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Chapter 10

Pharmacological Actions of *Citrus* Species

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Abstract

The genus *Citrus* belongs to family Rutaceae, which is characterized by trees and bushes. *Citrus* species are extensively cultivated throughout the world because of their multiple health benefits for humans and their applications in pharmaceutical and food industries. This chapter is a survey covering *in vitro* and *in vivo* studies that demonstrate the pharmacological activities of various *Citrus* species. The species *Citrus aurantium*, *Citrus sinensis*, *Citrus limon*, and *Citrus bergamia* are well known and several studies have been carried out to evaluate the pharmacological effects of their extracts, essential oils, and isolated constituents. These studies have found that they possess anxiolytic, anti-inflammatory, hypoglycemic, anthelmintic, anticancer, and anti-infective properties.

Keywords: *Citrus*, Pharmacology, *Citrus aurantium*, *Citrus sinensis*, *Citrus limon*, *Citrus bergamia*

1. Introduction

The genus *Citrus* belongs to family Rutaceae, which is characterized by trees and bushes. Fruits of this genus, such as oranges, lemons, and tangerines, are widely cultivated in the tropical and subtropical areas of the world [1].

In medicine, *Citrus* fruits are used in the treatment of various diseases. Research shows that the intake of *Citrus* fruits can reduce the incidence of gastric cancer [2]. In addition,

some isolated compounds from these fruits have effects on the central nervous system. For example, limonene, which is present in high concentrations in *Citrus aurantium*, showed a strong anxiolytic effect when tested in both animals and humans [3, 4].

To further understand the therapeutic potential of different *Citrus* species, we carried out a survey of *in vitro* and *in vivo* studies demonstrating their pharmacological actions, and summarized them in this chapter.

2. *Citrus* species with pharmacological activity

2.1. *Citrus aurantium* L

The species *C. aurantium* L., popularly known as bitter orange, *laranjeira-amarga*, or *laranjeira-cavalo*, is a native plant of Southeast Asia, a region that corresponds to China and India. It was first introduced to Syria and Egypt by the Arabs and was subsequently brought to Europe [1]. In the medieval times, it was widely used in the Mediterranean region as a cardiac and vascular stimulant, digestive, sedative, tranquilizer, appetite stimulant, general tonic, and antidote against poisons [5]. In traditional Chinese medicine, bitter orange is used as a gastrointestinal stimulant and general tonic [6].

Ethnopharmacological studies in Brazilian communities (documentation of the empirical uses of medicinal plants in traditional communities) describe the popular use of *C. aurantium* L. fruit peels, flowers, and leaves in the treatment of the central nervous system disorders such as insomnia, anxiety, and hysteria [7, 8]. Another study reports that tea made from the leaves of *C. aurantium* L. can relieve stomach cramps and constipation, combat stomach acidity, and relieve fever, while tea from the seeds is reported to control diabetes [9].

Studies have focused on the investigation of *C. aurantium* L. effects on the central nervous system, especially its anxiolytic effect. Several studies on animals and humans have demonstrated the anxiolytic effect of this species. For example, the essential oil obtained from *C. aurantium* L. peels was found to show an anxiolytic effect on rats after a single dose, denoted by an increase in the residence time in the open arms of the elevated plus maze [10]. In addition, anxiolytic activity was observed in experimental models of generalized anxiety and obsessive-compulsive disorder. At the same time, the mice did not show any signs of motor impairment, even after 15 consecutive days of treatment [7].

In a study conducted by Leite et al., 12 rats were evaluated in two models of anxiety: elevated plus maze and open field maze models. The rats were previously made to inhale the essential oil from *C. aurantium* L. at concentrations of 1.0, 2.5, and 5.0% for 7 min in an acrylic box. The authors observed a decrease in the emotional reactivity of the animals in both experimental models, suggesting a possible central action [11]. Moreover, the results of another study strongly suggest the involvement of 5-HT 1a receptor, a subtype of serotonin receptors, in its anxiolytic activity, suggesting a potential mechanism by which *C. aurantium* L. affects the central nervous system [12].

