

## An overview on phytopharmacology of *Pelargonium graveolens* L.

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Since ancient, *Pelargonium graveolens* L. is well organized for its therapeutic values. Only recently, its new medicinal aspects have been awarded by scientists. Regarding new multi-functional properties of *P. graveolens* and valuable ongoing reports we were prompted to update phytochemistry and pharmacology of it. Data were collected using journals, articles, scientific books and websites such as Scopus and PubMed. *P. graveolens* extracts and essential oil are important in drug development with many pharmacologic properties in China and Middle East especially in Egypt and Morocco. *P. graveolens* has been used in traditional medicine for the relief of hemorrhoids, dysentery, inflammation and cancer, as well as in the perfumery, cosmetic and aromatherapy industries all over the world. *P. graveolens* has recently been shown to have antioxidant, antibacterial, antifungal activities and acaricidal effects. The valuable therapeutic aspects of *P. graveolens* are mostly correlated to the existence of volatile constituents, terpenoids and flavonoids. Due to being widespread and the easy collection of this plant and also remarkable biological activities and containing a high amount of essential oil, this plant has become a medicinal plant in pharmacy especially in aromatherapy. This overview presents comprehensive analyzed information on the phytochemical and clinical properties of *P. graveolens*.

**Keywords:** Geraniaceae, *Pelargonium graveolens* L., Phytopharmacology

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Affordability and accessibility of the medicinal plants have made them as an important part of many people's life all over the world. The medicinal plants selection is a conscious process, which has led to an enormous number of medicinal plants being consumed by many cultures in the world<sup>1</sup>. According to the World Health Organization (WHO), due to the lack of access to modern medicines and poverty, about 65-80% of the people in developing countries depend on plants for their primary healthcare<sup>2</sup>. Regarding the lack of safe modern drugs, evaluation of active and effective plants for diseases such as diabetes has been recommended by WHO. It is estimated that close to 25% of the biological active components in currently synthetic drugs were first identified in natural sources especially in plant<sup>3</sup>.

Commonly known as Geranium, *Pelargonium graveolens*, is an aromatic, perennial and flowering plant which belongs to Geraniaceae family in the order of Geraniales that contains about 230 genera and more than 2500 species<sup>4</sup>. *Pelargonium* species probably originates from South Africa and introduced

to Europe in the 17<sup>th</sup> century and have since been hybridized all over the world<sup>5</sup>. Nowadays the major production of geranium takes place in China and Middle East especially in Egypt and Morocco<sup>6</sup>. *Pelargonium* genus has 750 species scattered widely around the world growing as annuals<sup>7</sup>. *P. graveolens* has been known as "Shamdani Atri" in Iran. *P. graveolens* is a shrubby perennial plant growing to a height of 1 m if left unpruned. In the tropical areas it is grown as an annual. The leaves are lobed and contain essential oil. The plant has typical small, pink flowers. Leaves and stalks are the essential parts of this plant. The essential oil is extracted from fresh plant material mainly using steam distillation.

*P. graveolens* essential oil is largely utilized in the perfumery, cosmetic and aromatherapy industries all over the world. It has since become indispensable aromatherapy oil<sup>8</sup>. Geranium oil responds well to the balancing effects of constipation, insomnia, restlessness, nervousness, anxiety, worry, high blood pressure, anger, frustration, emotional upsets, hypercholesterolemia, slow to lose weight and low metabolic forces<sup>9</sup>. The oil has potential immune

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modulating effects on natural killer cells<sup>10</sup>. Geranium oil improves circulation, treats congestion especially for the breast tissue, promotes healthy immune system, stimulates and cleans the lymphatic system and is helpful for detoxification, overcoming addiction, hemorrhoids, phlebitis, indigestion and fluid retention<sup>11</sup>. Other geranium essential oil usages which are becoming more and more popular include relieving dysentery, inflammation, hemorrhoids, heavy menstrual flows and cancer. The oil is clinically used for treating diabetes, diarrhea, jaundice, gallbladder problems, liver problems, gastric ulcers and urinary stones. The leaves are used as a form of herbal tea to de-stress, fight anxiety, ease tension, improve circulation and cure tonsillitis<sup>12</sup>.

Traditionally, roots have been used medicinally for a multitude of ailments; both the rhizome and herb have been used for different purposes since ancient times to treat malaria, abdominal and uterine disorders. They were also used in decoction to wash patients suffering from fever<sup>13</sup> and also directly chewed or powdered and mixed with food.

