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REVIEW PAPER

Valeriana officinalis – a review

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ABSTRACT

Introduction and aim. *Valeriana officinalis* has been recognized in traditional medicine and used since ancient times for a variety of health ailments. It is mainly appreciated for its sedative and sleeping properties. Currently, scientists are conducting numerous studies on the exact chemical composition of valerian and the properties they carry in the human body.

Material and methods. This paper presents a narrative review on valerian.

Analysis of the literature. The desire to summarize information on the uses and properties of *V. officinalis* is presented. *V. officinalis* exhibits sedative, sleep-inducing and antidepressant properties. Studies show broad effects on the human nervous system, for example, reducing stress.

Conclusion. By discovering new properties of valerian, its properties are expanding significantly day by day. Its main use is primarily in the treatment of sleep disorders and nervous system disorders. However, it is also used in headaches, depression, anti-cancer therapy, urinary and digestive disorders. More and more people are turning to valerian as an alternative to drugs that have more side effects.

Keywords. insomnia, valerian, valeriana, *valeriana officinalis*

Introduction

Valeriana officinalis was used as early as in ancient Greece and Rome by Galen and Hippocrates to treat various ailments such as digestive problems and urinary tract diseases, but also in the 16th century for accelerated heartbeat, headaches and nervousness (Fig. 1). According to the WHO, "Traditional medicine is used in the maintenance of health as well as in the prevention, diagnosis, improvement or treatment of physical and mental illness" (WHO, 2000).

The word valerian comes from valere (Latin), which translates as "to be in good health".[1] Over 200 different species of valerian are known worldwide. The most common in Europe and North America is *V. officinalis*, which is also known as valerian in colloquial speech. Valerian essence is obtained from the roots of this plant.[2] Nowadays, valerian is commonly used as a sleep aid and stress reliever.[1] This natural extract is often prescribed and recommended for sleep disorders. Insomnia, which affects more and more people in modern society, is a sleep disorder in which patients have difficulty falling asleep and staying asleep. The role of sleep is not completely understood. We know that it has a key function in the body's physiological processes, recovery and mood.[3] This problem affects approximately 30% worldwide.[4] In the treatment of insomnia, mainly sedative-hypnotic drugs are used. However, due to their numerous side effects they are very often replaced by herbs, which are a good alternative to the adverse effects of drugs.[2] This medicinal herb has sedative, hypnotic and anxiolytic effects that are supposed to improve the process of falling asleep and relieve tension in the

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nervous system.[2,5] Mirzaee et al. in 2015 in their study also proved the effectiveness of valerian in migraine headaches.[6] Serotonergic effects similar to antidepressants have also been seen.[7] Researchers have been interested in the potential of valerian in cancer therapy. They believe it may affect cancer cell death.[8] Side effects of valerian are rare, mostly mild and short-lived. These mainly include dizziness or nausea.[1] However, the U.S. Food and Drug Administration recognized valerian as "generally safe" for use.[9] According to the European Medicine Agency, valerian root essence relieves nervous tension and sleep disorders.[2]

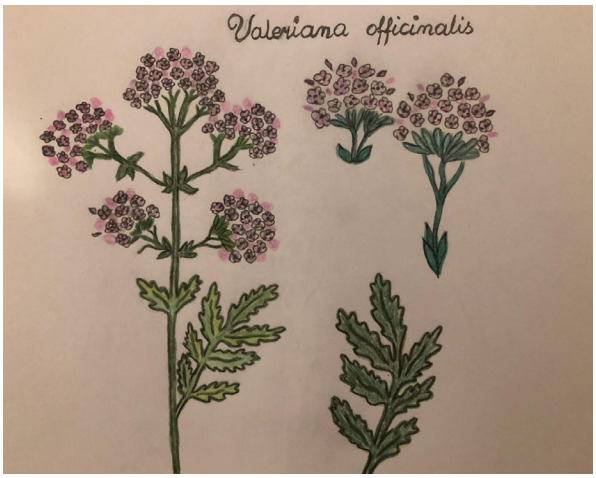

Fig. 1. *Valeriana officinalis*

Aim

The purpose of the article was to provide an overview of *Valeriana officinalis*.

Material and methods

This article is a review to discuss the latest progress made in *Valeriana officinalis* research. Scientific articles were reviewed by searching for information on valerian using the online database with scientific articles, including PubMed, Google Scholar and other available scientific databases. The following keywords were used to search for scientific articles: *Valeriana officinalis*, valerian, valeriana. Table 1 shows the steps of the literature review.

