Genus *Pelargonium*: General Aspects, Potential Pharmacological Applications, Extraction Methods and Applications in Industry

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**ABSTRACT**

*Pelargonium* is a genus belonging to the Geraniaceae family, found within the Angiospermae division, the Dicotyledoneae class, and the Geraniales order. It is the second biggest genus of the family; it has about 280 taxa. In the past, *Pelargonium* species were characterized by presenting large and red roots, from which preparations were used in the treatment of diarrhea, dysentery, anemia, and weakness. This article is a bibliographic search carried out in different databases that focus on chemical and physical features of *Pelargonium* and also some of the extraction methods. Currently, there are a variety of studies that affirm the different properties of the species of the genus *Pelargonium*, among which the activities stand out: antituberculous, antioxidant, antitumor, antibacterial, antifungal, antiviral, and immunomodulatory. Therefore, they are used in both the pharmaceutical and food industries. The most relevant species of this genus is *Pelargonium sidoides*, which has a broad range of biological properties, from which a standardized hydroalcoholic root extract was formulated, known as EPs® 7630, which has been authorized by the EMA and is listed in the European Pharmacopoeia. It is important to continue with the clinical studies to be able to analyze the other properties that *Pelargonium* has in order to contribute to the pharmaceutical industry.

**Keywords:** *Pelargonium*, *P. reniforme*, *P. sidoides*, root.

1. **Introduction**

*Pelargonium* L’Héritier in Aiton is a genus belonging to the Geraniaceae family and the Angiospermae division, the Dicotyledoneae class, and the Geraniales order. It is considered a brother genus of Geranium, Erodium, Monsonia, Hypseocharis, Rhychnotheca, and Sarcocaulon (Blerot et al., 2016). It has a great variety of floral morphologies and life forms, representing the second-largest genus of the Geraniaceae family, with around 280 taxa. It is morphologically different from the rest of the family since it has a hypanthium consisting of a spur of nectar adhered to a nectary. It usually features a zygomorphic floral symmetry (Reyes, 2010; Roeschenbleck et al., 2014).

The main distribution of the genus, which is 90%, is located in southern Africa. The most remarkable species diversity is located in the southwestern area of South Africa, where the rainfall comes exclusively during the winter. There is a distribution of species outside of southern Africa, which populate mountain habitats throughout the Rift Valley in West Africa and South Australia, Madagascar, the Arabian Peninsula, Anatolia, and New Zealand (Roeschenbleck et al., 2014).

The mild climate with low humidity is ideal for the *Pelargonium’s* growth. These species grow in short grassland areas and, in some cases, with shrubbery and trees in stony soils, which vary in their composition of sand, clay, shale, and basalt (Saraswathi et al., 2011). Furthermore, they can adapt to different climates and soils (tropical, subtropical, mediterranean, or arid), making their global distribution easier (Blerot et al., 2016). *Pelargonium’s* growth ways range from annual herbaceous plants and shrubbery to stem succulents and geophytes (Roeschenbleck et al., 2014). They can reach more than a meter in height (Reyes, 2010).

The stems are thick, with more ramifications at the base, and pairs of green stipules in a triangulated shape attached to the bud area. The leaves join the stem through
a long petiole (Reyes, 2010), and it has a great variety of shapes and sizes. They can be covered with fine hairs and rugged, sticky, or velvety texture. The leaf's borders can be “curly” or “crusty” in some species. The flowers are asymmetrical pentameres, and they are presented in pseudo-umbels, with 5 to 10 foils. In addition, they can feature different colors that range from white, pink, mallow, lavender, pale yellow, and burgundy to a combination of them (Saraswathi et al., 2011). These flowers are hermaphrodites, present 2 to 7 fertile stamens, and are pollinated by several animals, such as bees, flies, butterflies, hawks, and birds (Blerot et al., 2016).

