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REVIEW ON ROLE OF CITRUS FRUIT IN HEALTH

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ABSTRACT

Citrus fruits are among the most important fruit trees grown in the world, prized for their refreshing juice and health benefits. Citrus fruits are thought to have numerous therapeutic properties, including anti-cancer, anti-viral, anti-tumor, anti-inflammatory properties, effects on capillary fragility, and ability to reduce platelet aggregation. Recently, therapeutic value has been reported in relation to cardiovascular disease and age re lasted macular degeneration. These many health benefits of citrus fruits are related to the high amounts of photo chemically and bioactive compounds such as flavonoids, carotenoids, vitamins and minerals found in citrus fruits. It acts as antioxidant and it also stimulates the immune system. Induces protective enzymes in the liver or blocks damage to genetic material. His current work is investigating the health care uses of citrus fruit and its constituents, and compiling the chemical composition of the plant.

KEYWORDS: Citrus, Grapefruit Vitamin C, Heart Disease, Obesity Control.

INTRODUCTION

Citrus belongs to the Citrus family and is one of the most important fruit crops grown worldwide. Sweet orange (Citrus sinuses) is the major fruit of this group, but a counts for about 70% of the citrus production. This group also includes small citrus fruits, such as the

tangerine tree (Citrus reticulate), the grapefruit tree (Citrus vitis), the lime tree (Citrus aurantifulia), and the lemon tree (Citrus lemon). The Citrus Tree is an evergreen tree that produces fruits of different shapes and sizes (from round to oblong) full of aroma, flavor and sap. The rough, tough, brightly colored green-to-yellow skin or rind known as pericarp or flavedo, covers the fruit and protects it from damage. The glands contain essential oils that give the fruit its unique citrus aroma fruits. The inner part forms the pulp and is divided into separate segments or sacs by a thick root membrane or endocarp (seeds or sacs depending on the cultivar). This part is rich in soluble sugars, ascorbic acid, pectin, dietary fiber, various organic acids, and potassium salts that give the fruit its unique citrine flavor. Although the exact origin of Citrus has not been determined, most researchers speculate that originated in Southeast Asia. Citrus fruits were then brought to America by the Spaniards in and to Mexico, Florida, Brazil and California among others in with his orange orchards, the largest in the world.

Citrus lemon (L.), commonly known as Limo or Nibu in Pakistan and sub continental regions. It below northeastern India. Lemons are known for their various distinguishing characteristics and their importance in all a pects of life, including food, medicine, and nutrition. But most importantly, it is medically and nutritionally important. Because its juice helps in many ways, including fever, which is so common among us, and lowering blood pressure, which is considered the most important step towards chronicity. Its leaves, which are treated as waste, such as when sick, can also be used for oil extraction and serve as a medicinal and food, as well as being of great importance as a natural preservative is. Lemon has been found to be more effective not only when used by itself, but when combined with Honey for sore throats and water for weight loss. To prove that it is useful in many respects, scientists and researchers have conducted many experiments in all parts, not just mice.

Citrus fruits are an excellent food source with abundant amounts of vitamin C. In addition, fruits are rich in other macronutrients such as sugar, fiber, potassium, folic acid, calcium, thiamine, niacin, vitamin B6, phosphorus and magnesium. Copper, and riboflavin pantothenate. However, secondary metabolites are a particularly popular topic in current research. These components, also called phytochemicals, are small molecules that are not strictly necessary for plant survival, but have pharmacological activity. Citrus fruits contain numerous secondary metabolites, including flavonoids, alkaloids, coumarins, limonoids, carotene ids, phenolic acids, and essential oils. These active secondary metabolites exhibit

multiple biological activities that are of vital importance to human health including antioxidant, anti-inflammatory, anticancer, and cardiovascular and neuroprotective effects. Traditional medicinal herbs of some Asian countries such as China, Japan and Kore In, nine Chinese herbal medicines were included in the Chinese Pharmacopoeia as appropriate medicinal uses of six citrus fruits.

MEDICINAL IMPORTANCE

Recently, people seem to be interested in changing their lifestyles and replacing medicines with natural foods and herbs and their derivatives. It is much more important to use Along with some magical ingredients, lemon is not only used as a traditional his medicine, but also serves as an ingredient in many medicines. Each of its ingredients has its own characteristic remedy, which of course is very important. From common childhood and adolescent obesity to serious ailments such as cancer and urinary tract infections, Lemon works wonders. Meters.

Obesity

Obesity is a medical condition in which excess body fat accumulates to the point that it is detrimental to health. Mixing a glass of hot water with lemon not only reverses the condition by breaking down adipose tissue and body fat, but the pectin in lemon can control food carving. Lemon peel extract is also used as a treatment for obesity in children and adolescents. The citrus in lemons helps reduce body lipids and her lipoprotein layer.

