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– A REVIEW

CITRUS FRUITS: A RICH SOURCE OF PHYTOCHEMICALS AND THEIR ROLES IN HUMAN HEALTH

DONATUS EBERE OKWU

Department of Chemistry, Michael Okpara University of Agriculture Umudike, P.M.B 7276.
UMUAHIA. Abia State, NIGERIA
E-mail: okwudonatus@yahoo.com

ABSTRACT

Citrus fruits are the main fruit trees grown throughout the world and are well – appreciated for their refreshing juice and health benefits. Numerous therapeutic properties have been attributed to citrus fruits, like anticancer, antiviral, anti-tumor, anti-inflammatory activities, and effects on capillary fragility as well as an ability to inhabit platelet aggregation. More recently, therapeutic values related to cardiovascular diseases and age related macular degeneration have been reported. These numerous health benefits of citrus fruits are linked to the high amounts of photochemical and bioactive compounds such as flavonoids, carotenoids, vitamins and minerals available in citrus fruits. These phytonutrients may act as antioxidants, stimulate the immune systems; induce protective enzymes in the liver or block the damage of the genetic materials. The phytonutrients and vitamins may be responsible for the antioxidant, anticancer and anti-inflammatory properties of the citrus species. The citrus species have numerous applications in herbal medicine and as fruits in Nigeria.

In this review, the protective effects of citrus flavonoids and carotenoids against cancer, tumor growth, cardio diseases and macular degeneration along with various healing benefits and nutritional values of citrus fruits have been discussed.

Key words: Citrus, Phytochemicals, Vitamins, Antioxidants, Anti-inflammatory, Herbal medicine.

INTRODUCTION

Citrus fruits, which belong to the family of rutaceae are one of the main fruit tree crops grown throughout the world. Although sweet orange (*Citrus sinensis*) is the major fruit in this group accounting for about 70% of citrus output. The group also encompasses small citrus fruits such as tangerine tree (*Citrus reticulata*), grapefruit tree (*Citrus vitis*), lime tree (*Citrus aurantifulia)* and lemon tree (*Citrus limonum*)[1].

Citrus trees are evergreen trees that produce fruits of different forms and sizes (from round to oblong), which are full of fragrance, flavor and juice. It has a rough, robust and bright color from green to yellow skin or rind known as epicarp or flavedo, which covers the fruits and protects from damages. The glands contain the essential oils that give the fruit its typical citrus fragrance. It consists of a white, thick and spongy mesocarp or albedo which together with the epicarp forms the pericarp or peel of the fruit. The internal part constitutes the pulp which is divided into separate segments or juice sacs (with or without seeds, according to varieties) by a thick radical film or endocarp. This part is rich in soluble sugars, ascorbic acid, pectin, fibers, different organic acids and potassium salt that gives the fruit its characteristic citrine flavor[2, 3]. The exact origin of citrus fruits is not clearly identified, although most researchers place its origin to be South East Asia[3]. Later, the citrus fruits were transported to America by the Spaniards, specifically to Mexico, Florida, Brazil and California, where we currently find the largest orange orchards in the world[3].

Citrus fruits are consumed as fresh or utilized for processed citrus products and citrus-by-products. Approximately, one third of total citrus production is utilized for processing. This proportion in the case of oranges is more than 40% of globally produced oranges utilized for processing. In addition, orange utilization also apply to their juice used as flavorings in beverages[4, 5]. The most important processed citrus fruits product is orange juice. Orange juice can be presented in different forms. The major types of orange juice are the freshly squeezed orange juice and frozen concentrated orange juice[1, 6]. The juice is squeezed from fresh fruit and packaged in paper cartons, glass or plastic containers, without being pasteurized. The product is clearly labeled and located in the produce or dairy section of the grocery shop with a shelf life of only a few days.

It is also typically processed and prepared at home. Traditionally, an important proportion of orange juice consumers have preferred to freshly squeeze oranges at home. The frozen concentrated orange juice is obtained by removing through evaporation, the water from the orange juice of fresh, ripe oranges that have been graded, sorted, washed and strength ration to normal single-strength orange juice[1, 4]. If it is not concentrated, the juice is processed and pasteurized by flash heating immediately after squeezing the fruits, without removing the water content from the juice.

Another is the refrigerated orange juice that has been processed to obtain the frozen concentrate and then reconstituted by adding back the water that had been originally removed. Reconstituted single strength juice is normally reconditioned by the packager or the beverages industry and sold as a ready-to-serve product[1, 4]. In addition, citrus fruits can

be processed to obtain other food products such as dehydrated citrus products or marmalades and jams[4].

Citrus essential oils are another by-product of citrus fruits. Essential oils are volatile oils obtained from the citrus fruits peel's sacks. They are used by the food industry to give flavor to drinks and foods. They are also a component for the pharmaceutical industry for the preparation of drugs, soaps, perfumes and other cosmetics as well as for home cleaning products[1, 4].

Citrus fruits processing accounts for approximately one third of total citrus fruit production, more than 80% of it is orange processing, mostly for orange juice production. Fresh orange consumption expanded in many developing countries, such as Mexico, India, Argentina, Brazil and China[4].

Citrus fruits are well endowed with a variety of phytonutrients (Table 1). Phytonutrients are vital in both; health promotion and disease prevention[7, 8]. The dietetic and therapeutic properties of all citrus fruits are similar due to their phytonutrient contents[1].

