

Science Supports *Viola's* Traditional Medicinal Value

Dorene Petersen and Glen Nagel

Exquisite wild violet (*Viola odorata* L.) flowers fluttering in a gentle wind, like small, purple butterflies never fail to delight. Equally delightful is embarking on an exploratory journey, unearthing recent scientific studies, research reviews, and ancient texts that shed light on the constituents and the medicinal uses of *Viola odorata* L. (also abbreviated as *V. odorata*). This includes many that substantiate the traditional uses. The journey reveals a wealth of benefits through a historical and geographical landscape, from ancient Persian-Greek traditional medicine, known as Unaani, to Nicholas Culpeper (1616-1654),^[1] global pharmacopoeias, to recent research published in Pubmed, Science Direct, and the Cochrane library

From the family Violaceae the two main medicinal species mentioned in literature and research are *V. odorata*^[2] and *Viola tricolor* L. subsp. *curtisii* (E. Forst.) Syme.^[3]

Viola odorata traditionally has been used since the time of the Greek physicians Asclepius (8th century B.C.) and Hippocrates (460 B.C. to 375 B.C.).^[4] Many of the early uses that Culpepper discusses were said to be heavily influenced by the ideas of Paracelsus von Hohenheim (1493–1541) and followed the theory of the Doctrine of Signatures. At the time of Paracelsus, this doctrine was a useful evaluation tool that associated the plant's shape to medicinal uses. Unscientific but intriguing, nonetheless. Given that the leaf of the violet does have a shape that could at a stretch be a lung, the Doctrine of Signatures may have indeed influenced Culpepper's statement that "...the fresh or dried flowers and leaves are beneficial for pleurisy and all lung diseases, to lenify the sharpness of hot rheums and the hoarseness of the throat."

Similar uses of *V. odorata* leaves, flowers and roots in many forms from powders, pills, extracts, to syrups are recorded in the traditional medicine texts of Persia and Iran. The Persian physician Ibn-Sīnā, also known as Avicenna (ca. 970–1037), wrote about the virtues of violets.^[5] It was known as a plant with a cold and wet temperament and has been used for hot and dry diseases such as fever, excessive thirst, and uremic pruritus. It also was widely recommended in Iranian traditional medicine for pulmonary diseases such as cough, pneumonia, and pleurisy.^[6]

The Chemistry of *Viola odorata*

A 2017 review paper examines more closely the chemical composition and medical use of *V. odorata*. Ancient Persian texts as well as a complete review of electronic databases reveals 22 relevant studies, including three human studies and 16 *in vitro* studies up to 2017.^[7]

The plant's chemistry represents a diverse array of chemical constituents. The flowers contain an essential oil, a blue pigment, as well as monoterpenes and sesquiterpenes including linalool,

benzyl alcohol, cadinol, globulol, viridiflorol, sugar and a trace amount of melatonin. The leaves also contain an essential oil along with quercetin and salicylic acid, flavonoids, tannins, alkaloids such as violin (also found in the roots), and saponins. Two other studies state that the plant peptides (cyclotides), including cycloviolacin-O2 found in *V. odorata* show therapeutic potential.^{[8] [9]} Further, a 2010 study demonstrated that cyclotide cycloviolacin O2 from *V. odorata* has potent bactericidal activity against Gram-negative bacteria, further adding to its remarkable therapeutic repertoire. This is particularly good news given that Gram-negative bacteria are resistant to treatment with many antibiotics, and even botanical or essential oil treatments.^[10]

A water extract of another member of Violacea, the European wild pansy or heart's ease, *V. tricolor*, also is a source of bioactive cyclotides which inhibit proliferation of activated lymphocytes and provide support for disorders related to an overactive immune system. Further studies to evaluate its clinical potency would need to be performed but the immunologic effects and anti-inflammatory action reveal *V. tricolor's* medicinal potential.^[11]

Further, it is not a surprise, given the heart-shape of the leaves and the common name of heart's ease, that there is interest in using *V. tricolor* as a cardioprotective agent. Both *in vitro* and animal research has demonstrated that *V. tricolor* extracts have vasorelaxant and hypotensive effects. A 2020 *in vitro* animal study using the whole plant fluid extract of *V. tricolor* showed vasodilator, cardio-depressant, and anti-hypertensive effects. While the precise cardioprotective mechanism is still unclear, high performance liquid chromatography revealed the presence of gallic acid which has a potential role in cardiovascular diseases. Hence, *in vitro* and *in vivo* studies show the potential role of *V. tricolor* in treatment of cardiovascular diseases.