Table 1. Stages of literature search

Search stages	Search phrases
1	MeSH: *valeriana officinalis*, valerian, valeriana, *in vivo, in vitro*
2	Peer-reviewed articles
3	Available abstract

A literature review includes 47 selected scientific articles, published since 2004. Older articles were excluded due to presenting only the latest reports and knowledge base about *V. officinalis*. The exclusion criteria were taken into account when selecting the appropriate items shown in Table 2.

Table 2. Exclusion criteria used for the analysis

Exclusion criteria
– Languages of papier other than Polish, English and French
– Date of publication: published below 2004
– A short paper without details
– Unable to data extract

At the initial stage, 1057 publications were identified. Subsequently, after removal of duplicates, (n=1004) articles remained. Articles (n=887) were rejected at the inclusion and exclusion criteria stage. Articles (n=117) meeting the conditions were selected, and further (n=70) articles were rejected at the detailed analysis stage. By subjecting them to detailed analysis, finally (n=47) scientific papers were extracted. The process of reviewing the articles is shown in the PRISMA 2009 Flow diagram.

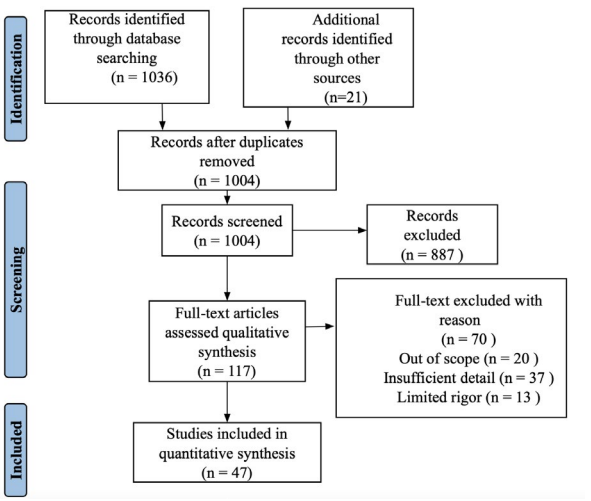

Fig. 2. PRISMA 2009 flow diagram

Analysis of literature

Chemical composition

V. officinalis has several biochemical components that act together to develop the full effectiveness of *V. officinalis*. Some of the main components are being listed below (Tab. 3):

Gamma-aminobutyric acid (GABA) is a nonstandard amino acid which is an amino acid that has undergone a chemical modification after the translational process. It affects the central nervous system as an inhibitory neurotransmitter that controls neurophysiological functions.[17] Studies have shown that higher levels of GABA in the body reduces anxiety and promotes relaxation. GABA acts when it enters the synaptic

cleft to bind on postsynaptic GABA receptors. Two major postsynaptic GABA receptors can be found on the postsynaptic neuron. The ionotropic receptors and metabotropic receptors. The binding of GABA to the ionotropic receptors, also called GABA-A receptor, opens channels so negatively charged chloride ions can enter. This results in a hyperpolarized cell and thus inhibits the creation of action potential. The binding of GABA to the metabotropic receptors, also called GABA-B receptor, leads to the exit of positively charged potassium ions in the cell through the potassium channels which also results in hyperpolarized cells and inhibits the conduction of action potential.[18,19] Simplified can be said that due to the binding of GABA and the receptors, action potential of neurons are being inhibited and this in return reduces the neuron excitability. So if there is not enough GABA in the body or if the binding process does not take place correctly, patients often suffer from diseases like epilepsy, anxiety, movement disorders and insomnia.[17,18,20]

Table 3. Classification of chemicals found in *V. Officinalis*

Chemical composition	
Gamma-amino-butyric acid	A neurotransmitter with inhibitory effects throughout the nervous system.[10]
Valepotriates	A group of unstable iridoids, exert a regulatory effect on the autonomic nervous system.[11]
Sesquiterpenes	Colorless lipophilic compounds.[12]
Flavonoids	A group of organic chemical compounds found in plants that act as dyes, antioxidants and natural insecticides and fungicides.[13]
Alkaloids	Complex organic molecules containing a heterocyclic nitrogen ring, which have been widely exploited for their diverse pharmacological properties.[14]
Triterpenes	Members of isoprenoids that are derived from a C30 precursor, squalene; the most abundant secondary metabolites present in marine organisms.[15]
Monoterpenes	A class of isoprenoids produced from geranyl diphosphate.[16]

