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BRIEF REVIEW ON ORANGE
(CITRUS SINESIS)

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Abstract

It makes sense that oranges are among the most widely consumed fruits worldwide. Worldwide, oranges (*citrus sinensis*) are highly prized for their nutritional and therapeutic qualities. The entire orange plant, including its ripe and unripe fruits, juice, peels, leaves, and flowers, has been utilized as a traditional medicine for ages. Citrus sinensis is a member of the Rutaceae family. The fruit is a juicy, indehiscent berry with a broad size range of 4 to 12 cm. Anti-bacterial, anti-fungal, anti-diabetic, cardioprotective, anti-cancer, anti-oxidant, and anti-hypertensive,anti -proliferative and Cytostatic effects are some of orange's main medical qualities. The entire plant's phytochemical composition includes rutin, limonene, citral, neohesperidin, naringin, rhamnose, eriocitrin, and vitamin C.

Keyword - *Cirus Sinensis*, Botanical description ,Phytoconstituents,Pharmacological activity.

Introduction

Natural products offer greater structural variety on a wider scale than synthesized molecules, making them an excellent source of chemicals for drug development. Natural products have historically been important sources of bioactive compounds and will continue to be key players in the development of novel pharmaceuticals[1] There are three kinds of Citrus, Fortunella (Kumquat), and Poncirus Trifoliata in the subgenus Citrus (Swingle), family Rutaceae, and subfamily Aurantioideae. There are eighteen recognized species and three genera, but there are also many natural mutations that lead to a large number of hybrids that are found all over the world. [2]

Among citrus, Citrus sinensis (L.) Osbeck is the most prevalent and significant species. The primary ingredient found in Citrus sinensis (L.) Osbeck essential oil is limonene. Sweet orange peel essential oil has demonstrated antibacterial and antifungal properties, with a greater efficacy against Gram-positive bacteria. The quantity of phenolic compounds in Citrus sinensis (L.) Osbeck is correlated with its antioxidant activity. In Citrus sinensis (L.) Osbeck, flavonoids are arguably the most significant naturally occurring phenolic; they have biological activity such as the ability to scavenge radicals.(3CS overview) In January 2021–2022, the world produced about 48 million tons of oranges, with the United State [3]. Brazil, China, the European Union, and Mexico being the top producers. Orange juice is mostly extracted from them in a number of nations; as of January 2021–2022, 1.7 million tons of orange juice were produced. [4]

Botanical Description

Southern China is the natural home of sweet oranges. It has since become widely dispersed and naturalized in India's subtropical zone. Particularly Brazil, China, Japan, Turkey, and India are the countries where it is grown. Sweet oranges require a dry environment with distinct summer and winter seasons and little precipitation. It grows on a variety of soil types that are susceptible to salt and range from clay to light sandy. Medium black, red, alluvial river bank loamy soil in Maharashtra state and Gujarat's Goradu soil are ideal for growing sweet oranges. Botanical classification of orange

Kingdom: Plantae
Division: Magnoliophyta
Class: Dicotyledons
Sub Class: Sapindales
Order: Rosidae
Family: Rutaceae
Sub family: Aurantoideae
Genera: Citrus
Species: sinensis [5]

Citrus Sinensis is a evergreen blooming tree has a compact crown with primarily spiky branches, and it can grow up to 7.5 meters in height, while it can occasionally reach up to 15 meters. Smooth, dark green leaves that are 3-5 mm broad and 6.5–15 cm long alternate with toothed blades that are formed differently—oval or elliptical—and are attached to the stem by winged petioles. The abundant oil in the leaves emits a powerful, distinct citrus scent.Small, waxy white, fragrant flowers with five white petals and twenty to twenty-five yellow stamens are axillary in whorls of six (5 cm wide).Fruits range widely in size and form, from round to rectangular. When these reach their maximum size, they appear brilliant yellow to orange in hue rather than green, which is their predominant color. The spherical, 4–12 cm fruits have a leathery, strongly adherent, 6 mm thick peel covering the luscious, segmented inner pulp, which, depending on the cultivar, may or may not contain seeds. Fruits are bursting with taste, aroma, and juice. [6]