Viola odorata Medicinal Uses

Traditional Persian medicine has numerous mentions of the value of *V. odorata* for central nervous system problems such as insomnia, epilepsy, headache, nasal ulcers, and fevers. Also mentioned are cardiovascular conditions such as palpitations and tachycardia, along with respiratory conditions such as chronic lung problems, coughs, common colds, and pneumonia.^[12] Interestingly, the British Pharmacopoeia also lists violet leaf *V. odorata folium* as an expectorant.^[13] Urinary tract issues such as fluid retention, painful or difficult urination, and flank pain also were mentioned as ailments that responded to *V. odorata*. The authors of the review thought this action was due to the presence of flavonoids in *V. odorata*. The most reported route of administration, however, was topical. Topical powders and poultices were used for skin conditions, inflammation, stomach, and liver disease and even anal swelling, apparently in recent times often misdiagnosed as hemorrhoids.^[14] Additionally, the research review revealed evidence of treatment of cancerous or malignant tumors and chronic inflammation.^[15] Avicenna and Culpepper both mention many of the ailments above as being effectively treated by the humble but impactful *V. odorata*.

In support of the traditional belief that *V. odorata* has potential for respiratory conditions, a 2015 study addressed the growing problem of asthma in children and the need to find alternatives to traditional drug treatments. Researchers aimed to investigate the effect of violet syrup on cough alleviation in children with intermittent asthma. The results reinforced Culpepper's and Avicenna's writings. In this human, double-blind, placebo-controlled study, the authors demonstrated the effectiveness of a *V. odorata* flower syrup on the cough of children with intermittent asthma. The study enrolled 182 children between the ages of 2 and 12 all with intermittent asthma. They were randomized in a group receiving either violet flower syrup or placebo. Each group used no other medicine except for treatment with short-acting bronchodilators. The children in each group were evaluated in terms of the duration until 50% cough reduction and 100% cough suppression were achieved. The *V. odorata* cough syrup was composed of dried viola flowers, 12 grams per 100 cc. Each child received 2.5 cc or 5 cc, 3 times a day for 5 days.^[16] The results from each group revealed no significant difference in cough reduction based on sex, age, place of living, and educational status of parents. Significant results showed the duration required to yield more than 50% cough reduction and 100% cough suppression was significantly less in the violet syrup group compared to placebo groups (statistically highly significant $P < .001$). There was significantly less wheezing occurrence in pulmonary examinations after the intervention in the violet syrup group than in the placebo group (also statistically highly significant).

This human study supports the long history of *V. odorata* flower syrups being used for coughs and upper respiratory mucus. Previously studies focused on the respiratory tracts of mice, which revealed that *V. odorata* flowers were anti-inflammatory and anti-asthmatic as well as effective in inhibiting the total serum levels of IgE and pro-inflammatory cytokines such as IL-3 and IL-4. Cytokines synchronize immune system responses to disease, in this case serving an anti-inflammatory function. This use of the syrup effectively decreased response of the airways and decreased eosinophilia, which are the body's white cells that attack disease and excessive mucus.