Table 1. Phytonutrients content of citrus species on dry weight basis expressed as mg/100 g.[1]

Species	Alkaloids	Flavonoids	Tannins	Phenols	Saponins
C. reticulata	0.38 ± 0.10	0.26 ± 0.11	0.02 ± 0.10	0.03 ± 0.20	0.03 ± 0.11
C. aurantifolia	0.33 ± 0.11	0.29 ± 0.20	0.04 ± 0.11	0.02 ± 0.10	0.22 ± 0.30
C. limonum	0.54 ± 0.20	0.57 ± 0.10	0.01 ± 0.10	0.05 ± 0.11	0.42 ± 0.10
C. vitis	0.64 ± 0.11	0.26 ± 0.11	0.03 ± 0.20	0.08 ± 0.01	0.21 ± 0.11
C. sinensis	0.62 ± 0.10	0.19 ± 0.20	0.04 ± 0.11	0.01 ± 0.10	0.08 ± 0.10

Data are mean ± standard deviation of triplicate determinations

The term phytonutrients refer to plant nutrients with particular biological activities in supporting human health[9]. Phytonutrients are mainly natural bioactive compounds from plants with general benefits to human health. The secondary metabolities of plants provide

humans with numerous biologically active products, which have been used extensively as food additives, flavours, colors, insecticides, drugs, fragrances and other chemicals[9].

These plant secondary metabolites include several classes such as terpenoids, flavonoids and phenolics compounds having diverse chemical structures and biological activities and exist widely in citrus fruits.

Phytochemicals in citrus

The chemical compounds available in plants is called phytochemicals. Phytochemicals constitute one of the most numerous and widely distributed groups of substances in the plant kingdom. Plants produce chemicals known as secondary metabolites that are not directly involved in the process of growth but acts as deterrents to insects and microbial attack. Alkaloids, cyanogenic glycosides, flavonoids, terpenoids and phenolic compounds all fit in this category[7, 8, 10]. Phytochemicals that possess many ecological and physiological roles are widely distributed as plant constituents. Citrus plants synthesize and accumulate in their cells a great variety of phytochemicals including low molecular phenolic (hydroxy benzoic and hydroxycinnamic acids, acetophenones, terpenoids, flavonoids, stilbenes and condensed tannins[1, 5, 11, 12]. There are about 40 limonoids in citrus with limonin and nomilin being the principal ones[13]. These compounds, which occur in high concentration in grapefruit (*C. vitis)* and orange juice (*C. sinensis*) partly provide the bitter taste in citrus.

Limonoids possess the ability to inhibit tumor formation by stimulating the enzyme glutathione S-transferase (GST)[13]. GST is a detoxifying enzyme that catalyzes the reaction of glutathione with dangerous electrophiles to form less toxic and more importantly water-soluble compounds that can be easily excreted from the body[13, 14]. Orange and lemon oil contain substantial amounts of GST that also possesses anti-cancer activity[7, 13]. Citrus pulp and the albedo (the white of the orange) are rich in glucarates. These substances are being studied extensively for their potentials in preventing breast cancer and to lower the risk and symptoms of premenstrual syndrome[13].