Valepotriates: Is one of the active compounds in the extract of *V. officinalis*. This organic compound belongs to the group of esterified iridoids. Valepotriates have a sedative effect on the body, which is based on the increased release of the inhibitory neurotransmitter GABA. Examples for valepotriate are valtrate, didrovaltrate, and isovaleric acid. In which isovaleric acids are responsible for the smell of the plant.[21-23]

Sesquiterpenes: Are one of the main compounds in essential oil of valeriana. Sesquiterpenes belong to the group of terpenes that consist of fifteen carbon atoms (three isoprene units) which can be either acyclic or ring shaped. One of the components of sesquiterpenes is valerenic acid. Valerenic acid inhibits GABA breakdown and this in return leads to sedation.[24-27]

Flavonoids: are natural compounds with the function to control the activity of cells and to combat free radicals. Due to the antioxidant effect of flavonoids, free molecules can be destroyed which can be harmful for the body. Flavonoids are divided into six subgroups, based on the chemical structure flavones, flavanones, flavonols, flavan-3-ols, isoflavones, and anthocyanins.[28,29] Examples of flavonoids in valeriana are linarin and apigenin. Studies in which linarin was injected into the mice, had shown that linarin in *V. officinalis* has sedative and sleep induced effects. The actual mechanism of linarin in the brain has not been solved until today but it is assumed that sedative effects can amplify due to various combinations of linargin, hesperidin, valerenic acid and 6-methylapigenin.[30]

Alkaloids: Are organic compounds that contain nitrogen and have complex ring structures. They can act as poisoning, pain reliever or anesthetics, so the field of application of alkaloids is broad. Examples for alkaloids are actinide and valerine. For the synthesis of actinidine are the precursors lysine and quinolinic acid needed. Actinide belongs to the psychoactive group of alkaloids. It behaves agonistic in relation to benzodiazepine receptors and acts then on gamma-aminobutyric acid receptors so intracellular chloride can flow in. This process leads then to the inhibitory effect on the central nervous system.[23,31]

Triterpenes: Are chemical compounds that consist of three terpene units. Almost 200 different structures of triterpenes are known and they are being divided by the amount of rings that they contain. Triterpenes are used for their anti-inflammatory, antiviral and antitumoral effects. An example for triterpenes is ursolic acid. It inhibits the nuclear signaling of factor-kappa B in cancer cells, keeps inflammatory levels down and also increases the antioxidants in the brain, so stress on brain cells decreases.[32,33]

Monoterpenes: Belong to the class of terpenes with two isoprene units. Four different types of monoterpenes are known: acyclic, monocyclic, bicyclic and tricyclic, classified according to the shape. Monoterpenes show anti-inflammatory effects by regulating the increase of cytokine release. Furthermore, effects such as antiviral, antioxidant and antitumor have been observed. Examples for monoterpenes in *V. officinalis* are bornyl acetate, borneol. Bornyl acetate belongs to the group of bicyclic monomeres and it has already been used for skin care and natural antiseptic disinfectant. Anti-inflammatory effects such as suppressing the proinflammatory cytokines TNF-α and IL-1β release, which both are involved in the disease Atherosclerosis. Generally can be said that monoterpenes have a wide range of positive effects for the body.[34-36]

