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REVIEW PAPER

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BY-PRODUCTS OF FRUITS PROCESSING AS A SOURCE OF PHYTOCHEMICALS*

The processing of fruits results in high amounts of waste materials such as peels, seeds, stones, and oilseed meals. A disposal of these materials usually represents a problem that is further aggravated by legal restrictions. Thus new aspects concerning the use of these wastes as by-products for further exploitation on the production of food additives or supplements with high nutritional value have gained increasing interest because these are high-value products and their recovery may be economically attractive. It is well known that by-products represent an important source of sugars, minerals, organic acid, dietary fibre and phenolics which have a wide range of action which includes antitumoral, antiviral, antibacterial, cardioprotective and antimutagenic activities. This review discusses the potential of the most important by-products of apple, grape and citrus fruits processing as a source of valuable compounds. The relevance of this topic is illustrated by a number of references.

Key words: by-products of fruits processing; apple; grape; citrus fruits; phytochemicals phenolics.

Nowadays, there is a growing interest in finding phytochemicals as an alternative to synthetic substances, which are commonly used in the food, pharmaceutical and cosmetic industry. This idea is supported by the consumer's concern about the safety of products containing synthetic chemicals because these synthetic molecules are suspected to cause or promote negative health effects. Recent studies showed that the phytochemicals in fruits and vegetables are the major bioactive compounds with human health benefits. Epidemiological studies have pointed out that the consumption of fruits and vegetables imparts health benefits, *e.g*. reduced risk of coronary heart disease and stroke, as well as certain types of cancer. Apart from dietary fibre, these health benefits are mainly attributed to organic micronutrients such as carotenoids, polyphenolics, tocopherols, vitamin C and others.

Food has now assumed the status of "functional food", which should be capable of providing the additional physiological benefit, such as preventing or delaying onset of chronic diseases, as well as meeting basic nutritional requirements. Any food or ingredient that has a positive impact on an individual's health, physical performance is a state of mind in addition to its nutritive value. Manufacturers who care and are willing to meet the requirements of the consumers for safe and functional food are introducing natural antioxidants during the production and/or processing. It has been evident that the consumption of food rich in natural antioxidants, as well as food enriched with them, ensure the desirable antioxidant status and helps in prevention of the development of diseases caused (linked) by oxidative stress. The scheme represents the health benefit of food enriched with natural antioxidants (Figure 1).

Epidemiological studies have related the dietary consumption of horticultural products, mainly fruits and vegetables, with a decrease in the incidence of cancer and cardiovascular disease mortality. Clinical studies support the role of the plant food phytochemicals as health-promoting functional food components. Table 1 represents some functional food components. The role of antioxidant phytochemicals in the prevention of these diseases has been mainly attributed to the prevention of LDL oxidation through a scavenging activity against peroxyl and hydroxyl radicals.

The processing of fruits, vegetables, and oilseeds result in high amounts of waste materials such as peels, seeds, stones, and oilseed meals. Figure 2

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Figure 1. The health benefit of food enriched with natural antioxidants.

Table 1. Examples of functional food components

Class/components	Source	Potential benefit
	Carotenoids	
Beta-carotene	Various fruits	Neutralizes free radicals which may damage cells; bolsters cellular antioxidant defences
Lutein, Zeaxanthin	Citrus	May contribute to the maintenance of healthy vision
	Flavonoids	
Anthocyanidins	Berries, cherries, red grapes	Bolster cellular antioxidant defences; may contribute to the maintenance of brain function
Flavanols - catechins, epicatechins, procyanidins	Apples, grapes	May contribute to the maintenance of heart health
Flavanones	Citrus foods	Neutralize free radicals which may damage cells; bolster cellular antioxidant defences
Flavonols	Apples	Neutralize free radicals which may damage cells; bolster cellular antioxidant defences
Proanthocyanidins	Cranberries, apples, strawberries, grapes, wine, peanuts, cinnamon	May contribute to the maintenance of urinary tract health and heart health

