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Phytochemistry, Nutritional, and Pharmacological Potential of *Citrus Limonum*

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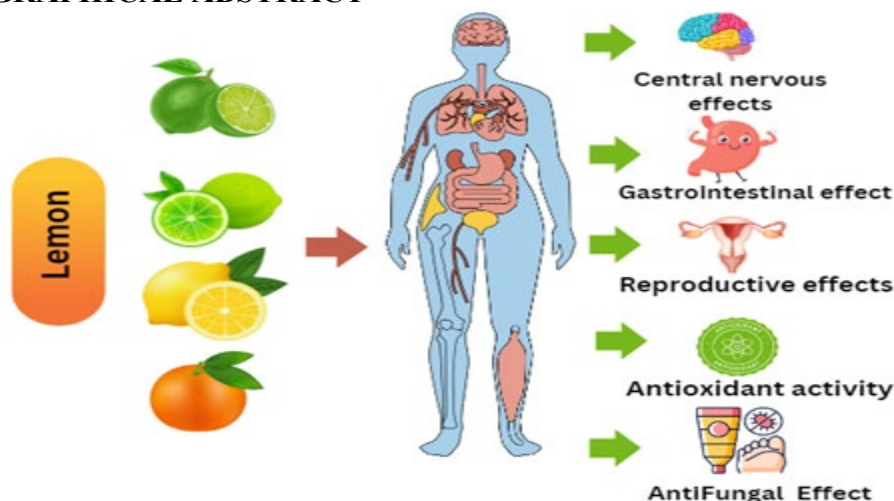
ABSTRACT

The current research aimed to provide an overview of the phytochemical configuration, nutritional value, and therapeutic uses of Citrous Limonum (lemon). Its fruit contains a variety of phytochemicals including citric acid, polyphenols, terpenes, limonene, flavonoids, vitamin C, sugar, pectin, citric acid, malic acid, flavonoids, carotenoids, terpineol, feller, camphenium, citrain, calcium oxalates, and mucilages. Vitamin C is abundant in citrous fruits, as well as macronutrients (dietary fibre and simple sugar) and micronutrients (copper, magnesium, phosphorus, calcium, potassium, pantothenic acid, riboflavin, vit B6 niacin thiamin, and folate). Lemon oil is composed of 70% limonene and 20% monoterpenes, along with significant amounts of aldehydes, such as citral, alcohols (linalool), and esters (coumarin). Lemon peel contains high concentrations of flavonoids, glycosides, coumarins, steroids (beta, gamma, sitosterol), dietary fibers, carbs, and volatile oils, all of which are necessary for good health and appropriate development. However, citrus fruits are low in calories, salts, and cholesterol. They find uses in herbal remedies due to their antioxidant, antifungal, anti-cholesterol, anticancer, antiulcer, antidiabetic, antibacterial, and anti-inflammatory characteristics. It is also important to mention that the excessive use of lemon may also be associated with some risks, such as the lowering of sperm count.

Keywords: dietary, lemon, medicinal, nutritional, vitamin C

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GRAPHICAL ABSTRACT



1. INTRODUCTION

Plants have tremendous importance for human beings due to their useful phytochemical ingredients [1, 2], as well as nutritional [3, 4] and medicinal [5, 6] contents. Herbal medicines have experienced exponential growth in recent years because of their natural origins and little to no negative consequences. Indeed, they are becoming more and more important in both developed and developing nations. Medicinal plants, minerals, and organic matter are used in many traditional remedies [7]. Medicinal plants, according to the World Health Organization (WHO), are the best sources of many medications. India is the world's second-largest producer of medicinal herbs, after China. Citrous fruits, which contain a wide range of biological activity and are rich sources of secondary metabolites, have long been used in traditional Asian medicine [8].

Citrus limonum (also called *Citrus limon* or lemon) is one of the most beneficial plants in traditional medicine. It is natural to Asia's subtropical and tropical climates [9]. Evergreen shrubs or small trees with strong fragrances and fragrant blossoms are known as citrous plants (Figure 1). The fruits (Figure 2) come in a variety of shapes (elongated, round, and oblong) with a diameter of 3.8 cm to 14.5 cm [10]. Lemon varieties include eureka, bush lemon, Lisbon, variegated pink, ponderosa, villafranca, yuzu, verna, and yen ben. The fruit can be brilliant yellow or greenish yellow in colour, resembling limes, though lemons are slightly larger and maintain their yellow hue as they mature [11].