The researchers concluded that viola flower syrup is a potential natural cough suppressing treatment for children with intermittent asthma. They recommended that studies continue with larger sample sizes and other dosages to confirm the results of this study and select the best dosage.^[17]

Culpepper mentions the efficacy of *V. odorata* for the "heat and sharpness of urine"^[18] and, while not directly related, one of the challenges of late-stage kidney disease is treating a condition called uremic pruritus. Uremic pruritus, also known as "chronic kidney disease-associated pruritus" (CKD-aP), is chronic itching that occurs with patients who have advanced or end-stage renal disease.^[19] It is known to affect about 20% to 50% of patients with renal failure and often causes long-term pain and suffering.^[20] A 2019 study^[21] concluded that the efficacy of treatment of hemodialysis pruritus with an infused oil of *V. odorata* flowers was more effective than just massage alone. The oil was formulated using fresh flowers in sweet almond oil in a ratio of 1-part oil to 1-part flowers. This was prepared in an incubator at 37 degrees Celsius (98.6° F). The

final violet oil was standardized by optical absorption for gallic acid, revealing 27.6 mg/l of gallic acid. Every patient was randomized to receive 3 ml to 5 ml of the violet oil massage or dry massage. On alternate days, the patients received six treatments of 5 ml of oil massaged into the hand for seven minutes. Unobtrusive hand massage was chosen as a convenient administration method because the massage was given during dialysis sessions to both males and females.

Each patient was given a physical exam, had all medical history recorded, and completed a Scale and Visual Analogue Scale (VAS) questionnaire. A score of zero indicated a lack of pruritus while a score of nine represented severe symptoms.¹

This study was the first of its kind to evaluate the effect of massage with or without violet flower oil. The results showed that massage with violet flower oil was more effective in the treatment of uremic pruritus than massage alone.

In conclusion, this study showed that massage alone can reduce skin dryness score, severity, location, and frequency of pruritus with hemodialysis patients. It appears that violet oil massage can further heighten the effect in lowering the dryness score because of the sedative, antipruritic, anti-inflammatory, and anti-hypertensive action in hemodialysis patients. This non-toxic, simple traditional remedy needs to be evaluated further by additional clinical studies.^[22]

Viola odorata shows preliminary promise in treating difficulty urinating associated with an enlarged prostate. While short, a 2017 two-week, double-blind, placebo-controlled trial of a traditional Persian remedy blend of an infusion of violet *V. odorata* flowers, borage (*Echium amoenum*), and Chinese lantern (*Physalis alkekengi*), evaluated how effective it was for treating symptomatic benign prostate hyperplasia (BPH) in men. Prostate problems are common in the aging male population. At least 70% of 60-year-olds and 90% of men over 70 have benign prostatic hyperplasia. There are many theories why, but stromal and glandular cells of the prostate can become hyperproliferative (a high rate of growth) and result in a host of lower urinary tract symptoms.

There are many drug treatments and surgical procedures for the treatment of BPH but there is as strong desire for a natural, effective, and low side-effect treatment. A total of 86 male patients with symptoms of BPH were chosen in this randomized, double blind, 2-week placebo controlled single center trial.^[23] The inclusion criteria focused on male patients with confirmed BPH, aged between 40 and 75, with a prostate volume more than 30, and an International Prostate Symptom Score of more than 13. The exclusion criteria included patients with diabetes, hypertension, cardiovascular disorders, hyperlipidemia, history of cardiac apoplexy, cerebral apoplexy, ischemic attack, and treatment with anti-BPH drugs within a month of the beginning the trial. The plants were all collected in different habitats ranging from a farm to the wild forests of Northern Iran. The plant

¹ The visual analogue scale (VAS) is a simple, valid, reliable and optimal instrument with ratio scale properties for describing the severity, intensity and frequency of skin dryness and pruritus.

materials were air dried in the shade and 50 g of each were ground and extracted with 80% ethanol, and then macerated for 48 hours. The solvent was removed by rotary evaporator and the extracts were mixed into a hydro-alcoholic solution with a final concentration of 1.5%, 1% and 1.5% for the *P. alkekengi*, *E. amoenum*, and *V. odorata* respectively.

