Journal of the Saudi Society of Agricultural Sciences (2016) xxx, xxx-xxx



Journal of the Saudi Society of Agricultural Sciences

King Saud University

www.ksu.edu.sa www.sciencedirect.com





## **REVIEW ARTICLE**

# Citrus peel as a source of functional ingredient: A review

# Shafiya Rafiq<sup>a</sup>, Rajkumari Kaul<sup>a</sup>, S.A. Sofi<sup>a</sup>, Nadia Bashir<sup>a</sup>, Fiza Nazir<sup>b</sup>, Gulzar Ahmad Nayik<sup>c,\*</sup>

<sup>a</sup> Department of Food Science and Technology, Sher-e-Kashmir University of Agricultural Sciences and Technology, Chatha, Jammu, J&K 180009, India

<sup>b</sup> Division of Post Harvest Technology, Sher-e-Kashmir University of Agricultural Sciences & Technology, Shalimar, Srinagar, J&K 190025, India

<sup>c</sup> Department of Food Engineering and Technology, Sant Longowal Institute of Engineering and Technology, Longowal 148106, Punjab, India

Received 12 June 2016; revised 27 July 2016; accepted 28 July 2016

#### **KEYWORDS**

Citrus; Citrus peel; Nutraceuticals; Bioactive components; Polyphenols; Flavonoids; Dietary fibre **Abstract** Citrus plants belonging to the family Rutaceae which include fruits such as orange, mandarin, lime, lemon, sour orange and grapefruitappear as a well known promising source of multiple beneficial nutrients for human beings. Processing of citrus by-products potentially represents a rich source of phenolic compounds and dietary fibre, owing to the large amount of peel produced. These citrus fruit residues, which are generally discarded as waste in the environment, can act as potential nutraceutical resources. Due to their low cost and easy availability such wastes are capable of offering significant low-cost nutritional dietary supplements. The utilization of these bioactive rich citrus residues can provide an efficient, inexpensive, and environment friendly platform for the production of novel nutraceuticals or for the improvement of older ones. This review systematically summarized the potential components present in citrus peel, which generally discarded as waste. © 2016 The Authors. Production and hosting by Elsevier B.V. on behalf of King Saud University. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

#### Contents

1.	Introduction	00
2.	Phenolic compounds	00

\* Corresponding author. Fax: +91 1672 280057.

E-mail addresses: shafiyarafiq3@gmail.com (S. Rafiq), gulzarsliet@gmail.com, gulzarnaik@gmail.com (G. Ahmad Nayik). Peer review under responsibility of King Saud University.



#### http://dx.doi.org/10.1016/j.jssas.2016.07.006

1658-077X © 2016 The Authors. Production and hosting by Elsevier B.V. on behalf of King Saud University. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

Please cite this article in press as: Rafiq, S. et al., Citrus peel as a source of functional ingredient: A review. Journal of the Saudi Society of Agricultural Sciences (2016), http://dx.doi.org/10.1016/j.jssas.2016.07.006

	ANTIGEL IN FRE35	
2	S. Rafiq et	al.
	Flavonoids	
	Conclusion	
	References	00

ADTICIE IN DDECC

#### 1. Introduction

Risk of chronic diseases can be reduced by frequent consumption of fruits and vegetables. A common component of food products is dietary fibre which consists of variety of nonstarch polysaccharides such as cellulose, hemi celluloses, pectin,  $\beta$ -glucans, gums and lignin (Elleuch et al., 2011) and due to their beneficial effects on food nutritional properties are consumed as foods. Consumption of dietary fibre plays a significant role in the prevention, reduction and treatment of chronic diseases such as bowel, gastrointestinal disorders, obesity, diabetes, cardiovascular disease, cancer and also promotes physiological functions such as lowering blood triglycerides and glucose control (Figuerola et al., 2005). Byproducts from fruits, vegetables and whole grains are assuring sources of dietary fibres and functional compounds (Larrauri, 1999). The recommended dietary fibre intake of 25-30 g/day can help to overcome the fibre deficit diet and has been related to several physiological and metabolic effects (Drzikova et al., 2005). Cholesterol ester accumulation which led to the risk of heart disease can be controlled by phenolic compounds present in fruits and vegetables (Meyer et al., 1997; Williams and Elliot, 1997). In addition to this, other properties such as anti-inflammatory and anticarcinogenic have also been reported (Carrol et al., 1999; Maeda-Yamamoto et al., 1999). The phenolic compounds are known to comprise of an antioxidant activity (Shahidi, 1997).

