



## PELARGONIUM GRAVEOLENS (ROSE GERANIUM) – THERAPEUTIC AGENT FOR ANTIBACTERIAL, ANTIOXIDANT, ANTIFUNGAL AND DIABETICS, ANTI-INFLAMMATORY

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**ABSTRACT** This review article is a draw upon published research articles for evaluation of the therapeutic abilities of *Pelargonium graveolens*. This article comprises and investigate the collected evidence for preserving the therapeutic abilities of *P. graveolens*. Various articles were reviewed and many different medicinal applications of the *Pelargonium* genus were discovered. Many other types of species of geranium were found in different geographical regions. But, the main focus in the reviewed articles, however, was on the species *Pelargonium graveolens* (*P. graveolens*). *P. graveolens* shown many positive benefits. *Pelargonium graveolens* (Geranium) is a source of finest quality of fragrance and its essential oils (EOs) are used as antibacterial and antifungal agent. The major benefits that were reviewed were the plant's antibacterial, antioxidant and anti-fungal activities. Other noteworthy benefits that were reviewed include hypoglycemic, anti-inflammatory and anti-reprotoxic activities as well as fairly low toxicity levels.

### KEYWORDS :

#### INTRODUCTION

Medicinal plants have emerged as major source drugs for the treatment of various diseases like cancer, diabetes, and cardiovascular complications. Medicinal plants are an important source of new chemical substances with considerable therapeutic effects [3]. Numerous natural products have been tested in various animal models for the development of new anti-inflammatory agents. Plant essential oils (EO) are used as folk medicine against various kinds of inflammatory diseases. The World Health Organization projected that 80% of people in emerging nations depend on medicinal plants for primary health care need. Natural products derived from medicinal plants are considered safe and effective compared to synthetic modern drugs based on the long history of use by humans as food and medicine [1,2].

Nowadays traditional herbal medicines are used to treat health issues by more than 80% of the world population [4,5]. More than 9000 plants have been identified and recorded for their therapeutic properties. About 1500 species are known for their aromatic properties [6]. Natural aromatic drugs are having great demand in various fields like cosmetics, food, pharmaceuticals, and perfumes. EOs have been used for their aroma, taste, medicinal properties, and as bactericides and preservatives [7]. Therefore, EOs are a safe, environmentally friendly, cost-effective choice for nutrition and environmental protection. EOs and extracts have gained their role as preservatives due to certain chemical compounds they contain, such as terpenes, terpenoids, carotenoids, and phenolics [8,9].

*Pelargonium graveolens* (*P. graveolens*), which is also known as “*P. graveolens*”, “pelargoniums”, “rose-scented geranium”, and “geraniums.”, commonly known as rose geranium. It has been more than 250 species within the *Pelargonium* genus and that are mainly found in the southern parts of Africa [10]. 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 [11,12]. Essential oils are the secondary metabolites of the plants. These oils are volatile, natural, and complex compounds which are very important in plant reproduction as they assist in the dispersion of seed and pollen by attracting some insects. They are, more importantly, used to resist the plants against bacteria, viruses, pests, and fungi [4].

#### Objectives of Review

- Review on published research articles for evidence and comprise the collected evidence in an evaluation of the therapeutic abilities of *Pelargonium graveolens*.
- This research review was 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.
- The major focus in the reviewed articles, however, was on the species *Pelargonium graveolens* (*P. graveolens*). *P. graveolens*

displayed many positive benefits. The major activities were reviewed were the plant's antibacterial, antioxidant and antifungal activities. Other activities are anti-inflammatory activities in rats and invitro anti-diabetic activity. Other noteworthy activities that were reviewed include hypoglycemic and anti-reprotoxic activities at fairly low toxicity levels.

- The main aim of this comprehensive research article 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, antidiabetic, anti-inflammatory activities and repro-toxic and toxic effects of the plant's essential oils.