The initial cariological research suggested a division of the genus into two significant clades, one with large chromosomes (>1.5 μm in length) and another with small chromosomes (<1.5 μm in length). Other studies have established the genus division into five compatible clades (A1, A2, B, C1, and C2). The clades A and B correspond to the small chromosomal clades, and clade C corresponds to the large chromosomal clade. Moreover, through floral morphology, leaf components, and nuclear markers analysis, it has been possible to establish the existence of four main clades (A, B, C1, and C2) instead of five. However, the classification of Pelargonium is still not considered a challenge (Blerot et al., 2016).

In 2014, a sub-generic division of Pelargonium was exposed, a division composed of the sub-genera Magnipetala, Paucisignata, Parvulipetala, and Pelargonium. At the same time, every one of these is subdivided into different phylogenetically arranged sections. The Reniformia section, belonging to the Parvulipetala sub-genus, contains species such as P. sidoides DC and P. reniforme Curtis, which are the most recognized of the genus due to their applications as traditional remedies (Roeschenbleek et al., 2014).

Around 35 indigenous medicinal plants were described in Cape Town during the years 1650 to 1800, of which six belonged to the Pelargonium genus. These presented big, red roots, from which formulations were developed to treat diarrhea, dysentery, anemia, and weakness. Some of these red-rooted Pelargonium were identified as Pelargonium myrhhifolium (L.) L’Herit. var. myrhhifolium, Pelargonium pinnatun (L.) L’Herit., Pelargonium triste (L.) L’Herit. and Pelargonium antisydsericicum (Brendler & van Wyk, 2008).

In 1867, the Englishman Charles Henry Stevens, who suffered from tuberculosis, travelled to South Africa to cure his illness. During this trip, the man met Kagaitse, a Zulu healer, who offered him boiled root preparation, which he had to take twice a day. After three months of treatment, Stevens overcame tuberculosis and introduced this natural medicine to England. However, it was not relevant due to the lack of knowledge regarding the plant’s botanical origin, chemical composition, and pharmacological activities. Eventually, Dr. Sechehaye gathered information about the plant and began to treat tuberculosis patients with the preparation utilized by Stevens. In 1930, he published the results of the treatments for the first time. He came to the conclusion that, in many tuberculosis cases, excluding acute or complicated cases, it was possible to establish healing effects from the preparation of the

**2. Materials and Methods**

To carry out the article, a bibliographic search was carried out in the databases: Elsevier, ResearchGate, Taylor & FrancisOnline, PubMed, Ovid, ScienceDirect, SpringerLink, WileyOnlineLibrary, PlosOne, Ebco, Proquest, and Google Patents. The publication dates of the articles comprised the period from 2002 to 2019. Keywords were used; Pelargonium, P. sidoides, P. reniforme, EPs®, 7630, taxonomy, history, pharmacological, alimentary, extraction, and formulation. Review articles, meta-analysis, preclinical studies, clinical studies, patents, and theses were used.
3. Results and Discussion

3.1. Potential Pharmacological Applications

The indole alkaloids elaecarpidine and its isomer 20-H epielaeocarpidine have been identified in some Pelargonium species. There have been found, as well, the flavonols and coumarins: scopoletin, 7-hydroxy-5,6-dimethoxycoumarin, as well as its methyl ether and glucoside. In addition, other compounds have been identified, such as common organic acids, ellagitannins, cinnamic acid derivatives, and phytosterols. Besides, approximately 230 compounds of the Pelargonium essential oils have been detected, these being a complex blend of monoterpenes and sesquiterpenes and compounds like alcohol, esters, aldehydes, ketones, and phenols. Other kinds of chemical products are included, such as flavonoids and derivatives of salicylic acid (Kolodziej, 2007; Saraswathi et al., 2011).

Due to its medicinal properties, P. sidoides is the most important Pelargonium species in the pharmaceutical industry and is botanically related to P. reniforme curt (Schoetz et al., 2008). The species used for the production of essential oils are also of great relevance, with these being often known as “geranium oils”; P. graveolens, P. radens, and P. capitatum.

Traditionally, both P. sidoides and P. reniforme have been used to treat a great variety of ailments. However, P. sidoides has had greater relevance in the health area nowadays. Therefore, it has been harvested on a large scale to be exported to Europe and other regions, aiming to explore and apply its medicinal properties in the medicine manufacturing process (Victor & Aphane, 2014).