Citrus (Citrus L. from Rutaceae) is one of the most popular world fruit crops, contains active phytochemicals that can protect health. In addition to this, it provides an ample supply of vitamin C, folic acid, potassium and pectin. The contribution of citrus species in deterrence of life threatening diseases have been assessed (Proteggente et al., 2003; Gorinstein et al., 2004; Anagnostopoulou et al., 2006; Guimarães et al., 2009) and it has been reported that citrus fruits, citrus fruit extracts and citrus flavonoids exhibit a wide range of promising biological properties due to their phenolic profile and antioxidant properties (Middleton and Kandaswami, 1994; Montanari et al., 1998; Samman et al., 1996). Citrus fruits are highly consumed worldwide as fresh produce, juice and most often the peel is discarded as waste which contains a wide variety of secondary components with substantial antioxidant activity in comparison with other parts of the fruit (Manthey and Grohmann, 2001). Global production of citrus fruit has significantly increased during the past few years and has reached 82 million tons in the years 2009–2010, of which oranges – commercially the most important citrus fruit accounts for about 50 million tons (USDA, 2010) and 34% of which was used for juice production, yielding about 44% peel as by-product (Li et al., 2006). Therefore, a large amount of peel is produced every year. Citrus peel, the primary waste, is a good source of molasses, pectin and limonene and is usually dried, mixed with dried pulps and sold as cattle feed (Bocco et al., 1998). Citrus peels are subdivided into the epicarp or flavedo (coloured peripheral surface) and mesocarp or albedo (white soft middle layer) as shown in Fig. 1. A number of studies have recognized the presence of polyphenols, vitamins, minerals, dietary fibres, essential oils and carotenoids content which makes citrus a health-benefit promoting fruit. To this regard several examples about the use of citrus fruits as therapeutic remedies can be cited: oranges to cure scurvy (Magiorkinis et al., 2011) orange, lime, and lemon juices as remedies for the prevention of kidney stones formation (Pak, 2004), grapefruits as agents able to lower blood pressure and to interfere with calcium channel blockers (Sica, 2006), citrus flavonoids as effective in vivo agents able to modulate hepatic lipid metabolism (Cha et al., 2001), orange juice to prevent and modulate inflammatory processes (Assis et al., 2013), kumquat peel polyphenolics as effective antioxidant agents (Sadek et al., 2009), grapefruit juice having anti-genotoxic effects (Alvarez-Gonzales et al., 2010) and several others. Rarely occurring valuable biologically active components such as oxyprenylated natural products for example, 3,3-dimethylallyloxy-(C5), geranyloxy-(C10), and the farnesyloxy-(C15) related compounds have been recognized in the last 12 years in citrus varieties (Munakata et al., 2012; Curini et al., 2006). Citrus fruits were also seen to be a good source of many natural compounds:

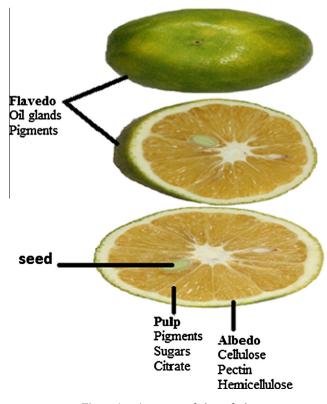


Figure 1 Anatomy of citrus fruit.

prenyloxycoumarins such as auraptene, bergamottin, imperatorin, heraclenin, oxypeucedanin and many others which have been isolated from the citrus juice and peel extracts (Epifano and Genovese, 2013; Epifano, 2014). There is a growing acceptance that phenols, amino acids, essential oils, pectin, carotenoids, flavonoids, and vitamin C present in citrus fruits exert beneficial effects in the prevention of degenerative diseases (Wang et al., 2014). Antioxidants are currently employed to retard the formation of compounds that result in decrease in sensory and nutritional quality such as butylatedhydroxyanisole, butylated hydroxytoluene (BHA, BHT) and studies have shown that these are sometimes toxic (Burlow, 1990). Clinical trials on rats have shown that these synthetic antioxidants such as BHA stimulate the development of cancerous cells (Ito et al., 1983). These findings have shifted the researchers as well as consumers preference for natural foods and food ingredients that are believed to be healthgiving and unadulterated than their synthetic analogues (Cozzi et al., 1997; Farag et al., 1986). Thus, identification and isolation of bioactive compounds from by-products of the food processing industries can result in value addition (Moure et al., 2001). This review refers to main three components of citrus peel, which have very high functional properties.

#### 2. Phenolic compounds

Major bioactive compounds known for health benefits are phytochemicals, especially phenolics in fruits and vegetables. Studies have reported that plant phenolics are not only present in edible parts of plant but their presence with multiple biological effects have also been reported in non-edible parts of the plants. The mechanisms behind the contribution of phytophenolics in health promotion and disease prevention are related to cell differentiation, pro-carcinogenes deactivation, DNA repair maintenance, suppression of N-nitrosamine formation and change of oestrogen metabolism, amongst others (Shahidi, 1997). Major mechanisms for the antioxidant effect of phenolics in functional foods include free radical scavenging and metal chelation activities. Reactive oxygen species (ROS), such as the superoxide radical  $(O_2^{-})$ , hydrogen peroxide (H<sub>2</sub>O<sub>2</sub>), hypochlorous acid (HOCl) and the hydroxyl radical (HO') have found to be supportive in pathogenesis of human beings. (Halliwell, 1996; Halliwell et al., 1992; Aruoma, 1994, 2003). Phytophenols provide effective means for preventing and treating free radical-mediated diseases such as cancer (Huang et al., 2001), diabetes (Boynes, 1991), neurodegenerative diseases (Perry et al., 2000), process of ageing (Hensley and Floyd, 2002) and cardiovascular dysfunctions by scavenging free radicals and quenching ROS (Hool, 2006). In addition, many of the antioxidants found in plants exhibit a wide range of biological effects, including antibacterial, antiviral, antiinflammatory, antiallergic, antithrombotic and vasodilatory actions (Cook and Sammon, 1996).