#### *P. graveolens* As Preservative

*P. graveolens* is used in food industry for its antimicrobial activity. The essential oil of rose geranium has proved through multiple studies to be effective in fighting bacteria and fungi. While the antimicrobial action of this oil against food spoilage pathogens has shown promising results so that it has been highly used in the food industry as a preservative [13,14].

*P. graveolens* shown positive benefits in many different studies with considerable therapeutic effects. The therapeutic effects include antibacterial, antifungal, antioxidant, antidiabetic and anti-inflammatory activity. [Libyan geranal]. In addition to this the plant of rose geranium had been traditionally used for treatment of fever, colds, sore throats, nephritis, wounds, inflammation, heavy menstruation, hemorrhoids, dysentery, gastrointestinal diseases, tuberculosis, hyperglycemia, insomnia, heart disease, asthma, nausea and vomiting to name a few [11,12,17,18].

#### RESULTS

##### Anti-fungal activity

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

Mohamed Nadjib Boukhatem et al., studied 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 krusei*, *Rhodotulra glutinis*, as well as two strains of *C. albicans*. This study also looked into the activity of the plant against bacteria. The results were interpreted on the basis of a zone of inhibition (defined as areas of zero microbial growth). The result of the geranium oil extract against the microbes showed that the oil was more effective on the yeasts than the bacteria [13]. The oil 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* [13,20-23].

Medicinally, the antifungal properties of *Pelargonium graveolens*

have been shown to be effective against *Malassezia* species. The oil was effective against *Malassezia* species. Pityriasis versicolor (PV) is one of skin diseases thought to be caused by the *Malassezia* genus. Naeini et al. tested *P. graveolens* against various strains of *Malassezia* species like *Malassezia furfur*, *Malassezia globosa*, and *Malassezia obtuse* that were isolated from patients with PV [24,25]. Rose geranium oil was found to be active against all the strains but was effective against *M. obtuse*, the oil created an inhibition zone of greater than 50mm against *M. obtuse*. Ketoconazole (drug used to treat diseases of *Malassezia* species) was used as control group for comparison it was found that *P. graveolens* produced an inhibition zone twice the size of the one produced by the control group drug [24,26].

Anis Ben Hsouna and Naceur Hamdi executed another study for *Pelargonium graveolens*, it was tested against mycotoxins (*Asperillus niger*, *Aspergillus flavus*, *Fusarium graminearum*, *Fusarium oxysporum*, *Fusarium culmorum*, *Rhizopus nigricans* and *Alternaria alternate*) [27] 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 defined as the lowest concentration of the total essential oil at which microorganism does not show visible growth after incubation [7] The ethyl acetate extract strongly inhibited the growth of the *Aspergillus* species while the n-hexane extract produced zero antifungal activity [27,28]

Chrysa Androutsopoulou et al executed the antifungal activities of essential oil and extract of rose geranium. They evaluated the antifungal activities over the course of one week (7 days). The experimental results show that all EOs in the concentrations of 100% and 50% were particularly effective against the fungus. At the end of the third day, the fungus stabilizes almost in diameter in all the oils and stops growing, while in the control it grows until it occupies the whole petri dish, which is why in the last days of the experiment its growth rate is low. As the time goes, the growth rate reaches saturation. This happens because the natural preservatives contain nutrients that initially favor the growth of the fungus. Nevertheless, this particular resistance can disappear [29]. The EO of rose geranium has the greatest effect on the fungus. At lower concentrations rose geranium EO, even at a concentration of 5%, maintained activity.

From the above observations they concluded that 90% extracts were efficient. In this, the fungi grow until the third day and then their growth stops, while in the control sample the growth is limited by the petri dish and stops. Potato Dextrose Agar (PDA) used as a nutrient base for luxuriant growth of most fungi [30]. In 50% plant extracts, they have a moderate effect whereas in the 25%, plant extracts have similar effect [31].