Morphologically, P. sidoides differ from P. reniforme in flowers and leaves. P. reniforme has pink-colored flowers and lanceolate petals with distinctive stripes and reniform type leaves, whereas P. sidoides presents rope-shaped leaves and flowers with a dark red color, which are commonly observed in almost black color (Kolodziej, 2007; Victor & Aphane, 2014).

Regarding the plants’ chemical composition, it has been identified that both species roots show important variations in the types of coumarins they contain, although they share the scopoletin, 6,7,8-trihydroxycoumarin and 8-hydroxy-5,6,7-trimethoxycoumarin coumarins; therefore, these compounds can be used as chemical markers. Besides, P. sidoides show coumarin sulfates and glucosides and the umckalin compound, which is considered a characteristic metabolite of the species, whereas P. reniforme has the reniforme compound, a unique metabolite of the species (Kolodziej, 2007; Schoetz et al., 2008).

P. graveolens is an aromatic and erect bush with an approximate 1.3 m height and 1 m length. It presents carved and soft to the touch leaves, which have numerous glandular trichomes and small pink-colored flowers (Blerot et al., 2016). The main components are geraniol, linalool, citronellyl formate, menthone, isomenthone, and nerol (Szutt et al., 2019). Besides, P. capitatum is a slightly scented sub-shrub with approximately 1 m in height and 1.6 m in length. It presents hairy leaves with interspersed glandular trichomes. Their main components are caryophyllene, viridiflorol, 10-epi-gamma-eudesmol, citronellyl formate, and citronellol. Finally, P. radens is an erect bush, approximately 1.5 m in height and less than a meter in width. It has leaves that are hard to touch with many interspersed glandular trichomes. The main components are citronellic acid, menthone, and isomenthone (Blerot et al., 2016; Lalli et al., 2006).

3.2. Pharmacological Properties of Pelargonium

3.2.1. Anti-Tuberculosis

During the year 2009, it was identified that compounds such as quercetin-3-d-glucoside, myricetin, gallic acid, and methyl gallate, which exist in P. reniforme’s aqueous extract, were capable of modulating the intracellular survival of the mycobacteria M. fortuitum and M. tuberculosis, which are present in murine peritoneal macrophages. (Kim et al., 2009) Another study determined that a raw root extract of P. sidoides exhibited an increased inhibition of M. tuberculosis growth. (Kolodziej et al., 2003) It has also been seen that acetone, chloroform, and ethanol extracts of P. reniforme’s roots present activity against M. tuberculosis, although to a lesser extent than the standard anti-tuberculosis medicine (Mativandela et al., 2006). On the contrary, it has been described that the umckalin, scopoletin, 6,8-dihydroxy-5,7-dimethoxy-2H-benzopyran-2-one,6,8-dihydroxy-7-methoxy-2H-benzopyran-2-one, catechin, and epigallocatechin compounds, isolated from the butanolic root extract of P. sidoides do not exhibit any activity against M. tuberculosis, and they present no activity against THP-1 macrophage cell lines, which are infected with the bacteria. As a result, it is supposed that the described cases on the effective use of the plant against tuberculosis can be due to indirect effects or due to an immune system activation (Mativandela et al., 2006).

3.2.2. Antioxidant

The antioxidant activity of a mother tincture of P. sidoides has been confirmed, attributed to gallic acid, trihydroxycoumarin, dihydroxycoemarin sulfates, proanthocyanins, and phenolic glycosides. Furthermore, due to the presence of hydrolyzable flavonoids and tannins, it has been informed of the antioxidant activity of P. reniforme. These compounds protect the cells of the reactive oxygen species (ROS) and eliminate the superoxide radicals, nitric oxide, and peroxyl (Latté & Kolodziej, 2004).