The fruit is divided into two unique sections: the endocarp, or pulp, which has juice sac glands, and the pericarp, commonly known as the peel, skin, or rind. The skin's distinct smell is attributed to the epidermis of epicuticular wax, which is home to several tiny aromatic oil glands. The outer flavedo, or epicarp, which is mostly composed of parenchymatous cells and cuticle, makes up the pericarp. The tissue mass compressed into the intercellular space is made up of tubular-like cells that are linked together to form the albedo or mesocarp, which is located beneath the flavedo. The fruit typically has several to many seeds inside of it along with a tasty pulp. Usually, eleven juice segments that range in flavor from sour to sweet make up the fruit pulp. Frost sensitivity is present in orchards. Vitamins, particularly vitamin C, as well as phytochemical substances like pectin, liminoids, synephrine, hesperidin flavonoids, polyphenols, and liminoids are responsible for these health advantages. An orange is thought to contain more than 60 flavonoids and 170 phytonutrients. [7]

Traditional / Ethnomedicinal uses

Citrus sinensis is effective in the management of arthritis, asthma, Alzheimer's disease, Parkinson's disease, macular degeneration, diabetes mellitus, gallstones, multiple sclerosis, cholera, gingivitis, optional lung function, cataracts, ulcerative colitis, crohn's disease, high blood pressure, arteriosclerosis, stomach ulcers, kidney stones, cancer prevention, cholesterol reduction, and immune system strengthening. 12.5% of the daily need for fiber is provided by a single orange [8]

Chemical Composition

Cultivars, planting location, fruit variety, fruit portion, maturity stage, year of harvest, and postharvest storage conditions all affect the chemical makeup of *Citras sinensis.* Despite this, the fruit is a rich source of numerous significant phytoconstituents that are found in the leaves, seeds, flowers, juice, and peels of *Citras sinensis*. Many groups of chemical compounds, such as volatile oil, flavonoids (such as flavanones, glycosides, and polymethoxylated flavones), carbohydrates, peptides, fatty acids, steroids, alkanes, hydroxyamides, carotenoids, vitamins, and Minerals have been studied and reported by various scientists.[Table1]

Table 1-Phytoconstituents of citras sinensis [9-17]

Sr no.	Class	Compound
	Volatile Compounds	limonene , γ-terpinene ,β-pinene , linalool , sabinene , myrcene ,α-terpineol , α-pinene α-Thujene , Camphene ,Sabinene , *n*-Octanal , α-Phellandrene , decanal, terpinen-4-ol, terpiolene, citronellal, neral, α-copaene, valencene, nootkatone.
	Flavonoids	Didymin, Eriocitrin, Hesperidin, Narirutin, Neoeriocitrin, Poncirin , 6,8-di-*C*-Glu-Apigenin, 6,8-di-*C*-Glu-Diosmetin, Rhoifolin, Isorhoifolin,Diosmin, Neodiosmin, Heptamethoxyflavone, Nobiletin, Sinensetin, Tangeretin, Taxifolin, Acacetin
	Steroids	ß-Sitosterol , B-Sitosterol-3-O-B-D-glucopyranoside
	Hydroxylamide, alkane,	(E)-N-(1,3,4,5-Tetrahydroxyhexadecan-2-yl)dec-4-enamide, Tetracosane, Ethyl pentacosancate , Tetratriacontanoic acid
	Vitamins	Vitamins A, Vitamins D, Vitamins E, Vitamins K, Vitamins B1, B2, B3, Vitamins B5, Vitamins B6, Vitamins C
	Peptides	Citrusin-I, Citrusin-II, Citrusin-III
	Carotenoids	β-Cryptoxanthin, α-Carotene, Lutein, Zeaxanthin ,Phytoene
	Carbohydrate	Glucose, Fructose ,Sucrose
	Mineral	Calcium , Iron ,Sodium ,Potassium, Manganes, Magnesium , Zinc ,Copper, Phosphorous
.	Fatty acid	Linoleic acid , Palmitic acid , Isopropyl linoleate , Pentadecanoic acid ,Stearic acid , Butyl linoneate , Glutaric acid .