Patients were assigned to receive 1 ml of the extract twice a day for two weeks. Baseline exams and exams after two weeks were performed for safety and to assess efficacy of treatment. The following were monitored during the treatment period:

- The value of hemoglobin, hematocrit, platelets, neutrophils, lymphocytes, and basophiles in blood
- Levels of serum electrolytes, fasting blood sugar, creatinine, BUN, elements, and liver enzyme
- Records of physical activities
- Serum examinations for measuring prostate specific antigen (PSA)

The International Prostate Symptom Score (IPSS) was utilized for evaluating the validity of patient's symptoms and responses to therapeutic protocol and further comparing the results among control and case groups.

The results demonstrated that all the men in treatment experienced significant decreases in symptoms of urinary excretion abnormalities including nocturia, incomplete urination, frequency, intermittency, urgency, and weak flow, plus prostate volume and excessive urine volume. The one exception was the symptom of urinary urgency, which did not change. IPSS scores significantly decreased in the treatment group compared to the placebo group. The prostate volume was considerably reduced in the treatment group. There were no significant changes in blood parameters between the two groups. The quality-of-life scores increased in the treatment group. In conclusion, the traditional Persian herbal medicine formula of the herbs *P. alkekengi*, *E. amoenum*, and *V. odorata* showed significant improvement in male patients with BPH. The combination indicated improvement in many of the expected lower urinary tract symptoms. Future research should examine each herb in the formula to investigate further action.^[24]

The sedative and anti-inflammatory actions of *V. odorata* also may be effective for allergic rhinitis or hay fever. A 2020 study showed that *V. odorata* flower oil had significant positive effects on the symptoms of adults with allergic rhinitis.^[25] The researchers enrolled 81 patients in this double-blind, randomized, placebo-controlled clinical trial. Patients were aged 18 to 60 with a diagnosis of mild to moderate allergic rhinitis, and with no impairment to daily activities. The exclusion criteria were pregnancy, lactation, concomitant respiratory illness, concomitant use of

herbal medicine or steroid medications, and a history of allergy to violets. The fresh *V. odorata* flowers (200 g) were extracted in 1 liter of 70% ethanol and shaken for 5 days. The extract was dried under pressure to 40 g of material which was then dissolved in 4 liters of sweet almond oil. The oil was standardized to total phenolics at 28 mg/ml, expressed as gallic acid equivalence per ml of oil.

The participants were divided into two randomly assigned groups. One group received violet flower oil preparations every 12 hours, one drop per nostril. The placebo oil was used for the control group. Each group received treatment for two weeks. In this short period, the symptom scores between the groups reflected significant improvement by the violet oil group in reduction of symptoms of nose itching, sneezing, nasal congestion, rhinorrhea, eye itching, eye burning, eye tearing, sleep quality, daily activity, and fatigue compared to the placebo group. The effects of the violet oil preparations increased over time, becoming more effective and stronger from day 7 to day 14. All these improvements were significant.

In conclusion, *V. odorata* flower oil preparation was well accepted with no significant adverse events reported in the violet group compared to placebo. The findings demonstrate that *V. odorata* has potential as a natural, effective, and safe treatment of allergic rhinitis.^[26] There is a need for longer studies to explore additional benefits from *V. odorata* flower oil.

Historical texts reveal that *V. odorata* flowers have the potential for improving sleep quality and for providing support for insomnia. Culpepper said, “[I]t likewise easeth pains in the head caused through want to sleep”^[27] and this is supported by a 2017 critical review that concludes that the administration of *V. odorata* flower oil to patients with insomnia in a form of nasal drops for a one month period resulted in improvement of sleep and insomnia scores.^[28] The *V. odorata* flower oil mentioned in the 2017 review is the infused oil.