HYPERTENSION

Hypertension is known to be more common in the elderly than in the young, and is associated with flavonoids such as erioctitrin, hesperidin, and diaosmin, as well as vitamin C and lemon peel water extract. It is also treatable. It also reduces blood cholesterol levels of a mixture of lemon juice and sugar can lower both diastolic and systolic blood pressure Hypertension The discovery of lemon juice therapy in the treatment of idiopathic hypo calcium citrate stones is a major step toward nutritional replacement of pharmaceuticals. Citrus fruits and juices are used as pharmacologic therapy, and potassium citrate is used for recurrent stone hypocitricuria.

CANCER

Cancer is an abnormal cell division that is most often fatal, but can be undone by the alkaloid contain therein by this little magic bullet called the anti-cancer plant Lemon is useful as a medicine plant in cancer chemotherapy. Lemon is said to be an antibacterial plant and food. Lemon leaf oil extract inhibits bacterial growth caused by monoterpenes and alkaloids. Lemon juice and warm water are the best antibacterial mouthwashes.

In addition, the lemon itself, its juice, leaf oil, citric acid, alkaloids, and many other nutrients are “osteopro sis, insomnia, asthma, nausea, vomiting, motion sickness, acne spots, sore throats.”, scurvy, antipyretic, and last but not least PH balance, etc.

Citrus Limon (L.) Balm. f. (lemon) is a tree 2.5-3 m tall. There are his leaves that are evergreen lanceolate. The bisexual flowers are white with a purplish tint to the petal edges. They are collected in small clusters or occur singly and grow in leaf axils. The fruit is an oblong, pointed green fruit that turns yellow when ripe. Inside is a juicy pulp divided into segments (like an orange). The pericarp of C. lemon consists of a thin waxy exocarp, below which is the outer part of the mesocarp, also known as flavedo. This part contains oil sac and carotenoid pigments. The interior of the mesocarp, also called albedo, consists of spongy white parenchyma. The endocarp or “pulp” is divided into segments by the spongy white tissue of the mesocarp. C. Limon trees prefer sunny locations. It grows in loamy, well-drained, moist soils with a wide pH range of. The original natural habitat location of C. Limon is not precisely known. However, C. Limon is believed to be native to northwestern or northeastern India. C.limon is primarily recognized as a cultivar. In southern Italy he has been cultivated since, in the 3rd century AD, and in Iraq and Egypt since 700. Arabs introduced C. Limon to Spain in and it has been cultivated since 1150. Marco Polo's

expedition also brought 1297 C. Limon to China. Also in 1493 Christopher he was one of the first new species brought to the North American continent in seed form by Columbus. In the 19th century, worldwide commercial production of C.limon started in Florida and California. Currently, the largest producer of C. Limon is the USA. Italy, Spain, Argentina and Brazil also play a significant role.

CITRUS FRUITS DIVIDED INTO DIFFERENT GROUPS AS FOLLOWS

a. Sweetge (Citrus sinensis L.): including ordinary orange, navel orange, blood orange and Valencia orange.
b. Sour orange (Citrus aurantium): bitter orange and their varieties
c. Tangerine and tangerine (Citrus reticulata of Swingle) or (Citrus delicious of Tanaka): this group is a category of easy-peel citrus, includes varieties with yellow and orange peel, such as Satsuma mandarin, Dancy mandarin, some varieties can they ripen already in December like Clementine and Satsuma tangerines, late varieties can be harvested in Augus or shine like Murcott and Pixie tangerines.
d. Lemon (Citrus Limon): Fruits ripen throughout the year a group including Eureka, Lisbon and Meyer lemon
e. Lime (Citrus aurantifolia): including Mexican lime, Indian lime, Tahitian lime, bear lime and key, fruits ripen throughout the year.
f. Other species: such as Lemon, Kumquat and Pomelos.

These citrus fruits are a valuable source of phytochemicals which are beneficial to the human organism as vital bioactive substances drugs, Phytochemicals are naturally present in citrus juices and play a role in physiological functions and metabolic changes of the human body, citrus fruits and juice also have a unique value essential nutrients and these nutrients protect against several chronic diseases. Citrus fruits have potential health benefits such as in addition, antimicrobial, anti-inflammatory, antiviral and anti-cancer that citrus juice contains a lower amount of cholesterol which helps for diabetics.