#### Anti-bacterial activity

Drug resistant bacteria are more prevalent now a days. So medicine has turned back to traditional medicines. *Pelargonium graveolens* has ability to combat bacteria. Various studies were performed to evaluate *Pelargonium graveolens* against a number of different Gram-positive and Gram-negative bacteria [13]. The multiple strains of bacteria in this study were *Staphylococcus aureus*, *Staphylococcus epidermidis*, *Bacillus subtilis*, *Escherichia coli*, *Citrobacter freundii*, *Proteus vulgaris*, *Serratia marcescens*, *Salmonella typhimurium*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, and *Enterobacter aerogenes*. *S. aureus*, *B. subtilis*, and *E. coli* tested [13].

The result of this was 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. While, the rose geranium oil was effective against the Gram-negative bacteria *E. coli*, *P. vulgaris* and *E. aerogenes* but the rose geranium oil showed no effect on *P. aeruginosa* and *K. pneumoniae*. The difference was shown when viewed against *S. aureus*, *E. faecalis*, *B. subtilis*, and *S. epidermidis* as these Gram-positive bacteria displayed greater inhibition zones than the Gram-negative bacteria [13,17]

Similar study was performed, by Anis Ben Hsouna et al., that showed similar findings to the study before-mentioned [18]. Additionally, this study evaluate that rose geranium oil showed promising results against 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 shows Gram-negative bacteria to be

less susceptible to the *Pelargonium graveolens* oil [18]

Chrysa Androutsopoulou et al executed the antibacterial activities of the different kinds of EOs and extracts were assessed by the agar dilution method. It can be seen that all essential oils and extracts had some antibacterial activity on the tested strains, nevertheless the antibacterial properties varied significantly with different strains. Essential oil of *P. graveolens* showed antibacterial activity (85%) against *E. coli* in 100% concentration. While in lower concentration it did not affect *E. coli* growth.

On the other hand, the extract showed good antibacterial activity (68%) against *E. coli* in 90% concentration and shows average efficacy in 50% and 25% concentrations (59% and 46% respectively). Also for *S. aureus*, the essential oil had good antibacterial activity (55%) in 100% concentration. In lower concentrations, it was not effective. The extract was not effective against this bacterium while only in 90% concentration it appeared to have a minor inhibition (40%). Finally, the *P. graveolens* oil had a small activity against *Salmonella* spp. (51%), in 100% concentration. Its activity was negligible at lower concentration. The extract was almost efficient in 90%, 42%, while in lower concentrations, it had no effect [31].

#### Anti-oxidant activity

The oxidation-reduction reactions are very important for the functioning of human body, this makes the need for oxidative processes. While to much oxidation causes oxidative stress and so many other negative effects. These effects could lead to some diseases like cancer, heart diseases and diabetes [11,19,32]. According to the Modern theory of free radical biology shows that reactive oxygen is key factors in certain diseases which are mentioned above. While, the risk factors for such diseases were reduced by alteration of the diet and adding natural antioxidants.

Rose geranium has been examined for this purpose.

Milka Maksimovic and Sanja Carvar tested hydrolysis of *Pelargonium graveolens* stems and leaves against thymol in 1,1-diphenyl-2-picrylhydrazyl (DPPH) solution. As DPPH is vibrant violet color and when free radicals are captured and reduced the solution becomes yellow. This results concluded that the stems of rose geranium essential oil possessed higher antioxidant activity than the leaves whereas the hydrosols from both the stems and leaves were ten times higher the thymol control [11,33-35]

#### Reprotoxicity

There are certain toxins present in the environment which causes the negative effects. These toxins are proved to be causing problem in male reproduction which results in decline in the quality and quantity of human semen. Deltamethrin (DL) is one such toxin. While, to prevent the negative effects of this toxin and others toxins, there is need to traditional medicine [36]. *Pelargonium graveolens*, is the best answer for traditional medicine which is known for its antioxidant effects.

