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Pelargonium graveolens (Rose Geranium) – A Novel Therapeutic Agent for Antibacterial, Antioxidant, Antifungal and Diabetics

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Abstract

Objectives: Draw upon published research articles for evidence and comprise the collected evidence in an evaluation of the preserving and therapeutic abilities of *Pelargonium graveolens*.

Design: The articles used as research for this research review were discovered by searching public databases with keywords such as *"Pelargonium graveolens", "P. graveolens"*, "pelargoniums", "rose-scented geranium", and "geraniums." Then the articles were reviewed, summarized, and organized based on findings.

Results: Many articles were reviewed and many different benefits to the *Pelargonium* genus were discovered. The major focus in the reviewed articles, however, was on the species *Pelargonium graveolens (P. graveolens). P. graveolens* displayed many positive benefits. The major benefits that were reviewed were the plant's antibacterial, antioxidant and anti-fungal activities. Other noteworthy benefits that were reviewed include hypoglycemic and anti-reprotoxic activities as well as fairly low toxicity levels.

Conclusion: *Pelargonium graveolens* antibacterial activity shows promise and could move to human trials. However, more research needs to be performed on Gram-negative bacteria because the essential from the plant does not have as strong of an effect as it does on Gram-positive bacteria. As an antioxidant, results are very positive and human trials could ensue. Regarding anti-fungal activity, the essential oil outperformed the drugs currently in place to treat fungal activity and in doing so led to the conclusion that *P. graveolens* could be used as a viable anti-fungal. *Pelargonium graveolens's* antioxidant ability is linked to its hypoglycemic effects against diabetes as diabetes has been linked to oxidative stress. Human trials in this area could also ensue. Against toxins that affected the male reproductive system, *P. graveolens* showed to reverse the negative effects and more research should be done to look into the potential for human trials. In most cases thus far observed, *P. graveolens's* toxicity level was relatively low and within limits to be harmless to humans. However, it was not low enough to be considered without any hesitation and more research should be performed to look for ways to lower this level.

Introduction

Pelargonium graveolens (*P. graveolens*), commonly known as rose geranium is one of more than 250 species within the Pelargonium genus and that are native to the southern parts of Africa [1]. However, not all species of the genus reside there. Some have branched out and thanks to the spice trade and medical plant collection by sailors some species can now be found growing naturally in Australia, eastern Africa, New Zealand, the Middle East, the islands of Helena, Tristan de Chuna and Madagascar [2,3]. While most noteworthy because of the scents they produce, it is actually the essential oils that provide the benefits that society reaps. Essential oils are the secondary metabolites that plants produce. These oils are volatile, natural, and complex compounds that are known to be important in plant reproduction as they assist in the dispersion of seed and pollen by attracting some insects. They are, more importantly, intended to protect the plant against bacteria, viruses, pests, and fungi [4]. It is these benefits that are pushing the essential oil into common industries today, such as food and medicine.

Uses in food industry

P. graveolens in the food industry is being used for its antimicrobial activity. The essential oil has shown through multiple studies to be effective in fighting bacteria and fungi. This antimicrobial action has led to testing of the oil against

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food spoilage pathogens and has shown promising results. Enough so that it has been highly considered in the food industry as a preservative agent [5].

The most recent, and likely most relevant, use of the plant is in the medical field. *P. graveolens* has shown potential in many different studies for its abundance of positive benefits. These benefits include antibacterial, antifungal and antioxidant activity, and others. Traditionally, the plant has been used to treat a variety of symptoms including: nephritis, wounds, fever, colds and sore throats, inflammation, heavy menstrual flow, hemorrhoids, dysentery, cancer gastrointestinal diseases, hyperglycemia, insomnia, heart disease, asthma, nausea and vomiting, fever and tuberculosis to name a few [2,3,6,7].

The intent of this comprehensive research article review is to review the clinical tests that determine the benefits of *Pelargonium graveolens* as a preservative and therapeutic agent via the examination of the antibacterial, antioxidant, antifungal and hypoglycemic activities, and repro-toxic and toxic effects of the plant's essential oils.