Clinical trials testing the anxiolytic effect of *C. aurantium* have also demonstrated satisfactory results. In a certain study, preoperative patients received distilled *C. aurantium* L. flower 2 h before the procedure, then the STAI scale was used for anxiety evaluation. In comparison to the control group, the patients from experimental group showed a reduction in preoperative anxiety [13]. In another study, patients with chronic myelogenous leukemia inhaled essential oil of *C. aurantium* L. before the procedure of medullary material collection. The results indicated that the patients subjected to this intervention showed a decrease in the anxiety levels and remained relaxed during the procedure. In addition, *C. aurantium* L. oil, even at a single exposure, showed an activity comparable to that of the anxiolytic used as the positive control. This ensures its efficacy in controlling anxiety in patients subjected to unpleasant diagnostic procedures [3].

Its anxiolytic effect was also tested before labor. In a certain study, 18–35-year-old primiparous women were subjected to aromatherapy with *C. aurantium* L. oil during labor, and the results showed a significant reduction in the anxiety during labor in those women. Another clinical trial conducted on 126 primiparous women investigated the effects of aromatherapy with *C. aurantium* L. on pain during the first stage of labor. The women received 4 ml of *C. aurantium* L. in distilled water soaked in gauzes every 30 min. The results showed pain relief in the women subjected to this procedure. When asked whether aromatherapy using *C. aurantium* L. was satisfactory or not, 88.1% of the participants said that they were satisfied with the method applied and 92.1% said that they would use this method in future procedures. These studies show that aromatherapy with *C. aurantium* L. is a simple, inexpensive, and noninvasive intervention that can be beneficial for pregnant women [14]. However, because vaginal birth is a painful and serious process that is often feared by primiparous women, further studies are still required [15].

Several studies have been conducted to identify other possible actions of *C. aurantium* L. constituents, other than their effects on the central nervous system. Researchers isolated the flavonoids such as nobiletin, naringin, and hesperidin from *C. aurantium* L. and evaluated their anti-inflammatory effect on rat cells *in vitro*. Results demonstrated the suppression of proinflammatory mediators, which confirms the anti-inflammatory action of the isolated flavonoids [16]. Flavonoids isolated from *C. aurantium* L. were also evaluated for possible anticancer activity in murine lung cells. They demonstrated an anticancer effect through the regulation of apoptosis and cell migration, providing scientific support for the use of *C. aurantium* L. flavonoids in the treatment of human lung cancer [17].

Using a rat model of diabetes, researchers evaluated the possible hypoglycemic effect of neohesperidin derived from *C. aurantium* L. Treatment with neohesperidin was shown to increase glucose tolerance and insulin sensitivity, and to decrease blood glucose levels in the rats of the experimental group. These results demonstrate its hypoglycemic effect, and thus, its potential application for the prevention of diabetes and its complications [18].

Finally, although *C. aurantium* L. has been known for millennia, and a large number of studies have been focusing on its effects in the last decade, further research is needed to elucidate new mechanisms of action and therapeutic properties.

2.2. *Citrus sinensis*

The species *C. sinensis*, popularly known as sweet orange, also belongs to family Rutaceae. This fruit is of Asian origin, where it has been known for about 4000 years. With the expansion of trade and shipping routes, orange was introduced to various regions of the world for cultivation. Information from 1471 to 1472 reported the presence of sweet orange in Liguria, a region in Italy, before its introduction by the Portuguese to the Iberian Peninsula in 1498. In the eighteenth century, there were reports about varieties of sweet orange in Palestine, possibly introduced by an Armenian monk. In the Americas, Portuguese colonists introduced it to Bahia/BR in the sixteenth and eighteenth centuries, and Jesuits introduced it to California/USA, where they settled and started subsequent plantations [19].

An ethnobotanical survey in a Brazilian community identified the species *C. sinensis* as the most cited by women in attention to basic health, indicating the use of its leaves prepared in the form of tea as a soft tranquilizer for mild cases of anxiety and insomnia [20]. In addition, the flower and fruit are used by the population as tranquilizers and for relief of headache, migraine, fever, flu, allergy, and cough. We can conclude that sweet orange is among the main species of medicinal plants commonly used by the Brazilian community [21].

The traditional use of *C. sinensis* as a sedative can be attributed to hesperidin, which was identified in a study as the active principle in this plant responsible for sedation. Hesperidin performs its sedative action through interaction with and stimulation of adenosine receptors. Its effect is opposite to that observed after consumption of coffee and tea, which antagonize the adenosine receptors and thus maintain the wakefulness state [22]. Researchers investigated the properties of hesperidin extracted from *C. sinensis* through *in vitro* experiments, revealing its strong cytotoxic activity against human carcinoma cell lines and its antioxidant activity against DPPH free radical. According to these results, hesperidin can be considered a promising future drug. Orange peels are a cheap and available source from which hesperidin can be extracted in an efficient way and with high purity [23].