On the other hand, the raw acetone extracts of P. botalimum and P. crispum have proven to execute a potent antioxidant activity attributed to the flavonoid derivatives (Lalli et al., 2008). It has been established that the hydroxyls obtained from the stems and leaves of P. graveolens show significant antioxidant activity. Besides, it reaches even ten times more activity than the thymol due to the phenolic derivatives. Therefore, formulations of this species are promising food supplements (Cavar & Maksimović, 2012).

3.2.3. Antitumor

The solid anticancer activity of a commercial P. sidoides mother tincture has been proven, this being against the lymphoblast cellular line of human T leukemic cells. The blocking of the G0/G1 phases of the cell cycle and
apoptosis have been identified. Due to the presence of polyphenolic compounds in the plant (Pereira et al., 2015). Besides, it has been observed that the methanolic extract of *P. quercetorum* has a significant antiproliferative effect against the lung cancer cell lines (Aztopal et al., 2015). The tetracosane, heneicosane, and 2-methyl eicosan are the most abundant compounds in this species; thereby, it is believed that they are responsible for said activity. Moreover, anticancer activity has been confirmed with *P. graveolens*' essential oil in human promyelocytic leukemia cells. Said activity can be due to the presence of monoterpenes, such as citronelol and transgeraniol (Fayed, 2009).

### 3.2.4. Antibacterial

Studies have shown that the root extract of *Pelargonium sidoides* has strong antibacterial properties against one of the periodontal pathogens, *Aggregatibacter actinomycetemcomitans*. This effect is mediated by compounds like oxygenated coumarins, flavonols, and prodelfinidines. In addition, the antibacterial activity of root methanolic extracts of *P. reniforme* and *P. sidoides* has been proven, which had an inhibitory activity over microorganisms responsible for this activity. It is believed that bactericide efficiency is achieved by inhibiting bacterial adhesion (Kolodziej & Kiderlen, 2007).

It has been informed that the commercial extract of *P. sidoides*, EPs® 7630, inhibits the growth of *Streptococcus pyogenes*, *Proteus mirabilis*, *Staphylococcus aureus*, *Escherichia coli*, *Streptococcus pneumoniae*, *Haemophilus influenzae*, and *Staphylococcus epidermidis* (Iekabsone et al., 2019). Another study has proven that this commercial extract presents inhibitory activity against *Helicobacter pylori* by reducing the bacterial density due to the block of the adhesion of the bacteria to the host's gastric cells. It was suggested that the negatively charged extract components are responsible for the effect (Beil & Kilian, 2007).

The essential oil of *P. graveolens* has shown antimicrobial activity against *Salmonella enteritidis*, *Pseudomonas aeruginosa*, *Escherichia coli*, *Staphylococcus aureus*, and *Bacillus subtilis*. An antimicrobial effect has been observed, more effective than chloramphenicol and amoxicillin. It looks like β- citronellol, a prominent part of the oil, and its likely synergistic effect with other components is responsible for the antibacterial effect (Ghanadni et al., 2012).

### 3.2.5. Antifungal

It has been seen that aerial and root part extracts of *P. sidoides* present anticyptococcal activity and antipathogenic properties in virulence factors against *Cryptococcus neoformans*. These effects are mediated by the inhibition of the laccase and urease activities and the reduction in the size of the fungus capsule. It is believed that some of the compounds responsible for the activity are: isoorientin, orientin, vitexin, and luteolin 7- O-β-D-glucoside. Besides, compounds like gallic acid, fraxetin, and scopoletin, present in this plant, have reports of activity against *Candida albicans* (Samie et al., 2019).

The main compounds of the rose-scented oil from the *Pelargonium* species’ leaves, citronelol, linalool, geraniol, isomenthone, geranyl formate, and citronellyl formate, have proven activity against *Candida albicans* and *Cryptococcus neoformans* (Rath et al., 2013). Also, the *Pelargonium zonale* stem's extract has indicated an inhibition of the activity against *Candida albicans*, through changes in the morphology of the fungal cells and the cellular metabolic activity (Lewtak et al., 2014).