Many species of citrus are hybrids and it has innumerable variants. These variants were generated from only a few original species, yet the true number of wild citrus species still remains unknown [12, 13]. According to some estimates, there are just 25 true-breeding citrus species [14]. Meyer lemons are frequently golden orange when fully grown. After orange and mandarin, *Citrus limon* is the third most important citrus species with a production of 4.4 million tons during the year 2001-2002. Argentina is the world's greatest producer and exporter of lemons. The country rapidly increased lemon production [15] with the export of 733 918 tons in 2017. The second and third highest lemon exporters were Spain (688 256 tons) and Turkey (451 911 tons) in 2017 [16].

Citrus is a leading fruit crop in Pakistan in terms of total yield and cultivated area. Punjab (a province of Pakistan) ranks highest with 2.289 million tons of citrus production per annum. Pakistan is the 12th highest producer of citrus in the world and has an annual production of 2.351 million tons over an area of 183.149 thousand hectares [17]. Citrus fruits including oranges, lemons, and limes are widely cultured and juiced. Their peels are thrown away as waste products during the production of citrus juice. Citrus flavonoids have considerable biological potential which includes antibacterial, anti-diabetic, antioxidant, and anticancer effects [18]. Keeping in view the importance of phytochemical ingredients [19], as well as nutritional [20, 21] and medicinal [22] importance of plant constituents or plant-based materials, the current study was performed to review the nutritional and medicinal value of *C. Limonum*.



Figure 1. Lemon Flowers and Buds
<https://gardeningnirvana.files.wordpress.com/2014/04/lemon-blossoms.jpg>



Figure 2. Lemon Fruit
<https://cdn.britannica.com/84/188484-050-F27B0049/lemons-tree.jpg>

2. PHYTOCHEMISTRY

Phytonutrients are bioactive chemicals obtained from plants and they have a significant impact on human health [23]. Lemons are rich in citric acid (about 47g/l juice) [24] and also contain a variety of phytochemicals, such as polyphenols, terpenes, limonene, flavonoids, vitamin C, sugars, pectin, citric acid, malic acid, flavonoids, carotenoids, terpineol, feller, camphenium, citrain, calcium oxalates, and mucilages. *Citrus limon* (lemon) essential oil can be extracted from rind, which makes up approximately 45% of the lemon. Lemon peel contains around 200 volatile and non-volatile chemicals. Lemon oil contains around 70% limonene and 20% monoterpenes. It also contains coumarin, aldehydes, alcohols, and esters, such as citral and linalool [25]. Figure 3 displays some important chemical constituents of lemons.

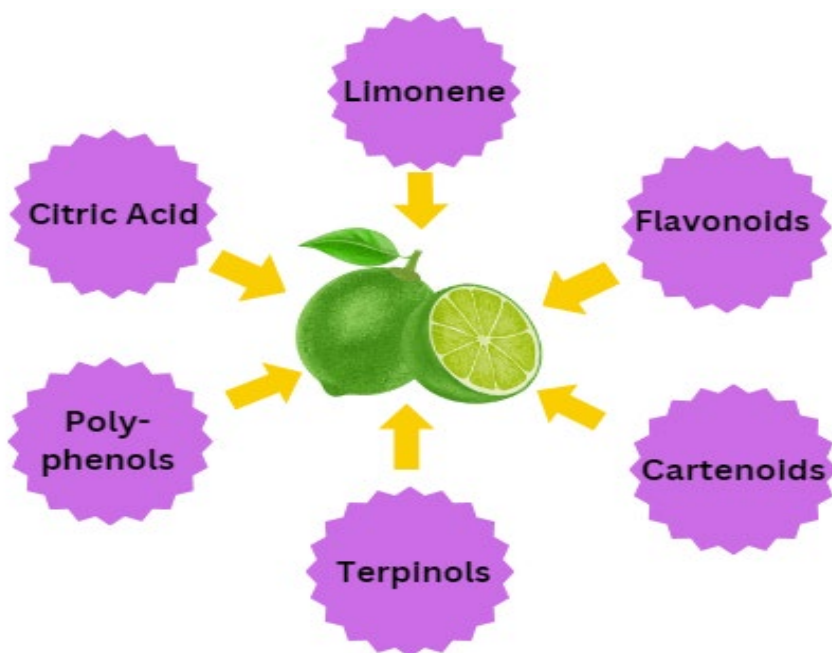


Figure 3. Important Chemical Constituents of Lemons

Limonene is a monocyclic monoterpene (Figure 4) and a multifunctional compound which exhibits potent therapeutic potential. It is also used in beverages (for scent addition), foods, soaps, and perfumes [26].

