

REVIEW ARTICLE

Antihypertensive, Antidepressant and Sedative Actions of Banafsha (*Viola Odorata*): A Review

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ABSTRACT

Viola odorata (Banafsha) is an important herb of Unani medicine. Banafsha is having more acceptability and compatibility with the human body. Due to its multiple therapeutic actions, Banafsha is used in different disease and disorders in human being. The plant is known to treat different systemic ailments due to the presence of phenolic compounds, triterpenes, sterols, resins, tannins, volatile oil, glycosides, flavonoids, saponins and anthocyanins. In Unani System of Medicine, the Banafsha is used in hypertension, depression, chronic insomnia, Dry cough, and as Demulcent, Laxative & Purgative etc. Different studies show *Viola odorata* as antihypertensive drug was tested on Guinea pig atria and rat aorta, and it was found effective. It was also found effective in depression as tested on mice; molecular docking results depict that compounds 1-3 can interact with 5HT₃, 5HT_{1A} and 5HT_{2A} receptors, and are more specific to the 5HT₃ receptor subtype. The findings of this study clearly suggest that compounds 1-3 possess antidepressant-like effects which might be mediated via the serotonergic system. The *Viola odorata* produce sleep in insomniac patients. They conducted study as an experimental pretest-posttest evaluation on VO efficacy in 50 patients with chronic insomnia in Iranian Traditional Medicine Clinic of Mashhad University of Medical Sciences, Mashhad, Iran. All patients are completing the questionnaire on Insomnia severity Index (ISI) before and after the completion of experiment. The result shows the improvement in the sleeping and ISI index of the patients ($p < 0.05$). Hence, study shows that the VO drop is safe, acceptable and effective drug in chronic insomnia. Many pharmacological activity mentioned in Unani medicine is validated and many activity needs further exploration owing to immense therapeutic scope in this drug.

Keywords: Banafsha, Pharmacological action, Unani system of medicine, *Viola odorata* Linn.

Received 04.04.2021

Revised 22.06.2021

Accepted 13.08.2021

How to cite this article:

I Ahmad, M Naseem, M Yasir, Q Shoeb, A Manyar, A Y Ahmed, P Mujahed. Antihypertensive, Antidepressant and Sedative Actions of Banafsha (*Viola Odorata*): A Review. Adv. Biores. Vol 12 [5B] September 2021. 406-411

INTRODUCTION

Current Studies shows that more than 60% of world's population relies on Herbal medicines. Herbal Medicines are having important role in treatment of diseases and disorders from last several centuries. As per WHO, More than three quarter of African and asian population uses Herbal medicines turnover worth 60 million USD. The worldwide demand of herbal medicines has increased in last few decades. Now a days, modern medicines uses different plant derived compounds (herbal medicines) as a basis for pharmaceutical drugs. Herbal medicines are also called as phytotherapy and phytomedicines. As per WHO, modern drugs in America contains 25% of herbs. In modern Pharmacopoeia, about seven thousands compounds are derived from plant. Currently 120 compounds derived from plant are used in

modern medicines. More than 80% of these drugs show same effect as observed from traditional plant derived substance. It is more beneficial to use herbal remedies in Diabetes, severe renal diseases (disease related to kidney), Cancer, Asthma and some skin infections. Herbal remedies are also applied and effective in European countries. In Germany, apothecaries dispense herbal drugs. Extract of herbal drugs, essential oils and herbal teas are also prescribed in Germany and other European countries. Herbal remedies are more popular in India, as Indian Government has constituted separate body i.e AYUSH (Ayurvedic, Yoga and Naturopathy, Unani, Siddha and Homeopathy). Standardization of herbal drugs is also carried out to determine the quality and quantity of herbal medicines. Standardization can be carried out by chromatographic techniques mainly thin layer chromatography and other techniques are also used to identify and quantify the herbal medicines. One of the important herbal medicines obtained from herbs is Banafsha plant. Banafsha is used as Unani and ayurvedic medicine since several years. It has number of pharmacological applications. The Banafsha is used in three varieties. Firstly herb i.e. flower, stem and leaves, secondly as dried flower i.e. Gul e Banafsha and third one is dried aerial part without flower i.e. Berg e Banafsha. The flower and other part of the plant are used as drug. [1-10]

The aim of current study is to explore the existing data about its pharmacological actions and uses especially in Unani System of Medicine.