One of the most popular world fruit crops namely citrus (Citrus L. from *Rutaceae*) contains a host of active phytochemicals that can protect health. In addition to this, it provides an ample supply of vitamin C, folic acid, potassium and pectin. Citrus species of various origins have been evaluated for their phytochemical composition and its contribution in health promotion (Proteggente et al., 2003; Gorinstein et al., 2004; Anagnostopoulou et al., 2006; Guimarães et al., 2009) and it has been recognized that citrus species exhibit promising biological properties including antiatherogenic, antiinflammatory, antitumor activity, anticlotting and strong antioxidant activity (Middleton and Kandaswami, 1994; Montanari et al., 1998; Samman et al., 1996). During the winter months a citrus fruit variety grown in north Indian states, mainly in Punjab and Rajasthan namely Kinnow or Tangerine (Citrus reticulata) is processed into juices by the industry and fruit vendors and 30-34% of kinnow peel is obtained as a major processing by-product. This Kinnow peel is found to be a rich source of health beneficial compounds including vitamin C, carotenoids and polyphenolic antioxidants (Anwar et al., 2008). On the other hand the major causes of food deterioration especially meat products are lipid oxidation and auto-oxidation. Synthetic antioxidants have been used from years to prevent this lipid oxidation which may produce changes in meat quality parameters such as colour, flavour, odour, texture and even nutritional value (Fernandez et al., 1997). To overcome the disadvantages of using synthetic anti-oxidants in meat products, Devatkal et al. (2010) replaced them with kinnow rind powder extract successfully and the results revealed that extracts are rich sources of phenolic compounds having free radical scavenging activity and concluded that the extracts of citrus powders have potential to be used as safer alternative to synthetic ones. Another encouraging study was carried out by Benamrouchea and Madania (2013) to confirm that by-products (peels and leaves) of two orange varieties cultivated in Algeria (Citrus sinensis L. and Citrus aurantium L.) as potent antioxidants. During the last decade interesting phytochemicals such as 4'-Geranyloxyferulic (GOFA) and boropinic acid have been discovered as valuable pharmacological effects as cancer chemo preventive, antiinflammatory, neuroprotective, and anti-helicobacter pylori agents. C. sinensis and kumquat (Fortunella japonica) are the richest sources of phytochemicals such as GOFA (0.141  $\pm$  0.011 mg/g of exocarp fresh weight) and boropinic acid  $(0.206 \pm 0.002 \text{ mg/g} \text{ of exocarp fresh weight)}$  respectively (Genovese et al., 2014). Comparative literature data on total phenol content of peel (flavedo + albedo) extracts of citrus fruits measured by the Folin-Ciocalteu assay are shown in Table 1.

#### 3. Flavonoids

Flavonoids are polyphenolic compounds having a phenyl benzopyrone structure, representing as two benzene rings (C6) joined by a linear three-carbon chain (C3), with a carbonyl group at the C position. Although flavonoids are generally regarded as non-nutritive agents, their potential role in the prevention of major chronic diseases has attracted the focus of many researchers. The citrus flavonoids include a class of glycosides, namely, hesperidin and naringin and another class of O-methylatedaglycones of flavones such as nobiletin and tangeretin, which are relatively two common polymethoxylated flavones (PMFs) (Li et al., 2014). In citrus fruits, peels are reported to possess highest amounts of PMFs compared to other edible parts of the fruit (Manthey and Grohmann, 2001; Wang et al., 2014). The citrus flavonoids have been found to have a health-related property, which include anticancer, antiviral and antiinflammatory activities, reduce capillary fragility, and restricts human platelet aggregation (Huet,

### **ARTICLE IN PRESS**

Citrus fruit	Total polyphenol (μg/g FW)	Method of extraction	Expression of results	Origin	Reference
Grapefruits Sweet oranges Lemons	1550 <sup>a</sup> 1790 <sup>a</sup> 1900 <sup>a</sup>	Homogenization of 10 g of fresh peel in 125 mL 95% ethanol followed by boiling in water bath	CAE	Grown in Israel	Gorinstein et al. (2004)
White grapefruits Jaffa sweetie grapefruits	282 <sup>b</sup> 376 <sup>b</sup>	Vortexing of 50 mg of lyophilized sample in 5 mL 80% methanol for 1 min. Heating at 90 $^{\circ}$ C for 3 h with vortexing every 30 min	GAE	Grown in Israel	Gorinstein et al. (2004)
Lemons (cv. Meyer)	598 <sup>a</sup>	Extraction of 2 g of frozen citrus peel powder with 16 mL of 72% ethanol for 3 h $$	GAE	Bought in New	Li et al. (2006)
Lemons (cv. Yenben)	1190 <sup>a</sup>	Centrifugation, filtration and evaporation of Solvent under pressure. Dissolving of extract in water		Zealand	
Grapefruit a Mandarin (cv. Ellendale)	1616 <sup>a</sup> 1211 <sup>a</sup>				
Sweet orange (cv. Navel)	736 <sup>a</sup>				
Lemons Mandarins Sweet orange	1882–2828 2649–6923 4509–6470	Extraction of 100 mg of lyophilized sample with 12 mL of 80% methanol over 3 days Centrifugation, decantation and use of extract as is	GAE	Grown in Mauritius	Ramful et al. (2010)

 Table 1
 Comparative literature data on total phenol content of peel (flavedo + albedo) extracts of citrus fruits measured by the Folin-Ciocalten assay

GAE: gallic acid equivalent.

<sup>a</sup> Values were converted from original values expressed in mg/100 g FW.

<sup>b</sup> Values were converted from original values expressed in µmoL/g FW.

1982; Benavente-Garcia et al., 1997). Some glycosylated flavanones can be easily converted into the corresponding dihydrochalcones, which are potent natural sweeteners (Bor et al., 1990). The wide biochemical functions of flavonoids in orange peel have been studied extensively recently. They increased serum antioxidant capacity against lipid peroxidation (Assini et al., 2013) and reduced the elderly oxidative stress. These compounds possess the beneficial effects of anti-inflammation, antitumor (Romagnolo and Selmin, 2012; Park and Pezzuto, 2012), and antiatherosclerosis (Mulvihill and Huff, 2012). In Addition to this, these also serve as supplementary of drug chemotherapy (Meiyanto and Hermawan, 2012), diabetes health food (Aruoma et al., 2012), and neuroprotective drug (Hwang et al., 2012). Ramful et al. (2010) examined flavedo extracts of different varieties of citrus fruits grown in Mauritius for their total phenolic, flavonoid and vitamin C contents and antioxidant activities. Flavonoid derivatives, expressed in quercetin equivalents, in Mauritian citrus flavedos were generally high (> 2000  $\mu$ g/g FW for the majority of samples analysed) and the reason probably might be high sunlight conditions which could induce the accumulation of flavonoids (Li et al., 1993). Using the same assay system but with Catechinas standard, three types of flavonoids generally occur in citrus fruits: flavanones, flavones and flavonols. HPLC analyses of nine flavedo extracts showed that the flavanone glycoside hesperidin is found to be present in highest concentrations (83-234 mg/g FW) in all the extracts (Londono-Londono et al., 2010). The flavanones glycosides