C. sinensis extracts have shown potent anthelmintic properties *in vitro* when compared with the positive control, indicating that it is equipotent to conventional anthelmintic drugs. However, *in vivo* studies should be conducted to establish this efficacy and to identify the active components responsible for the anthelmintic activity [24].

Researchers induced liver cirrhosis in rats for 16 weeks and treated the animals with *C. sinensis* dried peel extract orally for 9 weeks. After the completion of the treatment, the animals were euthanized to evaluate the biochemical and histopathological changes associated with liver cirrhosis. The histopathological examination of the liver tissue and the biochemical findings demonstrated the curative effect of the extract, suggesting its potential therapeutic application in liver fibrosis and cirrhosis [25].

Another study investigated the effects of the *C. sinensis* peel extract when administered orally to rats at a concentration of 25 mg/kg and revealed its antidiabetic potential. The researchers administered a single dose of alloxan (120 mg/kg) to the rats, which triggered an increase in serum glucose levels and α-amylase activity. Then, a group of the rats was administered *C. sinensis*, which normalized all the adverse changes induced by alloxan. This

reinforces the antidiabetic properties of the orange peel extract, which might be applied in the development of therapies for diabetes control [26].

In 2010, Faturi et al. demonstrated that the essential oil from *C. sinensis* had an anxiolytic effect when inhaled by rats. The animals were subjected to the elevated plus maze test, and the residence time of each rat in the open arms was measured. The possibility that the anxiolytic effect could result from any other inhaled aroma was discarded, since no anxiolytic activity was observed with *Melaleuca alternifolia* essential oil. The authors also reported that the animals were not previously exposed to the essential oil of sweet orange or any solutions that could contain the essence [27].

In a clinical study conducted on patients waiting for dental care, a group of the patients inhaled sweet orange essential oil in the waiting room, a second group listened to music, and the third group, which was the control group, did not receive any intervention. The results showed that the patients who inhaled the essential oil were calmer and had lower anxiety levels than the patients of the other groups [28].

Results obtained by Goes et al. in 2012 demonstrated the anxiolytic effect of the *C. sinensis* essential oil on healthy individuals while performing an anxiogenic task. The anxiolytic activity was evidenced by the significant difference in the level of anxiety between the group exposed to *C. sinensis* and the control group, providing scientific support for the use of this essential oil as a tranquilizer in aromatherapy [29].

The results presented here support the use of *C. sinensis* as an aid to combat insomnia and anxiety. Research also indicates that the natural constituents of sweet orange can be used in the pharmaceutical industry, as natural cytotoxic agents, anthelmintics, antidiabetic agents, or for the treatment of liver cirrhosis.

2.3. *Citrus bergamia*

Citrus bergamia, commonly known as bergamot [30], is a plant belonging to family Rutaceae, subfamily Esperidea, and is defined as a hybrid between bitter orange (*Citrus aurantium*) and lemon (*Citrus limon*) [31]. The botanical and geographical origins of this plant are still unknown. The name "bergamot" seems to be derived from Berga, a Spanish city from which the plant was transported to Calabria in Southern Italy. *C. bergamia* is cultivated almost exclusively along the southern coast of Calabria; over 90% of its world production comes from this region. However, it is also cultivated to a lesser extent in other countries, such as Greece, Morocco, Iran, Ivory Coast, Argentina, and Brazil [32].

The fruit of *C. bergamia* is mainly used for the extraction of its essential oil, which is used in perfumes, drugs, cosmetics, food, and clothing [33]. Throughout the cultivation and the processing of *C. bergamia*, tons of wastes of low commercial value, but of great industrial potential, are generated. These wastes contain high levels of nutrients, pigments, and bioactive components with low toxicity [34].

There are evidences that *C. bergamia* contains antibacterial and antifungal active constituents, in addition to its anti-inflammatory, antiproliferative, neuropsychopharmacological, neuro-

protective, and analgesic effects, [35] as well as its cardiovascular properties in rodents [32]. Bergamot juice, which is obtained from the endocarp after the extraction of the essential oil, was found to exhibit hypoglycemic and hypolipidemic activities, as well as anti-inflammatory [36–38] and anticancer properties [39].