As mentioned, the research review of traditional Persian medicine texts and research papers identified that *V. odorata* extracts were considered a traditional, herbal anti-metastatic treatment. Coupling this background with the presence of the constituent cycloviolacin-O2 found in *V. odorata* reveals the potential cytotoxic activity (toxic effects on cells). Cycloviolacin-O2 is thought to participate in the defense mechanism of *V. odorata* and has shown strong cytotoxic activity against a variety of drug-resistant and drug-sensitive human tumor cell lines, specifically primary chronic lymphocytic leukemia and ovarian carcinoma cells.^[29] In a 2020 study,^[30] researchers attempted to detect and compare the effects of *V. odorata* extract on malignant breast cancer cell lines (specific types of breast cancer cells) and breast cancer stem cells (cells from which all other specialized cells are created, such as for organs). The research was carried out on two frequently studied human breast cancer cell lines. Then, researchers performed an analysis and comparison on breast cancer stem cells treated with an alcoholic extraction of *V. odorata* on apoptosis and malignant characters of the breast cancer cell lines.

The results revealed that the extract of *V. odorata* induced cell death in the human breast cancer cell lines and their derived breast cancer stem cells through cell apoptosis. The *V. odorata* extract also demonstrated anti-migratory, anti-invasion, and anti-colony formation activity in the two human breast cancer cell lines. The research demonstrated a reduction of both the size and volume of tumors generated by the two breast cancer cell lines in a chicken embryo model. This study shows that the nontoxic extract of the traditional anticancer herb *V. odorata* has significant anticancer activity of human breast cancer cell lines. The data also suggested that the *V. odorata* extract targets mostly cancerous cells, not normal cells, and acts in a cell dependent manner. The study suggests future studies on *V. odorata* extract to treat breast cancer and other cancers as well.

A Final Word About *V. odorata*

In summary, *V. odorata* contains numerous therapeutic compounds that can be useful for various health conditions including digestive, cardiovascular, respiratory, skin, and oncology conditions and diseases. There are multiple clinical research studies to date, and a few of these are on humans. *V. odorata* has a long history as a traditional remedy and demonstrates a promising future that will be supported by well-designed clinical studies. Couple this with the fact that there are no reported food, drug add comma or supplement interactions associated with *V. odorata*, it is a valuable herb to grow in any home apothecary garden.

When *V. odorata* is in season, herbalists can prepare some simple violet remedies to enhance the home apothecary medicine chest. There is nothing more satisfying than gathering a basket of fresh violet flowers or leaves on a warm summer day and preparing your own infused oil. Violet flowers are best gathered in the early morning on a warm summer day.

The following recipes provide amounts for the use of dried herbs. If you are using fresh herbs, double the quantity and leave them to wilt for six hours to reduce the water content. High water content will spoil the final product.

Violet Flower and Marshmallow Root Cough Syrup

1 ounce violet (*V. odorata*) flowers

1/2 ounce marshmallow (*Althaea officinalis*) root

1 1/2 pints distilled or filtered water

1 cup raw sugar

Honey, in the amount of the violet and marshmallow infusion

Glycerin, optional, 4 tablespoons for every 8 tablespoons of syrup

Prepare an infusion of the violet flowers and marshmallow root in the water. Let the mixture steep for 30 minutes, then strain and measure.

For each cup of infusion, use one cup of honey.

Combine the sugar, honey, and lemon juice, and simmer over a low heat until it thickens and forms a syrup. Add the strained violet and marshmallow infusion. Return to heat if necessary to increase thickness. The optional vegetable glycerin can be added to help preserve the syrup for up to one week. Bottle and store in the refrigerator.

Infused Violet Flower and/or Violet Leaf Oil

The following three methods can be used to prepare either the fresh or dried *V. odorata* flowers or leaves. Note when using fresh violet flowers make sure to strain your finished product carefully and let the infused oil sit for 24 hours and then decant the oil. You may notice a small amount of water settling on the bottom of the oil. Leaving this water in the oil can lead to contamination and molding.

Water Bath Method

1 cup sweet almond (*Prunus amygdalus* var. *dulcis*) oil

1/2 ounce dried herb, or 1 ounce fresh herb

Pour the oil over the herbs in a stainless-steel bowl. Heat over a water bath (a saucepan one-quarter filled with water) or double boiler, which should be simmering. Make sure the bowl is not sitting on the bottom of the pot but is floating in the water. Keep the lid on the oil. Stir occasionally and simmer the oil and herb over the water bath for 30 minutes. Be sure the oil does not become too hot. It should not smoke or bubble. It can burn easily and will develop an acrid smell if it overheats, which is very difficult to disguise.