Botanical Name: *Viola odorata* Linn.

Family: Violaceae

Regional Names:

English: Wood violet, Sweet violet, Common violet, Garden violet

Urdu/ Hindi: Banafsha, Banafsa, Vanafsha, Banaphsa.

Arabic: Banafsaj, Farfeer

Persian: Kokash

Marathi: Bagabanosa,

Tamil: Vayilethe, vayilettu, ratnapurus, Ratnapurucu,

Sanskrit: Banafsha, Banapsa, Vanaphsa, Vanspika. [11-20, 30]

Description: The *Viola odorata* (Gul-e-Banafsha) contains a violet color flower. It is branched, short, knotted and leaf-stalk and stipules. The branches are very thin, they arise from single root. Each branch contains one flower. Blue and sky blue flowers are common in this species. The flower can be white yellow or pinkish in color. The Kashmiri banafsha plant contains small size flowers. The whole plant i.e. flower, branches and leaves are used as drug. The flower contains sweet and attractive scent which is used in different cosmetic preparations like Perfumes, fragrances and spray. The plant grows from surface having height of half or one hand. The root is thick, knotty and dry. [21-29]

Mizaj (Temperament): According to holistic Unani concept the basic nature or temperament of this drug is Barid (cold) in first stage and Ratb (moist) in second stage. The pharmacological actions depend on this fundamental nature of plant.

Uses: It is used in hot cough (sualharr), irritation of urinary bladder (suzish-i mathana), pharyngitis (suzishwawaram-i-halaq), catarrh (zukam), coryza (nazla), diphtheria (khunaq), pleurisy (dhat al-janb), eczema (nar-i-farsi), ailments of infants (amrad-i- itfal), headache due to excessive heat (suda-harr), bilious diarrhoea (ishal-i safrawi). It is helpful in heartburn, reduces blood pressure, also helpful in headache, dry cough, conjunctivitis. It is used in the form of Decoction and infusion to treat cold, runny nose and cough. Almond oil and fresh flower of Banafsha in combination is used to treat constipation and cold. According to renowned Unani Pharmacologist, IbneBetar, Banafsha induces sleep moderately. It reduces excess heat and dryness of all the body organs. Nilofar, Gaozaban and Aslussus may be considered as its alternative in these functions. (30)

Adverse effects: Although commonly adverse effects are not observed clinically but following are mentioned old literature: Nausea, indigestion, Vomiting, palpitation, weakens the appetite, restlessness. (30)

REPORTED PHARMACOLOGICAL ACTIVITIES:

Antihypertensive Activity:

Siddiqi et al. studied about the *in vivo* and *in vitro* study of *Viola odorata* Linn, Pharmacological effects like antihypertensive action of *Viola odorata* were studied. The effect of *Viola odorata* leaves extract (Vo.Cr) was observed on Atria of Guinea pig. It inhibits the rate and force of contraction of atria. The plant extract contains Phenolics, Saponins, Flavonoids, Alkaloids, Coumarins and Tannins. The extract of *Viola odorata* plant shows phentolamine sensitive vasoconstriction on thoracic aortae of Rat. The plant extract shows a

rightward shift of Ca⁺⁺ concentration-response curves as well as suppression of PE (1 μM) control peaks in Ca⁺⁺-free medium and also caused a concentration-dependent relaxation, similar to that caused by verapamil. The relaxation curve while observing the effects of Plant Extract (Extract of *Viola odorata*) showing partial inhibition, which involves Nitric oxide (NO) mediated pathway, in presence of L-NAME. (31)

Ali H Eid *et al* studied about *Viola odorata* as anti-hypertensive drug. The drug was tested on guinea pig atria and rat aorta. The drug was administered in a dose of 0.39mg/ml and 0.40 mg/ml. It observes the increase in the nitric oxide level (NO) which causes vasodilatation hence producing antihypertensive effect (32). Duke *et al* studied about antihypertensive activity of *Viola odorata* and *viola tricolor*. (33)