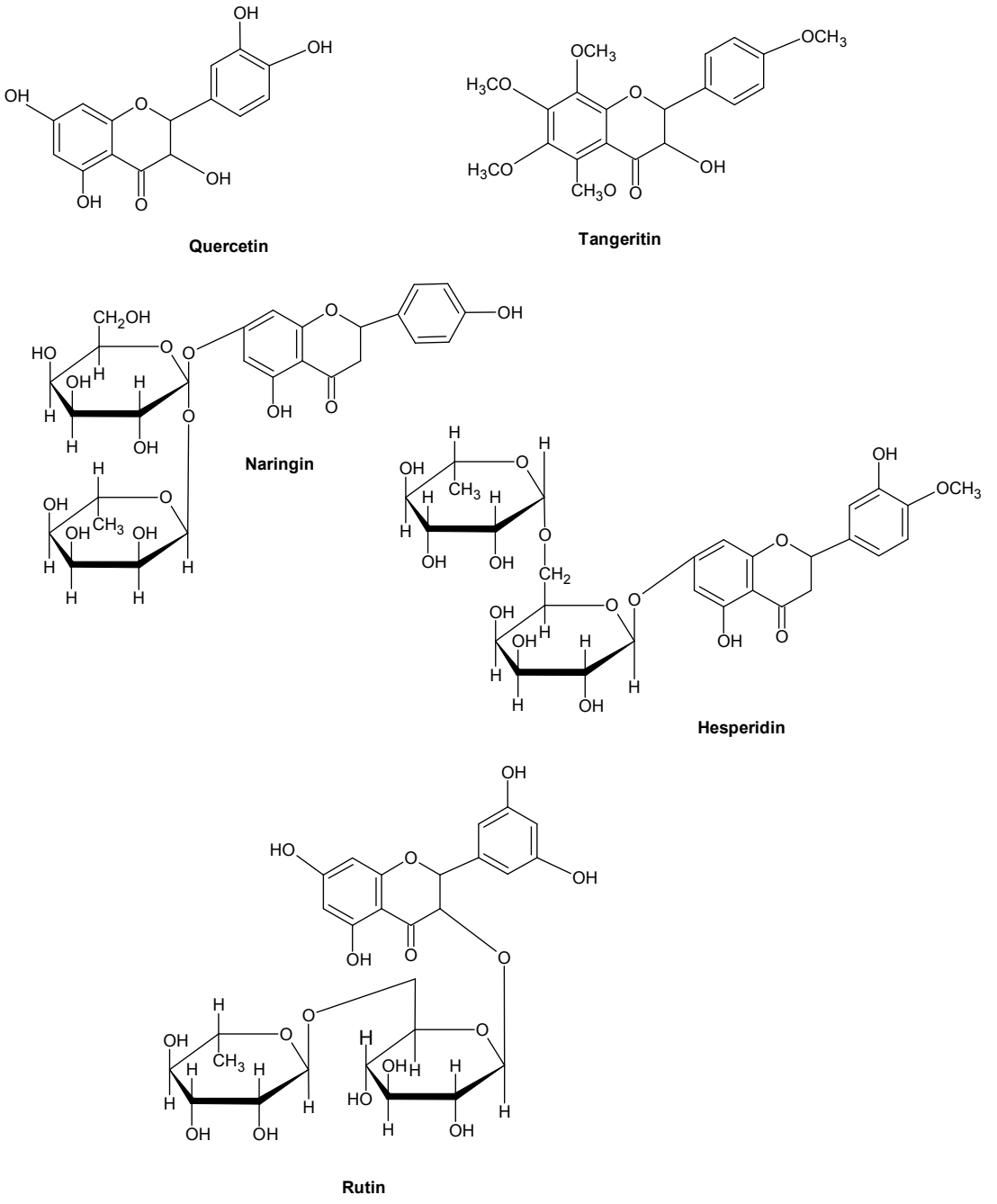

Fig. 1: Chemical structures of citrus flavonoids

Flavonoids are another phytochemicals found in citrus fruits. The flavonoids have strong inherent ability to modify the body's reaction to allergens, viruses and carcinogens. They show anti-allergic, anti-inflammatory, anti-microbial and anti-cancer activity[8]. Quercetin, myricitin, rutin, tangeritin, naringin and hesperidin (Fig.1) are found amongst the common flavonoids in citrus fruits[1]. These flavonoids are responsible for the bitter taste of some grape fruits, lemons and oranges. Quercetin is a flavonoid and more specifically a flavonol that constitutes the aglycone of the glycoside rutin. Quercetin is found to be the most active due of the flavonoids and many medicinal plants owe much of their activity due to their high quercetin content[7, 8].

Quercetin has demonstrated significant anti-inflammatory activity because of direct inhibition of several initial processes of inflammation. For example, it inhibits both; the production of histamine and other allergic/inflammatory mediators[3, 11].

In addition, it also exerts potent antioxidant activity and ascorbic acid sparing action[3,11]. Quercetin also shows remarkable anti-tumor properties. Quercetin may have positive effects in combating or helping to prevent cancer, prostatitis, heart diseases, cataracts, allergies/inflammations and respiratory diseases such as bronchitis and asthma[5]. Hesperidin is a flavonoid glycoside found abundantly in citrus fruits. Its aglycone form is called hesperetin. Hesperidin is believed to play a role in plant defence. It acts as antioxidant according to *in vitro* studies[5,11].

Hesperidin reduces cholesterol[11,12] while hesperidin has anti-inflammatory effects[11]. Hesperitin also showed an ability to penetrate the blood brain barrier in an *in vitro* model[5, 11].

Another useful citrus flavonoid glycoside is rutin and it is also known as rutoside or quercetin-3-rutinoside, In humans, rutin attaches to the Fe^{2+} ion and it is, preventing it from binding to hydrogen peroxide and creating a highly reactive free radical that may damage cells. It is also an antioxidant and therefore, it plays an important role in inhibiting some cancers. Furthermore, rutin strengthens the capillaries and therefore, it can reduce the symptoms of hemophilia. It also helps to prevent edema of the legs[3]. Rutin, as ferulic acid can reduce the cytotoxicity of oxidized low density lipoprotein (LDL) cholesterol and lower the risk of heart diseases[11]. Tangeritin is a polymethoxyleted flavone that is found in tangerine and other citrus peels. Tangeritin shows potential as an anti-cancer agent. It strengthens the cell wall and protects it from invasion[15].