Ahlem Ben Slima et al., performed the study in that DL was administered to healthy, male, virgin mice. Under examination, the mice produced a significant decrease in sperm count and motility, testicular catalase and superoxide dismutase activity, also GSH (a natural antioxidant) and ascorbic acid levels. In addition to this, an increase in abnormal morphology was observed. According to all these effects they conclude that the Deltamethrin induced oxidative stress in the mice testes. When these mice were treated with the *P. graveolens*, the negative effects were reversed [36]. Slima et al. found that *P. graveolens* essential oil shown a strong protective effect against oxidative stress damage and that a dose of 67 mg/kg/day was sufficient to decrease protein oxidation in the testes as well as reduce oxidative stress and lipid peroxidation. The *P. graveolens* oil also improved the poor quality of the sperm [36,28].

#### Antidiabetic Activity

Nowadays diabetes mellitus is a prominent and continuously growing issue around the world. Approximately, the current adult prevalence of this disease sits at 285 million people. Unfortunately, this number will grow everyday 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 [19]. Not the only these symptoms but other symptoms reported in connection with

diabetes is an alteration in the intermediary metabolism of carbohydrates, lipids, and proteins [19]

Diabetes mellitus is in progression today due to the oxidative stress specially created by a hypoglycemic-induced generation of radicals. These radicals show an abnormally high free radical level leading to membrane lipid peroxidation, protein glycation and a decrease in antioxidant defenses simultaneously producing membrane damage [19]

The current treatment for diabetes mellitus includes synthetic drugs or insulin. However, these two solutions create new side effects of their own. The patients who are being treated with either one or both drug regimens shows the side effects like drug-resistance, hypoglycemia, edema and weight gain [19] Clearly, these symptoms are counterproductive to their intended purpose and a problem to have to deal with in an attempt to make one healthier. Due to this, research has turned towards traditional medicine.

Pelargonium graveolens oil has been used traditionally to treat diabetic patients was put to test [19]. Maher Boukis et al., evaluated *P. graveolens* amongst alloxan-induced diabetic rats. The test results conclude that a dose of 150mg/kg body weight was the most effective dose of geranium oil to treat diabetes mellitus. The diabetic rats showed significant hypoglycemic effects when dosed once with rose geranium oil. When the rats were diagnosed as diabetic (rats with blood glucose levels above 10 mmol/dm<sup>3</sup> after two weeks of alloxan injections) an increase in liver and kidney Thiobarbituric Acid Reactive Substances (TBARS) levels was observed. But when 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 [19]. It was observed that hyperglycemia decreases the antioxidant system in response to increased lipid peroxidation and the formation of free radicals. The rose geranium essential oil fights this by reducing oxidative stress via the prevention of the generation of free radicals, thus inhibiting the development of diabetes [28]

Diabetes is a chronic disorder of metabolism produced due to an absolute or relative lack of insulin and characterized by hyperglycemia, glycosuria, and hyperlipidemia (15). Post-prandial hyperglycemia (PPHG) is one of the key risk factors associated with diabetes. PPHG caused by the fast uptake of glucose in the intestine under the influence of hydrolyzing enzymes  $\alpha$ -amylase and  $\alpha$ -glucosidase that change polysaccharides through oligosaccharides to monosaccharides (16). Inhibition of  $\alpha$ -amylase and  $\alpha$ -glucosidase enzymes produces a reduction in their hydrolysis and thereby controlled blood glucose levels (39). Therefore, an important strategy for controlling PPHG is to inhibit  $\alpha$ -amylase and  $\alpha$ -glucosidase enzymes (40). These enzymes are main targets for the management of PPHG particularly in pre-diabetic patients or those with impaired glucose tolerance [37]. Natural products like  $\alpha$ -amylase and  $\alpha$ -glucosidase inhibitors have attracted considerable interest in the drug discovery research (41-43) The clinically used inhibitors of carbohydrate metabolizing enzymes such as acarbose, voglibose, and miglitol are non-specific in their action. This causes the side effects such as flatulence (44).