Results

Anti-bacterial activity

Drug resistant bacteria are becoming a more prevalent issue every day. In a search for an answer, medicine has turned back to traditional medicines. *Pelargonium graveolens* is known for its abilities to combat bacteria. A number of studies were performed to examine exactly how effective the plant is against different bacteria. To start looking into the effects, a study evaluated *Pelargonium graveolens* against a number of different Gram-positive and Gram-negative bacteria [5]. The bacteria in this study were *Staphylococcus aureus, Staphylococcus epidermidis, Bacillus subtilits, Escherichia coli, Citrobacter freundii, Proteus vulgaris, Serratia marcescen, Salmonella typhimurium, Klebsiella pneumonia, Pseudomonas aeruginosa, and Enterobacter aerogenes. S. aureus, B. subtilis*, and *E. coli* had multiple strains that were tested [5]. This study showed that a zone of inhibition was recognized with both Gram-positive and Gram-negative bacteria. However, the zone was greater in the Gram-positive bacteria. Specifically, the rose geranium oil was effective against the Gram-negative bacteria *E. coli, P. vulgaris* and *E. aerogenes* but had no effect on *P. aeruginosa and K. pneumonia*. The bias was shown when viewed against *S. aureus, E. faecalis, B. subtilis*, and *S. epiedermis* as these Gram-positive bacteria displayed greater inhibition zones than the Gram-negative bacteria [5,6].

Another study, by Anis Ben Hsouna et al., showed similar findings to the study afore-mentioned [7]. Additionally, this study looked into the oil's preference of Gram-positive bacteria over Gram-negative bacteria. It concluded that the Gram-positive bacteria were preferred because they lacked the hydrophilic polysaccharide chain that acts as a barrier for Gram-negative bacteria. This difference is what allows Gram-negative bacteria to be less susceptible to the *Pelargonium graveolens* oil [7].

Dorman et al. produced a study that focused on the volatile oils of different plants, *Pelargonium graveolens* included [8]. The results of the study stated that all of the twenty-five tested bacterial strains (nine Gram-positive and sixteen Gram-negative) displayed some degree of susceptibility towards the *P. graveolens* oil and *P. graveolens* displayed a bias towards Gram-positive bacteria over Gram-negative bacteria. However, this study also looked into whether or not the bias could be lessened and the susceptibility of Gram-negative bacteria could be increased [7]. Dorman found that through the addition of an alkyl substituent in the non-phenolic ring structure, more Gram-negative bacteria were affected, thus indicating that the alkylation influences Gram sensitivity and that if an alkylic side chain could be added to the oil, its effects could be enhanced and used as a very effective disinfectant, food preserving agent or chemotherapeutic agent [8-11].

In yet another study, strictly the essential oil of *Pelargonium graveolens* was evaluated against the six bacterial strains of *Listeria monocytogenes, Salmonella enteritidis, Escherichia coli, Staphylococcus aureus, Pseudomonas aeruginosa, and Bacillus subtilis* [4]. These results conclude that all of the strains with the exception of *L. monocotyogenes* and *E. coli* were susceptible. *S. aureus* proved to once again be the most susceptible. The essential oil proved to be more effective than the controls of amoxicillin and chloramphenicol, thus suggesting it could make a better antibacterial agent than the current drugs in place [4].

Anti-oxidant activity

The human body functions on reduction-oxidation reactions, thus making the need for oxidative processes a necessity. However, too much oxidation leads to oxidative stress and a number of other negative effects. Some of those effects could lead to diseases like cancer, cardiovascular disease and diabetes [2,12-14]. Modern theory regarding free radical biology insinuates that reactive oxygen species are key factors in certain diseases (like those aforementioned) and risk factors for such diseases hold the potential to be reduced via alteration of the diet to an appropriate pattern and adding natural antioxidants. *Pelargonium graveolens* has been investigated for this purpose. Sanja Ćavar and Milka Maksimović tested hydrosols of *P. graveolens* stems and leaves against thymol in a 1,1-diphenyl-2-picrylhydrazyl (DPPH) solution. DPPH is a vibrant violet color and when free radicals are captured and reduced, the solution turns yellow; therefore, it is a great tool to visualize oxidations.2 The results of this study concluded that rose geranium essential oil from the stems possessed higher antioxidant activity than the leaves and that the hydrosols from both the stems and leaves were ten times higher than the thymol control [2,15-17].