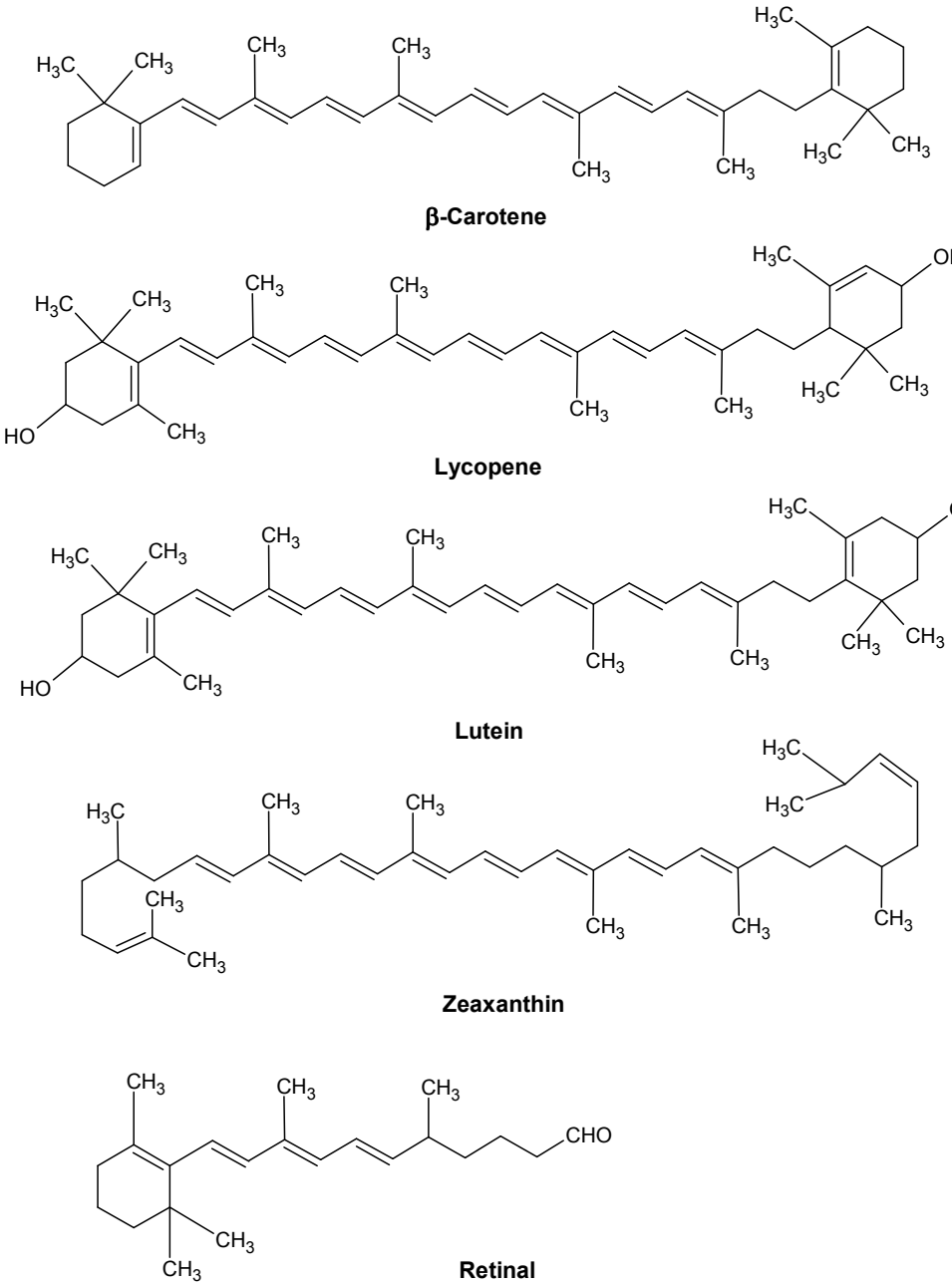

Fig. 2: Citrus carotenoids

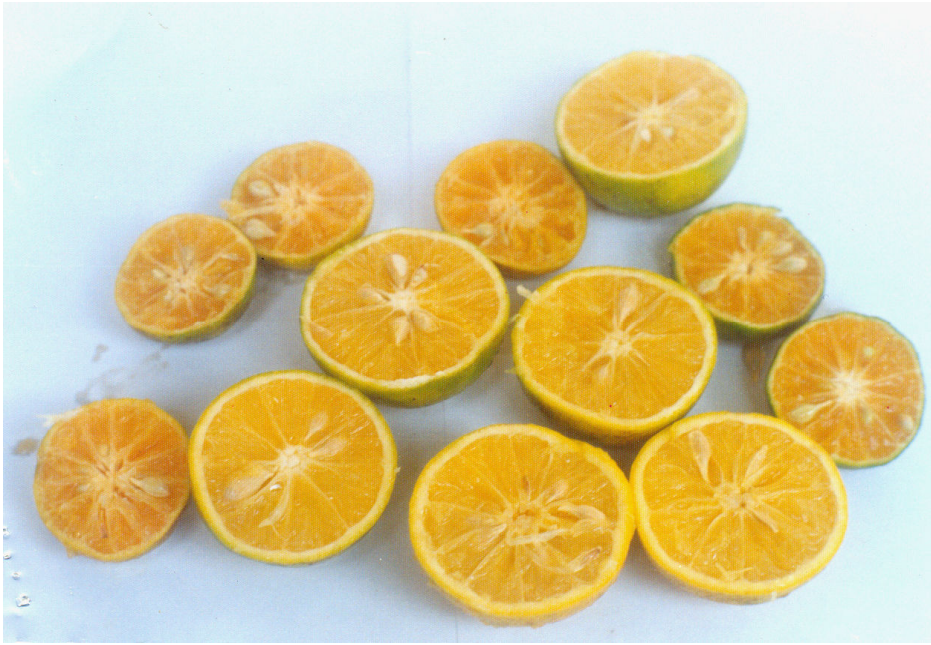

Fig. 3

Fig. 4

The citrus bioflavonoids that include hesperidine, quercetin, rutin (a glycoside of quercetin) and tangeritin, in addition to possess antioxidant activity and an ability to increase intracellular levels of ascorbic acid, rutin and hesperidin exert beneficial effects on capillary permeability and blood flow[6, 11]. They also exhibit some of the anti-allergie and anti-inflammatory benefits of quercetin[11, 12]. Hydroxyethylrutosides (HER) have been used in the treatment of capillary permeability, easy bruising, hemorrhoids and varicose veins[6, 11, 12]. Another group of phytochemicals found in citrus are carotenoids (Fig 2). Pink grapefruit have a high content of β-carotene while other citrus fruits such as tangerines and oranges contain high levels of other carotenoids (lutein, zeaxanthin, cryptoxanthin)[16] that have significant anti-oxidant activity. These carotenoids are associated with a lower incidence of age-related macular degeneration, the leading cause of blindness in human after the age sixty five[17].