poncirin, didymin, narirutin and flavone glycosidesdiosmin and isorhoifolin were present in all flavedo extracts where as the flavanone glycoside naringin was present only in Mandarin variety (Tomás-Barberán and Clifford, 2000). Several reports highlighted the structure-antioxidant activity relationship of flavonoid subclasses in citrus extracts. Data evidence suggests that glycosylation, O-methylation, O-glycosylation influence greatly the antioxidant potency of citrus flavonoids (Di-Majo et al., 2005). Antioxidant activity decreases with glycosylation and was enhanced with hydroxylation and the presence of C2-C3 double bond in conjugation with a 4-oxo function (Rice-Evans et al., 1996). Strong associations between high dietary intakes of natural compounds with a reduced risk in development of neurodegenerative diseases, such as Alzheimer's disease, Parkinson's disease, amyotrophic lateral sclerosis and multiple sclerosis have consistently been reported in numerous epidemiological studies (Glass et al., 2010). These natural compounds possessed neuroprotective ability and resulted suppression of activated microglia-mediated neuroinflammation (Lee et al., 2003; Pan et al., 2008; Zheng et al., 2008). Dried tangerine peel (Citri reticulatae) is used as traditional Chinese medicine, pericarpium called chen-pi to cure a wide array of ailments, including bronchial asthma, dyspepsia, and cardiac circulation, (China Pharmacopoeia Committee, 2010). A number of scientific studies report it as a rich source of many flavonoids, especially flavanone glycosides and polymethoxy flavones, which play a great contribution in protection against life threatening diseases such as cancer, atherogenesis, (Tripoli

Table 2	Sources of	dietary	fibre (%	dry matter).	
---------	------------	---------	----------	--------------	--

Sources of fibre	Total dietary fibre content	Analytical methods	References
Lime peel	66.7–70.4	Enzymatic chemical method: NSP + Klason lignin	
Orange peel	64.3	Enzymatic gravimetric method	Figuerola et al. (2005)
Grapefruit peel	44.2-62.6	Enzymatic gravimetric method	Figuerola et al. (2005)
Limon peel	60.1–68.3	Enzymatic gravimetric method	Figuerola et al. (2005)

et al., 2007; Benavente-Garcia and Castillo, 2008) and neurodegeneration disorders (Youdim et al., 2004; Hwang et al., 2012). Inhibiting microglial activation-mediated neuroinflammation has become a convincing target for the development of functional foods to treat neurodegenerative diseases. Tangerine peel (*Citrireticulata epericarpium*) has potent antiinflammatory capacity; however, its anti neuro-inflammatory capacity and the corresponding active compounds remain unclear. Hesperidin has been found as the most predominant flavonoid in tangerine peel, followed by tangeretin and nobiletin. It has been reported that hesperidin, nobiletin, and tangeretin individually possess mild inhibitory activity against neuroinflammation but their collective effect is found to be significant (Su-Chen and Chun-Ting, 2014).

#### 4. Dietary fibre

Dietary fibre which is often classified as soluble dietary fibre and insoluble dietary fibre consists of a mixture of plant carbohydrate polymers, both oligosaccharides and polysaccharides e.g., cellulose, hemicelluloses, pectin substances, gums, resistant starch, inulin and in association with some noncarbohydrate moiety (Fuentes-Zaragoza et al., 2010). Few sources of dietary fibre (% dry matter) are shown in Table 2. The fibre source should have SDF/IDF ratio close to 1:2 to be acceptable as a food ingredient (Jaime et al., 2002). Dietary fibre not only helps in evading hydrolysis, digestion and absorption in the human small intestine, but also achieves one of these functions: faecal bulking efficiency, enhances colonic fermentation, maintains insulin level and reduces preprandial cholesterol levels (Champ et al., 2003; Fuentes-Zaragoza et al., 2010). Health conscious people prefer natural supplements fearing that synthetic ingredients may be the source of toxicity, fibre-rich by-products, rich in dietary fibre and bioactive compounds act as a prize to food processors. Supplementation with dietary fibre can result in safer and economical foods with multiple health benefits. The average daily requirement of dietary fibre is 21-25 g per day for women and 30-38 g per day for men (Food and Nutrition Board, Institute of Medicine, 2001). Most nutritionists and diet experts suggest that 20-30% of our daily fibre intake should come from soluble fibre. In addition to health related benefits dietary fibre shows some functional properties such as water holding capacity, oil holding capacity, viscosity or gel formation, bile acid binding capacity emulsion stabilization, and enhances shelflife. Cereal, fruit and vegetable by-products produced in large amounts every day can be utilized as a value added products. They supply dietary fibre as well as bioactive compounds such as polyphenols and essential oils, providing economic benefit to the producer as well as consumer. One typical example is the residue obtained from the industrial processing of citrus peel (Braddock, 1999). Garcia et al. (2002) reported that the addition of cereal or fruit fibre, specifically 1.5% orange fibre, can be used as a fat replacer in dry fermented sausages. Citrus fibre, which possesses bioactive functions due to the presence of polyphenol-like components, can be used as effective inhibitors of lipid oxidation in meat products, thereby improving their oxidative stability and prolonging their shelf life (Fernandez-Gines et al., 2003; Sayago-Ayerdi et al., 2009). Citrus fibre could also be used for reduction of residual nitrite levels (Fernandez-Gines et al., 2003). Citrus peel could be considered to be a potential source of pectin which is composed of white, spongy and cellulosic tissue (Terpstra et al., 2002). Frequent consumption of dietary fibre is associated with low risk of life threatening chronic diseases such as bowel, gastrointestinal disorders, obesity, diabetes, cardio vascular disease, cancer and also promoting physiological functions including reduction in blood cholesterol level and glucose attenuation (Figuerola et al., 2005). The effectiveness of citrus peel in lowering the plasma liver cholesterol, serum triglyceride level, serum total cholesterol, liver total lipids, and liver cholesterol (Terpstra et al., 2002) is proven by many epidemiological studies. The peel fibre derived from orange fruit is involved in the improvement in intestinal function and health (Chau et al., 2005). Peel, pulp and peel fibre from Citrus hystrix and Citrus maxima (red and white variety), could be used as potential dietary fibre sources in the enrichment of foods because of their high physicochemical properties.

