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Review of the Ethnopharmacology, Phytochemistry, and Pharmacology of the *Veronica officinalis*, An update (2020-2024)

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ABSTRACT

The present article offers an extensive examination of Veronica officinalis, a perennial herbaceous plant renowned for its medicinal significance in traditional medicine. From ethnopharmacology to pharmacology, recent research findings from 2020 to 2024 are synthesized, illuminating the diverse therapeutic properties of this botanical species. Known colloquially as speedwell, V. officinalis has been integral to Balkan traditional medicine, addressing a spectrum of conditions such as liver, kidney, and bladder disorders, as well as snakebites and skin lesions. Recent studies have underscored its antioxidant, antimicrobial, anti-neoplastic, and anti-inflammatory attributes, indicating its potential in addressing contemporary healthcare challenges. Analysis of its chemical composition reveals bioactive compounds pivotal to its pharmacological efficacy. By elucidating the therapeutic potential of V. officinalis, this review aims to advocate for its utilization as a natural remedy and stimulate further exploration into its applications within modern healthcare paradigms.

Introduction

Among the various creatures with medical significance, plants are notably prominent, with Veronica officinalis standing out as one of the beneficial genera. *V. officinalis* belongs to the Plantaginaceae family. *V. officinalis*, a member of this genus, is a perennial herbaceous plant [Figure1](1). The genus *Veronica* is predominantly found in regions characterized by a Mediterranean climate, spanning from sea level up to high alpine regions (2) and they can be found flourishing in both damp and arid habitats (3).

The utilization of *V. officinalis* in traditional medicine can be attributed to the specific phytochemical constituents of the studied species (4).

In this review, we provide an updated overview of *V. officinalis*, encompassing ethnopharmacology, phytochemistry, and pharmacology from 2020 to 2024. We emphasize its diverse medicinal attributes, synthesizing recent findings to deepen understanding of the plant's therapeutic potential and implications for contemporary healthcare practices[Figure2].

Results

The rule of V. *officinalis* in traditional medicine

V. officinalis, a plant studied herein, holds a significant place in the traditional medicine of Balkan communities. Mocan et al. conducted research revealing antioxidant properties in ethanol extracts of phenolic compounds from *V. officinalis*, measuring at 157.99 ± 6.58 mg Trolox equivalents/g d.w (5). Similarly, Valyova et al. affirmed antioxidant activity in phenolic extracts of *V. officinalis* in their investigation (6). The aerial parts of speedwells find application in treating various ailments including liver, spleen, kidney, and bladder disorders, as well as in addressing snakebites, facilitating wound healing, and managing skin lesions, eczema, and ulcers (7,8,9).

Anti-bacterial

Despite advancements in controlling bacterial illnesses, the rise of drug-resistant bacteria and the emergence of new pathogenic strains continue to pose challenges, prompting the urgent need for novel antibiotics. Throughout history, plants have been utilized for treating infectious diseases, indicating their potential in this regard. Scientific studies have validated the therapeutic properties of medicinal plants in combating such infections. Hence, exploring the medicinal properties of plants presents a pragmatic strategy for identifying new antibacterial agents to address significant public health concerns(10,11).

Nazlić et al. conducted a study where ethanolic extracts obtained from *V. officinalis*, *V. teucrium*, and *V. orchidea* displayed significant antibacterial activity against Gram-positive bacterial pathogens, including diverse strains of *Listeria* spp. and *Bacillus cereus*(12). This observed susceptibility is linked to the distinct cell wall structure of Gram-positive bacteria, contrasting with the complex outer membrane found in Gram-negative bacteria. This structural disparity affects compound uptake into the cells and simultaneously bolsters their multifaceted efflux pump system (13,14,15).

In a study conducted by Rajakumar et al., it was found that *V. officinalis* demonstrated significant antimicrobial activity against various pathogens. The study involved obtaining microbiological samples from root canals undergoing retreatment and culturing them on selective media for 24 hours to cultivate specific bacterial species. Methanolic extracts of plants were then prepared and stored at 4°C until required. The susceptibility of endodontic bacteria to these extracts at varying concentrations was evaluated using the disc diffusion method, with the inhibition zone diameters measured. Minimum inhibitory concentration (MIC) and Minimum bactericidal concentration (MBC) were determined to pinpoint effective plant concentrations against resistant bacteria. The tests were performed in triplicate, and the average results were statistically analyzed using one-way ANOVA in SPSS version 20.0 to assess the inhibition zones of the herbal extracts against the microbiota. However, it exhibited resistance (R) against *E. faecalis* and *S. aureus* at lower concentrations. The MBC for S. aureus was determined to be 637.5 mg, while no bactericidal effect was observed against E. faecalis. Nevertheless, the plant showed potential inhibition against S. mutans, which could be attributed to differences in cell membrane permeability and cell wall structure. The reduced microbial activity and efficacy of *V. officinalis* might be attributed to factors such as the potential inactivation of active components during extraction processes, or variations in the concentration levels of active ingredients due to geographical location and cultivation methods. This study stands out as the first report on the antimicrobial properties of *V. officinalis* species. The MIC of *V. officinalis* extract against *Staphylococcus aureus* and *Streptococcus mutans* is 212.5, while for *Enterococcus faecalis*, it is 425. This suggests