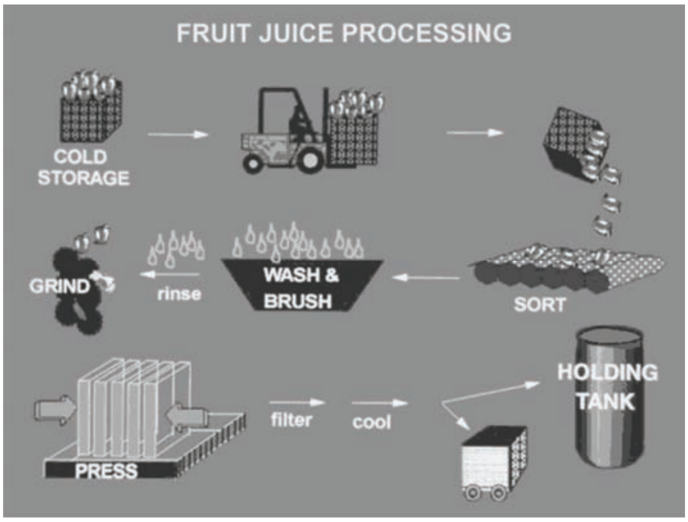

Figure 2. Scheme of fruit juice processing.

shows a scheme of fruit juice processing during which fruit pomace remained.

The fruit processing results in various amounts of fruit pomace depending on the raw material. Some date of fruit pomace yields, expressed as percent of the processed raw material weight are presented in Table 2, together with the accordingly estimated annual worldwide produced wastes [1].

Table 2. Annual worldwide processed quantities and resulting wastes of selected fruits

Fruit	Annual processed (million Mt)	By-products/processed fruit (%, wet basis)	Estimated annual waste (million Mt)
Orange and other citrus fruits	31.2	50	15.6
Apple	12.0	25-35	3.0-4.2
Pear	1.7	NA[a]	-
Peach (canned)	1.0	NA	-
Grape	50.0	15-20	5.0-9.0
Cooking banana	30.0	30	9.0
Kiwifruit	1.0	30	< 0.3

[a]No available

A disposal of these materials usually represents a problem that is further aggravated by legal restrictions. Plant waste is prone to microbial spoilage; therefore, drying is necessary before further exploitation. The cost of drying, storage, and transport possess additional economical limitations to waste utilization. Therefore, agroindustrial waste is often utilized as feed or fertilizer. Thus new aspects concerning the use of these wastes as by-products for further exploitation on the production of food additives or supplements with high nutritional value have gained increasing interest because these are high-value products and their recovery may be economically attractive. Oreopoulou and Tzia [1] present a general flow diagram for the recovery of various dietary components from fruit pomace (Figure 3). Depending on the fruit some of the indicated steps may be omitted.

It is well known that by-products represent an important source of sugars, minerals, organic acids, dietary fibre, and bioacitive compounds such as phe-