Valeriana officinalis in vitro on studies

Kara et al. evaluated oxidative stress and cytotoxicity on human hepatocellular carcinoma and human colorectal adenocarcinoma cell lines. The results showed that valerian root extract did not induce oxidative stress in HepG2 and Caco2 cell lines. Valerian is not an alternative for cancer treatment. But in tolerable concentrations, it can be recommended due to its property of not inducing oxidative stress.[8] De Brito et al. studied the interaction of valerian in cortical spreading depression and analyzed the protective effect against cytotoxic effects of rotenone in in vitro cultures of rat C6 glioma cells. *In vitro* studies on rat C6 glioma cells showed a protective effect against rotenone-induced cytotoxicity.[37] Shi et al. showed in their in vitro study that valerian extract reduces breast cancer cell proliferation. This could make valerian a therapeutic agent for breast cancer. The authors also suggest the potential effectiveness of valerian acid as an HDAC inhibitor.[38] Hellum et al. in their work on *in vitro* cells, they presented the effect of valerian on mechanism-based inhibition of CYP2D6 activity. The study demonstrated the action of valerian components as inhibitors on CYP2D6 enzyme activity. However, they note that this type of inhibition is irreversible, making it impossible to ignore the deleterious or toxic responses of valerian action in in vivo studies.[39] Hellum et al. presented the effect of valerian on CYP activity in human hepatocytes. In the results, we see that statistically significant inducing properties on CYP2D6 and CYP3A4 were found. The researchers suggested in their work that valerian is one herb whose data may be clinically relevant in future in vivo CYP studies.[40] In a subsequent study, the same authors evaluated the effect of the induction potential dose of commercially used herbal products on the metabolic activity of CYP2C19 and CYP2E1 in human hepatocyte cultures. In the case of valerian, the results showed that it is a weak inducer of CYP2C19 and in the case of CYP2E1 it did not show inducing properties.[41] Lefebvre et al. investigated the in vitro effects of products containing valerian root extracts on the metabolism and transport of P-glycoprotein via the cytochrome P450 CYP3A4 pathway. The results showed that valerian extracts have the ability to inhibit metabolism through the cytochrome P450 3A4 pathway and transport by P-glycoprotein.[42]

Valeriana officinalis in vivo on studies

Sudati et al. conducted an in vivo study on flies evaluating protection against the harmful effects of rotenone. The results confirmed the effectiveness of valerian in reducing rotenone-induced toxicity in *Drosophila melanogaster*. These authors also suggest the usefulness of the results obtained in future studies of movement disorders such as Parkinson's disease.[43] Bogacz et al. conducted an in vivo study of the effects of compounds in valerian root on CYP3A4 gene expression, as well as on nuclear receptors PXR, CAR, RXR, GR, and HNF-4a in male rats. The results showed decreased expression levels of CYP3A1 (homolog of human CYP3A4), RXR, and HNF-4a and increased for CAR. The data show an effect on decreasing CYP3A4 expression. They suggest further in vivo studies in evaluating the safety of pharmacotherapy by the possibility of interaction with synthetic drugs metabolized by this enzyme.[44] Benke et al. in their in vivo studies in mice, showed that neurons expressing GABA(A)-containing beta3 receptors are a major cellular substrate for the anxiolytic effects of valerian extracts.[45] Torres-Hernández et al. through the data obtained in an in vivo study using zebrafish larval swimming behavior, demonstrated the high psychoactivity of valerian extract with respect to a behavioral-molecular approach.[46] Dimpfel in his study, he used rats with implanted electrodes and monitored EEG wave frequencies and then administered valerian root extract in one of the test groups. Results compared to a matrix of synthetic drugs showed that valerian exhibited effects similar to physiological sleep. The changes that occurred resembled natural sleep and may suggest the effectiveness of valerian in acting on health.[47]

Conclusion

V. officinalis commonly known as herb is a very common species, accompanying us since ancient times. Over the centuries its composition, chemical properties, and effects on the human body have been studied in order to use it in herbal medicine as a sedative, anti-depressant, and sleep inducer. A single oral dose of *V. officinalis* modulates intraventricular facilitatory circuits by acting as an anti-anxiety agent. Other, lesser known applications of valerian should not be overlooked either, such as its diuretic and cognitive enhancing properties. The various substances contained in valerian provide a broad spectrum of the plant's medicinal properties. It is a good option for treating insomnia, which nowadays affects more and more people, and for relieving nervous tension connected with stress. Scientists have confirmed numerous aspects of valerian and its positive effects on the human body in their studies. Of particular value here is the GABA content, which inhibits the action potential of neurons, reducing their excitability, and valepotriates, which increase the release of GABA. The rhizome and root are available in the form of capsules, tablets or alcoholic extracts, so everyone can choose the form that is most convenient for them. Valerian can also be consumed in the form of valerian honey, which has a pleasant taste. In pharmacies or herbal stores it appears under different trade names. Note that consumption of valerian also carries gastrointestinal side effects such as nausea and abdominal cramps.

Declarations

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Author contributions

Conceptualization, W.M. and D.A.; Writing – Original Draft Preparation, W.M. and D.A.; Writing – Review & Editing, W.M. and D.A.

Conflicts of interest

The authors declare no conflict of interest.

Data availability

Data supporting the results of this study shall, upon appropriate request, be available from the corresponding author.

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