Anti-fungal activity

Pelargonium graveolens, in addition to being known for its antibacterial and antioxidant activity, was also thought to possess strong antifungal qualities as well. This is a major benefit in the food industries as many food spoilage pathogens are fungi.

A study by Mohamed Nadjib Boukhatem et al., looked at the antimicrobial activity of *P. graveolens* against a variety of spoilage agents. The tested fungi included *Candida lipolytica, Candida tropicalis, Candida sake, Candida parapsilosis, Candida kruse, Rhodoturla glutinis, as well as two strains of C. albincans*. This study also looked into the activity of the plant against bacteria. The results were interpreted as of a zone of inhibition (defined as areas of zero microbial growth). The result of the essential oil extract against the microbes showed that the oil was more effective on the yeasts than the bacteria [5]. It was particularly effective against *C. tropicalis and C. albicans. C. albicans* was even found to be more susceptible to the essential oil than the most susceptible bacterium, *S. aureus* [5,18-21].

Medicinally, the antifungal properties of *Pelargonium graveolens* have been shown to be effective against *Malasezia* species. Pityriasis versicolor (PV) is one of many skin diseases thought to be caused by the *Malassezia* genus. Naeini et al. tested *P. graveolens* against strains from *Malassezia* species (*Malassezia furfur, Malassezia globosa, and Malassezia obtusa*) that were isolated from patients with PV [22,23]. It was found that the rose geranium essential oil was active against all the tested strains, but was particularly effective against M. obtuse, against which the oil created an inhibition zone of greater than 50mm. In comparison to the control group, which consisted of Ketoconazole (the drug currently used to treat diseases of *Malassezia* species), it was observed that *P. graveolens* produced an inhibition zone twice the size of the one produced by the control group [22,24].

In another study, executed by Anis Ben Hsouna and Naceur Hamdi, *Pelargonium graveolens* was tested against several known mycotoxins: *Asperillus niger, Aspergillus flavus, Fusarium graminearum, Fusarium oxysporum, Fusarium culmorum, Rhizopus nigricans and Alternaria alternate* [7]. The study tested the rose geranium oil in different extracts (n-hexane, ethyl acetate, and methanol) and the results were compared in terms of Minimum Inhibitory Concentrations (MICs). MIC was operationally defined as the lowest concentration of the total essential oil at which the microorganism does not demonstrate visible growth after incubation [7]. The n-hexane extract produced zero antifungal activity. The ethyl acetate extract inhibited the growth of the Fusarium species and strongly inhibited the growth of the *Aspergillus* species.

Diabetic effects

Diabetes mellitus is a prominent and continuously growing issue around the world today. In fact, the current adult prevalence of this disease sits at 285 million people. Unfortunately, this number is only expected to grow and, by the year 2030, reach an estimated 439 million. The disease is marked by hyperglycemia (high blood sugar) with an insulin impairment and or insulin action [12]. However, these are not the only symptoms. Also reported in connection with diabetes is an alteration in the intermediary metabolism of carbohydrates, lipids, and proteins [12].

Currently, studies are showing that the development and progression of the disease is brought on by oxidative stress; specifically, stress created by a hyperglycemia-induced generation of radicals. These radicals produce an abnormally high free radical level leading to membrane lipid peroxidation, protein glycation and a decrease in antioxidant defenses simultaneously resulting in membrane damage [12].