#### 5. Conclusion

Recent research concerning functional properties of citrus byproducts especially peel has added to our knowledge. Due to the low cost and easy availability of fruit residues which otherwise would be discarded as waste in the environment should be regarded as potential nutraceutic resources, capable of offering significant low-cost, nutritional dietary supplements. Rich in bioactive compounds, these unwanted cast-offs of manufacturing could be recycled as value added food supplements, that provide advantageous dietary fibre and polyphenols. They serve as non-caloric bulking agents, enhance water and oil retention, improve emulsion and could prevent us from a wide range of diseases caused due to oxidative stress. The extracts from fruit peel hold promise in food industry as sources of bioactive compounds. In addition, an established use of the citrus peel would also help alleviate pollution problems caused because of the poor disposal of such residues. More research is needed to establish bioavailability and real benefits of these peel extracts obtained from citrus peel in vivo.

#### References

Alvarez-Gonzales, I., Madrigal-Bujaidar, E., Sanchez-Garcia, V.Y., 2010. Inhibitory effect of grapefruit juice on the genotoxic damage

induced by ifosfamide in mouse. Plant Foods Hum. Nutr. 65, 369-373.

- Anagnostopoulou, M.A., Kefalas, P., Papageorgiou, V.P., Assimopoulou, A.N., Boskou, D., 2006. Radical scavenging activity of various extracts and fractions of sweet orange flavedo (*Citrus sinensis*). Food Chem. 94, 19–25.
- Anwar, F., Naseer, R., Bhanger, M.I., Ashraf, S., Talpur, F.N., Aladededune, F.A., 2008. Physicochemical characteristics of citrus seeds and oils from Pakistan. J. Am. Oil Chem. Soc. 85, 321–330.
- Aruoma, O.I., 1994. Nutrition and health aspects of free radicals and antioxidants. Food Chem. Toxicol. 32, 671–683.
- Aruoma, O.I., 2003. Methodological considerations for characterizing potential antioxidant actions of bioactive components in plant foods. Mutat. Res. 523–524, 9–20.
- Aruoma, O.I., Landes, B., Ramful-Baboolall, D., 2012. Functional benefits of citrus fruits in the management of diabetes. Prev. Medi. 54, 12–16.
- Assini, J.M., Mulvihil, E.E., Sutherland, B.G., 2013. Naringenin prevents cholesterol-induced systemic inflammation, metabolic dysregulation, and atherosclerosis in Ldlr/mice. J. Lip. Res. 54, 711–724.
- Assis, C.R.C.L., Hermsdorff, H.H.M., Bressan, J., 2013. Anti-inflammatory properties of orange juice: possible favorable molecular and metabolic effects. Plant Foods Hum. Nutr. 68, 1–10.
- Benamrouchea, S.L., Madania, K., 2013. Phenolic contents and antioxidant activity of orange varieties (*Citrus sinensis* L. and *Citrus aurantium* L.) cultivated in Algeria: peels and leaves. Ind. Crops Prod. 50, 723–730.
- Benavente-Garcia, O., Castillo, J., 2008. Update on uses and properties of citrus flavonoids: new findings in anticancer, cardiovascular, and anti-inflammatory activity. J. Agric. Food Chem. 56, 6185– 6205.
- Benavente-Garcia, O., Castillo, J., Francisco, R., Ana-Ortuno, M., Delrio, J., 1997. Uses and properties of citrus flavonoids. J. Agric. Food Chem. 45, 4505–4515.
- Bocco, A., Cuvelier, M.E., Richard, H., Berset, C., 1998. Antioxidant activity and phenolic composition of citrus peel and seed extracts. J. Agric. Food Chem. 46, 2123–2129.
- Bor, A., Borrego, F., Benavente, O., Castillo, J., DelRio, J.A., 1990. Neohesperidindihydrochalcone: properties and applications. LWT-Food Sci. Technol. 23, 371–376.
- Boynes, J.W., 1991. Role of oxidative stress in the development of complication in diabetes. Diabetes 40, 405–411.
- Braddock, R.J., 1999. Handbook of Citrus By-products and Processing Technology. John Wiley, New York.
- Burlow, S.M., 1990. Toxicological aspects of antioxidants used as food additives. In: Hudson, B.J.F. (Ed.), Food antioxidants. Elsevier, Amsterdam, pp. 253–268.
- Carrol, K.K., Kurowska, E.M., Guthrie, N., 1999. Use of citrus limonoids and flavonoids as well as tocotrienols for the treatment of cancer. International Patent WO 9916167.
- Cha, J.Y., Cho, Y.S., Kim, I., Anno, T., Rahman, S.M., Yanagita, T., 2001. Effect of hesperedin, a citrus flavonoid, on the liver triacylglycerol content and phosphatidatephosphohydrolase activity in oroticacidfed rats. Plant Foods Hum. Nutr. 56, 349–358.
- Champ, M., Langkilde, A.M., Brouns, F., Kettlitz, B., Collet, Y., Le, B., 2003. Advances in dietary fibre characterisation. Definition of dietary fibre, physiological relevance, health benefits and analytical aspects. Nutr. Res. Rev. 16, 71–82.
- Chau, C.F., Sheu, F., Huang, Y.L., Su, L.H., 2005. Improvement in intestinal function and health by the peel fibre derived from Citrus sinensis L cv Liucheng. J. Sci. Food Agric. 85, 1211–1216.
- China Pharmacopoeia Committee, 2010. Chinese Pharmacopoeia (II). Beijing, China.
- Cook, N.C., Sammon, S., 1996. Flavanoids chemistry, metabolism, cardioprotective effects, and dietary sources. Nutr. Biochem. 7, 66– 76.