Recently in 2021, the antidiabetic activity has been proposed by Javed Ahamad and Subasini Uthirapathy evaluate antidiabetic activity through  $\alpha$ -glucosidase inhibition assay. They first calculated the chemical composition of *P. graveolens* EO by GC/MS and its antidiabetic activity was produced through inhibition of  $\alpha$ -glucosidase enzyme in *in vitro* models. The enzyme inhibition assay results show that the EO of *P. graveolens* inhibits  $\alpha$ -glucosidase enzyme in *in vitro* study. Also the results show that the EO of *P. graveolens* was found comparable with standard acarbose in inhibition of  $\alpha$ -glucosidase enzyme. As  $\alpha$ -Amylase and  $\alpha$ -glucosidase enzymes are present in brush border of gastrointestinal tract and it is responsible for breakdown of polysaccharides and disaccharides, respectively. Inhibition of these enzymes leads reduction of monosaccharides available for absorption in blood and ultimately it controls sudden increase of blood glucose level after meals.

The increased blood sugar level after a meal is known as PPHG (Post-prandial hyperglycemia) and type 2 diabetes controlled by inhibiting  $\alpha$ -glucosidase enzyme. The inhibitors of  $\alpha$ -amylase and  $\alpha$ -glucosidase enzymes such as acarbose and miglitol are non-specific in their action. Inhibition of both these enzymes caused decreased metabolism of

polysaccharide this produce flatulence and distension as side effects due to bacterial fermentation from undigested carbohydrates (38). This study concludes the antidiabetic effects of *P. graveolens* EO in controlling PPHG through inhibition of  $\alpha$ -glucosidase enzyme (38).

#### Anti-inflammatory Activity

Anti-inflammatory drugs which are available commercially exert an extensive variety of side effects and are either too potent or too weak. Due to this, the search for new anti-inflammatory compounds has been a priority for the pharmaceutical industry. Medicinal plants are very important source of new chemical substances with potential therapeutic effects (3). Various natural products have been tested in many animal models for the development of new anti-inflammatory agents. Plant essential oils (EO) are used as folk medicine used for various kinds of inflammatory diseases (14).

Mohamed Nadjib Boukhatem et al evaluated the anti-inflammatory activity of the essential oil of rose geranium (RGE). Initially, they investigated the chemical composition of geranium oil. The major components were citronellol (29.13%), geraniol (12.62%), and citronellyl formate (8.06%). Then they evaluated the anti-inflammatory activity in carrageenan-induced paw edema, five different groups were established and RGE was administered orally in three different doses (14)

RGE (100 mg/kg) was able to significantly decrease the paw edema as compared to the effect observed with diclofenac, the positive control. Also, RGE showed a potent anti-inflammatory activity by topical treatment in the method of croton oil-induced ear edema. When the dose was 5 or 10 ml of RGE was induced per ear of rats, the inflammation was reduced by 73 and 88%, respectively. This is the first report to evaluate a significant anti-inflammatory activity of Algerian RGE. Also, they produce the histological analysis which confirmed that RGE inhibited the inflammatory responses in the skin. They conclude their results as RGE may have significant potential for the development of novel anti-inflammatory drugs with improved safety profile (14).

#### DISCUSSION

*Pelargonium graveolens* which is commonly known as rose geranium is an herbal plant that has been used as traditional medicine for centuries. Rose scented geranium has been used mainly cultivated in South Africa, which has been used by people in that area for wounds, fevers, cold, inflammation, and more [11,17]. Traditional medicines are investigate to combat with drug resistant microbes. Thus, traditional medicines are now the area of interest in the medical community. Rose geranium was known for many beneficial qualities and this review has compiled a number of them. Number of studies have shown that the plant possesses great antibacterial activity against Gram-positive bacteria [13,27,45]. *P. Graveolens* also possesses the ability to fight Gram-negative bacteria but so far the greatest results have been seen with the addition of an alkyl substituent to help it [46]. More research needs to be done to determine best way to produced prominent effects against Gram-negative bacteria is with the addition of the alkyl substituent. If the best results will achieve without the addition of the alkyl substituent, the extra effort and cost that would be saved by most of the drug companies might be able to influence to produce *Pelargonium graveolens* as an antibiotic.