CHEMICAL COMPOSITION OF C. LIMON

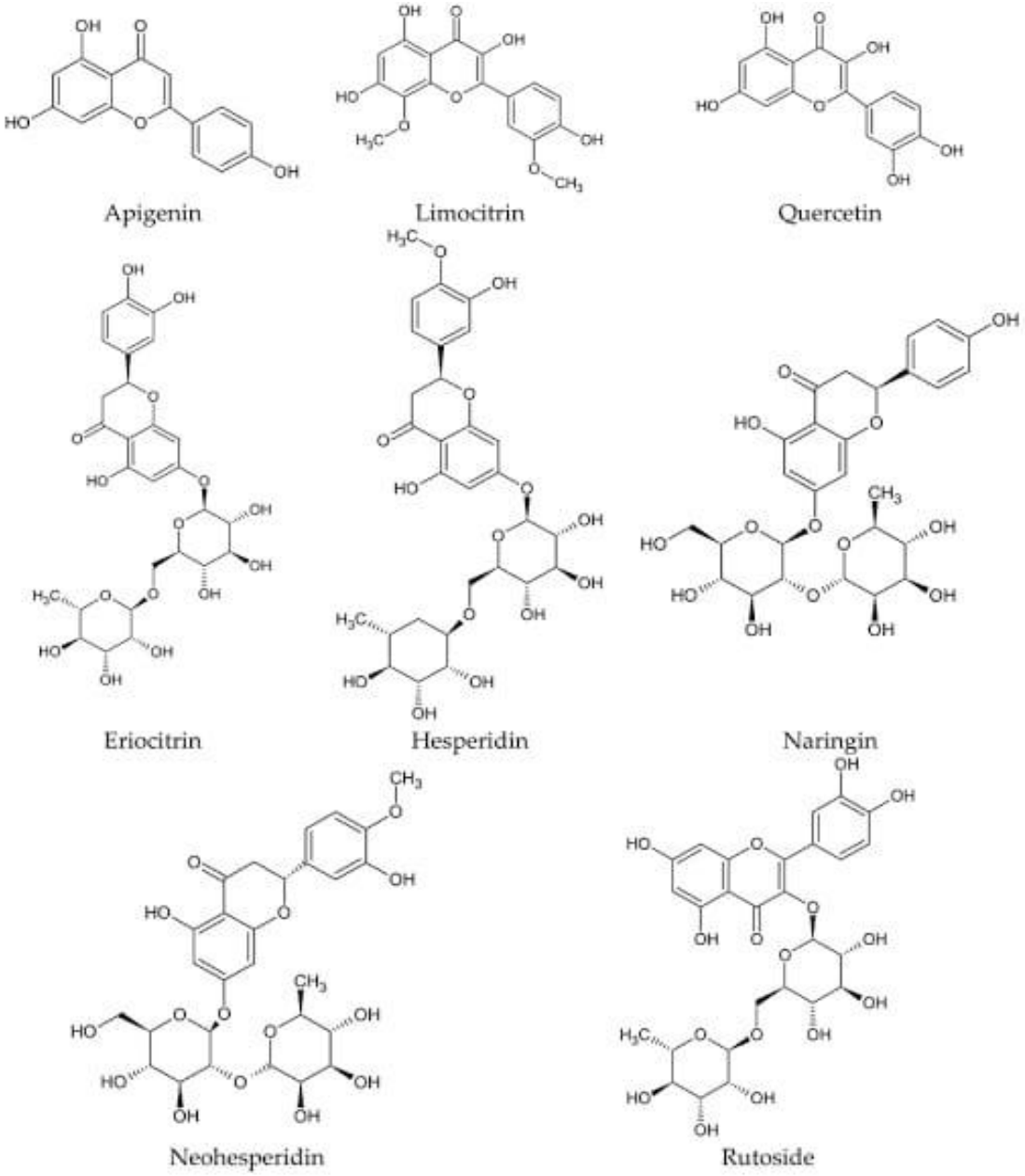
The chemical composition of C. Limon fruits is well known. It was not intended only for the whole fruit, but also especially for the pericarp, juice, pulp and essential oil. Ingredients leaves and fatty oil extracted from the seeds of C. Limon are also known. Due to the large number of C. Limon varieties, cultivars and hybrids, various research centers are engaged in the task of analyzing chemical composition of raw materials obtained from them.

The most important group of bioactive substances in C. Limon fruits and their juice, determining their biological activity is flavonoids such as: flavones – eriodictyol, hesperidin, hesperetin, naringin; flavones – apigenin, diosmin; flavonols — quercetin; and their derivatives (Figure 2). IN whole fruit, additional flavonoids are additionally detected: flavonols — limocitrin (Figure 2) and spinachetin, and flavones – orientin and vitexin (Tables 3 and 4). Some flavonoids, eg neohesperidin, naringin and hesperidin (Figure 2), are characteristic of C. Limon fruits. Compared to other citrus species. Limon has the highest eriocitrin content.

Another important group of compounds found in both juice and fruit are phenolic acids. There are mainly two such compounds in the juice – ferulic acid and synaptic acid and their derivatives. On the contrary, the presence of p-hydroxybenzoic acid was confirmed in the fruit. In fruit, there are also coumarin compounds, carboxylic acids, carbohydrates, as well as amino acids, B complex vitamins, and importantly vitamin C (ascorbic acid).