For a long time, *P. graveolens* root decoction and infusion of the roots is employed for its palliative and curative effects in treating the gastrointestinal disorders and respiratory tract infections while the aerial parts are used to heal the wounds<sup>14</sup>. The fairly high concentrations of oligomeric proanthocyanidins (9%) occurring in this indigenous medicine may, at least in part, explain the traditional use of it for the treatment of gastrointestinal disorders such as diarrhea and the application of the aerial parts as wound healing. Since systemic analysis and review of biological activities and potentials of *P. graveolens* have not been reported, we interested to prepare the currently accessible information on ethno biological and local knowledge issues, ethnomedicinal aspects, pharmacologically important compounds identification and pharmacologic studies on this useful plant. This overview introduces *P. graveolens* as a potent plant by highlighting the new findings for novel multi-functional and clinical applications as well as its traditional indications.

## Materials and methods

The data presented in this paper were collected using all scientific data come from encyclopedia, articles, books, journals and websites such as Pubmed, Scopus and Google Scholar.

## Chemical composition

Many chemical constituents such as volatile substances, terpenoids, flavonoids, phenolics, coumarins, cinnamic acids and tannins have been isolated from the plant<sup>15,16</sup>. Citronellol (29.90%), trans-geraniol (18.03%), 10-epi- $\gamma$ - eudesmol (8.27%), isomenthone (5.44%), linalool (5.13%), geranyl acetate (4.52%),  $\gamma$ - Cadinene (2.89%), geranyl butyrate (2.53%), geranyltiglate (2.50%) and gemacrene D (2.05%) were identified as the major constituents of the *P. graveolens* aerial parts essential oil<sup>17</sup>. Phytochemical investigations in 1996 resulted in characterization of the indole alkaloids, elaeocarpidine, and its 20-H isomer epielaecarpidine in the leaves of geranium<sup>18</sup>.

## Potential of *P. graveolens* in phytotherapies

Various studies have revealed the different pharmacological properties of *P. graveolens* in a range of *in vitro* and *in vivo* test models. The aerial parts of the plant, in particular, have been demonstrated to possess antibacterial, antifungal, acaricidal and antioxidant activities at different doses/concentrations. These have been described in greater detail in the following subsections.

## Antibacterial and antifungal activities

*P. graveolens* has been found to possess good antibacterial activity against *S. aureus*, *Proteus vulgaris*, *B. cereus* and *Staphylococcus epidermidis*<sup>18</sup>.

*P. graveolens* oil is being used as potent oil on the pathogenic vaginal bacteria such as *Atopobium vaginae*, *Gardnerella vaginalis*, *Bacteroides vulgates*, *Streptococcus agalactiae*, H<sub>2</sub>O<sub>2</sub>-producing lactobacilli, non H<sub>2</sub>O<sub>2</sub> producing lactobacilli, *C. albicans*, *C. glabrata*, *Candida parapsilosis* and *Candida tropicalis*<sup>18,19,20,21</sup> and has been used to extend the shelf life of foods, beverages, pharmaceutical and cosmetic products. The essential oil from the fresh aerial parts of the plant exhibited antimicrobial activity against *B. subtilis*, *S. aureus*, *Enterococcus fecalis*, *C. glabrata*, *C. krusei*, *C. neoformans*, *Mycobacterium tuberculosis* and *Mycobacterium intracellulare*. Geranium oil has shown inhibition properties on *S. aureus* and *C. albicans*<sup>22</sup>. Presence of  $\alpha$ -pinene (37.4%),  $\beta$ -pinene (16%) and limonene (13.3%) in high concentrations are believed to actively inhibit the growth of microorganisms<sup>23,24</sup>. The profound antimicrobial activity of *P. graveolens* may partly explain their

wound-healing properties<sup>13,25</sup>. The extract broad spectrum antimicrobial activity may be caused by the coumarins and phenolic acids<sup>26</sup> and may be potential sources of effective agents for wound infections<sup>11,3,27,28,29</sup>.