Ilkay Erdogan Orhan *et al.* performed experiment on inhibitory potential of the dichloromethane, ethyl acetate, ethanol, and aqueous extracts of *Viola odorata* L. (VO) was investigated against tyrosinase (TYR) and cholinesterases by microplate assays. The antioxidant activity was tested using six *in vitro* assays. Only the ethanol extract inhibited TYR (80.23 ± 0.87% at 100 μg mL), whereas none of them were able to inhibit cholinesterases. The extracts were more able to scavenge NO radical (31.98 ± 0.53–56.68 ± 1.10%) than other radicals tested, and displayed low to moderate activity in the rest of the assays. HPLC analysis revealed that the aqueous extract of VO contained a substantial amount of vitexin (18.81 ± 0.047 mg g extract), while the ethanol extract also possessed rutin (1.31 ± 0.013 mg g extract) and vitexin (4.65 ± 0.103 mg g extract). Furthermore, three flavonoids (rutin, isovitexin, and kaempferol-6-glucoside) were isolated from the ethanol extract. This is the first report on TYR inhibitory activity of VO as well as presence of vitexin and isovitexin in this species. (34)

Kandpal Asheesh *et al* studied about Vasodilatation effect of the *Viola* plant extract. It is mediated through multiple pathways like inhibition of Ca⁺⁺ influx via membranous Ca⁺⁺ channels, its release from intracellular stores and Nitric Oxide-mediated pathways, which possibly explain the fall in Blood Pressure. The plant also showed antidiabetic effect and reduction in body weight which may be due to the inhibition of synthesis and absorption of lipids and antioxidant activities. Thus, this study provides a pharmacologic rationale to the medicinal use of *Viola odorata* in hypertension and dyslipidemia. (35)

Khalid Hussain Janbaz *et al* performed experiment on Rabbit aorta. The drug exert relaxant effect on phenylephrine (1 μM)- and K⁺ (80 mM)-induced contractions in isolated rabbit aortic preparations. The *V. odorata* crude extract on application to isolated rabbit aortic preparation, exerted relaxant effect on phenylephrine (1 μM)-induced contractions in isolated rabbit aortic preparations up to the extent of 5 mg/mL tissue bath concentrations with EC₅₀ values of 5.37 mg/ mL (95% CI: 3.97-6.65 mg/mL; n=5), whereas K⁺ (80 mM)-induced contractions in isolated rabbit aorta were relaxed at lower tissue bath concentrations with EC₅₀ values of 1.5 mg/mL (95% CI: 0.34-6.66 mg/mL; n=5). The standard Ca²⁺ channel blocker (verapamil), relaxed the phenylephrine (1 μM) and K⁺ (80 mM)-induced contractions with respective EC₅₀ of 1.08 mg/mL (95% CI: 0.08-2.52; n=5) and 0.55 mg/mL (95% CI: 0.04-2.10; n=5). Thus, the drug providing rationale for its folkloric uses to treat hypertension. (36)

Antidepressant activity:

Nasiarakarim *et al* studied about Antidepressant potential of novel flavonoids derivatives from sweet violet (*Viola odorata* L). The *Viola odorata* has been used in the treatment of neuropsychiatric disorder. The present study was performed to isolate phyto constituents including three flavonoids 5,7,4'-trihydroxy-3',5'dimethoxyflavone, 5,7- Dihydroxy-3,6-dimethoxyflavone and 5,7,4'-trihydroxy- 3'-methoxyflavone from the whole plant of *Viola odorata* Linn and to investigate the antidepressant-like effects of these compounds and their possible mechanism of action using antagonists of the dopaminergic, serotonergic and adrenergic system.

Classical animal models of depression were used to evaluate anti-depressant activity. The models used were forced swimming Test (FST) and Tail Suspension Test (TST). The mice were used to evaluate the aforesaid activity. The mice were divided into various groups and were administered with either fluoxetine (FLX), vehicle control or test compounds 1-3 intraperitoneally (i.p.). For experiments involving mechanism determination, mice were pre-administered with 5-HT, dopamine and adrenergic antagonists. The brain 5-HT levels were determined following FST. To determine the binding affinity of compounds 1-3 to serotonergic receptors, the molecular docking studies were carried out. The results indicated that compounds 1-3 at the dose of 1-30 mg/kg, intraperitoneally significantly decreased the immobility time in the forced swimming Test (FST) and Tail Suspension Test (TST) in mice. The reduction in immobility time was reversed by pre-treating the mice with 5-HT receptor antagonists including WAY100635 (5-HT_{1a} antagonist) and pCPA (5-HT synthesis inhibitor) 100 mg/kg intra-peritoneally, Ondansetron (5-HT₃ antagonist) and ketanserin (a 5-HT_{2a} antagonist) but not with prazosin (α₁-adrenergic antagonist) and haloperidol (D₂ dopaminergic antagonist) or SCH23390 (D₁ dopaminergic antagonist). Furthermore, in neurochemical assays, as compared to vehicle, compounds 1-3 cause a significant increase in the 5-HT level