Another interesting group of compounds found in C. Limon fruits are limonoids. Limonoids are highly oxidized secondary metabolites with polycyclic triterpenoid backbones. They occur primarily in citrus fruits, including lemons, in which they are found mainly in the seeds, pulp and peel. They exist mainly two such compounds in C. Limon fruits – limonin and nomilin (Figure 3). Studies showed that the concentrations of compounds of this group are dependent on fruit growth and maturation stages. Young citrus fruits contain the highest amount of these compounds compared to ripe.

Analysis of macro elements in C. Limon fruits showed the presence of: calcium in the pulp and peel (Ca), magnesium (Mg), phosphorus (P), potassium (K) and sodium (Na). In C. Limon seed oil, the main components are fatty acids such as arachidonic acid, behenic acid and linoleic acid as well as tocopherols and carotenoids (Table 5). Recent studies have shown this C. Limon fruit pulp oil contains more fatty acids compared to other citrus species such as C. aurantium, C. reticulata and C. sinensis. The following fatty acids were identified in C. Limon pulp oil: behenic acid, erucic acid, gondoic acid, lauric acid, linoleic acid, α-linolenic acid, margaric acid, palmitic acid, palmitoleic acid, pentadecanoic acid and stearic acid.



Some Health Benefits of Citrus

Citrus fruits have a wide spectrum of biological activity maintaining physical health (Table 3). Also sweet orange and lemon fruits have a wide variety of bioactive compounds that list a 60-70% control of liver diseases.

However, citrus juice, especially grapefruit, contains enzymes, especially the P-45 enzyme, which is considered a natural tool for controlling obesity and contained a number of different proteins that burns human fat Lemon fruits have numerous bioactive compounds and lemon juice contains more than 200 compounds that include regulators of the human body. Lemony

and sweet though orange juices have a controlled wide range of bioactive compounds about 60-70% of liver disease through control lipids.

THE MAIN HEALTH BENEFITS OF CITRUS FRUITS

Anti-carcinogenic properties: Citrus flavonoids have ant carcinogenic and antitumor activities.

Cardiovascular properties: Citrus flavonoids show an anti-adhesive and anti-aggregation effect against aggregation of red blood cells.

Hyperglycemia: Citrus flavonoids play an important role prevention of the progression of hyperglycemia, in part through binding with starch, increasing liver glycolysis and glycogen concentration and reduction of hepatic gluconeogenesis.

Anti-inflammatory, anti-allergic and analgesic activity: Citrus flavonoids such as hesperidin, diosmin, quercetin and others flavonoids have shown dose-dependent anti-inflammatory activity by influencing the metabolism of arachidonic acid and histamine edition.

Antimicrobial activity: One of the properties of flavonoids with their physiological action in plants are their antifungal and antiviral activity.

Anti-anxiety, antidepressant and anti-allergic activity: Apigenin exhibits antidepressant activity, some flavonoids do antiallergic.

Citrus and lipid control: Many clinical studies have reported this citrus juice is useful for controlling high cholesterol and major lipid problem of the human body, due to the higher content soluble and insoluble fiber in citrus juice.

HEALTH BENEFITS OF BIOACTIVE COMPOUNDS OF CITRUS FRUITS

5.1. IN VITRO STUDIES

5.1.1. FLAVONOIDS

The antioxidant activity of citrus bioactive compounds, especially flavonoids, carotenoids, terpenes, and limonoids, can alleviate oxidative stress-related disorders; therefore, they have a potential application against obesity, inflammatory diseases, atherosclerosis, and neurodegenerative diseases. And cancer. (Table 3).Pancreatic lipase (PL) is a key enzyme involved in the hydrolysis of triglycerides gastrointestinal tract and its inhibition may improve obesity by minimizing lipids absorption. Hesperidin, neohesperidin, naringin, narirutin and eriocitrin were found be the main component of citrus peel extracts of grapefruit, pomelo, kumquat, tangerine and ponkan. Interestingly, among these flavonoids in this study, hesperidin, the most dominant flavonoid in the ponkan bark extract, showed the