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Figure 1. This image showcases Veronica officinalis in its natural habitat.

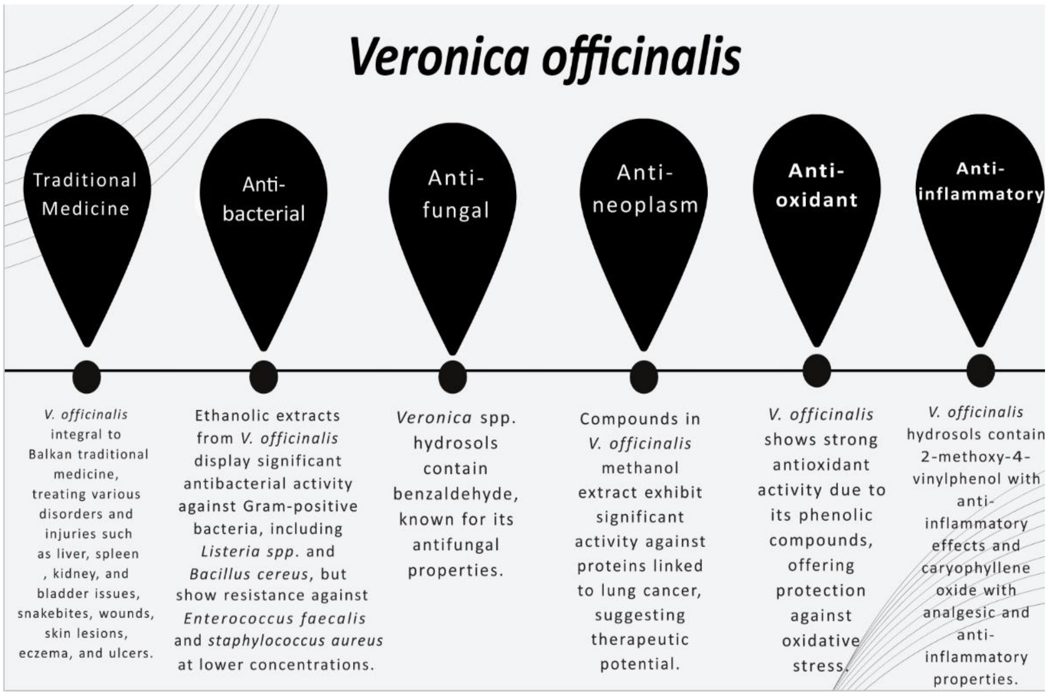

Figure 2. Summary of Properties and Uses of Veronica officinalis.

that the extract is effective in inhibiting the growth of these bacteria, with a lower concentration needed for S. aureus and S. mutans compared to *E. faecalis* (16).

Anti-fungal

Fungal infections present a diverse array of challenges to human health, spanning from minor skin conditions to life-threatening systemic illnesses. The extent and impact of these infections are influenced by both the specific type of fungus involved and the strength of the patient's immune system. Despite notable advancements in the development of new and effective medications, the persistence of drug resistance and other obstacles continue to pose significant challenges in treatment protocols. Consequently, there has been ongoing exploration into the potential of

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different herbal compounds for the management of fungal infections(17,18).

In the research conducted by Nazlić and colleagues, free volatile compounds (FVCs) were isolated from the aqueous fractions (hydrosols) of 10 Croatian *Veronica* spp. obtained by hydrodistillation and microwave-assisted extraction. They highlighted that benzaldehyde stands out as the simplest and most widely utilized aromatic compound known for its antifungal properties(19).

