did not result in any fatalities. Similarly, a study by Khan et al. investigating the anticonvulsant, anxiolytic, and sedative effects of V. officinalis revealed toxicity at even higher doses of 3 and 5 g/kg body weight. Notably, these doses also did not lead to the death of the tested rats, although a reduction in locomotor activity was recorded.

Application in Food Production

In 2010, the European Food Safety Authority (EFSA) published a scientific opinion that recognized V. officinalis, addressing health claims associated with various food products and ingredients. This opinion highlighted the herb's antioxidant activity, its role in safeguarding cells from premature aging, its antioxidant content, and its protective effects on DNA. The findings suggest that V. officinalis is capable of shielding cells and tissues from oxidative stress damage while enhancing the body's physiological resilience. Within the food industry, vervain is recommended as a flavoring agent, particularly in the manufacturing of beverages and alcoholic drinks.

Application in Cosmetology

V. officinalis products are predominantly employed in the field of cosmetology due to the presence of essential oil characterized by its unique scent. The European Commission's Cosmetic Ingredient Database (CosIng) identifies several raw materials suitable for cosmetic production: extracts from the green parts and flowers, which are approved for use as emollients and skin conditioners; extracts and floral water from the flowers, intended for skin conditioning; water from the flowers and leaves, which can be used as a flavoring agent and for skin conditioning; and oil and absolute derived from the leaves, sanctioned as a component in perfumes. The global cosmetics market offers a wide range of products containing V. officinalis, such as soaps, hair shampoos, body lotions, massage oils, and body scrubs.

Conclusion

The application of V. officinalis herb in contemporary phytotherapy is rooted in its historical utilization within folk medicine across various nations and its role in traditional Chinese medicine. Recent professional investigations into the biological properties of extracts derived from this herb substantiate its longstanding application in traditional phytotherapy. Furthermore, the latest research highlights additional potentially beneficial uses, including antioxidant, antimicrobial, anti-inflammatory, neuroprotective, anticancer, analgesic, and anticonvulsant properties. This research is being conducted in scientific institutions globally, including countries such as Germany, Austria, Spain, Turkey, Egypt, Ethiopia, Pakistan, India, Japan, China, and Poland. The growing interest in V. officinalis is attributed not only to its widespread presence across all continents but also to its significant medicinal attributes. The herb's well-documented and diverse chemical composition—comprising iridoids, phenylpropanoid glycosides, flavonoids, terpenoids, phenolic acids, and essential oils—contributes to its therapeutic efficacy. Currently, V. officinalis is officially recommended for treating respiratory ailments, including colds, fever, chest tightness, bronchitis, asthma, whooping cough, and sinusitis, as well as nervous system disorders such as stress, anxiety, depression, chronic fatigue syndrome, nervous exhaustion, insomnia, sexual neurosis, and headaches. Additionally, it is indicated for digestive issues like abdominal colic, jaundice, gallbladder inflammation, and intestinal worms, as well as urinary tract conditions such as urinary stones, infections, and reproductive system disorders like dysmenorrhea. Moreover, V. officinalis extracts may be applied topically for wounds, insect bites, oral and throat inflammation, muscle spasms, and rheumatic conditions.

A significant portion of scientific investigations concerning V. officinalis has concentrated on phytochemical analyses. Extensive studies have been conducted on the chemical composition of extracts derived from various parts of the plant, including its essential oil. Researchers have examined a range of extracts, such as methanolic, methanolic, ethyl acetate, chloroformic and those obtained through supercritical carbon dioxide extraction . These investigations have demonstrated that variations in chemical composition are influenced by the plant's origin, the specific part being studied, the extraction methods employed, and the use of solvents with differing polarities.

Numerous researchers have examined the significant pharmacological attributes of plant extracts, including those derived from herbs, leaves, and roots, highlighting their antibacterial, and antioxidant properties. Nonetheless, existing studies do not definitively identify which specific component is accountable for each activity. It is essential that future investigations concentrate on linking the mechanisms of biological activities to particular compounds.

Research has also been conducted in vivo using mouse and rat models. These studies have demonstrated various activities, including antitumor and immunostimulating effects, anti-inflammatory properties, cicatrization, gastroprotective effects, anxiolytic and sedative actions, analgesic effects, anticonvulsant properties, sleep promotion, and antidepressant effects. Our review of the scientific literature revealed only one study involving vervain extracts in human subjects, which was a comprehensive multicenter clinical trial focusing on patients with chronic generalized gingivitis. The contemporary uses of V. officinalis are rooted in its extensive traditional applications. Nevertheless, further assessment is necessary to determine the effectiveness, potency, and appropriate dosages of both the plant material and its extracts. Additionally, certain uses recognized in folk medicine, such as antispasmodic, diuretic, and antipyretic activities, as well as applications related to the respiratory system, including expectorant and secretolytic effects, and digestive system disorders like diarrhea, dysentery, stomach pain, and intestinal worms, still require scientific validation.

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