#### 3.2.6. Antiviral

The EPs® 7630 medicine has proven antiviral activity against several viruses, especially the ones responsible for respiratory diseases, such as respiratory syncytial virus, human coronavirus, parainfluenza virus, and coxsackie virus, as well as the seasonal influenza A virus strains (H1N1, H3N2), through the inhibition of the activity of neuraminidase and hemagglutination (Theisen & Muller, 2012). However, this preparation is inactive against other viruses, such as; adenoviruses, rhinoviruses, and measles. Said antiviral effects are attributed to the gallic acids and other phenolic compounds present in the plant (Brendler & van Wyk, 2008).

The aqueous extract of *P. sidoides* has proven to be capable of inhibiting the replication of the HSV-1 and HSV-2 virus (Michaelis et al., 2011). Furthermore, this aqueous extract showed a potent anti-HIV-1 activity by directly interfering with the viral infectivity and blocking the virus's particles union to the objective cells. It has been determined that said activity was mediated by multiple low-cytotoxic polyphenolic compounds present in the plant (Helfer et al., 2014).

#### 3.2.7. Immunomodulatory

Recent studies have informed that EPs® 7630 can increase innate immune defense by activating monocytes, inducing proinflammatory cytokines, and modulating their mediator production capacity and neutrophils and Th17 and Th22 adaptive cell generation (Witte et al., 2015). In addition, it has been established that this extract can stimulate the host's defense by enhancing the liberation of antimicrobial peptides. Besides isolated *P. sidoides*, simple phenols, flavan-3-ols, proanthocyanidins, and hydrolyzable tannins compounds could enhance the ARNm of iNOS proteins and cytokines levels in parasitized cells (Brendler & van Wyk, 2008). Moreover, geraniol, the main compound of the *Pelargonium* essential oils, has proved the prevention of graft rejection in live models, mediated by a reduction in the immune system's response. It has also been proven, in live models, to exercise suppression regarding the adherence of neutrophils induced by TNF-α (Chen & Viljoen, 2010).

### 3.3. Pelargonium Applications in Pharmaceutical and Food Area

Nowadays, the preparation of EPs® 7630 is made from the *P. sidoides* roots’ ethanolic extract (11% w/w), and it is the most popular medicinal product obtained from *Pelargonium* species in the pharmaceutical industry. This has been the object of many chemical studies, clinical and non-clinical, from which it has been awarded immunomodulatory, antiviral, and antibacterial properties mainly. In addition, it is found in a film-coated tablet fashion, which
contains the dry extract, which is prepared from the liquid extract. It contains six main compound groups: purine (2%), coumarins (2%), peptides (10%), carbohydrates (12%), minerals (12%), and oligomeric procollagens derivatives (EMA, 2018). At present, it is indicated for the treatment of acute bronchitis. It offers an effective alternative in treating this condition in cases where an antibiotic is not required (Chuchalin et al., 2005).

Numerous clinical essays have informed about the use of this formulation to treat the common cold in adults. It has been proven that early administration reduces the severity of the symptoms and the duration of the illness (Chuchalin et al., 2005). Furthermore, its effectiveness has been reported regarding the early treatment of acute respiratory tract infections in kids, quickly decreasing the symptoms and, as a result, the risk of bacterial super-infection (Careddu & Pettinazzo, 2018). Moreover, some studies have proven the prevention of asthma attacks during viral superior respiratory tract infections, a significant reduction of cough frequency, a high secretolytic activity, and the reduction of trachea and bronchi injuries (Bao et al., 2005). It has been proven that early administration reduces the occurrence of viral superior respiratory tract infections, a significant reduction of cough frequency, a high secretolytic activity, and the reduction of trachea and bronchi injuries (Bao et al., 2005). At present, it is indicated for the treatment of acute bronchitis. It offers an effective alternative in treating this condition in cases where an antibiotic is not required (Chuchalin et al., 2005).

3.4. Pelargonium Extraction Methods

3.4.1. Procedure for the Preparation of Extracts of Pelargonium sidoides and Pelargonium reniforme

The roots of Pelargonium sidoides and Pelargonium reniforme undergo percolation or a two-stage maceration. Percolation and double maceration are carried out with mixtures at different proportions of water:ethanol, such as 10%–92% w/w ethanol or 10%–60% w/w ethanol. The extracts obtained, after drying, have a total phenolic content of 15%–18% (Erdelmeier et al., 2007).