Pink grapefruit also contains a high level of lycopene, the red pigment that has a significant anti-tumor activity. Carotenoids are the pigments responsible for the colors of many plants. They serve as light harvesting complexes in photosynthesis. Carotenoids are referred to be the orange-red colors found in fruits such as oranges, tomatoes and carrots as well as the yellow colors of many flowers[18, 19]. They are also added as colorants to many manufactured food drinks, fruit juice and animal feeds either in the form of natural extracts or as pure compounds manufactured by chemical synthesis[18, 19]. The production of carotenoids by bio-technology is of increasing interest. Carotenoids are essential to plants for photosynthesis, in protection against destructive photo-oxidation.

Carotenoids are important in human health. Carotene plays an essential role as sources of vitamin A. The most active role is protection against serious disorders such as cancer, heart diseases and degenerative eye diseases. It is an antioxidant and acts as regulators of the immune system[18]. Carotenoids are a class of hydrocarbon (carotene) and their oxygenated derivatives (xanthophyls) .They consist of eight isoprenoid units joined in such a manner that the arrangement of isoprenoid units is reversed at the center of the molecule so that the two central methyl groups are in 1,5-position relationship[20].

In mammals, such as humans and monkeys, the most important metabolic products of carotenoids are the retinoids, including vitamin A and retinal[21, 22]. It was demonstrated[18] that the formation of vitamin A from β-carotene could occur either by central or by eccentric cleavage of β carotene. α-carotene, β-carotene and β-cryptoxanthin can be converted to retinal or vitamin A in the intestine and liver by the enzyme 15-15[1] β-carotenoid dioxygenase[18]. Such *in vivo* formation of retinal appears to be homeastatically

controlled, such that conversion to retinol is limited in persons having adequate vitamin A[20]. Age-related muscular degeneration (ARMD) associated with ageing can lead to a total blindness in healthy people. However, there is a significant reverse relationship between the incidence of ARMD and the ingestion of citrus fruits rich in provitamin A. Citrus carotenoid was demonstrated to have significant reductions in the risk of developing neo-vascular ARMD as a function of plasma levels of α- carotene, β-carotene, cryptoxanthin, lutein and zeaxanthin[19, 23]. Based on epidemiological data, it can be assumed that diets rich in carotenoid containing fruits are associated with significant decreased risks for a variety of degenerative diseases. Several epidemiological studies have supported the observation that a high content of blood carotenoids decrease the risk of cataract formation[19, 23].

The ability of carotenoids, to act as antioxidant has been reported[24]. Antioxidants are secondary phyto-constituents or plant metabolites that inhibits or prevents oxidation of susceptible substrate. *In vitro* studies have demonstrated that lycopene has the highest antioxidant activity of all the carotenoids[25, 26]. It has the ability to quench singlet oxygen (more than that of β-carotene) to trap peroxyl radicals, to inhibit the oxidation of DNA and inhibition of lipids per oxidation[27] and in some studies to inhibit the oxidation of low-density lipoprotein (LDL)[28, 29]. Carotenoids are known to suppress these growths of tumors in *in vitro* (test tube) and *in vivo* (animal) studies[29]. The various carotenoids such as hycopene, β-carotene, α-carotene, lytein and canthaxanthin can decrease malignant transformation of cells[29]. There have been positive reports on dietary carotenoids improving fertility or reproduction capacity in a number of animals[30].

The vitamin constituents of citrus fruits using juice have been determined (Table 5). The fruit juice contained ascorbic acid, niacin, riboflavin and thiamin in varying quantities. Citrus is the main source from which primates device vitamin C[1]. Ascorbic acid in the body aids in iron absorption from the intestines. It is required for connective metabolism especially the scar tissue, bones and teeth[8, 20]. It is necessary as an anti-stress and protector against cold, chills and damp[1]. It prevents muscle fatigue and scurvy that is characterized by skin hemorrhages, bleeding gums, fragile bones, anemia and pains in joints and defects in skeletal calcification[1]. The function of ascorbic acid also accounts for its requirement for normal wound healing[7, 31]. It acts also as antioxidants in the skin by scavenging and quenching free radical generated by ultra violet radiation stabilization. The production of collagens is also dependent on vitamin C. It helps in the promotion and restoration of skin and improvement of fine wrinkles[2].

Antioxidant activity of citrus flavonoids

Antioxidants are secondary metabolites found naturally in plants such as citrus fruits. An antioxidant can be defined as anything that inhibits or prevents oxidation of a substrate[32]. Aerobic cells undergo metabolism producing free radicals. The oxygen consumption inherent in cell growth leads to the generation of a series of free radicals causing oxidative stress. The interaction of these species with molecules of a lipid nature produces new radicals: hydroperoxides and different peroxides[11]. This group of radicals comprising hydroxyl, superoxide and lipids peroxides may interact with biological systems in a clearly cytotoxic manner. These species interact with such life essential molecules as nucleic acids and proteins, producing oxidative reactions involving alterations and protein exchange[11, 33]. Citrus phenolic compounds particularly flavonoids have been reported to posses an important antioxidant activity toward radicals. The citrus flavonoids have the ability to capture electrons, block and/or scavenge the radicals. The citrus flavonoids form a tautomeric dislocation, which prevents the propagating chain reactions of these oxygen free radicals[11, 34]. The different radicals responsible for the cell oxidation process are the following: singlet oxygen ($^1O_2$); superoxide anion (O_2), hydroxyl radical ($OH^\bullet$) and peroxyl radical R-O-$O^\bullet$[11, 33, 34].