in the brain tissue. These increases were reversed in the mice groups pretreated with pCPA. Moreover, molecular docking results also depict that compounds 1-3 can interact with 5HT₃, 5HT_{1A} and 5HT_{2A} receptors, and are more specific to the 5HT₃ receptor subtype. In conclusion, the findings of this study clearly suggest that compounds 1-3 possess antidepressant-like effects which might be mediated via the serotonergic system.(37)

Bakhshaei S. *et al.* studied about *Viola odorata* (Sweet violet) is an herbal plant from the Violaceae family. It is native to Asia and Europe and also introduced to North America and Australia. In traditional Iranian folk medicine it has been used to treat depression respiratory ailments, congestion, sore throat, insomnia, anxiety blood pressure as well as coughs. Sweet violet contains glycoside, mucilage, methyl salicylate as well as alkaloid. Based on recent studies, the main compounds in the Violet's leaves are glycoside of salicylic acid that has been used for to treat body pains and headaches. Also, Violet's flower has been used as an antidepressant, anti-insomnia laxative, lipid-lowering, anti-inflammatory, blood pressure lowering and anti-septic treatment.(38)

In Chronic Insomnia:

FarhadJafari et al studied about use of traditional medicines in chronic insomnia. The *Viola odorata* produce sleep in insomniac patients. They conducted study as an experimental pretest-posttest evaluation on VO efficacy in 50 patients with chronic insomnia in Iranian Traditional Medicine Clinic of Mashhad University of Medical Sciences, Mashhad, Iran. The Intranasal drop of *Viola odorata* (Violet Oil) was used in insomnia. Two drops of Violet oil (66 mg) were administered in nostril before sleeping for one month. All patients are completing the questionnaire on Insomnia severity Index (ISI) before and after the completion of experiment. The result shows the improvement in the sleeping and ISI index of the patients ($p < 0.05$). Some patients observed mild complications on administration of VO drops. No any serious case was observed. Hence, study shows that the VO drop is safe, acceptable and effective drug in chronic insomnia. (39)

Hamedi et al studied about herbal medicinal oil. In Iran, conventional production methods of herbal oils are widely used by local practitioners. Administration of oils is rooted in traditional knowledge with a history of more than 3000 years. Scientific evaluation of these historical documents can be valuable for finding new potential use in current medicine.*Viola odorata* oils are used for patients having chronic insomnia. Different testing on insomniac patients shows effective result. (40, 41)

CONCLUSION

The present study shows idea about use of *Viola odorata* (Banafsha) in Hypertension, Hyperlipidemia and in Chronic Insomnia. *Viola odorata* as antihypertensive drug was tested on rat aorta and Guinea pig atria, and it was found effective. It was also found effective in depression as tested on mice; molecular docking results depict that compounds 1-3 can interact with 5HT₃, 5HT_{1A} and 5HT_{2A} receptors, and are more specific to the 5HT₃ receptor subtype. The findings of this study clearly suggest that compounds 1-3 possess antidepressant-like effects which might be mediated via the serotonergic system. The *Viola odorata* produce sleep in insomniac patients. They conducted study as an experimental pretest-posttest evaluation on VO efficacy in 50 patients with chronic insomnia in Iranian Traditional Medicine Clinic of Mashhad University of Medical Sciences, Mashhad, Iran. All patients are completing the questionnaire on Insomnia severity Index (ISI) before and after the completion of experiment. The result shows the improvement in the sleeping and ISI index of the patients ($p < 0.05$). Hence, study shows that the VO drop is safe, acceptable and effective drug in chronic insomnia.

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