- Cozzi, R., Ricordy, R., Aglitti, T., Gatta, V., Petricone, P., DeSalvia, R., 1997. Ascorbic acid and b-carotene as modulators of oxidative damage. Carcinogenesis 18, 223–228.
- Curini, M., Cravotto, G., Epifano, F., Giannone, G., 2006. Chemistry and biological activity of natural and synthetic prenyloxycoumarins. Curr. Med. Chem. 2, 199–222.
- Devatkal, S.K., Narsaiah, K., Borah, A., 2010. Anti-oxidant effect of extracts of kinnow rind, pomegranate rind and seed powders in cooked goat meat patties. Meat Sci. 85 (1), 155–159.
- Di-Majo, D., Giammanco, M., La-Guardia, M., Tripoli, E., Giammanco, S., Finotti, E., 2005. Flavanones in citrus fruit: structureantioxidant activity relationships. Food Res. Int. 38, 1161–1166.
- Drzikova, B., Dongowsky, G., Gebhardt, E., Habel, A., 2005. The composition of dietary fibre-rich extrudates from oat affects bile acid binding and fermentation in vitro. Food Chem. 90, 181–192.
- Elleuch, M., Bedigian, D., Roiseux, O., Besbes, S., Blecker, C., Attia, H., 2011. Dietary fibre and fibre rich by-products of food processing: characterisation, technological functionality and commercial applications: a review. Food Chem. 4, 411–421.
- Epifano, F., Genovese, S., 2013. Recent acquisitions on naturally occurring oxyprenylated secondary plant metabolites. In: Brahmachari, G. (Ed.), Chemistry and Pharmacology of Naturally Occurring Bioactive Compounds, first ed. CRC Press, Boca Raton, pp. 239–257.
- Epifano, F., 2014. Analysis of Biologically Active Oxyprenylated Ferulic Acid Derivatives in Citrus Fruits. Springer Science+Business Media, New York.
- Farag, R.S., Badei, A.Z., Heweij, F.M., El-Baroty, G.S.A., 1986. Antioxidant activity of some spices essential oil on linoleic acid in aqueous media. J. Am. Oil Chem. Soc. 66, 792–799.
- Fernandez, J., Perej-Alvarez, J.A., Fernandez-Lopez, J.A., 1997. Thiobarbituric acid test for monitoring lipid oxidation in meat. Food Chem. 59, 345–353.
- Fernandez-Gines, J.M., Fernandez-Lopez, J., Sayas-Barbera, E., Sendra, E., Perez Alvarez, J.A., 2003. Effect of storage conditions on quality characteristics of bologna sausages made with citrus fibre. J. Food Sci. 68, 710–715.
- Figuerola, F., Hurtado, M.L., Estevez, A.M., Chiffelle, I., Asenjo, F., 2005. Fibre concentrates from apple pomace and citrus peel as potential fibre sources for food enrichment. Food Chem. 91, 395– 401.
- Food and Nutrition Board, Institute of Medicine, 2001. Dietary reference intakes. Proposed definition of dietary fibre. A report of the panel on the definition of dietary fibre and the standing committee on the scientific evaluation of dietary reference intakes. National Academy Press, Washington, DC.
- Fuentes-Zaragoza, E., Riquelme-Navarrete, M.J., Sanchez-Zapata, E., Perez-Alvarez, J.A., 2010. Resistant starch as functional ingredient: a review. Food Res. Int. 43 (4), 931–942.
- Garcia, M.L., Dominguez, R., Galvez, M., Gavlez, D., Casas, C., Selgas, M.D., 2002. Utilisation of cereal and fruit fibres in low fat dry fermented sausage. Meat Sci. 60, 227–236.
- Genovese, S., Fiorito, S., Locatelli, M., Carlucci, G., Epifano, F., 2014. Analysis of biologically active oxyprenylated ferulic acid derivatives in Citrus fruits. Plant Foods Hum. Nutr. 69 (3), 255– 260.
- Glass, C.K., Saijo, K., Winner, B., Marchetto, M.C., Gage, F.H., 2010. Mechanisms underlying inflammation in neurodegeneration. Cell 140, 918–934.
- Gorinstein, S., Cvikrova, M., Machackova, I., Haruenkit, R., Park, Y. S., Jung, S.T., Yamamoto, K., Ayala, A.L.M., Katrich, E., Trakhtenberg, S., 2004. Characterization of antioxidant compounds in Jaffa sweeties and white grapefruits. Food Chem. 84, 503–510.
- Guimarães, R., Barros, L., Barreira, J.C.M., Sousa, M.J., Carvalho, A.M., Ferreira, I.C.F.R., 2009. Targeting excessive free radicals with peels and juices of citrus fruits: grapefruit, lemon, lime and orange. Food Chem. Toxicol. 48 (1), 99–106.