highest pancreatic lipase inhibitory activities, suggesting its promising application in the treatment of obesity. Citrus peel flavonoid nobiletin suppresses the inflammatory response in lipopolysaccharide (LPS)-stimulated RAW264.7 cells by increasing autophagy by reducing inflammatory cytokine levels (inducible nitric oxide synthase (iNOS) and cyclooxygenase-2 (COX-2)) and interleukin-6 (IL-6) activation/signal transducer and activator transcription 3 (STAT3)/forkhead box O3a (FOXO3a) signaling pathway responsible for induction of macrophage autophagy. Dysregulation of IL-5 secretion by antigen-specific T helper 2 (Th2) cells was associated with eosinophilic inflammation in asthma. Th2 cytokine expression is regulated by transcription factors, including nuclear factor of activated T cells (NFAT). In addition, heme oxygenase-1 (HO-1) expression is known to suppress asthmatics Antioxidants 2022, 11, 239 12 of 28 modulation of the phosphoinositide 3-kinase (PI3K)/protein kinase B immune response (AKT), extracellular signal-regulated kinase (ERK)/c-Jun N-terminal kinase (JNK), nuclear factor erythroid 2-related factor 2 (Nrf2), and peroxisome proliferator-activated receptor γ (PPARγ) signaling. The citrus flavonoid gardening A and hesperidin exhibited a robust suppressive effect on IL-5 secretion in PMA/ionomycin-treated murine lymphoma EL-4 cells by reducing NFAT protein expression. In this study, hesperidin and gardenin A induced HO-1 protein expression and suppressed IL-5 production through divergent paths; hesperidin up regulated HO-1 production through Nrf2 protein expression in combination with activation of ERK/JNK and PI3K/Akt signaling pathways, while gardenin A induced HO-1 expression through the PPARγ transcription factor. In addition to the health benefits described above, bioactive substances are present in citrus fruits the juices have been shown to have direct antiviral activity. Dong et al. Reported that hesperidin restricted influenza virus replication and progression in A549 human lung carcinoma cells by up regulating the p38 signaling pathway. Hesperidin, hesperidin and Naringenin has been shown to inhibit key proteases involved in coronavirus replication and prevent virus entry into host cells. The flavonoids (hesperidin, naringin, tangeritin and rutin) rich in the hydro-ethanolic extract of the bark of C. reticulata Blanco showed antiproliferative effects against human breast cancer BT474. In this study, extract treatment reduced by 500 µg/ml BT-474 cell viability by 47% and 60% after 24 or 48 h of treatment, respectively.

5.1.2. CAROTENOIDS

Carotenoids are widely investigated for their anticancer activity. Carotenoids are well known for their antioxidant function in the normal cellular environment. However, in cancer cells with an innately high intracellular level of ROS, carotenoids are they can act as potent pro-

oxidant molecules and promote ROS-mediated apoptosis. In our study, we demonstrated that the anticancer activities of β-cryptoxanthin are derive from tangerines to human cervical carcinoma (HeLa) cells are mediated through pro-oxidative action that enhances ROS generation, followed by increased expression of caspase-3, -7 and -9, Bax and p-53 on mRNA, with concomitant suppression of anti-apoptotic Bcl-2. These events trigger nuclear condensation, loss of mitochondrial membrane potential, activation of caspase-3 proteins, and ultimately cleavage DNA core. In this study, β-cryptoxanthin significantly inhibited proliferation HeLa cells with an IC50 value of 4.5 µM after 24 hours of treatment.

5.1.3. ESSENTIAL OIL (terpenes and limonoids)

Lumy essential oil rich in limonene (48.9%) and linalool (18.2%) exhibit strong antioxidant and free radical scavenging properties with antiacetylcholinesterase activity. Additionally, in this study, Lumy essential oil was shown to be neuroactive effects by significantly reducing burst frequency (MBR), assessed spontaneously electrical activity of rat cortical neuronal networks. In neuronal cells, K+ imbalance, activation (phosphorylation) of extracellular signal-regulated protein kinase (ERK1) and production of reactive oxygen species (ROS) occur. Associated with the progression of Alzheimer's disease (AD). In addition, the enzyme acetyl cholinesterase (AChE), which participates in the hydrolysis of acetylcholine, plays an important role. Role in triggering neuropsychiatric symptoms in AD. Limonene has shown protection effects on Aβ1–42 oligomer-triggered toxicity in primary cortical neurons (in vitro model AD) by suppressing AChE hyper function, ROS production and voltage-gated K + channel KV3.4 and down regulating phosphorylated (p)-ERK. Citrus limonoids (limonexic acid, limonin and nomilin) have been shown to induce apoptosis and inhibit proliferation (IC50 values < 50 µM after 72 h) of pancreatic cancer Panc-28 cells, by increased cleavage of caspase-3, reduced the mitochondrial membrane potential and up regulation of X-associated B-cell lymphoma 2 (Bcl-2) expression protein (Bax)/Bcl-2 proteins. Moreover, limonoids up regulated in this study Antioxidants 2022, 11, 239 13 of 28 expression of cyclin-dependent kinase inhibitor (p21) and showed anti-inflammatory activity through down regulation of the expression of pro-inflammatory proteins Cox-2, nuclear factor-kappa β (NF-κB) and IL-6.IL-6.