The anti-infective properties of *C. bergamia* derivatives can be observed from the action of its essential oil against bacteria, mycetes, and larvae, and the action of its juice against *Helicobacter pylori*. Compounds derived from its fruit peel extract have antimicrobial properties. Studies report that its essential oil has antibacterial and antifungal activities against *Campylobacter jejuni*, *Escherichia coli* O157, *Listeria monocytogenes*, *Bacillus cereus*, *Staphylococcus aureus*, and dermatophytes. The essential oil of *C. bergamia* shows *in vitro* activity against *Candida* species, which suggests its potential application in the topical treatment of fungal infections by Candida. It also demonstrates *in vitro* activity against dermatophytes [40].

In addition, favorable results were obtained regarding its pharmacological properties in nervous system disorders. Sometimes, the essential oil from *C. bergamia*, usually extracted from the peel, is used in aromatherapy to relieve stress and anxiety [41].

In a study carried out on rats to investigate the anxiolytic activity of *C. bergamia*, the essential oil was administered to the rats at different concentrations and its effects were compared with those of diazepam. The results of this study indicated that *C. bergamia* showed an anxiolytic action, which was observed when the rats were subjected to the elevated plus maze and hole-board tests. The researchers observed a reduction in the activity of the hypothalamic-pituitary-adrenal axis, reducing corticosterone response to stress [42].

Clinical studies have also reported beneficial effects of *C. bergamia* essential oil in cardiac control, blood pressure reduction, and stress response management, in addition to its effect on the central nervous system [43]. Although the mechanisms by which the effects on the central nervous system are mediated have not yet been fully elucidated, it has been suggested that this action might be mediated by the release of amino acids that modulate the synaptic plasticity [32].

Some studies demonstrated that the essential oil from *C. bergamia* also shows anticancer activity. For example, Berliocchi et al. demonstrated *in vitro* antiproliferative activity of *C. bergamia* essential oil against SH-SY5Y human neuroblastoma cells. In this work, the lethal effect of *C. bergamia* was mediated by activating multiple pathways that lead to cell death by both necrosis and apoptosis [44]. Compounds derived from bergamot oil, such as limonene, monoterpenes related to limonene, alcohol, and perillic acid, were also found to inhibit the proliferation of breast cancer cells, and to show chemopreventive and chemotherapeutic effects in models of mammary tumors [45].

However, the poor water solubility, weak stability, and limited bioavailability of essential oils have prevented their use in cancer therapy. Nevertheless, due to the favorable results regarding the anticancer action of the essential oil from *C. bergamia*, some attempts have been made to use bergamot in cancer therapy. For example, in 2013, Celia et al. developed liposomes of *C. bergamia* essential oil, which improved its water solubility and increased its *in vitro* anticancer activity against SH-SY5Y human neuroblastoma cells [46].

In order to elucidate the mechanisms by which the essential oil from *C. bergamia* has anticancer activity, Russo R et al. conducted a study in 2013 to identify the components involved in the cell death process. The results of the study suggested an important role of the combined action of monoterpenes in the process of cell death [35].

Regarding the protective cardiovascular properties, Di Donna et al. established a rat model in 2014 to investigate the hypocholesterolemic effect of 3-hydroxy-3-methyl-glutaryl flavanones enriched fraction (HMGF), extracted from *C. bergamia* fruits, in comparison with that of statin (simvastatin). Both HMGF and simvastatin reduced total cholesterol, triglycerides, very low density lipoproteins (VLDL), and low-density lipoproteins (LDL). However, only HMGF caused an increase in high-density lipoprotein (HDL). In addition, HMGF showed no genotoxic effects and was cytotoxic only at high concentrations. Thus, the authors concluded that daily supplementation of HMGF in the diet can be very effective against hypercholesterolemia, featuring the cardiovascular protective properties of bergamot [47].

Although all the pharmacological effects of *C. bergamia* indicate potential clinical applications in the future, only clinical studies investigating its anxiolytic effects in aromatherapy were published heretofore [32].

2.4. Citrus limon

The Latin name of lemon is *C. limon (Linnaeus) N. Burman*. It belongs to family Rutaceae, and it is sometimes called limoeiro or limoeiro-azêdo [48]. It originated in Southeast Asia and is believed to have been introduced to Europe by Muslims across the Iberian Peninsula and Sicily [5]. Currently, Spain is considered the main producer country of this genus in the Mediterranean region. Lemon is considered the third most important species of the genus *Citrus*, as it contains many relevant natural chemical compounds, including citric acid, ascorbic acid, minerals, and flavonoids [49].