- Halliwell, B., 1996. Antioxidants in human health and disease. Ann. Rev. Nutr. 16, 33–50.
- Halliwell, B., Gutteridge, J.M.C., Cross, C.E., 1992. Free radicals, antioxidants and human disease: where are we now? J. Lab. Clin. Med. 119, 598–620.
- Hensley, K., Floyd, R.A., 2002. Reactive oxygen species and protein oxidation in aging: a look back, a look ahead. Arch. Biochem. Biophys. 397, 377–383.
- Hool, L.C., 2006. Reactive oxygen species in cardiac signaling: from mitochondria to plasma membrane ion channels. Clin. Exp. Pharmacol. Physiol. 33, 146–151.
- Huang, R.P., Golard, A., Hossain, M.Z., Huang, R., Liu, Y.G., Boynton, A.L., 2001. Hydrogen peroxide promotes transformation of rat liver non-neoplastic epithelial cells through activation of epidermal growth factor receptor. Mol. Carninog. 30, 209–217.
- Huet, R., 1982. Constituants des agrumesa' effetpharmacodynamique: 1982. les citroflavonoïdes (Constituents of citrus fruits with pharmacodynamic effect: citroflavonoids). Fruits. 37, 267–271.
- Hwang, S.L., Shih, P.H., Yen, G.C., 2012. Neuroprotective effects of citrus flavonoids. J. Agric. Food Chem. 60, 877–885.
- Ito, N., Fukushima, S., Hasegawa, A., Shibata, M., Ogiso, T., 1983. Carcinogenicity of butylated hydroxyanizole in F344 rats. J. Nat. Cancer Inst. 70, 343–344.
- Jaime, L., Molla, E., Fernandez, A., Martin-Cabrejas, M.A., Lopez Andreu, F.J., Esteban, R.M., 2002. Structural carbohydrates differences and potential source of dietary fibre of onion (*Allium cepa* L.) tissues. J. Agric. Food Chem. 50 (1), 122–128.
- Larrauri, J.A., 1999. New approaches in the preparation of high dietary fibre powders from fruit by-products. Trends Food Sci. Technol. 10, 3–8.
- Lee, H., Kim, Y.O., Kim, H., Kim, S.Y., Noh, H.S., Kang, S.S., Cho, G.J., Choi, W.S., Suk, K., 2003. Flavonoid wogonin from medicinal herb is neuroprotective by inhibiting inflammatory activation of microglia. Faseb. J. 17, 1943–1944.
- Li, S., Lo, C.Y., Ho, C.T., 2006. Hydroxylatedpolymethoxy-flavones and methylated flavonoids in sweet orange (Citrus sinensis) peel. J. Agric. Food Chem. 54, 4176–4185.
- Li, S., Wang, H., Guo, L., Zhao, H., Ho, C.T., 2014. Chemistry and bioactivity of nobiletin and its metabolites. J. Funct. Foods 6, 2–10.
- Li, Y., Ou-Lee, T.-M., Raba, R., Amundson, R.G., Last, R.L., 1993. Arabidopsis flavonoid mutants are hypersensitive to UV-B irradiation. Plant Cell. 5, 171–175.
- Londono-Londono, J., de Lima, V.R., Lara, O., Gil, A., Pasa, T.B.C., Arango, G.J., Pineda, J.R.R., 2010. Clean recovery of antioxidant flavonoids from citrus peel: optimizing an aqueous ultrasoundassisted extraction method. Food Chem. 119, 81–87.
- Maeda-Yamamoto, M., Kawahara, H., Tahara, N., Tsuji, K., Hara, Y., Isemura, M., 1999. Effect of tea polyphenols on the invasion and matrix metalloproteinases activities of human fibrosarcoma HT1080 cells. J. Agric. Food Chem. 47, 2350–2354.
- Magiorkinis, E., Beloukas, A., Diamantis, A., 2011. Scurvy: past, present and future. Eur. J. Int. Med. 22, 147–152.
- Manthey, J.A., Grohmann, K., 2001. Phenols in citrus peel byproducts. Concentrations of hydroxycinnamates and polymethoxylated flavones in citrus peel molasses. J. Agric. Food Chem. 49 (7), 3268– 3273.
- Meiyanto, E., Hermawan, A., 2012. Natural products for cancertargeted therapy: citrus flavonoids as potent chemopreventive agents. Asian Pacific J. Canc. Prevent. 13 (2), 427–436.
- Meyer, A., Yi, O., Pearson, D., Waterhouse, A.L., Frankel, E., 1997. Inhibition of human low-density lipoproteins oxidation in relation to phenolic antioxidants in grapes. J. Agric. Food Chem. 43, 1638– 1643.
- Middleton, E., Kandaswami, C., 1994. Potential health-promoting properties of Citrus flavonoids. Food Technol. 11, 115–119.
- Montanari, A., Chen, J., Widmer, W., 1998. Citrus flavonoids: a review of past biological activity against disease. In: Manthey, J.A.,

Buslig, B.S. (Eds.), Flavonoids in the Living System. Plenum Press, New York, pp. 103–113.