Pharmacological Activity

1) Antibacterial activity

By evaluating the zone of inhibition, the in vitro antibacterial activity of *C. sinensis* essential oil against S. aureus, E. coli, and S. agalactia was evaluated. According to results gathered using the well diffusion method, essential oil significantly reduced the growth of several tested bacterial strains. With a zone of inhibition measuring 14.33 ± 2.08 mm, this essential oil had the best antibacterial activity against E. coli. S. aureus and S. agalactiae had corresponding zones of inhibition of 10.67 ± 1.53 mm and 11.33 ± 1.16 mm. All bacterial strains' growth was considerably ($p < 0.05$) suppressed by the application of citrus oil. Based on the zone of inhibition value, the bacterial strains were ranked as follows: S. aureus > S. agalactiae > E. coli. Therefore, S. agalactiae has the fastest rate of growth and the lowest value of zone of inhibition, whereas E. coli has the highest value and the least growth. [18]

With a 6 mm inhibition zone diameter when applying essential oil extracted from hydrodistillation and a 4 mm inhibition zone diameter when applying essential oil derived from solvent free microwave extraction, orange essential oils have typically only been demonstrated to inhibit against Bacillus cereus .The circumference around the well in the agar plate containing the bacterium indicates the antibacterial activity against that strain of bacteria. Bacillus cereus cultures of essential oils from hydrodistillation and solvent free microwave extraction techniques exhibit the strongest antibacterial activity of orange essential oil. Nevertheless, the remaining Gram-positive and Gram-negative bacteria did not exhibit this antibacterial action of orange essential oil. Numerous bioactive substances that are frequently present in various plant species, such as thymol, citral, eugenol, limonene, pinene, and linalool, have been shown in earlier research to have potent inhibitory effect against these pathogens by interfering with the integrity of the bacterium. Furthermore, the hydrophobicity of essential oils results in a significant contact with lipid components, which is another way by which they penetrate cell membranes. This ultimately leads to bacterial cell structure breakage and component leaking. [19]

1) Antioxidant activity

The antioxidant ability of the extracts was assessed using the ferric reducing antioxidant power (FRAP), oxygen radical absorbance capacity (ORAC), and 2,2-diphenyl-1-picrylhydrazyl (DPPH) radical scavenging activity. The extracts from the peel of Citras sinensis showed varying levels of DPPH radical scavenging (8.35 to 18.20 mg TE/g), FRAP (95.00 to 296.61 mmol Fe(II)/g), and ORAC (0.31 to 0.92 mol TE/g). Among the extracts, 70% AEC had more antioxidant activity in all three tests, while WEC displayed much less antioxidant activity. Nonetheless, the extracts' DPPH, FRAP, and ORAC values were much lower than those of the ascorbic acid and gallic acid tested positive controls. Across all extracts, there was a significant amount of connection between the tests, particularly between FRAP values and TPC (R-square = 0.95, $P < 0.0001$) and TFC (R-square = 0.93, $P < 0.0001$). [20]

- **Mechanism of antioxidant activity of citras sinensis**

a) Inhibition of oxidant enzymes

Citrus fruit bioactive components may act as oxidant enzyme inhibitors to produce their antioxidant effects. Reactive nitrogen species (RNS) and other cellular ROS are primarily produced by oxidant enzymes, which also play crucial roles in biological systems' redox processes. Furthermore, the inhibition of Xanthine oxidase is one among the main processes underlying the antioxidant action of natural substances. Hesperetin inhibits Xanthine oxidase , which directly lowers the formation of free radicals within cells. In order to lessen the production of free radicals, coumarins can directly decrease the creation of Xanthine oxidase in cells. Polyphenols and other phytochemicals may thereby strengthen citrus fruits' antioxidant potential.