The hydroxyl radical is the most cytotoxic of all these radicals. Also, polyunsaturated fatty acids present in cell membranes are easily oxidized by both; enzymatic and oxidative preoxidation through free radical chain reaction[11, 34]. Initiation of lipid per oxidation can be induced by free radicals (superoxide, hydroxyl and singlet oxygen) produced in biological systems[11, 34]. These electrically inert species have the ability to interact and alter genetic constitution. They exhibit catatonic, mutagenic and carcinogenic actions. It has been reported that lipid peroxidation can be inhibited by flavonoids acting as strong radical scavengers and singlet oxygen quenchers[11, 34]. It has also been proposed that citrus flavonoids react with peroxyl radicals; thus, bringing about the termination of the radicals reaction[11].

Citrus flavonoids

Flavonoids are known for their ability to enhance the effects of ascorbic acid. Flavonoids protect the vascular system by strengthening, maintaining and repairing capillaries[34,35]. Plant flavonoids comprise anthocyanins, proanthocyanins, flavones, flavonols, flavonones, biflavinonoids, flavin-3-4-diol, isoflavones and catechins (Table 2). Flavonoids found in citrus species include quercetin, naringin, tangeritin. hesperidin and rutin (Fig.1). The biological function of flavonoids include action against allergies,

inflammation, microbes, ulcers, hepatotoxin, viruses and tumors[7, 8, 34, 38]. Flavonoids are plant water-soluble super antioxidants, which prevent oxidative cell damage and have strong anti-cancer activity and inhibit all stages carcinogensis[7, 8, 34, 38]. Flavonoids in the intestinal tract are known to lower the risk of heart disease[7, 34].

Table 2: Principal flavonoids isolated in citrus with structures and substitution pattern[11]

Flavonoid	*Citrus spp.*	C-ring structure	Substitution pattern
Naringin	*C. paradise* *C. aurantium*	FLA FLA	5, 4'-OH
Neoriocitrin	*C. aurantium*	FLA	5, 3'4'-OH 7-O-NeO
Hesperidin	*C. sinensis*	FLO	5, 3'-OH 4-OMe 7-O-Rut[b]
Rutin	*C. limonia*	FOL	5, 7 3', 4'-OH
Naringenin	*C. paradisi*	FLA	5, 3' 4'-OH
Eriodictyol	*C. aurantium*	FLA	5, 7 3', 4'-OH
Hesperin	*C. sinensis*	FLA	5, 7 3'-OH 4-OMe
Apigenin	C. paradisi	FLO	5, 7, 4'-OH
Luteolin	*C. Limonia* *C. aurantium*	FLO	5, 7 3', 4'-OH
Diosmetin	*C. sinensis*	FLO	5, 7 3'-OH 4-Ome
Kaempferol	*C. paradisi*	FOL	5, 7 3', 4'-OH
Quercetin	*C. Limonia*	FOL	5, 7, 3, 3', 4'-OH
Tangeretin	*C. aurantium* *C. paradisi* *C. Limonia*	FLO	5, 6, 7, 8, 4'-OMe

[a]FLA, Flavanone; FLO, Flavone; FOL, Flavonol
[b]NeO; Neoherperidoside; Rut; rutinoside

Most citrus species accumulate large quantities of flavonoids during the development of their different organs[37, 38]. All the flavonoids obtained in citrus sp. can be classified as flavonones, flvones and flavonols (Table 2). Among these groups, flavones and flavonols are found in low concentrations in citrus tissues. These flavonoids (flavones and flavonols) have been shown to have powerful antioxidant and free radical scavenging properties. Flavonoids have been reported to act as quenchers of singlet oxygen[11, 34, 39]. Research has also shown that citrus flavonoids are not only super oxide scavengers[11, 34] but also possessed hydroxyl radical scavenging activity. Flavonoids are excellent hydroxyl scavengers and according to the studies, these flavonoids possess a degree of effectiveness which depends on their structure. Methoxylated flavonoids are much more active than hydroxylated compounds[1, 11, 34]. Oxidative damage has been suggested to be contributory factor in development and complication of thrombosis Recently, the beneficial effects of antioxidants from citrus fruits against thrombosis have gained interest[1, 3, 6].

Nutritional profile of citrus fruits

Results on the proximate (Table 3) and mineral profile (Table 4) of the citrus clearly indicated that citrus fruits are sources of quality food (Okwu and Emenike 2007).