**Percolation examples (Erdelmeier et al., 2007):**

1) 1 kg of dried roots of *Pelargonium sidoides* is placed in 2 kg of 35% w/w ethanol for 24 hours and then transferred to a glass column. It is percolated for 10 hours with 8 kg of 5% w/w ethanol. The drug residue is squeezed lightly, and the extract is filtered through a Seitz Supra 1500 filter and concentrated by evaporation to dryness.

2) 40 g of dried roots of *Pelargonium sidoides* are placed in 80 g of an extraction solvent (11% w/w or 35% w/w ethanol) for 22 hours and then transferred to a glass column. It is percolated for 3 to 4 hours with 320 g of the solvent used for the extraction, the drug residue is squeezed lightly, and the extract is concentrated by evaporation to dryness.

3) 40 g of dried roots of *Pelargonium sidoides* are placed on a glass column and percolated for 8 hours with 400 g of 11% w/w ethanol. The drug residue is squeezed lightly; the extract is filtered through a Seitz Supra 1500 filter and concentrated to dryness.

**Maceration example (Erdelmeier et al., 2007):**

1) 20 g of dried Pelargonium sidoides roots are macerated with 140 g of an extraction solvent (11%, 20%, 35%, 60%, 90% w/w ethanol-water or water) at 50 °C for 30 minutes. The extract is separated by filtration, and the drug residue is macerated for a second time in the same way. After solid/liquid separation, the extract solutions are mixed and dried.
3.4.2. Procedure for the Preparation of Dry Extracts of Pelargonium sidoides y Pelargonium reniforme

Two solvents are used; solvent A composed of 10 parts of 96% ethanol, 20 parts of 85% glycerol, and 70 parts of water. And solvent B composed of 10 parts of 85% glycerol, 10 parts of xylitol and 80 parts of water (Herrmann & Thöle, 2010).

Examples (Herrmann & Thöle, 2010):

1) 28 kg of ethanol (35% w/w) are added to 14 kg of the ground root of Pelargonium sidoides and stored at room temperature for 20 hours. The mixture is percolated with 112 kg of ethanol (6% w/w) for 10 hours and then filtered. Subsequently, 1.25 kg of mannitol is dissolved in 15.4 kg of the liquid extract. It is dried at 50 °C under a vacuum. Then, 5.55 g of each of the obtained dry extracts is mixed with 100 ml of solvent A or B after mixing with 4.55 g of a carrier substance.

2) 28 kg of ethanol (35% w/w) are added to 14 kg of ground Pelargonium sidoides root and stored at room temperature for 20 hours. The mixture is percolated with 112 kg of ethanol (6% w/w) for 10 hours and then filtered. Subsequently, 1.19 kg of sucrose is dissolved in 14.7 kg of the liquid extract. It is dried at 50 °C under a vacuum. Then, 5.55 g of each of the obtained dry extracts (corresponding to 1 g of the native portion and 4.55 of mannitol) are mixed with 100 ml of solvent A or B.

3) 28 kg of ethanol (35% w/w) are added to 14 kg of the ground root of Pelargonium sidoides and stored at room temperature for 20 hours. It is percolated with 112 kg of ethanol (6% w/w) for 10 hours and then filtered. Subsequently, 1.25 kg of mannitol is dissolved in 15.4 kg of the liquid extract. It is dried at 50 °C under a vacuum. Then, 5.55 g of each of the obtained dry extracts (corresponding to 1 g of the native portion and 4.55 of mannitol) are mixed with 100 ml of solvent A or B.

4) 28 kg of ethanol (35% w/w) are added to 14 kg of the ground root of Pelargonium sidoides and stored at room temperature for 20 hours. The mixture is percolated with 112 kg of ethanol (6% w/w) for 10 hours and filtered. Subsequently, 1.34 kg of maltodextrin is dissolved in 16.5 kg of this liquid extract. It is dried at 50 °C under a vacuum. Then 5.55 g of each of the obtained dry extracts (corresponding to 1 g of the native portion and 4.55 of maltodextrin) are mixed with 100 ml of solvent A or B.