The current treatment for diabetes mellitus includes synthetic drugs or insulin. Both treatments have, over time, proven to help manage the disease. However, these two solutions create new problems of their own. Side effects noted by patients who are being treated with either one or both drug regimens are drug-resistance, hypoglycemia, edema and weight gain [12]. Clearly, these symptoms are counterproductive to their intended purpose and a hassle to have to deal with in an attempt to make one healthier. Thus, research has turned towards traditional medicine for an answer.

Rose geranium, which traditionally had been used as a diabetic, was put to the test [12]. In a study by Maher Boukis et al., *P. graveolens* was tested amongst alloxan-induced diabetic rats. The test evaluated the effects of different doses of rose geranium essential oil on the induced diabetic rats as opposed to those that were not induced and classified as normal control rats. The results showed that a dose of 150 mg/kg by body weight was the most effective dose of essential oil to treat diabetes mellitus. Once dosed with the oil, the diabetic rats displayed significant hypoglycemic effects. When the rats were diagnosed as diabetic (rats with blood glucose levels above 10 $mmol/dm^3$ after two weeks of alloxan injections) an increase in liver and kidney Thiobarbituric Acid Reactive Substances (TBARS) levels was observed. Then, after having been treated with the rose geranium essential oil, the liver and kidney TBARS levels significantly decreased, indicating that the oil made the rats less susceptible to peroxidative damage when under oxidative stress like diabetes [12]. It was observed that hyperglycemia depletes the antioxidant system in response to increased lipid peroxidation and the formation of free radicals. The rose geranium essential oil combats this by reducing oxidative stress via the prevention of the generation of free radicals, thus inhibiting the development of diabetes [12].

Reprotoxicity

The abundance of toxins in the environment and the negative effects from said toxins are becoming prevalent issues. The toxins are reported to be causing issues in male reproduction and cause a decline in the quality and quantity of human semen. Deltamethrin (DL) is one such toxin. In attempt to revert and prevent the negative effects of this toxin and others like it, attention was drawn back to traditional medicine [25]. An answer arose in Pelargonium graveolens, which is known for its antioxidant effects.

In a study performed by Ahlem Ben Slima et al., DL was administered to healthy, male, virgin mice. Upon examination, the mice displayed a significant decrease in sperm count and motility, testicular catalase and superoxide dismutase activity,

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and GSH (a natural antioxidant) and ascorbic acid levels. Additionally, an increase in abnormal morphology was observed. These effects when considered together lead to the conclusion that the Deltamethrin induced oxidative stress in the mice testes. When treated with the *P. graveolens*, the negative effects were reversed [25]. Slima et al. found that *P. graveolens* essential oil produced a strong protective effect against oxidative stress damage and that a dose of 67 mg/kg/day was sufficient to reduce protein oxidation in the testes as well as reduce oxidative stress and lipid peroxidation. The oil also improved the poor quality of the sperm [25].

Toxicity

Despite having proved to possess various benefits, *P. graveolens* still poses a threat in regards to toxicity. To keep an eye on the toxicity levels of different substances that are being used in either food or drugs, the USA's Food and Drug Administration (FDA) has created a list known as the Generally Recognized as Safe or GRAS list. The list recognizes *P. graveolens* oil as GRAS between 1.6 to 200 ppm [3]. In a study performed by Lalli et al., the *in vitro* toxicity of certain *Pelargonium* species was examined. Lalli et al. expressed toxicity in terms of the IC50 value. The IC 50 value was defined as the concentration the essential oil must be at to produce 50% decolorization of stable 2,2-diphenyl-1-picrylhydrazyl (DPPH) [6]. The lower the IC50 value the higher the toxicity. *Pelargonium graveolens* produced a fairly high IC50 value, meaning it is fairly non-toxic but levels should be monitored because it is not necessarily highly non-toxic either [6].