The leaf essential oil of *P. graveolens* exhibited a broad fungi toxic spectrum against *Aspergillus fumigatus*, *Aspergillus terreus*, *Aspergillus alternata*, *F. oxysporum*, *H. oryzae* and *T. viride*<sup>30</sup> first reported the anti-aflatoxigenic nature of *P. graveolens* oil with complete inhibition of aflatoxin B1 production even at 0.50 g/L—suggesting the relevance in enhancing shelf-life of commodities by controlling microorganisms and minimizing health hazards by inhibiting aflatoxin B1 elaboration in food by use of the essential oil of *P. graveolens*. The oil was found to be highly efficacious, showed better fungi toxicity against *A. flavus* at concentrations lower than the earlier reported oils and synthetic fungicides<sup>31</sup>.

The antimycotic investigation revealed that *P. graveolens* extracts showed significant growth inhibition against *Aspergillus flavus*, *A. niger* and *Penicillium notatum*<sup>30</sup>.

#### Acaricidal activity

Mites are a major source of multiple potent allergens, and have been causally associated with sudden infant death syndrome. Exposure to house dust mite allergens can result in broncho-constriction and inflammatory reaction of the airways. Most houses are co-inhabited by *Dermatophagoides farinae* and *D. pteronyssinus*. Control of dust mites depends on environmental and chemical methods such as fumigation and spraying with acaricidal compounds<sup>32</sup>.

However, repeated use of organophosphorus chemicals has resulted in the increase of resistance<sup>32</sup>.

*P. graveolens* leaves essential oil, at doses of 40, 20, and 10 µg/cm<sup>2</sup> gave 100% mortality against house dust mites. In the test with *D. farinae* adults, the *P. graveolens* oil gave a 62.5%, 27.5%, and 5.0% mortality of *D. farinae* adults at 5, 2.5, and 1.25 mg/cm<sup>2</sup>, respectively, 24 hrs after treatment. For *D. pteronyssinus* adults, the essential oil caused 53.1%, 15.2%, and 2.3% mortality at 5, 2.5, and 1.25 mg/cm<sup>2</sup>, respectively<sup>33</sup>.

These results indicate that the acaricidal activity of the essential oil of *P. graveolens* leaves can be mostly attributed to geraniol and β-citronellol, because geraniol was approximately 39 and 34 times more toxic than benzyl benzoate against *D. farinae* and

*D. pteronyssinus*, respectively. Additionally, β-citronellol was approximately 36 and 33 times more toxic to *D. farinae* and *D. pteronyssinus* than benzyl benzoate. Geraniol, β-citronellol, and their derivatives are most promising for possible use against *D. farinae* and *D. pteronyssinus* owing to their selective actions and their safety for mammals. Therefore, *P. graveolens* oil derived materials could be useful as fumigants for house dust mites, and can be very useful in removing allergens<sup>33</sup>.

#### Antioxidant properties

Antioxidants are of interest to biologists and clinicians because they help to protect the human body against damages induced by reactive free radicals generated in atherosclerosis, ischemic heart disease, cancer, Alzheimer's disease, Parkinson's disease and even in aging process<sup>34,35</sup>. There are many evidences that natural products and their derivatives have efficient anti-oxidative characteristics, consequently linked to anti-cancer, anti aging and anti-inflammatory activities<sup>34</sup>.

Anti-oxidative capacities of *P. graveolens* were evaluated by determining its effect on DPPH radical scavenging<sup>8</sup>.

In DPPH radical-scavenging activity assay, the IC<sub>50</sub> value of geranium oil was 66.45 µg/ml which was a little weaker than that of ascorbic acid (IC<sub>50</sub> value = 38.49 µg/ml) as standard<sup>8</sup>.

The antiradical scavenging activity of the oil might be attributed to the replacement of hydroxyl groups in the aromatic ring systems of the phenolic compounds as a result of their hydrogen donating ability. Geranium essential oil could be a possible source of antioxidant compounds since the extracts were relatively non-toxic<sup>11,36</sup>.

These observations prompt that the oil may have potential use as a therapeutic agent in managing diseases associated with free radicals and also has the potential employed as additives in the food or cosmetic industries<sup>8</sup>.

#### Cytotoxic activity

It is shown that *P. graveolens* oil has potential antitumor activity against uterine cervical neoplasia<sup>37</sup>.