5.1.4. OTHER BIOACTIVE SUBSTANCES

In addition to flavonoids, carotenoids, terpenes and limonoids, citrus pectin and coumarin has beneficial health properties. For example, citrus pectin oligosaccharides and their microbial

metabolites showed ant atherosclerotic effects on LPS treated human macrophages by regulating the expression of pro-inflammatory mediators (TNFα, IL-6, IL-10 and NF-κB mRNA). Additionally, cholesterol efflux was also present in this study accelerated by up regulation of liver X receptor-α (LXRα) and adenrnonete Triphosphate-binding cassette transporter (ABC) A1 and G1 (ABCG1) mRNA. Furthermore, pectin oligosaccharides suppressed cholesterol synthesis by down regulating 3-hydroxy-3-methylglutaryl coenzyme A reductase (HMGCR) mRNA. Coumarin, isolated from grapefruit, inhibited the levels of alanine transaminase (ALT) and aspartate transaminase (AST), and the activity of antioxidant enzymes, including glutathione peroxidase (GSH-Px), by inhibiting d-galactosamine. It showed hepatoprotective activity in treated normal human LO2 hepatocytes. Reduction of superoxide dismutase (SOD) and malondialdehyde levels (MDA).

5.2. IN VIVO STUDIES

Excessive caloric intake causes chronic hyperlipidemia and hyperglycemia, triggering atherosclerosis, liver steatosis, obesity, diabetes and cardiovascular complications. These metabolic diseases are associated with a whole range of metabolic complications. Hyperlipidemia is a disorder of lipid metabolism that results in abnormally elevated levels of low-density lipoprotein (LDL-c) and very low-density lipoprotein cholesterol. Lipoprotein cholesterol (VLDL-c), triglycerides (TG) and total cholesterol (TC) in the blood, as well as reduced levels of high-density lipoprotein cholesterol (HDL-c). Similarly, chronic hyperglycemia is a condition of persistent and abnormally high postprandial (after a meal) blood glucose levels, primarily due to poor insulin production. Several recent animal studies have demonstrated the beneficial effects of citrus flavonoids, carotenoids, terpenes, limonoids and other bioactive substances (e.g. pectin and coumarins) against metabolic syndrome (Table 4). In addition, the strong antioxidant activity of citrus bioactive substances have shown protection against primary dysmenorrhea (PD), pulmonary edema, cancer and neuropsychiatric and neurodegenerative diseases.

5.2.1. FLAVONOIDS

The citrus flavonoids are most widely investigated for their antihyperglycemic and antihyperlipidemic effects in animal models. Citrus flavonoids, such as hesperidin, have shown potential in attenuating hyperglycemia in streptozotocin (STZ)-induced diabetes in rats by releasing insulin from β cells of islets. In this study, hesperidin supplementation of 40 mg/kg for 45 days showed a significant decrease in plasma glucose levels and a significant

increase in the level of plasma insulin. It restored the compromised antioxidant status by increasing the activity of SOD, catalase (CAT), and glutathione peroxidase (GPx). Moreover, in this study, hesperetin alleviated hyperlipidemia by lowering the cholesterol, free fatty acid (FFA), TG, and phospholipid (PL) levels in diabetic rats, probably via the insulin-mediated reduction in the synthesis of fatty acids and cholesterol. Moreover, the authors suggested that the cholesterol-lowering effect of hesperetin is possibly due to the capability of hesperetin and other flavonoids to bind to bile acids, resulting in enhanced bile acid secretion and a reduction in cholesterol absorption. The flavanone aglycones present in fermented/non-fermented ougan (cv. Suavissima) juice exhibited anti-obesity properties in high-fat-diet (HFD)-fed C57BL/6J mice by reduced weight gain, decreased fat accumulation, enhanced glucose homeostasis and insulin sensitivity, lowered liver steatosis, enhanced white adipose tissue (WAT) browning, augmented brown adipose tissue (BAT) activity, and increased diversity of gut microbiota. The gastrointestinal microbiota composition plays a vital role in host physiology, nutrition, and metabolism. Changes in the gastrointestinal microbiota composition, the community of pathogenic symbiotic and microorganisms, are probably responsible for the anti-obesity effects of citrus bio actives, especially flavonoids. The abundance of gut microbiota, Firm cutes over Bacteroidetes, is linked to obesity-related metabolic syndrome. Moreover, the gut micro biome's branched-chain amino acid (BCAA) metabolism is considered responsible for metabolic syndrome. It is likely that microbial produced BCAAs, such as imidazole propionate, impair insulin signaling through the activation of mammalian target of rapamycin (mTOR) complex 1 (mTORC1) and P70S6K. Sterol regulatory element-binding proteins (SREBPs) play essential roles in regulating lipid homeostasis via mTOR. An extract rich in PMFs and hydroxy polymethoxyflavones (HOPMFs) (0.5% of HFD for 16 weeks) from citrus peel attenuated the obesity and modulated gut microbiota in male C57BL/6 mice fed a HFD by altering the gut microbiota, by increasing Prevotella and decreasing rc4–4 bacteria . In this study, PMFs and HOPMFs alleviated the total body weight, decreased the lipids in 3T3-L1 preadipocytes, and reduced the adipocyte size and adipose tissue weight in the HFD mice. Moreover, in this study, PMFs and HOPMFs decreased the levels of lipid droplets (LD) and perilipin 1 protein and sterol regulatory element-binding protein 1 (SREBP-1) expression. Similarly, in another study, a citrus PMF (nobiletin and tangeretin)-rich extract was shown to ameliorate HFD-induced metabolic syndrome via gut dysbiosis (decreased Firmicutes-to-Bacteroidetes ratio), and regulated branched-chain amino acid (BCAA) metabolism. In this study, the PMF-rich extract inhibited the phosphorylation of mTOR and P70S6K and decreased the expression of