3.4.3. Procedure for the Preparation of Essential Oil of Pelargonium odoratissimum

The vegetable material of Pelargonium odoratissimum is placed in a volatile oil extractor, then distilled water is added according to a solid-liquid ratio of 1:10–20 and is then soaked for 1 to 3 hours, occasionally shaking it. Then, the wet distillation is done, and after 3 to 6 hours, the essential oil is gathered through drying using anhydrous sodium sulfate. After the sealing, a transparent, yellow, and usable form of the volatile oil is obtained and preserved at −4 °C. This product can be used as an essence in makeup and laundry products or as a medicinal essence (Chen et al., 2015).

3.4.4. Procedure for the Preparation of the Rose-Scented Pelargonium Essential Oil

350 kg of Pelargonium leaves are placed in a false bottom in the distillation tank, and steam is poured into the false bottom. The vapors formed are passed through a cohabation column and condensed in a horizontal shell and tube heat exchanger. The distillate and collected oil are separated in a receiver/separator. The distillate is recycled to the distillation tank through the cohabation column from the receiver/separator. After completing the 4 hours of distillation, steam is injected into the steam jacket to boil the residual water that collects at the bottom of the alembic. The process continues for another 4 hours. The collected oil is dried over anhydrous sodium sulfate (Babu & Kaul, 2005).

3.5. Pelargonium Pharmaceutical Formulations

3.5.1. Formulation of Hedera Helix Extract, Pelargonium sidoides Extract and Zingiber officinale Extract

The formulation aims to administer orally, parenterally, ocularly, nasally, buccally, sublingually, and topically, with the oral being the preferred route. The volume of Zingiber officinale must be preferably 0%, 1%–4% w/v. The formulation contains at least one propolis extract, Glycyrrhiza glabra, and Echinacea purpurea (Cifter et al., 2014):

1) If the formulation contains propolis extract, the weight ratio of the Hedera helix, Pelargonium sidoides, Zingiber officinale, and propolis extracts is 6:10:4:1, respectively.

2) If the formulation contains Glycyrrhiza glabra, the weight ratio of the Hedera helix, Pelargonium sidoides, Zingiber officinale, and Glycyrrhiza glabra extracts is 7:12:5:5, respectively.

3) If the formulation contains Echinacea purpurea, the weight ratio of the Hedera helix, Pelargonium sidoides, Zingiber officinale, and Echinacea purpurea extracts is 7:12:5:8, respectively.

4) If the formulation contains Hedera helix, Pelargonium sidoides, Zingiber officinale, propolis, and Glycyrrhiza glabra extracts, the weight ratio is 6:10:4:1:4, respectively.

5) If the formulation contains Hedera helix, Pelargonium sidoides, Zingiber officinale, propolis, and Echinacea purpurea extracts, the weight ratio is 6:10:4:1:7, respectively.

6) If the formulation contains Hedera helix, Pelargonium sidoides, Zingiber officinale, Glycyrrhiza glabra, and Echinacea purpurea extracts, the weight ratio is 7:12:5:5:8, respectively (Nadjib et al., 2010).

The formulation must also contain 10%–25% w/v sorbitol, citric acid monohydrate, and sodium citrate dehydrate with a weight ratio of 1:2, 0.05%–2% eucalyptus, 0.005%–10% w/v of a sweetener such as; sucralose, saccharin sucrose, fructose, glucose, sorbitol, or a mixture of these, and solvents such as; propylene glycol, glycerin, water or ethanol or a mixture of them (Cifter et al., 2014).
One method to elaborate the formulation consists of adding every solvent to the fabrication container and mixing until obtaining a homogeneous mixture (A mixture). Then, add the inactive ingredients to the container carrying the A mixture and mix until obtaining a homogeneous mixture (B mixture). Then incorporate the extracts of the herb-based substances into the B mixture and mix until obtaining a homogeneous mixture (C mixture). Finally, the C mixture can become a different dosage (Cifter et al., 2014).