b) Interaction with redox signaling pathways

The antioxidant properties of citrus fruits might be attributed to the activation of nuclear factor E2-related protein 2 (Nrf-2) and the inhibition of nuclear factor kappa B (NF-κB) transcription factors. These two molecules play key roles in controlling the redox signaling pathways located in the cytoplasm and nucleus, respectively. Endogenous oxidants, including H2O2, function as second messengers and start a cascade of intracellular signaling processes that promote the synthesis of detoxifying enzymes and antioxidants..[21]

c) Direct reaction with ROS/RNS

Reactive oxygen species (ROS) and/or reactive nitrogen species (RNS) can directly interact with citrus bioactive components, exhibiting antioxidant activity. While modest levels of ROS/RNS are necessary for intracellular signaling defense responses to pathogens, higher concentrations of ROS/RNS play a critical role in the genesis of many human disorders. Phytochemicals found in C. sinensis may act as a barrier to prevent the accumulation of ROS and RNS and help the body get rid of them. O is cleared by vitamin C is direct reaction with HOO, OH, and irreversible dehydrogenation.

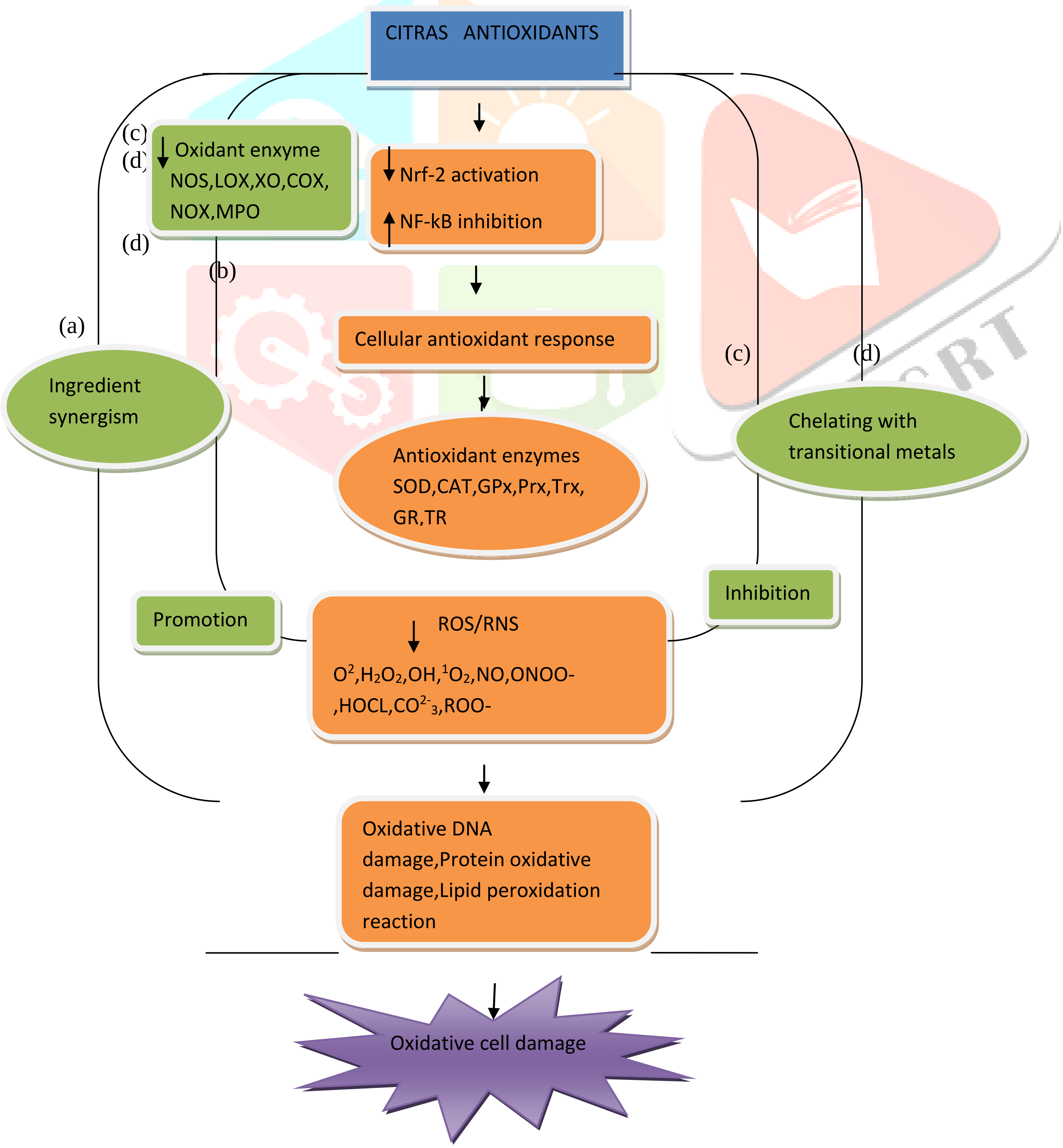
d) Chelators with transitional metals

Citrus fruit vitamin E has the ability to chelate transitional metals like Fe2+- and Cu2+. vitamin E from citrus fruits decreased the amount of ferrous iron to ferric iron. Hesperidin and coumarin both strongly chelate excess iron from the serum and deposit iron from the brain tissue, investigation of their effects on the iron-chelation activity of iron-overloaded mice's brain tissue. This finding supports the effectiveness of both compounds as antioxidant enzyme activators and chelators of iron ions. (6)

e) Ingredient synergism

Selenium and vitamin E collaborate to shield mitochondria from free radical harm and prevent peroxidation damage to their membranes. Even a small amount of vitamin E can effectively halt carotenoid oxidation in lipid-soluble environments, enhancing their antioxidant capabilities. Polyphenols, along with vitamins C and E, display synergistic effects due to their combined reduction.(22)