Recently, some of the therapeutic properties of *C. limon* have been recognized in the literature. Studies have found that the use of lemon helps neutralize the acidity of the gastric environment, by stimulating the production of potassium carbonate, indicating its protective effects on the gastric mucosa. It was also found to have analgesic, anti-anemic, anti-sclerotic, antipyretic, antiseptic, emollient, and moisturizer properties. The recognized actions of lemon cellulose are that it is anti-diarrheal, diuretic, intestinal mucosa protector, local hemostatic, vascular stimulant and protector, and vitamin [5].

Production networks of lemon generate large amounts of wastes and by-products, which are an important source of bioactive compounds with potential applications in animal feeding, processed foods, and health care [49]. Although its health benefits are always attributed to its vitamin C content, recently, it has been found that flavonoids also play an important role [48]. Some authors suggest that flavonoids present in lemon have different biological functions, including antioxidant, anti-inflammatory, antiallergic, antiviral, antiproliferative, antimutagenic, and anticancer activities [48].

Hesperidin, which is the main flavonoid in *C. limon*, influences the vascular permeability, increases the capillary resistance, and has analgesic and anti-inflammatory properties [49]. It

is also an effective antioxidant, since it is capable of scavenging free radicals that are involved in cancer. Some studies have shown that flavonoids present in lemon juice also have hypocholesterolemic properties [50].

Trovato et al. conducted a study on rats in 1996 and found that *C. limon* had a significant effect on the levels of cholesterol and triglycerides, suggesting that the prolonged consumption of its juice might offer significant protection from hypercholesterolemia [51].

Another study investigated the protective effect of the essential oil from *C. limon* against acute hepatic and renal damage induced by a high dose of aspirin in Wistar albino rats. The data obtained in this study demonstrated that the treatment with *C. limon* protected the liver and kidney from damages induced by aspirin [52].

Regarding the pharmacological effects on the central nervous system, a recent study conducted by Khan and Riaz evaluated the effects of lemon on the behavior of rats, using three different doses (0.2, 0.4, and 0.6 ml/kg), considered low, moderate, and high doses, respectively. The anxiolytic and antidepressant activities were evaluated twice, for 15 days, using the open field, elevated plus maze, and forced swimming tests. In the open field test, *C. limon* revealed an increase in the distance traveled, the number of central entries, and the number of rearing at moderate dose, while in the elevated plus maze, the number of open arm entries was found to be increased. Whereas in the forced swimming test, there was a decrease in duration of immobility and an increase in the duration of climbing. Thus, results suggest that *C. limon* at moderate dose has an anxiolytic effect [53].

It has been noted that disorders such as anxiety and depression can be managed through healthier variations in dietary patterns, since there is evidence that a diet rich in antioxidants and vitamins reduces these symptoms. Accordingly, a study was performed in order to evaluate the behavioral effects of *C. limon* and *Punica granatum* in rats. In this study, two combinations of doses were used: 0.4 + 5 ml/kg and 0.2 + 8 ml/kg of *C. limon* and *P. granatum*, respectively. As in the previous study, the antidepressant and anxiolytic effects were evaluated twice, for 15 days, using forced swimming, open field, and elevated plus maze tests. In the open field test, the use of *C. limon* and *P. granatum* showed an increase in the distance traveled and the number of central entries at the dose combination of 0.4 + 5 ml/kg. In the elevated plus maze test, the number of entries was increased at the highest dose combination (0.2 + 8 ml/kg). In the forced swimming test, there was a decrease in the immobility duration and an increase in the climbing duration at both dose combinations: 0.4 + 5 ml/kg and 0.2 + 8 ml/kg *C. limon* and *P. granatum*, respectively. Based on these results, the authors suggested that *C. limon* and *P. granatum*, at a combination of 0.4 + 5 ml/kg, show anxiolytic and antidepressant effects [54].

In another study conducted by Riaz et al. in 2014, the effect of *C. limon* and pomegranate juice on rats' memory was evaluated. It is known that memory is greatly influenced by factors such as diet, stress, and sleep quality. The results of this study indicated that *C. limon* contains essential phytochemicals and nutrients that improve the memory, particularly the short-term

memory. They also concluded that flavonoids in these juices could be responsible for this effect [55].