### 3.5.2. Formulation of Emulsion for Topical Use, Based on Aromatic Water of Pelargonium graveolens

A semi-solid formulation of the hydrophilic emulsion type is made. The oil phase (30%) contains; 10%-15% paraffin oil, 5% white wax, 4% stearic acid, 4% cetyl alcohol, and 1%-2% cetostearyl alcohol. And the aqueous phase (70%) contains; 65% geranium hydrosol (aromatic geranium water), 4%-5% glycerin, and 0.3%-2% triethanolamine. The protocol used is that of a conventional emulsion, where the two phases (oily and aqueous) are prepared at 70 °C separately and mixed by applying agitation. Then, a preservative is added to guarantee sterility, and it is packaged in aluminum tubes (Nadjib et al., 2010).

### 3.5.3. Solid Formulation Made from Pelargonium sidoides Extracts and Silicic Acid Compounds

As a first step, the extract of Pelargonium sidoides is made. The plant’s dried roots are cut to a size of about 10 mm or less, dipped in 35% ethanol. 5.3% ethanol is added in a volume of approximately eight times that of the dried root. Subsequently, the liquid extract is filtered. Then, it is sterilized at 120–121 °C for 30 seconds and cooled (Choi et al., 2016).

The development of the solid formulation that includes extract of Pelargonium sidoides and a compound of silicic acid consists of; placing the previously made extract in conjunction with a silicic acid compound in a high-speed mixer and mixing them together to adsorb the extract of Pelargonium sidoides on the silicic acid compound. Subsequently, microcrystalline cellulose, hydrated lactose, and povidone are added and mixed. The obtained mixture is dried and sieved. Then, croscarmellose sodium, colloidal silicon dioxide, and sodium stearyl fumarate are added to the sieved product and mixed. The obtained mixture is compressed in a tableting machine. Finally, coating the tablets with Opadry is performed (Choi et al., 2016).

### 3.5.4. Formulation of Herbal Supplements Made from Geranio Pelargonium

One or more crushing plants of the Geranium or Pelargonium genus are used, and water and alcohol are added to obtain a mixture that is then refluxed. The mixture is extracted to separate the essential oil phase from the aqueous phase. The aqueous phase is concentrated and dried to obtain a powder. The purified essential oil is combined with the powder to obtain the extract. This method (or modifications thereof) can be used to obtain an extract containing at least 1% methylhexaneamine (Akrong et al., 2012). Examples (Akrong et al., 2012):

1) Dietary supplement for appetite suppression: It is prepared as a powder to mix with water and consumed twice a day. One serving (about 8 g) contains 6 g Inulin Root (*Cichorium intybus*), 150 mg Anhydrous Caffeine, 10 mg Psyllium Powder Seed Husk (*Plantago ovata*), 10 mg Oat Powder (*Avena sativa*), 5.3 mg of methylhexaneamine (obtained from the extract of Geranium or Pelargonium), excipients and flavorings.

2) Pre-exercise supplement: Prepared as a powder to administer before exercise, 1 to 3 servings (tablespoon/serving) contain; 120 mg of caffeine, 5.3 mg of methylhexaneamine (obtained from Geranium or Pelargonium extract), 1 g of B-alanine, 1 g of citrulline, and 1 g of creatine.

### 4. Conclusion

*Pelargonium* is a genus with many species, widely characterized in taxonomy, phylogeny, distribution, and traditional uses. Among the most relevant *Pelargonium* species are *Pelargonium sidoides* and *Pelargonium reniforme*, which have a wide range of biological properties and are therefore helpful in the pharmaceutical and food areas, especially the standardized pharmacological extract EPs® 7630 that is currently widely used in the health area, mainly as immunomodulatory and antiviral. However, it is necessary to carry out more clinical studies that contribute to evaluating the other pharmacological properties that have been described, and based on this, analyze different pharmaceutical formulations with the potential to be introduced in the pharmaceutical industry.

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### Conflict of Interest

The author declares that there is no conflict of interest.

### References