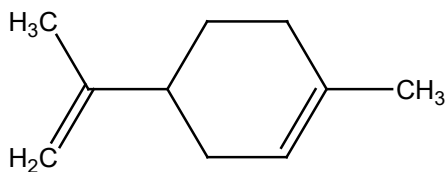


Figure 4. Chemical Structure of Limonene

The essential oil of *Citrus limon* leaves and peel also contains limonene as its primary constituent. Other components in leaf oil include β -caryophyllene, geranyl, neryl acetate, neral, myrcene, and β -pinene. Whereas, μ -terpinene, β -pinene, and myrcene are present in the peel oil [27]. The pericarp of Spanish lemon contains numerous flavonoids including limonitrine and hesperidoside. Lemon flowers contain caffeine and citrus acids including caffeic acid, ascorbic acid, and citric acid. The leaves of *citrus lemon* contain caffeine. Many health benefits are associated with lemons due to the presence of a variety of beneficial compounds. Lemons are rich in vitamin C (ascorbic acid) which is highly beneficial for human health. A 100 ml of citrus juice contains approximately 50 mg of vitamin C and 5 g of citric acid. However, there is a very quick loss of vitamin C when the lemon is squeezed. It loses about 20% of its potency when it is put for 24 hours in the fridge or placed at ambient temperature for 08 hours. Mineral-based items such as sodium (Na), calcium (Ca), potassium (K), copper (Cu), magnesium (Mg), iron (Fe), phosphorus (P), and zinc (Zn) have concentrations of 755.5, 8600, 8452.5, 4.94, 147.65, 1429.5, 13.94, and 6656 mg/100g, respectively in lemon [28]. Iron, copper, zinc, and manganese are essential nutrients that are widely employed in health, environmental research, and medicine [29]. Lemon peel samples are rich in calcium with a concentration of 8452.50 mg/100g. Calcium plays a key role in bone development and also regulates various cell processes and structural functions in living organisms [30]. For all livestock, phosphorus is a necessary nutrient. Magnesium has been linked to the maintenance of nerve electrical potential and the activation of certain enzymatic systems [28]. In addition to standard visual identification, methodologies to examine citrus species are also based on carotenoid, flavonoid patterns, hydrocarbon profiles, fatty acids, and enzyme concentration [31].

The outer skin or rind of citrus fruits is composed of a waxy and leathery layer (called epidermis), a subepidermal layer (called flavedo) containing color and oil sacks, a spongy layer (called albedo, a flavanone source)

beneath the flavedo, and a network of microscopic threads (vascular bundles) that pass through the skin (Figure 5). The inside flesh of the fruit is divided into segments which are often grouped and orientated around the soft centre core. A thin segment membrane, known as the septum, separates these segments [10, 32]. Changes in ascorbic acid, total sugar, and acidity concentration, as well as in fruit size and peel color, imply that the fruit is ripening and developing. Citrous fruits are ready to eat and process as soon as they are picked; their composition doesn't significantly alter thereafter [33].

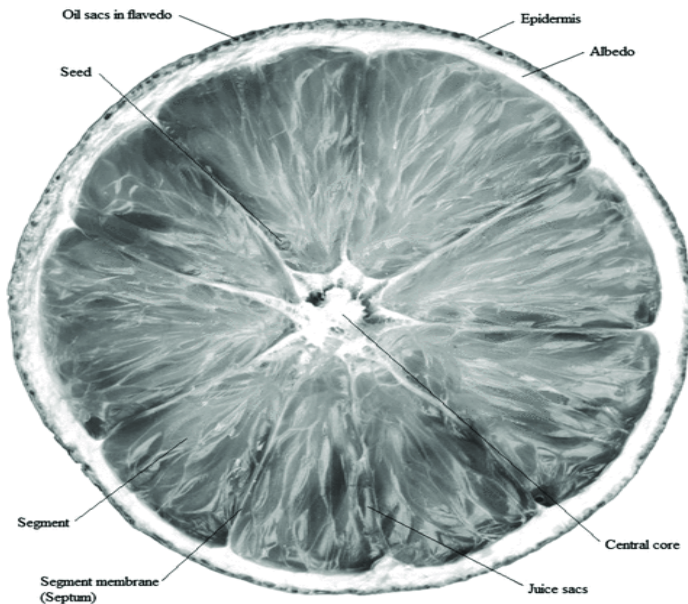


Figure 5. Typical Citrus Fruit with Different Structures

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3. NUTRITIONAL VALUE OF LEMON