Strain the plant material from the oil through four layers of unbleached muslin or some other very fine non-metal strainer. Strain twice, if necessary, as it is important to get all herbs out of the oil to prevent the oil from becoming rancid or moldy. If the oil has not extracted enough aroma from the plant material it is not recommended to add fresh material and reheat. You can, instead at this stage, add the fresh herb and prepare again using the solar method, described next.

Solar Method

Use the same quantities of herbs and oil as for the water bath method. The quantity of herb can be increased to produce a higher aroma intensity oil. Put the herbs in a jar with a tight-fitting lid and pour the oil over them. Make sure the herbs are completely covered with oil. Add 1 tablespoon of apple cider vinegar or white wine vinegar to help break down the plant material. Leave the jar to sit in the sun all day and in a warm cupboard at night for two weeks. You can leave it there longer if you choose, but at a minimum, two weeks.

Strain through four layers of unbleached cotton cheesecloth or muslin and repeat, if necessary, as plants can become moldy in oil. This process can be repeated two to three times to give stronger

oil. The final product should be strong enough to leave an aroma when massaged on the skin. Always test infused oils by rubbing them on the skin.

Crockpot Method

Use the same quantities of herbs and oil as for water bath method. Place the herbs and oil in a crockpot and leave on a low heat for two hours. Follow the previous directions for straining.

How to Preserve Infused Oils

This is only necessary when you prepare large quantities that you intend to store for a while. Add the following preservatives once you have completed the infusion process and strained the oil thoroughly. Add 500 IU of natural mixed tocopherols or Vitamin E to 1 cup of infused oil. The shelf life of infused oils increases if the equipment and the bottles are clean and sterile. Prepare your infused oils using the same hygienic precautions as if you were canning food.

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Dorene Petersen BA, DIP.NT, DIP.ACU, RH (AHG) is a New Zealand-trained Naturopath and aromatherapy, herbalism, and holistic wellness expert with decades of experience. She founded the American College of Healthcare Sciences (ACHS) in 1978 and has been President of the College since that time. Contact Dorene at dorenepetersen@achs.edu.

Glen Nagel ND, RH (AHG) is a practicing herbalist, licensed Naturopathic physician, and all-around herbal wise guy. He has a lifelong interest in plants and nature and believes in teaching with humor and hands-on experience. Glen is the Herbal Medicine Program Chair at ACHS.edu.

The Skinny on Violets: Two Approaches to Violets in Skin Care

Marge Powell

Violets have an exceptionally long history in the herbal apothecary related to skin conditions. Violets have earned a reputation of aiding oily, dry, and/or sensitive skin. Current research attributes this to the salicylic acid contained in the leaves and other parts of fresh violets. Salicylic acid disinfects and can dissolve tissue, which points to topical remedies to soften hard skin and treat corns and warts. Salicylic acid is also a known acne fighter. Sometimes people turn to willow bark as a source of salicylic acid, but willow bark contains salicin, which when taken orally is converted to salicylic acid by our digestive system. If used topically, our skin does not possess the enzymes to convert salicin to salicylic acid. Violet leaf is a rich source of salicylic acid and requires no conversion from salicin. In addition to the salicylic acid violet leaf contains vitamin C (an antioxidant and anti-inflammatory nutrient that improves skin tone and texture) and vitamin A (a widely accepted skin nutrient). When collected in spring violets contain twice as much vitamin C as the same weight of orange and more than twice the amount of vitamin A, gram for gram, when compared with spinach. Violet leaf is also fungicidal.

While violets could rest on their laurels as a soothing skin aid for eczema, rashes, hives, and other irritated skin conditions, it has a much more serious side. Violets have an active role in breast health, especially fibrocystic lumps, mastitis, plugged milk ducts, and as a natural adjunct