SREBPs in human liver HL-7702 cells and HFD-fed mice. Therefore, the authors hypothesized that the decreased BCAAs by the PMF-rich extract contribute to improving metabolic syndrome by inhibiting the mTOR/P70S6K/SREBP pathway. Among the four flavones tested for their anti-atherosclerosis potential in apolipoprotein E-deficient (ApoE−/−) mice, naringin showed the most potent anti-atherogenic effect, followed by hesperidin, naringenin, and hesperetin. In this study, oral naringin admiration alleviated atherosclerosis by enhancing bile acid synthesis. Hesperidin up regulated ABCA1 to enhance cholesterol reverse transport, while the aglycones naringenin and hesperetin inhibited cholesterol synthesis significantly by down regulating 3-hydroxy-3-methyl-glutaryl-coenzyme a reductase (HMGCR). Dietary administration of 0.05% PMF 5-demethylnobiletin has shown chemo preventive effects against azoxymethane/dextran sulfate sodium (DSS)-driven colorectal carcinogenesis in male CD-1 mice by reduced cell proliferation, increased apoptosis, and decreased mRNA and protein levels of proinflammatory cytokines IL-1β, IL-6, and TNF-α in the colon. In this study, a significant amount of 5-Demethylnobiletin metabolites, namely 5, 3′-didemethylnobiletin, 5, 4′-didemethylnobiletin, and 5, 3′, 4′-tridemethylnobiletin, was documented in the colonic mucosa of the treated mice. Surprisingly, these metabolites showed more potent effects than 5-demethylnobiletin on inhibiting the proliferation, inducing cell cycle arrest, and the apoptosis of HCT116 human colorectal cancer cells. Higher levels of circulating thyroid-stimulating hormone (TSH) are vital for greater longevity. The up regulation of sirtuin 1, which deacetylates transcription factors that contribute to cellular regulation, may positively up regulate the exocytosis of TSH-containing granules. Due to the antioxidant and anti-inflammatory properties, 15 mg/kg body mass (BM) of citrus naringenin has shown increased TSH secretion in 24-month-old male Wistar rats by up regulating the Sirt1 protein expression.

5.2.2. CAROTENOIDS

Provitamin a carotenoids (eg β-cryptoxanthin) from citrus fruits also have has shown efficacy against metabolic syndromes such as type 2 diabetes. IN body (gut and liver), provitamin a carotenoids are bio converted to retinol β-carotene 15, 15′-oxygenase (BCO1) activities. In type 2 induced by a high fructose diet male Wistar rat model of diabetes, feeding a citrus concentrate containing 0.086 mg βcryptoxanthin, 5.69 mg hesperidin, and 7.5 mg pectin for eight weeks reduced insulinemia, glycemia, and dyslipidemia by restoring LDL-c and TG levels to similar healthy group. Additionally, in this study, administration of purified β-cryptoxanthin alone or with a matrix containing hesperidin and pectin showed a synergy

between these components. Furthermore, β-cryptoxanthin from citrus fruits was shown in this study to restore vitamin A status in both control and prediabetic (high fructose-fed) rats; however, prediabetic rats showed lower absorptive bioconversion of β-cryptoxanthin to retinoids. The synergy between carotenoids and flavonoids is probably due to enhancement uptake of carotenoids in the presence of flavonoid glycosides.