Citrus fruits are rich in vitamin C [34] and macronutrients such as dietary fiber and simple sugar. They are also rich in micronutrients including copper, magnesium, phosphorus, calcium, potassium, pantothenic acid, riboflavin, vit B6 niacin thiamin, and folate. Lemon peel contains a high concentration of flavonoids, glycosides, coumarins, steroids (beta and gamma sitosterol), dietary fibers, carbs, and volatile oils, all of which are necessary for good health and appropriate development [35, 36]. However,

citrus fruits are low in calories and cholesterol [37]. Every 100 g of an edible portion of *C. medica*, *C. sinensis*, *C. limonum*, and *C. aurantifolia* contains moisture: 87.1, 88.4, 85.0, and 84.6 g; protein: 0.081, 0.8, 1.0, and 1.5 g; fat: 0.04, 0.3, 0.9, and 1 g; fiber: 1.1, 0.5, 1.7, and 1.3 g; carbohydrates: 6.9, 9.3, 11.1, and 10.9 g; minerals: 0.3, 0.7, 0.3, and 0.7 g; iron: 0.55, 0.7, 2.3, and 0.3 mg; carotene 0.009, 0, 0, and 15 µg, and energy; 30, 43, 57, and 59 Kcal, respectively [38, 39]. Table 1 displays important nutritional facts about citrus lemon [40].

Table 1. Nutritional Value of 100 Grams of Raw Lemon without Peel [40].

Nutrient	Amount	% values
Protein	1.10 g	-
Sugars	2.50 g	-
Dietary Fiber	2.8 g	-
Vitamin C	53.0 mg	88%
Carbohydrates	9.32 g	-
Energy	121 kJ (29 kcal)	-
Niacin (Vit. B3)	0.100 mg	1%
Calcium	26 mg	3%
Thiamine (Vit. B1)	0.040 mg	3%
Phosphorus	16 mg	2%
Magnesium	8 mg	2%
Iron	0.60 mg	5%
Riboflavin (Vit. B2)	0.020 mg	1%
Pantothenic acid (B5)	0.190 mg	4%
Folate (Vit. B9)	11 µg	3%
Fat	0.30 g	-
Potassium	138 mg	3%
Zinc	0.06 mg	1%
Vitamin B6	0.080 mg	6%

4. MEDICINAL USES OF CITRUS

The essential oil of lemon acts as a multipurpose remedy for the entire body and has a distinct and pleasant aroma. It can be inhaled, administered internally, or diluted for the treatment of various diseases. Citrus fruits including oranges and lemons are used as herbal remedies because they are rich in antioxidant, antiulcer, antidiabetic, antibacterial, and anti-inflammatory contents [41, 42]. The medicinal potential of lemon is due to

its antiscorbutic, depurative, anti-cancer, anti-inflammatory, antifungal, antimicrobial, and healing properties. However, lemon essential oil is poisonous during nursing, radiation exposure, and pregnancy [28]. Several citrus parts are clinically important due to their antibacterial and anti-cancer potential and also used for improving the patients' condition during rheumatism, arthritis, respiratory problems, kidney stones, mental health, and blood pressure [28]. Lemons and their derivatives also find applications in medical treatments for diverse conditions including osteoporosis, asthma, insomnia, vomiting, nausea, antifever, acne, scurvy, throat infections, and pH balance maintenance [43].

Both lemon and orange juice help to prevent the formation of kidney stones, although the role of the latter is more important [44]. Insoluble urate crystals are formed in the urine at relatively low urine pH [45]. The citrate helps to increase the alkalinity and thus protects against uric acid stone formation [46].

4.1. Lemon Peel Can Reduce Cholesterol

Several studies showed that eating lemon peel can effectively lower cholesterol levels [47].