Rose geranium possess the ability to capture not only free radicals but also prevent formation of a new generation of free radicals this reduces the oxidative stress and inhibits the development of diabetes. The investigations on diabetes mellitus was examined that disease could be brought on by oxidative stress [19]. From above evidence rose geranium has proved to be a great antioxidant.

As previously mentioned

The rose geranium plant has ability to combat multiple fungi known for being food spoilage pathogens makes it as a good anti-fungal as well as new food preservatives [13]. The rose geranium plant possesses great anti-fungal property. Rose geranium has been tested against mycotoxins and pathogens, it was found that *P. Graveolens* produced higher inhibition zones than the controls which were used for experiment [18,19].

Another activity evaluated was repro-toxicity. Toxicity which affects on male reproductive system was studied and it was found that, when the rose geranium oil was used to treat the detrimental effects seen on male sperm quality and quantity. Also, sperm quality was improved



and the oxidative stress effects caused by the toxins were decreased[47].Another effect of rose geranium oil was that it has a relatively low toxicity level and the toxicity levels were non-toxic[17].

The antidiabetic activity of rose geranium oil has been reviewed ,the diabetic rats showed significant hypoglycemic effects when dosed once with rose geranium oil. When the rats were diagnosed as diabetic (rats with blood glucose levels above 10 mmol/dm<sup>3</sup> after two weeks of alloxan injections) an increase in liver and kidney Thiobarbituric Acid Reactive Substances (TBARS) levels was observed. But when the same rats treated with the rose geranium essential oil, the liver and kidney TBARS levels significantly decreased, showing that the oil made the rats less susceptible to peroxidative damage when under oxidative stress like diabetes [19]. It was observed that ,due to increased lipid peroxidation and the formation of free radicals, hyperglycemia decreases the antioxidant. By reducing oxidative stress via the prevention of the generation of free radicals, the rose geranium oil thus inhibiting the development of diabetes [ 28]

Another evidence reviewed for antidiabetic activity of rose geranium through  $\alpha$ -glucosidase inhibition assay.  $\alpha$ -glucosidase inhibition produced by inhibition of  $\alpha$ -glucosidase enzyme in *in vitro* models. The results show that the EO of *P. graveolens* was found comparable with standard acarbose in inhibition of  $\alpha$ -glucosidase enzyme. This experiment concludes the antidiabetic effects of *P. graveolens* EO in controlling PPHG through inhibition of  $\alpha$ -glucosidase enzyme[44].

The anti-inflammatory activity of the essential oil of rose geranium (RGEO) was studied.By investigating the chemical composition of geranium oil,the anti-inflammtory activity in carrageenan- induced paw edema has been evaluated as a result significant decrease in the paw edema was observed as compared to the effect observed with diclofenac(the positive control) Also, RGEO produced a potent anti-inflammatory activity by topical treatment in the method of croton oil-induced ear edema(14).

## CONCLUSION

*Pelargonium graveolens* shows great potential as a therapeutic agent for its antifungal,anti bacterial,antioxidant,antidiabetic,reprotoxicity and anti-inflammatory activities.Rose geranium has shown various positive benefits as a traditional medicine.The antibacterial and antifungal properties show strong evidence to replace current therapeutic drug regimens.Very potent antioxidant and hypoglycemic activities has been shown in Rose Geranium. *P. graveolens* showed to reverse the negative effects against toxins which affects male reproductive system whereas more research should be studied for human trials.

Also essential oil was found to be potent inhibitors of  $\square$ -glucosidase enzyme.The present study also give a scientific basis for controlling PPHG in diabetic patients.RGEO is potentially effective as a anti-inflammatory agent for prevention and treatment of acute or chronic inflammatory skin diseases.Further evaluation of the chemical constituents of REGO might develop a new,effective and safe drug regimens.

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