Table 3. Proximate composition (%) and food energy (g Cal^{-1})values of citrus species [6]

Species	Moisture	CP	CF	Ash	Lipid	CHO	FE
C. reticulata	5.70 ± 0.10	11.81 ± 0.01	5.84 ± 0.10	4.40 ±0.20	0.84 ± 0.10	77.10 ± 0.10	363.20
C. aurantifolia	5.84 ± 0.20	10.94 ±0.20	6.24 ± 0.20	7.80± 0.10	0.64 ± 0.10	74.38 ± 0.10	347.04
C. limonum	6.14 ±0.11	14.44 ± 0.20	6.78 ± 0.11	5.80 ± 0.20	0.68 ± 0.11	72.30 ± 0.20	353.08
C. vitis	6.24 ± 0.10	13.13± 0.10	7.10 ± 0.20	5.10 ± 0.11	1.24 ± 0.10	73.42 ± 0.10	357.36
C. sinensis	4.28 ± 1.10	17.06 ± 0.10	5.88 ± 0.11	5.10 ± 0.20	1.10 ± 0.10	70.86 ± 0.11	361.58

Data are means of triplicate determinations ± standard deviation.
CP = Crude fiber, CP = Crude protein, CHO = Carbohydrates, FE = Food energy

They are not only sufficiently rich in calories but also contain adequate quantities of other essential nutrients such as proteins, vitamins (Table 5) and minerals[1, 6]. Citrus

fruits generally have low fat contents thus, presenting it as an ideal fruit for people suffering from cancer of the colon, coronary diseases or thrombosis[6]. More important is this that citrus fruits are usually recommended as part of weight reducing diets[2]. The fat content is low and mainly devoid of saturated fatty acids. Citrus fruits are good examples of healthy foods since they contain little fat[6, 40]. They provide dietary fiber, softer stools and enhance frequent waste elimination including bile acids, sterols and fat[40]. Citrus fiber acts as an authentic broom in the intestine; absorbing toxins and carrying out harmful substances such as bleary acids, the precursors of cholesterol[2, 6].

Table 4. Mineral composition (g 100^{-1}) citrus species[6]

Species	P	K	Mg	Na	Ca
C. reticulata	0.25 ± 0.10	0.47 ± 0.20	0.49 ± 0.11	0.33 ± 0.20	2.41 ± 0.22
C. aurantifolia	0.29 ± 0.11	1.00 ± 0.10	0.36 ± 0.11	0.36 ± 0.11	2.81 ± 0.10
C. limonum	0.38 ± 0.20	0.37 ± 0.11	0.33 ± 0.02	0.33 ± 0.02	2.00 ± 0.10
C. vitis	0.24 ± 0.10	0.28 ± 0.02	0.28 ± 0.11	0.28 ± 0.11	3.20 ± 0.11
C. sinensis	0.41 ± 0.22	0.82 ± 0.10	0.33 ± 0.30	0.33 ± 0.30	2.00 ± 0.10

Data are means ± standard deviation of triplicate determinations

Table 5: Vitamin composition of citrus juice expressed as mg/100 g

Species	Ascorbic acid Vitamin C	Thiamine Vitamin B_1	Riboflavin Vitamin B_1	Niacin Nicotinic acid
C. reticulata	31.66 ± 0.20	0.12 ± 0.10	0.01 ± 0.11	0.43 ± 0.10
C. aurantifolia	22.88 ± 0.10	0.11 ± 0.20	0.04 ± 0.22	0.03 ± 0.22
C. limonum	61.60 ± 0.11	0.88 ± 0.22	0.02 ± 0.10	0.14 ± 0.33
C. vitis	36.08 ± 0.20	0.09 ± 0.11	0.06 ± 0.11	0.36 ± 0.20
C. sinensis	19.36 ± 0.10	0.06 ± 0.10	0.11 ± 0.20	0.38 ± 0.10

Data are means ± standard deviation of triplicate determinations

Citrus fibers when taken swells with water; this however increases in volume many times. Consequently this gives consistency to the feces and facilitates its transit through the colon until it is expelled through the rectum, when the diet contains little fiber; the faces

are hard, dry and concentrated. This eventually causes the intestine to make effort to eliminate them. This causes or worsens several problems such as intestinal diverticulum, hemorrhoids and even cancer of the colon[2, 3, 6]. Even though citrus fiber does not provide energy, nor it passes to the blood directly; it is an indispensable component of a healthy and balanced diet[6]. This is because it is devoid of intestinal constipation. Fiber has a physiological effect on the gastrointestinal function of promoting the reduction of tracolonic pressure, which is beneficial in diverticular disease such as cancer of the colon and hemorrhoids[2, 6, 40].

Citrus fiber also has a biochemical effect on the absorption and reabsorption of cholesterol and bile acids, respectively. Citrus fiber aids the excretion of bile acids and prevents the reabsorption of bile acids and consequently, the absorption of dietary fat cholesterol pool and prevents the formation of plaque, whose components are cholesterol, some fats and protein[6, 40]. Citrus fruits have high calorific values. This may be done to the carbohydrate contents which supplies the energies in calories. The carbohydrate content, also acts as mild natural laxative for human being. They also add to the bulk of the diet[6]. The carbohydrate content of citrus fruits comprises mainly of dietary fiber, sucrose, glucose and fructose. With the exception of dietary fiber, all other carbohydrates (glucose, fructose and sucrose) are water soluble and sweet-tasting sugars. People with diabetes in moderation, remembering that the same amount of sugars is better tolerated, when taken in its natural form in fruits containing vitamins, organic acids and phytochemicals[3, 6].