4.2. Aromatherapy

Lemon is important for a healthy human skin but is also seemingly good for the mind. Consuming lemon or even inhaling its aroma (aromatherapy) effectively improves the mood and also lowers tension, nervousness, anxiety, tiredness, swelling, and lethargy [48]. Lemon is also used in a many air sprays and cooling devices. Some people inhale lemon drops to improve their mental concentration (attention), often by placing them on a handkerchief [28].

4.3. Anti-inflammatory Activity

Citrus peel is considered as an excellent source of anti-inflammatory and anti-nociceptive agents [49]. The essential oil of lemon may have one or more anti-inflammatory components, such as linalool, linalyl ate, limonene, and alpha-pinene [28].

4.4. Traditional Uses

Lemon juice provides a wide range of skin benefits and can aid in skin whitening [50].

4.5. Antioxidant Properties

Citrus fruits, juices, and peels are high in antioxidants, vitamin C, phenolic compound glycosides, and flavonoids.

4.6. Hypertension

Hypertension is common in older people as compared to younger ones; however, it can be treated with flavonoids such as erioctitrin, hesperidin, and diaosmin, vitamin C [51], and lemon peel water extract [52]. Lemon also helps to lower blood cholesterol levels [53]. Blood pressure can be lowered both systolic and diastolic by combining sugar and lemon juice [51].

One important step towards substituting medications with nutrition is the use of lemon juice therapy for idiopathic hypocitraturic calcium stones. For the purpose of treating hypocitraturia, potassium citrate is substituted with citrous juices and fruits in pharmacological treatments to remove kidney stones [54]. The use of lemon juice therapy for treating idiopathic hypocitraturia calcium stones represents a significant step in nutritional interventions. Citrus products are incorporated into pharmacological treatments, such as using potassium citrate to address recurring stones including hypocitraturia [43].

4.7. Scurvy

Lime is renowned for its effectiveness in treating scurvy, a condition caused by vitamin C deficiency. Common symptoms include frequent infections, cracked lips, ulcers in the mouth, and bleeding gums. Soldiers and sailors in the past used lime to prevent scurvy, a once-dreaded disease. Presently, it is given to staff working in contaminated areas, such as furnaces, painting shops, and mines, as a safeguard against scurvy [40].

4.8. Skin Care

Both lime juice and its oil offer significant skin benefits, whether consumed or applied externally. Rich in vitamin C and flavonoids, potent antioxidants, antibiotics, and disinfectants, they rejuvenate the skin, impart a radiant glow, and protect against infections. When used topically, the acids in lime scrub away dead cells, addressing issues such as dandruff, rashes, and bruises. Mixing lime juice or oil into bathing water provides a refreshing and revitalizing experience for the skin [40].

4.9. Antimicrobial Effect

The literature supports the efficacy of lemon peel as both an antimicrobial agent and as an astringent [55]. This is noteworthy due to the potential of excessive sebum secretion, a factor that may contribute to skin infection by certain flora, such as *Pseudomonas* and *Micrococcus*. In conditions like acne, it may act as a predisposing factor. The uncomplicated application of citrus juice may serve as a preventive measure against these diseases, contributing to the overall health and well-being of the skin [28].

With its rich content of monoterpenes, lemon demonstrates antibacterial properties, particularly through the inhibitory effects of lemon leaf oil on bacterial development. A blend of lemon juice and hot water proves effective as an antibacterial solution [43].

Lemon oil has the ability to directly regulate the formation of mould in certain foods or to act on packaged goods to produce inhibitory effects [56].

4.10. Central Nervous Effects

The depressive and anticonvulsant effects of *citrous limon* essential oil on the central nervous system (CNS) were investigated using animal models. In mice, *citrous limon* essential oil demonstrated CNS depressive and anticonvulsant properties, lowering motor activity and postponing the onset of convulsions brought on by PTZ and PIC [57].

4.11. Antidiabetic Effect

A metabolic condition known as diabetes interferes with the body's ability to use digested food as fuel for growth and energy. Human body uses glucose as its primary fuel source, which is produced when food is turned into blood sugar. For glucose to be able to enter the cells, insulin is necessary. The organic substances found in lemons known as polyphenols are particularly prevalent in lemon peel [58]. It has been discovered that polyphenols prevent fat accumulation, insulin resistance, hyperlipidemia, weight gain, and elevated blood glucose levels, among other features of obesity. Numerous essential oils included in citrus peel either eradicate or stop the formation of harmful germs. The anti-peroxidative and diabetes-lowering properties of citrus peel are partly attributed to its high total polyphenol content [59].