Fig 1. Schematic illustration of Citrus sinensis potential antioxidant process.



The literature currently in publication suggests five pathways: (1) chelate with transitional metals to yield less oxidative damage; (2) interact with redox signaling pathways to lead to the cellular antioxidant response; (3) directly react with ROS/RNS as a "free radical scavenger"; (4) interact with ingredient synergism to influence the entire antioxidant system.Lipoxygenases (LOX) and Nitric Oxide Synthase (NOS) Cyclooxygenases, or COX NADPH - Nicotinamide Adenine Dinucleotide Phosphate; NOX - NADPH Oxidase; Myeloperoxidase (MPO) Nf-kB, or nuclear factor kappa B, and Nrf-2, or nuclear factor erythroid 2-related factor2, Superoxide dismutase, or SOD Catalase (CAT), ROS (reactive oxygen species), GR-glutathione reductase, TR-thioredoxin, Prx-peroxiredoxin, GPx-glutathione peroxidase, and (1) inhibition of oxidant enzymes, reducing the cellular production of ROS/RNS, (2) interaction with redox signaling pathways, leading to the cellular antioxidant response, (3) direct reaction with ROS/RNS as a ‘‘free radical scavenger”, (4) chelate with transitional metals yielding less oxidative damage, (5) interaction of the ingredient synergism, which influence the whole antioxidant system. *NOS- Nitric Oxide Synthase, LOX- Lipoxygenases COX- Cyclooxygenases, ,XO –Xanthine oxidase,NOX-NADPH Oxidase, MPO-myeloperoxidase Nrf-2 – Nuclear factor erythroid 2-related factor2, Nf-kB- nuclear factor kappa B, SOD-superoxide dismutase, CAT-catalase, GPx- glutathione peroxidase, Prx-peroxiredoxin, GR-glutathione reductase, TR-thioredoxin, ROS-Reactive oxygen species, H2O2,- hydrogen peroxide, O2− superoxide anion, OH- hydroxyl radical, 1O2- singlet oxygen, NO- Nitric oxide, ONOO_ - peroxynitrite, HOCL-Hypochlorous acid, CO2−3- Carbonate, ROO_- Peroxy radical, ↑-Increase, ↓-Decrease. [23]