Anti neoplasm

Cancer is characterized by the unrestricted proliferation of cells, leading to the formation of tumors within the body(20,21). Cancer is a serious and potentially life-threatening condition. While various drugs and treatment methods are utilized to address it, there can be risks associated with these treatments. When conventional approaches fail to yield desired results, individuals may explore alternative methods. There's been an increasing interest in natural remedies, with some compounds derived from plants showing promise in combating tumors. Examples include vincristine, vinblastine, paclitaxel, and epipodophyllotoxins, all sourced from plant extracts and known for their anti-tumor properties(22,23).

In the study by Tüzün et al., it was found that Cyclododecane and 2,6-Dimethyl-3-(methoxymethyl)-pbenzoquinone, which were identified in the methanol extract of *V. officinalis*, exhibit significant activity against proteins associated with lung cancer. These compounds showed greater efficacy compared to other molecules investigated in the study. This suggests that these specific compounds could be valuable in targeting lung cancer proteins for therapeutic interventions (24). In this study, the Maestro Molecular modeling platform by Schrödinger (25,26) was utilized for conducting calculations. Various modules, including protein preparation (27,28), LigPrep (29,30), and Glide ligand docking (31,32), were applied in the molecular docking calculations. The OPLS4 method was employed for all calculations, providing a comprehensive approach to explore potential interactions between the investigated molecules and antioxidant proteins (33).

In the study conducted by Vrca et al., it was noted that while the essential oil (EO) of *V. officinalis* exhibited no antiproliferative activity at the tested time points (4, 24, 48, and 72 hours), the hydrosol (HY) of *V. officinalis* demonstrated significant antiproliferative effects on MDA-MB-231 and T24 cancer cell lines. Specifically, the *V. officinalis* HY showed notable antiproliferative activity on MDA-MB-231 cells after 48 and 72 hours, with IC_{50} values of 34.28% and 25.44%, respectively. Moreover, after 24, 48, and 72 hours, it displayed antiproliferative effects on the T24 cancer cell line with IC_{50} values of 21.83%, 13.41%, and 15.22%, respectively. These findings suggest the potential of *V. officinalis* HY as an effective agent against cancer cell proliferation. The hydrosol (HY) derived from *V. officinalis* exhibited apoptotic effects on the T24 cancer cell line, resulting in early apoptosis rates of 5.41 ± 0.83% and late apoptosis rates of 0.95 ± 0.22%. Microwave-assisted extraction (MAE) was utilized to extract volatiles in this study, offering a more efficient alternative to traditional hydro-distillation methods. The shortcomings of hydrodistillation, including high temperatures and prolonged extraction durations leading to compound decomposition, were addressed by employing MAE. Unlike microwave distillation, which occasionally isolates only a few components, MAE emerged as a superior technique due to its speed, ease of operation, and environmental friendliness. Moreover, MAE requires less energy compared to conventional extraction methods, facilitating the extraction of bioactive components effectively (34). The article by Batjargal, focuses on evaluating the anti-cancer pharmacological effects of Gurgem-7, a traditional Mongolian prescription(35).

Antioxidant

In aerobic cells, various redox processes generate oxidants and radicals that are

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exceptionally reactive and harmful to healthy cells. These substances have the potential to induce damage to the structure of DNA and proteins if left unchecked. To mitigate these detrimental effects, the body relies on antioxidants, which effectively neutralize free radicals and detoxify the system. Plant-based sources, along with products derived from them, encompass a diverse range of phytochemicals, including antioxidants. These compounds are thought to play a crucial role in reducing the risk of oxidative stress-related diseases by counteracting the harmful effects of oxidants and free radicals(35,36).

In the study conducted by Nazlić et al., the antioxidant activity of volatile compounds extracted from hydrosols was assessed using two methods: Oxygen Radical Absorbance Capacity (ORAC) and 2,2-diphenyl-1-picrylhydrazyl (DPPH) radical scavenging assay. Both Clevenger and microwave-assisted hydrodistillation techniques were employed to extract the hydrosols, and the antioxidant activity was evaluated accordingly. Notably, *V. officinalis* exhibited the highest antioxidant activity in terms of ORAC values for both extraction methods, with values of 217.54 ± 14.98 µmol TE/mL for Clevenger extraction and 359.9 ± 44.40 µmol TE/mL for microwave extraction(19). Results for the DPPH antioxidant activity method also showed that *V. officinalis* hydrosol has the highest activity, for both extraction methods. Besides this species, higher antioxidant activity showed *V. acinifolia*, *V. arvensis*, and *V. cymbalaria* for Clevenger-extracted hydrosols. In microwave-assisted extracted hydrosols, *V. cymbalaria* showed higher activity than other tested species, alongside *V. officinalis*. *V. officinalis* showed the highest antioxidant activities in both methods with an IC50 of 4.43 ± 2.44 (for Clevenger) and 3.70 ± 1.35 (for microwave-assisted extraction) mg/ml, respectively. *V. officinalis* is known that this species has been used in folk medicine for a long time and many studies support its biological activity. This activity could be due to the relatively high content of phenolic compounds and the group of acids, esters, and alcohols (19).