Rats were given a single intraperitoneal injection of alloxan (140 mg/kg bw) to cause diabetes in order to study the hypoglycemic effect of the

citrous limon peel hexane extract. *C. limon* peel hexane extract (200 mg/kg bw) was given orally and metformine hydrochloride (175 mg/kg bw) was the conventional medication. The outcomes demonstrated that hexane extract had a considerable hypoglycemic effect and that its activity was comparable to that of a prescription medication [60]. *Citrus medica* seed petroleum ether extract was investigated for its antidiabetic and hypolipidemic effects in a streptozotocin (STZ)-induced diabetic rat model. The oral dosage of seed extract was 200 and 400 mg/kg. After 15 days of medication, the *Citrus medica* seed petroleum ether extract significantly ($p < 0.05$) reduced fasting blood glucose, serum triglycerides, LDL, serum cholesterol, and VLDL. Nevertheless, a 15-day exposure to 200 mg/kg/day seed extract did not result in any change in HDL levels. Whereas, a daily dose of 400 mg/kg/day markedly raised HDL levels in diabetic rats [61].

4.12. Anticancer Effect

The pathophysiology of peptic ulcer is marked by an imbalance between factors that contribute to its development including offensive elements, such as acid, pepsin, and *H. pylori* and their protective mechanisms [62]. Indian medicinal plants and the products derived from them have been proven to be excellent therapeutic agents used for the treatment of various illnesses including conditions related to stomach. Additionally, the aqueous extract from fruits demonstrates antiulcer activity against gastric ulcers [63]. Many gastrointestinal diseases are traditionally treated at home with lemon fruit juice. A study was done on rats to find out how lemon juice affected ulcers in their stomach and duodenum. A significant ulcer healing effect was shown by lemon juice in a dose dependent manner [64]. Among citrus-scented medicinal plants, linn has been used to cure stomach ulcers, traditionally. Rats' ethanol-induced ulcer was tested against the fruit's aqueous extract. The rats were given two doses of the extract (250 and 500 mg/kg oral dose) and the antiulcer effect was contrasted with that of ranitidine (20 mg/kg oral dose). The fruit extract under investigation considerably decreased the formation of ulcers. Mucosal ulcers, inflammatory mucosal changes, and submucosal edoema all significantly decreased. Given that flavonoids have been demonstrated to have antiulcer capabilities, their presence may be responsible for the antiulcer action [65].

4.13. Anticancer Effect

Lemon, known for its potent alkaloids, is celebrated for its potential to counteract malignant cell growth, earning it the reputation of being an anticancer plant [43]. Limonene (a primary component of citrus fruits) lowers the chances of developing cancers of the lips, stomach, lungs, breasts, skin, and colon [66]. The essential components of lemon oil exhibit either cancer-fighting or antitumor properties, acting as preventive measures against cancer and inhibiting metastasis when the disease is already present [25, 40, 67].

4.14. Reproductive Effect

Vitamin C has been recognized for enhancing sperm quality. While consuming lemons may improve human sperm quality, the ideal concentration remains a critical consideration. For five weeks, male mice were given different quantities of lemon extract (25%, 50%, and 75%) as part of a true experimental design. Surprisingly, the highest improvement in sperm quality occurred with a 25% lemon extract concentration, surpassing the effects of higher concentrations. The study suggests that an optimal concentration of lemon extract, such as 25%, can positively impact sperm motility and morphology, highlighting the potential benefits of lemon consumption on sperm quality and quantity. Excessive concentrations, however, exhibit adverse effects, emphasizing the importance of moderation in utilizing lemon for this purpose [68].

4.15. Digestion

The captivating fragrance of lime triggers salivation, initiating primary digestion even before tasting it. Lime contains acids that are essential for stimulating the digestive system, as do the flavonoids in its aromatic oils. These compounds enhance the secretion of digestive juices, acids, and bile, aiding in the breakdown of food molecules. Additionally, they promote peristaltic movement, contributing to efficient digestion. This tradition is reflected in the practice of consuming lemon pickle with meals in India and its neighboring countries [11].