Also, geranium essential oil has shown potent cytotoxic effects against human promyelocytic leukemia cells with the LC<sub>50</sub> values of 62.50 µg/ml in NB4 cell line and 86.5 µg/ml in HL-60 cell line. The results found that the incubation of HL-60 cells

with geranium essential oil at all concentrations (25 – 200 µg/ml) for 24 hrs reduced the viability of these cells. The dead cells were increased by increasing the concentration of the oils. The HL-60 dead cell (%) was recorded by geranium essential oil (79.27%) for concentration of 200 µg/ml. The NB4 dead cells (%) were recorded by geranium essential oil (79.8%) for concentration of 200 µg/m. The antioxidant activity of geranium essential oil is positively correlated with its anticancer activity against HL-60 and NB4 cell lines<sup>8</sup>.

The essential oils and their main components possess a wide spectrum of biological activity, which may be of great importance in several fields, from food chemistry to pharmacology and pharmaceuticals<sup>38</sup>. Essential oils rich in monoterpenes are recognized as food preservatives<sup>39,40</sup>, and monoterpene essential oils are natural antioxidants<sup>41</sup> that are active against certain cancers<sup>42</sup>. Indeed, a number of dietary monoterpenes have antitumor activity that can prevent the formation or progress of cancer and cause tumor regression.

Most of the principle components present in geranium essential oil are monoterpenes. Monoterpenes have shown prevention of mammary, lung, skin, liver and for stomach cancers in rat models. The inhibition of HL-60 and NB4 cells may be due to the presence of monoterpenes.

Analysis of geranium essential oil has shown citronellol and trans-geraniol as the major constituents. These compounds are known to possess antioxidant and anticancer properties, so these activities may be attributed to the major contents of citronellol and trans-geraniol. It was reported that citronellol derived from the geranium oil, had anticancer<sup>43</sup>.

The anticancer activity of geraniol also investigated. It was found that significant (60-90%) inhibition of the anchorage-independent growth of human MIA PaCa2 pancreatic tumor cells was attained with geraniol<sup>44</sup>.

## Discussion

*P. graveolens* is believed to be native to South Africa, Europe and it is now hybridized all over the world. The flowering aerial parts of the plant have been famously used as medicinal herbs in the European, Chinese, Iranian, Indian and Arabic traditional medicines since ancient times. The claimed medicinal uses of this plant throughout the countries such as Iran, India, Turkey and European countries

include for the treatment of inflammatory- and pain-associated ailments (i.e., headache, neuralgia), nervous system-related ailments (i.e., restlessness, nervousness, anxiety, anger, frustration, emotional upsets), for relief of constipation and treating high blood pressure, high cholesterol, low metabolic forces and slow to lose weight. Most of these claims have been confirmed via *in vitro* and *in vivo* techniques of biological evaluation.

In the present paper, we have overviewed the relevant literature to congregate the botanical, ethnobotanical, phytochemical, and pharmacological information on *P. graveolens*. Based on the literature survey, *P. graveolens* demonstrated various pharmacological activities. However, detail and careful analysis of the reported data leads us to conclude that the plant only possessed promising antioxidant, larvicidal, antibacterial, antifungal and cytotoxic activities. Despite the large number of diseases for which the plant finds use as a medicine, our critical analysis of the literature revealed that its therapeutic efficacy has been assessed only in a few studies. In view of the wide range of medicinal uses of *P. graveolens* in European, Asian, Iranian, Indian and Arabic folklores as described in ethnobotanical surveys, it is necessary to conduct more clinical and pharmacological studies at molecular level to investigate untapped potential of this plant. For these reasons, extensive pharmacological and chemical experiments, together with human metabolism, will be a focus for future studies. Recent increase in interest on herbal medicines accompanied by increased laboratory investigation into the pharmacological properties of the bioactive ingredients and their ability to treat various diseases has contributed to numerous drugs/herbal extracts entering the international market.

## Conclusion

Clearly, herbal-based pharmaceuticals, cosmetics and flavoring are more welcoming every day. Numerous studies have been conducted to brighten both theoretical and practical aspects of the traditional usage of *P. graveolens*. The objective of this work has been to show the recent advances in the exploration of *P. graveolens* phytotherapy and to illustrate its potential as a therapeutic agent. With the current information, it is evident that *P. graveolens* has pharmacological functions. As the current information shows, it is also possible that volatile components and

might be useful in the development of new drugs to treat various diseases. It must be kept in mind that clinicians should remain cautious until more definitive studies demonstrate the safety, quality and efficacy of *P. graveolens*. Last but not the least, this review emphasizes the potential of *P. graveolens* to be employed in therapeutic drugs and provide the basis for future research on the application of transitional medicinal plants.

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