- Moure, A., Cruz, J.M., Franco, D., Dominguez, J.M., Sineiro, J., Nunez, M.J., Parajo, J.C., 2001. Natural antioxidants from residual sources. Food Chem. 72, 145–171.
- Mulvihill, E.E., Huff, M.W., 2012. Citrus flavonoids and the prevention of atherosclerosis. Cardiovasc. Hematol. Disord. Drug Targets 12 (2), 84–91.
- Munakata, R., Inoue, T., Koeduka, T., Sasaki, K., Tsurumaru, Y., Sugiyama, A., Uto, Y., Hori, H., Azuma, J., Yazaki, K., 2012. Characterization of coumarin-specific prenyltransferase activities in Citrus limon peel. Biosci. Biotechnol. Biochem. 76, 1389–1393.
- Pak, C.Y., 2004. Medical management of urinary stone disease. Nephron Clin. Prac. 98, 49–53.
- Pan, X.D., Chen, X.C., Zhu, Y.G., Zhang, J., Huang, T.W., Chen, L. M., Ye, Q.Y., Huang, H.P., 2008. Neuroprotective role of tripchlorolide on inflammatory neurotoxicity induced by lipopolysaccharide-activated microglia. Biochem. Pharmacol. 76, 362–372.
- Park, E., Pezzuto, J.M., 2012. Flavonoids in cancer prevention. Anti-Cancer Agents Med. Chem. 12 (8), 836–851.
- Perry, G., Raine, K.A., Nunomura, A., Watayc, T., Sayre, L.M., Smith, M.A., 2000. How important is oxidative damage? Lessons form Alzheimer's disease. Free Radic. Biol. Med. 28, 831–834.
- Proteggente, A.R., Saija, A., De Pasquale, A., Rice-Evans, C.A., 2003. The compositional characterisation and antioxidant activity of fresh juices from Sicilian sweet orange (*Citrus sinensis* L. Osbeck) varieties. Free Radic. Res. 37, 681–687.
- Ramful, D., Bahorun, T., Bourdon, E., Tarnus, E., Auroma, O.I., 2010. Bioactive phenolics and antioxidant propensity of flavedo extracts of Mauritian citrus fruits: potential prophylactic ingredients for functional foods application. Toxicology 278, 75–87.
- Rice-Evans, C.A., Miller, N.J., Paganga, G., 1996. Structure–antioxidant activity relationships of flavonoids and phenolic acids. Free Radic. Biol. Med. 20, 933–956.
- Romagnolo, D.F., Selmin, O.I., 2012. Flavonoids and cancer prevention: a review of the evidence. J. Nutr. Geront. Geriat. 31 (3), 206– 238.
- Sadek, E.S., Makris, D.P., Kefalas, P., 2009. Polyphenolic composition and antioxidant characteristics of kumquat (*Fortunella margarita*) peel fractions. Plant Foods Hum. Nutr. 64, 297–302.
- Samman, S., Wall, P.M.L., Cook, N.C., 1996. Flavonoids and coronary heart disease: dietary perspectives. In: Manthey, J.A., Buslig, B.S. (Eds.), Flavonoids in the Living System. Plenum Press, New York, pp. 469–481.
- Sayago-Ayerdi, S.G., Brenes, A., Goni, I., 2009. Effect of grape antioxidant dietary fibre on the lipid oxidation of raw and cooked chicken hamburgers. LWT Food Sci. Technol. 42, 971–976.
- Shahidi, F., 1997. Natural antioxidants an over view. In: Shahidi, F. (Ed.), Natural Antioxidants. AOCS Press, Illinois, pp. 1–11.
- Sica, D.A., 2006. Interaction of grapefruit juice and calcium channel blockers. Am. J. Hypertens. 19, 768–773.
- Su-Chen, H., Chun-Ting, K., 2014. Hesperidin, nobiletin, and tangeretin are collectively responsible for the anti-neuroinflammatory capacity of tangerine peel (*Citri reticulatae* pericarpium). Food Chem. Toxicol. 71, 176–182.
- Terpstra, A.H., Lapre, J.A., Vries, H.T., Beynen, A.C., 2002. The hypocholesterolemic effect of lemon peels, lemon pectin, and the waste stream material of lemon peels in hybrid F1B hamsters. Eur. J. Nutr. 41 (1), 19–26.
- Tomás-Barberán, F.A., Clifford, M.N., 2000. Flavanones, chalcones and dihydrochalcones– nature, occurrence and dietary burden. J. Sci. Food Agric. 80, 1073–1080.
- Tripoli, E., Guardia, M.L., Giammanco, S., Majo, D.D., Giammanco, M., 2007. Citrus flavonoids: molecular structure, biological activity and nutritional properties: a review. Food Chem. 104 (2), 466–479.

#### 8

# **ARTICLE IN PRESS**

- USDA: United States Department of Agriculture/Foreign Agricultural Service, 2010. Citrus: World Markets and Trade Available from: http://www.fas.usda.gov. Accessed 28.09.2010.
- Wang, L., Wang, J., Fang, L., Zheng, Z., Dexian, Z., Wang, S., Li, S., Ho, C.T., Zhao, H., 2014. Anticancer activities of citrus peel polymethoxyflavones related to angiogenesis and others. Biomed. Res. Int. http://dx.doi.org/10.1155/2014/453972.
- Williams, R.L., Elliot, M.S., 1997. Antioxidants in grapes and wines: chemistry and health effects. In: Shahidi, F. (Ed.), Natural

Antioxidants: Chemistry, Health Effects and Applications. AOCS Press, IL, pp. 150–173.

- Youdim, K.A., Shukitt-Hale, B., Joseph, J.A., 2004. Flavonoids and the brain: interactions at the blood-brain barrier and their physiological effects on the central nervous system. Free Radic. Biol. Med. 37, 1683–1693.
- Zheng, L.T., Ryu, G.M., Kwon, M., Lee, W.H., Suk, K., 2008. Antiinflammatory effects of cathecols in lipopolysaccharide-stimulated microglia cells: inhibition of microglia neurotoxicity. Eur. J. Pharmacol. 588, 106–113.