4.16. Effect on Bone Loss

Citrus aurantifolia cv. was evaluated for its anti-osteoporosis qualities in an ovariectomized rat model. Citrous extracts were administered and the tibia's trabecular bone mineral content and bone mineral density increased,

along with the levels of calcium and phosphorus. The findings showed that bone loss is lowered in ovariectomies rats by citrus extracts. So, it was recommended that clinically useful antiosteoporotic agents may be developed from citrus extracts [69].

4.17. Anti-cholinesterase Effect

Citrous aurantifolia peel and leaves from various growing zones were investigated for their anti-cholinesterase properties. IC₅₀ values of 91.4 to 107.4 µg/ml were found for the n-Hexane fractions from the peel and leaves, which demonstrated significant inhibitory activity against acetylcholinesterase [70].

4.18. Hypertension

Flavonoids such as eriocitrin, hesperidin, and diosmin, along with L-ascorbic acid and water extract from lemon peel, present promising avenues for treating hypertension common in older individuals. Lemon consumption is associated with reduced blood cholesterol levels. Additionally, a combination of lemon juice and sugar showed the potential of lowering both diastolic and systolic blood pressure [43].

4.19. Xanthine Oxidase Inhibitory Effect

The *Citrous limetta* peel extract (IC₅₀ = 40.16±0.88µg/ml) possesses an excellent potential of inhibiting the xanthine oxidase [71].

4.20. Decreasing the Risk of Renal Stone

Studies showed that women who drank half a liter of orange juice a day had higher urine pH values and increased excretion of citric acid which dramatically reduced the incidence of calcium oxalate stones [72].

4.21. Obesity

In obesity (a medical condition), excessive fat is collected in the body to such an extent that it may be harmful for health. Lemon juice, mixed with a glass of warm water, helps to break down adipose tissue and body fat, reversing the disease. It also has pectin which can limit food cravings [73].

Lemon peel extracts are also utilized to treat obesity in children and adolescents. Lemon's citrus content helps to lower the body's cholesterol and lipoprotein layer [74]. One of the primary health benefits linked with weight loss is the use of lemon juice and honey [75].

4.22. Toxic/Harmful Effects of Lemon

It was reported that sperm cells are destroyed by the use of lime juice, probably due to its higher acidity. Moreover, it was found that 50% juice of *Citrus aurantifolia* can kill 2000 of sperm cells in 30 seconds [76]. *Citrus limonum* seeds also showed anti-fertility effects on male albino rats, causing significant lowering of sperm count after 60-day treatment [39].

5. CONCLUSION

Currently, there is a global demand for herbal medicines containing bioactive compounds to treat various illnesses. Many traditional herbal remedies have gained recognition, worldwide. Citrus fruit is a notable example, known for its nutritional and therapeutic properties, particularly its high vitamin C content. *Citrus limon* is a rich source of diverse phytochemicals including citric acid, polyphenols, terpenes, limonene, flavonoids, vitamin C, sugars, pectin, citric acid, malic acid, flavonoids, carotenoids, terpineol, fennel, camphor, citral, calcium oxalates, and mucilages. Lemon oil contains 70% limonene and 20% monoterpenes, along with significant amounts of aldehydes, such as citral, alcohols (linalool), and esters (coumarin). Its medicinal properties are due to its antioxidant, antifungal, anti-cholesterol, anticancer, antiulcer, antidiabetic, antibacterial, and anti-inflammatory properties. Its fruits juice is effective in the removal of kidney stones and the consumption of its peel results in cholesterol reduction. Lemon fruit is also an excellent source of important nutritional contents especially vitamin C, macronutrients (dietary fibre and simple sugar), and micronutrients (copper, magnesium, phosphorus, calcium, potassium, pantothenic acid, riboflavin, vit B6 niacin thiamin and folate). Lemon peel contains high concentrations of flavonoids, glycosides, coumarins, steroids (beta, gamma, sitosterol), dietary fibers, carbs, and volatile oils, all of which are necessary for human health and appropriate development. Traditional medicine utilizes all parts of the citrus plant including the fruit juice, peel, and flowers. Furthermore, citrus fruit residues have low cost and are easily available. They are often discarded as waste, although they can be repurposed as a source of nutraceuticals. In brief, citrus plants represent a valuable source of bioactive compounds with potential applications in medicine and nutrition.

CONFLICT OF INTEREST

The authors of the manuscript have no financial or non-financial conflict of interest in the subject matter or materials discussed in this manuscript.

DATA AVAILABILITY STATEMENT

Data availability is not applicable as no new data was created.

FUNDING DETAILS

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