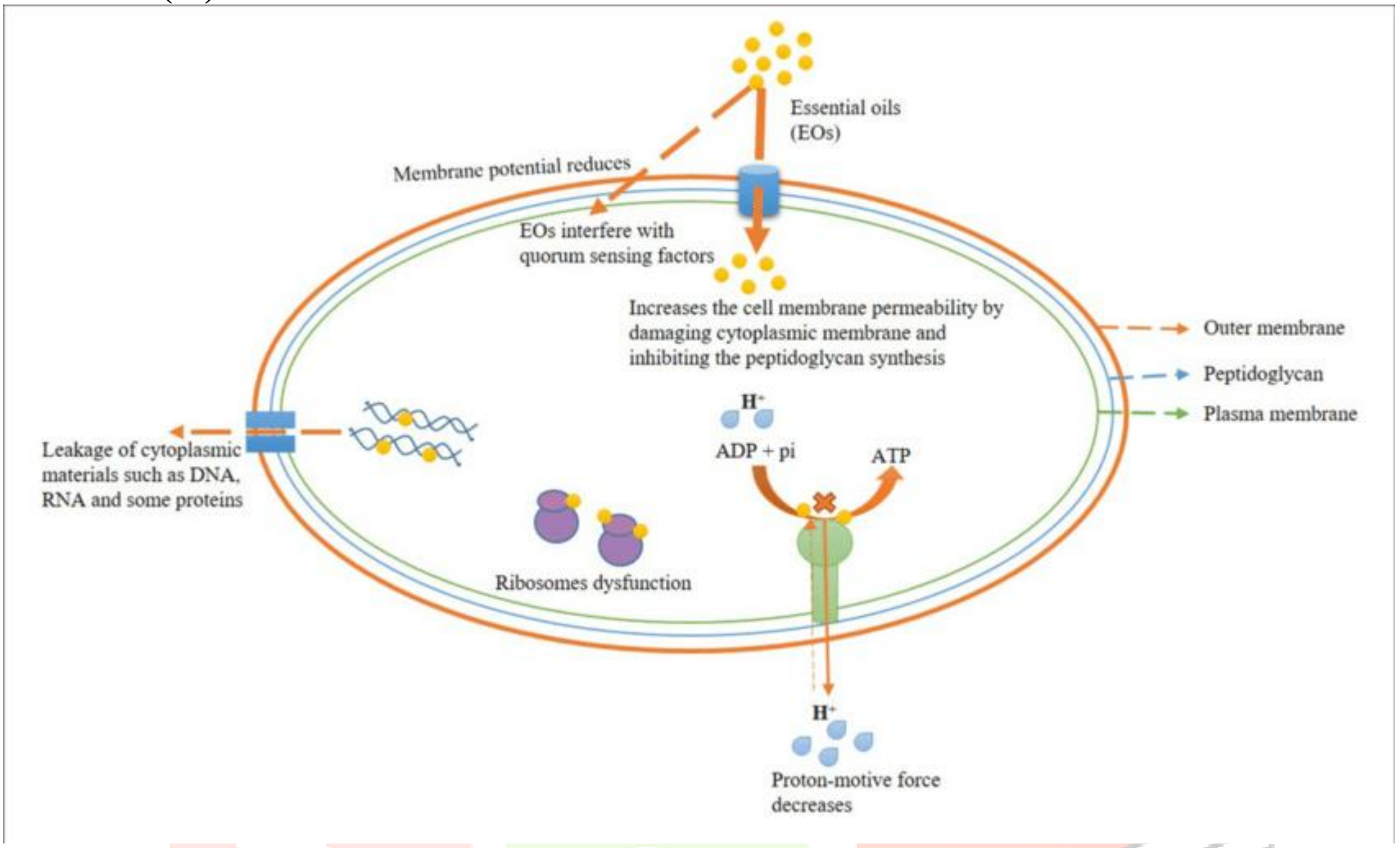
3) Anti-proliferative and Cytostatic effects