5.2.3. ESSENTIAL OIL (Terpenes and Limonoids)

Overproduction of endometrial prostaglandins (PGs), particularly prostaglandin F2α (PGF2α) and prostaglandin E2 (PGE2), is considered one of the key factors in the progression of primary dysmenorrhea (PD). I'm here. A higher ratio of PGF2α/PGE2 is believed to be a major indicator of PD. In female Sprague-Dawley rats, limonene-rich citrus essential oils, particularly sweet orange essential oil, reduced PGF2α levels and increased PGE2, thereby alleviating estradiol benzoate and oxytocin-induced PD., resulting in a decrease in the ratio of PGF2α/PGE2. Furthermore, in this study, citrus essential oils prevented a decrease in markers of antioxidant status such as total antioxidant capacity (T-AOC), SOD and CAT, and an increase in MDA levels. Anxiety and depression are the most common forms of neuropsychiatric disorders. Orange essential oil and its main component, limonene, reduced curiosity and motility, reduced weight gain, and reduced sucrose preference in a male Kunming mouse model of chronic unpredictable mild stress (CUMS)., showed antidepressant effects by restoring monoamine neurotransmitters by reducing levels of 5-hydroxytryptamine (5-HT), dopamine (DA), norepinephrine (NE), and brain-derived neurotrophic factor in the hippocampus. Increased levels of corticosterone (BNDF) and its receptors tropomyosin receptor kinase B (TrkB) and corticotropin releasing factor (CRF) corticosterone (CORT).

5.3. HUMAN STUDIES

Similar to in vitro and animal studies, case-control, cohort and interventional studies have also demonstrated the health benefits of bioactive compounds derived from citrus fruits. A pooled meta-analysis of 14 case-controls (13 hospital-based and two population-based) and two cohort studies showed that people with the highest citrus fruit intake had a 50% reduced risk of oral and pharyngeal cancer compared with lowest income. In this meta-analysis, the protective effect of citrus fruits was significantly greater in case-control studies (OR 0.47; 95% CI 0.40–0.55) compared with cohort studies (OR 0.73; 95% CI 0.55– 0.96).

CONCLUSION

Citrus fruits are known for their beneficial biological activities for the human body, citrus fruits are available all year round, Citrus fruits and their components are a rich source of flavonoids, carotenoids and bioactive compounds used in treatment hypertension, there are also active substances extracted from citrus fruits used against heart disease. However, citrus juice contains enzymes considered a natural tool to control obesity and it contained a number of different proteins that burn human fat.

All sour citrus fruits are said to provide more amount of calcium citrate than sweet varieties. Calcium citrate is a better match to all other salts available as a calcium salt supplement, antioxidant and antacid. Report the percentage yield of calcium citrate can help select a high yield salt source. The hydro distillation of orange peel was carried out which further lay a new method and less time-consuming and a less tedious method for extracting the volatile oil from citrus peel.

REFERANCE

1. D. E. Okwi and I. N. Emenike, Evaluation of the Phsytonutrients and Vitamins Contents of Citrus Fruits. In ternational J. Molecular Medicine and Advance Sciences, 2006; 2(1): 1-6.
2. G. D. P. Roger, New Life Style Enjoy It. Editorial Safelie SL Spain, 1999; 3: 75-76.
3. G. D. P. Roger, Encyclopedia of Medicinal Plants (Vol. 1). Education and Health. Library Editorial Safeliz S.L.Spsin, 2002; 265: 153-154.
4. M Avello., et al. "Use of Citrus limon l. (lemon) in treating blood pressure sudden rises". International Journal of Pharmacognosy and Phytochemical Research, 2014; 6.3: 606-611.
5. D Chaturvedi and RRN Shrivastava Shine. "Basketful Benefit of Citrus Limon". International Research Journal of Pharmacy, 2016; 7.6: 1-4.
6. M Hojjati and H Barnegat. "Original Article Chemical Composition and Biological Activities of Lemon (Citrus limon) Leaf". Nutrition and Food Science Research, 2017; 4.4: 15-24.
7. D Xia., et al. "Protective effects of C-phycocyanin on alcohol induced sub-acute liver injury in mice". Journal of Applied Phycology, 2016; 28.2: 765-772.
8. Economos C, Clay WD (1999) Nutritional and health benefits of citrus fruits. Food Nutr Agric, 24: 11–18.

9. Committee NP (2010) Pharmacopoeia of People's Republic of China, vol 2. China Medicinal Science and Technology Press, Beijing, 6.
10. An Ajugwo. "Nutritional value of lime and lemon in hypercholesterolemia induced rats LIME AND LEMON IN", 2016.
11. M Hashemipour., et al. "The effect of Citrus Aurantifolia (Lemon) peels on cardio metabolic risk factors and markers of endothelial function in adolescents with excess weight: A triple masked randomized controlled trial". Medical Journal of the Islamic Republic of Iran, 2016.
12. S Patel., et al. "Say Yes To Warm for Remove Harm: Amazing Wonders of Two Stages of Water!" European Journal of Pharmaceutical and Medical Research, 2015; 2.4: 444-460.
13. Y Kato., et al. "Effect on blood pressure of daily lemon ingestion and walking". Journal of Nutrition and Metabolism, 2014.
14. Mabberley, D.J. Citrus (Rutaceae): A review of recent advances in etymology, systematics and medical applications. Blumea J. Plant Taxon. Plant Geogr, 2004; 49: 481–498. [CrossRef].