Anti-inflammatory

Inflammation is the body's natural response to harmful stimuli, serving as a protective mechanism and signaling the initiation of the healing process. The term "anti-inflammatory" refers to substances or treatments capable of reducing inflammation(37).

In Nazlić et al.'s research, the compound 2-methoxy-4-vinylphenol was detected solely in the hydrosols of *V. officinalis*, regardless of the extraction method employed, with a consistent concentration of 11.12%. This phenolic element is noted for its varied biological attributes, with special attention drawn to its anti-inflammatory and analgesic qualities, particularly significant from a pharmacological viewpoint (19). In the composition of hydrosols from microwave-assisted extraction (MAE), caryophyllene oxide was detected in all isolates from MAE, in addition to the already mentioned β-ionone, which also dominates in the isolates from hydrodistillation. Preliminary pharmacological studies have shown that caryophyllene oxide administered intraperitoneally has analgesic and anti-inflammatory effects (19).

Chemical Composition of Essential Oil and Hydrosols of V. *officinalis*

In the research conducted by Vrca et al., it was observed that in the essential oil (EO) of *V. officinalis*, heptacosane emerged as the most prevalent compound, constituting 17.21% of the composition. Additionally, phytol and hexadecanoic acid were notably present in the EO composition. In contrast, in the hydrosols (HY) of V. officinalis, methyl eugenol was identified as the predominant compound, comprising 22.01% of the composition. Following methyl eugenol, (E)-β-damascenone and β-ionone were also prominent, with an identification percentage exceeding 14%(34).

In the study by Nazlić et al., the research found that *V. officinalis* hydrosols obtained through hydrodistillation contain the highest percentage (13.78%) of β-ionone among the

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identified volatile compounds. Additionally, in hydrosols obtained through microwave-assisted extraction (MAE), β-ionone (17.78%), caryophyllene oxide (15.91%), and (E)-β-damascenone (11.34%) were identified as dominant compounds in the composition of *V. officinalis*. Moreover, the phenolic compound 2-methoxy-4-vinylphenol was exclusively isolated in *V. officinalis* for both extraction methods, with a consistent percentage of 11.12% (19).

Other

In Nazlić et al.'s research, it was observed that polyphenols, natural compounds present in plants, serve to safeguard the plant from ultraviolet radiation and pathogenic threats. These polyphenols are recognized for their potent antioxidant capabilities and their potential to combat neurodegenerative diseases and cancer, making them a common inclusion in the diet (38, 39).

Conclusion

The extensive body of research presented underscores the multifaceted therapeutic potential of *V. officinalis*, a plant deeply rooted in traditional medicine practices across various cultures. Studies have revealed its diverse pharmacological properties, ranging from antioxidant and antimicrobial to anti-neoplastic and anti-inflammatory effects. Notably, *V. officinalis* extracts have demonstrated significant antibacterial activity against a spectrum of Gram-positive pathogens, shedding light on its potential as a natural source for novel antibiotic agents. Moreover, its efficacy against fungal infections and cancer cell proliferation further highlights its versatility in addressing complex health challenges.

The antioxidant prowess of *V. officinalis*, as evidenced by its high ORAC values, underscores its utility in mitigating oxidative stress-related diseases. Additionally, its anti-inflammatory attributes, particularly attributed to compounds like 2-methoxy-4-vinylphenol, position it as a promising candidate for managing inflammatory conditions. The chemical composition analysis of *V. officinalis* essential oil and hydrosols provides valuable insights into its bioactive constituents, further elucidating its pharmacological mechanisms.

In conclusion, the comprehensive exploration of *V. officinalis* reaffirms its status as a botanical powerhouse with profound implications for human health. By harnessing its medicinal properties, we stand to unlock novel therapeutic avenues and address pressing public health concerns, thereby paving the way for enhanced healthcare practices grounded in nature's bounty.

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Conflicts of interest

The authors declare no conflict of interest.

Authors' contributions

All authors were involved in the drafting of the manuscript and revising it critically for intellectual content, approved the final version for submission, and agreed to be accountable for all aspects of the work.

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