Pharmacology/Biological Studies

Recently, plant flavonoids have attracted attention as potentially important dietary cancer chemoprotetive agents[12, 41]. Also, the possible antitumor action of certain flavonoids has generated interest[11,42,44]. There is convincing epidemiologic evidence that the consumption of citrus fruits is beneficial in health and contributes to the prevention of degenerative processes particularly lowering incidence and mortality rate of cancer and cardio and cerebrovascular diseases[12, 41]. *In vivo* studies on inhibition of experimental induction of tumors have been essentially affected on citrus flavonols[11, 12]. The intake of quercetin in experimental diets lowered the incidence of colon tumors in azoxymethanol treated rats[45]. as well as fibrosarcoma in mice induced by 20-methylcolanthene (20-MC) produced 100% tumor incidence and the onset of tumors within 7 weeks while flavonoids treated mice produce tumors in the 9th week. It was reported[11] that the tumor incidences in mice treated with quercetin and luteolin-mixed diets were 52% and 60%, respectively in inhibiting tumor growth in mice. Subcutaneous administration of 20 –MC along with the flavonoids compounds (quercetin, luteolin) was found to have a significant effect on tumor

expression.

In vitro, flavonoids display anti-proliferative effect on various human neoplasic cell lines as observed in myeloid and lymphoid leukemia cells[46], gastric cancer cells, ovarian cancer cells. Prostrate cancer cells[47] and squanmous cell carcinoma[44]. Lipophilic citrus polymethoxylated flavonoids (such as nobiletin and tangeretin) inhibited the cell growth of squamous cell carcinoma in a dose dependent manner[11]. At 8 mg/mL these two flavonoids appeared to cause the death of the cells as incubation was prolonged[44]. Citrus flavonoids have been shown to effect cells of the vessel wall, blood platelet function, leukocyte function, blood coagulation, blood rheoalogy and ultimately thrombosis[11]. Citrus flavonoids show an antiadhesive and anti aggregation action on red blood cell dumping[11]. Methoxylated flavonoids (nobiletin, tangeretin) are much more active than hydroxylated compounds[11]. It was believed that their action might be similar to that of acetylsalicylic acid, which has been shown to inhibit platelet aggregation. Citrus flavonoids are effective inhibitors of platelet adhesion, aggregation and serotonin sacretion[11]. Citrus flavonoids prevent coronary heart diseases. The possible activity of citrus flavonoids in antiinflammatory and antiallergic responses were well documented[11, 12]. Hespeidin and diosmin influence the metabolism of arachidonic acid and histamine release. Diosmin behaves as a powerful protective agent against inflammatory disorders. Diosmin reduced edema formation and inhibited the synthesis for prostaglandin E2 (78.5%). Prostaglandin F2 (45.2%) and thromboxane B2 (59.5%)[11].

Intravenons injection of diosmin reduced hyperglycemia induced by injection of alloxan in rats[48]. Due to its hesperidin content as well as diosmin and other flavonoids, citrus fruits reinforces the stability of the capillary vessels and improves venos blood flow. It is useful in cases of swollen legs, edema, varicose veins, hemorrhoids, thrombosis and emboli[1, 3]. It is also recommended for people who suffer from high blood pressure. Quercetin have antiallergic activity while hesperidin, tangeretin and nobiletin, exhibited slight to moderate antiallergic activity[11]. The leaves fruits stems and roots of *Citrus sp like C. aurantufolia Swingle, C. aurantium L. C. paradisi Macfed and C. Sinesis (l).* Osbeck are employed in the treatment of malaria and fever in herbal medicine[49]. The flavonoids quercetin-3- rhamnoside and quercertin-e- rutinoside (rutin) were isolated as the active principles. The plants act by redox perturbation in the form of imposition of substantial oxidant stress during malaria infection[49].

The leaves of the citrus spp. are rich in an aromatic essence formed by d-limonene, I-linalol and other terpenes and hydrocarbons in lesser proportions. They are sedative and antispasmodic and their use is recommended for those people who are suffering from

nervousness, insomnia, palpitations, migraine or asthma[3]. Being also sudorific, they suit people suffering from fever. They also have vermifuge effect (to expel) parasites from the intestine[3]. The rind of the fruit contains 0.5% of essential oil whose main component is d-limonene, besides coumerines and flavonoids. It has invigorating properties for the digestive system and it is recommended for those persons who are suffering from lack of appetite, heavy digestion and poor functioning of the stomach. As a result of the content of vitamins, minerals and acids, citrus sp stimulates the activity of the digestive organs and has a revitalizing effect on the whole body[1, 6]. It suits people suffering from dyspepsia (difficult digestion). In the case of upset stomach or indigestion, a popular remedy is to administer the juice. Citrus fruits are highly recommended for persons suffering from kidney stones, gout and arthritis. Citrates (citric acid salts) with citrus juice containing especially potassium citrate, prevent the formation of kidney stones and ease their dissolution. This has been provel in scientific experiments for both; with urate stones and with oxalate stones[3]. This property of citrates combined with the aforementioned alkaline action, makes citrus juice a true medicine for people with kidney ailments[3]. Due to the high content of vitamin C, citrus fruits are used in the treatment of scurvy. The anti-scurvy effect of citrus fruits is very strong because of the balance composition of organic acids and minerals. The anti microbial activities of citrus fruits have been investigated and the extracts are useful in treating viral, bacterial and fungal diseases[15, 50].

CONCLUSION

It is significant to note that soft drinks that are so called lemonade or that they are made of lime not only lack medicinal properties but are also noxious for health due to their contents of carbonic gas, artificial coloring and aromatizes and sugar or other flavors[1, 3]. The herbal vitamins are dietary supplements and may be used safely as preventive health measure for nutritional values. Herbal vitamins are manufactured from parts of specific plants such as seeds, roots, stems, barks, leaves, berries or capsules or pills[1]. The best way to take advantage of the many medicinal virtues of lemon, lime, grapes and other citrus juice is to consume them just after they have been squeezed from the fruits.

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