Hesperidin extracted from *C. limon* was found to play an important vasodilator action. In 2016, Dobias et al. evaluated the effect of hesperidin on vascular responses in normotensive and hypertensive rats. Fifteen-week-old healthy Wistar rats and spontaneously hypertensive (SHR) rats were randomly assigned to receive either hesperidin (50 mg/kg/day) or a corresponding volume of water orally for 4 weeks. The vascular responses of isolated femoral arteries were studied using a myograph under control conditions and during the NO-synthase inhibition. Although hesperidin had no effects on blood pressure, it significantly improved endothelium-dependent vasodilation in Wistar and SHR rats. The contraction responses were increased in all the groups to a similar extent, but the relaxing responses were significantly attenuated in the SHR group only. The inhibition of the potassium channels (Kv) significantly reduced the endothelium-dependent vasodilator response only in SHR rats administered hesperidin. This indicates that hesperidin can improve endothelium-dependent vasodilation during hypertension [56].

Regarding the anti-inflammatory activities described for *C. limon*, in 2016, Amorim et al. conducted a study to confirm the hypothesis that essential oil (EO) from *C. limon*, *C. latifoli*a, *C. aurantifoli*a, and *C. limonia* have antinociceptive effects. Thus, they were tested each one on the formalin-induced licking behavior. This model is a widely used pain model in evaluating antinociceptive and anti-inflammatory drugs. The results of this study suggest that EO from *C. limon*, *C. aurantifoli*a, and *C. limonia* have an anti-inflammatory effect because they reduced the second phase response to formalin. This may occur through a reduction in inflammatory mediator liberation in mice paws or a direct action on one or more mediator receptors [57].

Since *C. limon* is widely used in traditional medications in India and China, we sought to explore the importance of flavonoids that are abundant in citrus fruits on platelet function. Nobiletin is a highly abundant flavonoid present in these and has been shown to reduce the adhesive properties of platelets. In 2015, Vaiyapuri et al. conducted a study to verify the pharmacological effects of a polymethoxy flavonoid, nobiletin, in the modulation of platelet function. Nobiletin was shown suppress a range of well-established activatory mechanisms, including platelet aggregation, granule secretion, integrin modulation, calcium mobilization, and thrombus formation. This study provided insight into the underlying molecular mechanisms through which nobiletin modulates hemostasis and thrombus formation. Therefore, nobiletin may represent a potential antithrombotic agent of dietary origins [58].

In conclusion, *C. limon* presents numerous curative properties, and thus it has been widely used as a traditional medicine for the treatment of various diseases [52]. However, more studies still need to be conducted in order for its application in clinical practice to be established and disseminated [59].

3. Conclusion

Citrus species are well known and have been commonly used by populations for hundreds of years for various purposes. This knowledge of their therapeutic potential has led to several studies that proved the pharmacological effects of the above-mentioned species (**Table 1**). The effect of *Citrus* species on the central nervous system was highlighted as the study objective in most of the publications. However, research has advanced in seeking other pharmacological actions, especially of isolated constituents of the species.

Citrus species	**Pharmacological action**
Citrus aurantium L.	Gastrointestinal stimulant and general tonic. Treatment of central nervous system disorders like insomnia, anxiety, and hysteria. Relieve stomach cramps and constipation, combat stomach acidity. Hypoglycemic effect. Anti-inflammatory. Anxiolytic effect.
Citrus sinensis	Sedative action. Anthelmintic properties. Treatment of liver cirrhosis. Antidiabetic properties. Anxiolytic effect.
Citrus bergamia	Antibacterial. Antifungal. Anti-inflammatory. Analgesic. Antiproliferative and anticancer properties. Neuropsychopharmacological. Neuroprotective. Anxiolytic activity. Hypoglycemic and hypolipidemic activities.
Citrus limon	Analgesic. Anti-anemic. Anti-sclerotic. Antipyretic. Antiseptic. Emollient and moisturizer properties. Anti-diarrheal. Diuretic. Intestinal mucosa protector. Local hemostatic. Vascular stimulant and protector. Antioxidant. Antiallergic. Antiviral. Anti-inflammatory. Antiproliferative, antimutagenic, and anticancer activities.

Table 1. Pharmacological action of different citrus species (studies *in vitro* and *in vivo*).

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