Discussion

Pelargonium graveolens possess the common name of rose scented geranium and even more commonly, rose geranium. It is an herbal plant that has been used for centuries by many tribes as a medicine. Native to southern Africa, it has served the people there as medicine for a number of ailments, such as wounds, fevers, cold, inflammation, and more [6,2]. Currently, drug resistant microbes are on the rise and the drugs currently in use are failing. Traditional medicine has been revived to investigate the possibility of herbs and plants to combat the now drug resistant microbes. Thus, traditional medicine is gaining interest in the medical community as it could possess the answer. *Pelargonium graveolens* was known to possess many beneficial qualities and this review has explored a number of them. Multiple studies have shown that the plant possesses great antibacterial activity against Gram-positive bacteria [4,5,7]. It also possesses the ability to combat Gram-negative bacteria but so far the greatest results have been seen with the addition of an alkyl substituent to help it [8]. Despite these positive outcomes, more research needs to be done to determine if more Gram-negative bacteria could be affected and if the best way to obtain results against Gram-negative bacteria is with the addition of the alkyl substituent. If there is a way to achieve the same outcome without the addition of the alkyl substituent, the extra effort and cost that would be saved might be able to influence some drug companies to make the effort to produce *Pelargonium graveolens* as an antibiotic.

Rose geranium has also proven to be a great antioxidant as it possesses the ability to not only capture free radicals, but also prevent a new generation of free radicals from forming, thus reducing oxidative stress and inhibiting the development of diabetes [12]. In an investigation on diabetes mellitus, it was discovered that disease could be brought on by oxidative stress [12]. As previously mentioned, *Pelargonium graveolens* has strong antioxidant abilities and when tested against mice that were induced with diabetes, the oil reversed the harmful effects. The effect from the experiment with the alloxan induced diabetic mice was revealing. More studies should be performed to try to replicate these results. If replicable, the oil could then be used in studies on humans to see if the same results appear and a new potential treatment for diabetes mellitus could arise. Research on the antioxidant effects of rose geranium is pretty conclusive; however, more could be done to actually see the antioxidant effect in humans. If applicable, humans could use the oil as (a) a simple antioxidant and (b) a potential treatment/preventative measure for diseases that are brought on by oxidative stress.

The plant has shown to be an anti-fungal agent. Its ability to combat multiple fungi known for being food spoilage pathogens makes it a great contender to become a new food preservative [5]. Additionally, rose geranium has been tested against mycotoxins and pathogens known to cause some serious skin diseases [7,22]. It was found in both studies that *P. graveolens* created greater inhibition zones than the controls used in the experiment. In both cases, the controls consisted of the drugs currently used to treat those specific ailments [7,22]. The fact that the Pelargonium essential oil performed better than the current drugs in place indicates that the plant possesses great anti-fungal abilities and should be considered as a treatment for fungal related illnesses.

Another concern that was raised was the issue of toxicity. Toxicity in regards to the male reproductive system was investigated and it was discovered that, with the increase of toxins being released into the environment, there has been a detrimental effect noticed amongst male sperm in quality and quantity. When a rose geranium essential oil was used to treat these detrimental effects, sperm quality was improved and a protective effect against the oxidative stress caused by the toxin was observed [11]. Another noted benefit of *P. graveolens* was that it possesses a relatively low toxicity level, meaning that all the benefits that have previously been discovered could be seen in humans as replacements for the current drug regime [6]. It should be noted, in the studies observed for this review, the *P. graveolens* toxicity levels were non-toxic. However, the levels were needed to be closely monitored [6]. More research should be directed towards seeking a method to decrease the oil's toxicity levels so it could be used as therapeutic agent without the incredibly close monitoring that has so far been placed upon the use of the oil.

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Conclusion

Pelargonium graveolens, rose geranium, has shown multiple positive benefits. Its antibacterial and anti-fungal abilities show strong potential to replace current therapeutic drug regimes as there is an increase in drug resistance microbes. More research is needed to conclude for certain that the potential is high. The plant's antioxidant and hypoglycemic qualities appear to be very potent and research into whether or not it could be used in human trials should be performed. Toxicity is a concern and should be monitored as further research progresses. However, on all fronts, *Pelargonium graveolens* shows great potential for a traditional solution in today's world as a preservative and, more eminently, a therapeutic agent.

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