Orange juice at five, ten, twenty, forty, and sixty percent v/v concentrations was made. The concentration of methotrexate was 50 µg/mL. Layers of filter paper and cotton wool were placed within the Petri plates. S. bicolor seeds totaling twenty were added to each Petri dish. The methotrexate-treated seeds received 10 mL of 50 µg/mL methotrexate, while the control seeds received 10 mL of distilled water. The test seeds were treated with various orange juice preparations, with 10 mL of each concentration given to the seeds in a particular Petri dish (i.e., the seeds in one Petri dish were treated with 5% v/v concentration, the seeds in another received 10% v/v, the seeds in a third received 20% v/v, the seeds in a fourth received 40% v/v, and the seeds in the final Petri dish received 60% v/v). After 24 hours of incubation in a dark environment, the seeds were checked for growth, and after 48 and 72 hours, the mean lengths (mm) of the radicles that emerged from the seeds were measured. The outcome demonstrated that during the trial, the standard medication exhibited a significant ($P < 0.001$) anti-proliferative impact in comparison to the control, methotrexate. After 72 hours, there was a greater suppression of radicle growth (87.32%). At a level of 5% (v/v), the juice had no significant effect at 48 hours, but after 72 hours, it had a marginally significant ($P < 0.05$) effect. Throughout the experiment, the 10% and 20% (v/v) juice doses had a highly significant ($P < 0.001$) anti-proliferative effect; however, the percentage inhibitions were larger at 72 hours. At 72 hours, the juice's percentage inhibition at 10% (v/v) was 72.37%, and at 20% (v/v), it was 91.96%. According to the experiment, Citras sinensis fruit juice may have cytostatic and anti-proliferative effects on rapidly proliferating cells, which in turn may lead to the development of malignant cells. [24]

4)Antifungal activity

Fresh *Citras sinensis* peel essential oils encouraging in vitro anti-Rhizopus stolonifer action may be explained by limonene, the main chemical component of the peels. It can also be inferred that the high limonene concentration of 95.2% in lima orange essential oils accounts for the significant antifungal activity. This monoterpene has already demonstrated encouraging efficacy against a variety of fungus, including various Candida species. Conversely, reported that limonene had strong antifungal properties against Trichophyton rubrum. Generally speaking, it was wisely determined that citrus essential oils have a long history of use in the food and pharmaceutical industries due to their antifungal properties. The activity of essential oils may take place through changes in the integrity, composition and permeabilty of cell membranes, oxidative stress, inhibition of intracell processes of ion transport and rupture of cell membranes. High concentrations of limonene, a monoterpene that may be connected to the encouraging in vitro antifungal activity against Rhizopus stolonifer, were seen in the essential oils of both citrus cultivars. This essential oil carries antifungal activity by mechanism of a) Effect on Membrane Ergosterol, b) Effect on Leakage of Cellular Ions, c) Effect on Mitochondrial Membrane Potential, d)Effect on DNA and Gene Expression [25]

Fig 2- Possible antibacterial activity of essential oil -Mg^{2+}- Magnesium ions, k^+-Potassium ions, Ca^{2+}-calcium ions(26)



5) Cardiovascular effect

The primary outcome of this investigation indicates that a four-week intake of commercial *citras sinensis* fruit juice led to a significant reduction in both DBP (diastolic blood pressuer) and SBP (systolic blood pressure) in participants who were in good health. A similar finding was also observed in middle-aged, healthy men who were normal weight, who consumed orange juice for four weeks. Furthermore, research has demonstrated that consuming fruit juice high in flavanones significantly lowers blood pressure in hypertensive individuals. Given the high concentration of flavanones in citrus fruits and the widespread use of citrus fruits, especially orange juice, attention to flavanones is especially participant Compared to natural juice, concentrated citrus products have higher levels of flavones (polymethoxylated flavones, hesperitin, and naringin). This is because the fruit is ground whole in order to extract the juice. The concentrated juice also contains higher concentrations of pectin and aromatic oils from the peel. Oranges and grapefruits are the primary sources of hesperidin and naringin. They may provide some protection against mutagenesis and lipid peroxidation, as well as antioxidant, antihypertensive, and hypocholesterolemic properties. Regular postprandial ingestion of *Citrus sinesis* juice has been shown to lower DBP and boost endothelium-dependent microvascular responsiveness in middle-aged, healthy, moderately overweight males. It was proposed that hesperidin was responsible for orange juice's health benefits. (27).

Conclusion

New pharmacological substances can and will be largely derived from natural items. Due to the inability of alternative drug discovery techniques to provide several lead compounds in important therapeutic areas, there has been a recent resurgence of interest in natural product research. The public needs to be made aware of the significance of *Citras sinensis* and the need for finding and discovering new and effective drug compounds, so this review is a great way to learn about this natural product. In light of the health benefits of *Citras sinensis*, it presents excellent options for treating or helping in a disease due to its bioactive compounds (drug candidates) that show important activities or for developing new products.

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