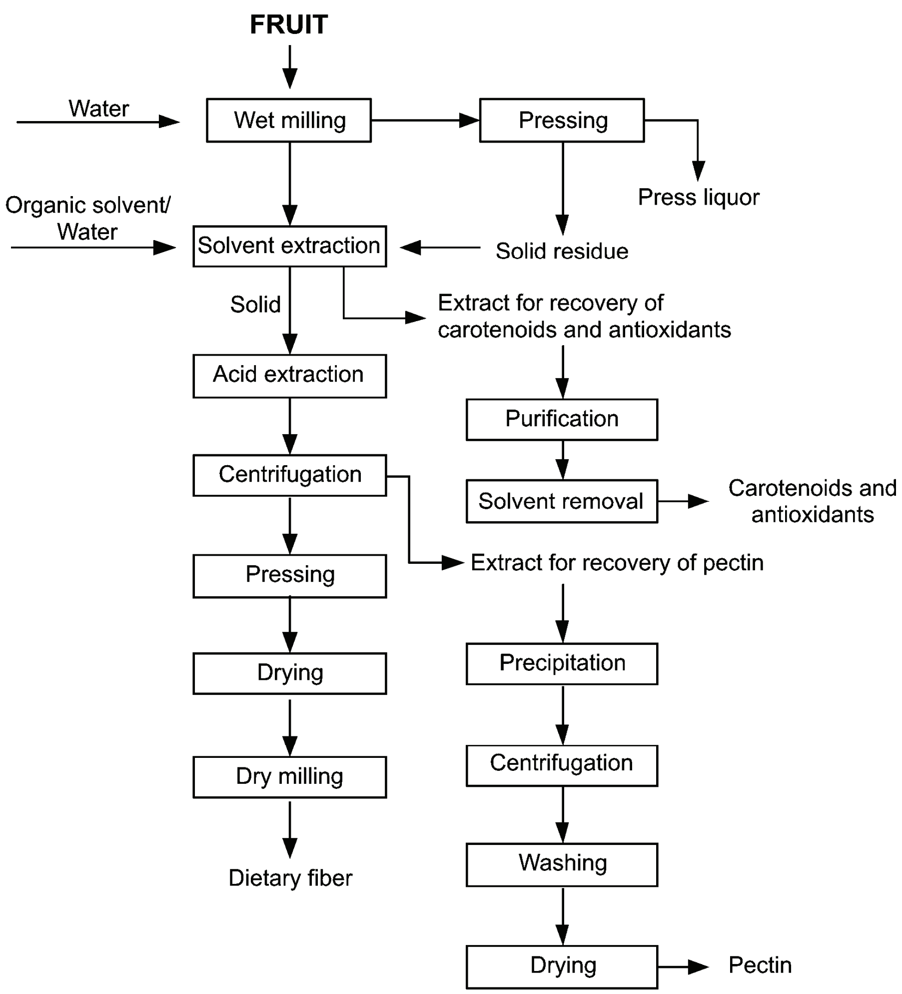

Figure 3. Flow diagram for the utilization of fruit pomace.

nolic compounds. Phenolics are a much diversified group of secondary plant metabolites, which includes simple phenolic, phenolic acids (benzoic and cinnamic acid derivatives), lignans, lignins, coumarins, flavonoids, stilbenes, flavonolignans and tannins [2]. Many of phenolic compounds have shown strong antioxidant properties as oxygen scavengers, peroxide decomposers, metal chelating agents, and free radical inhibitors [3, 4]. Besides antioxidant activity, phenolic compounds have a wide range of action which includes antitumoral, antiviral, antibacterial, cardioprotective, and antimutagenic activities.

Thus, new aspects concerning the use of these wastes as by-products for further exploitation on the production of food additives or supplements with high nutritional value have gained the increasing interest because these are high-value products and their recovery may be economically attractive. Far from claiming completeness, this review discusses the potential of the most important by-products of apple, grape and citrus fruits processing as a source of valuable compounds.

FUNCTIONAL COMPOUNDS FROM BY-PRODUCTS OF FRUIT PROCESSING

Apple

Apples are well-known and widespread fruit of the genus Malus (about 25 species) belonging to the family Rosaceae. The world apple production is estimated to nearly 27 million metric tons annually and around 9 million tons are produced in EU [5]. Apple pomace is the by-product of processing for the recovery of apple juice and amounts to up to 25-35% of the processed fruit [6]. Apple pomace is a rich source of polyphenols, minerals and dietary fibre [7,8]. Although it is conventionally used as an animal feed, the production of pectin is considered to be the most reasonable utilization approach from both economical and ecological points of view. Pectin consists of 10-15% of apple pomace, on a dry weight basis [1] and is recovered by acid extraction and precipitation. Pectin currently produced from apple pomace has more superior gelling properties than citrus pectin but presents a brown hue that may limit its incorporation into light-colour foods. The colour of apple pomace and extracted pectin is formed by the oxidation of phenolic constituents that are co-extracted with pectin and partially precipitated. Apple pomace has been shown to be a good source of polyphenols which are predominantly localized in the peels and are extracted into the juice to a minor extent. Major compounds isolated and identified include catechins, hydroxycinnamates, phloretin glycosides, quercetin glycosides, and procyanidins (Figure 4) [9-12].

A conventional apple juice production (straight pressing of apple pulp or pressing after pulp enzyming) resulted in a juice poor in phenolics and with only 3-10% of the antioxidant activity of the fruit they were produced from [13]. In view of the fact that most of the polyphenolics remained in the apple pomace, commercial exploitation of this by-product for the recovery of these compounds seems promising. Polyphenols are one of the phytochemical groups whose "protective" properties include antioxidant, antimicrobial, anticancer and cardiovascular-protective activities [14--16]. Different *in vitro* model systems were employed to evaluate the antioxidant properties of apple pomace polyphenols. For example, Lu and Foo [17] determined DPPH and superoxide ion radical scavenging activities of apple pomace polyphenols, and also their antioxidant property in the β-carotene/linoleic acid system. The polyphenols examined were epicatechin, its dimer (procyanidin B2), trimer, tetramer and oligomer, quercetin glycosides, chlorogenic acid, phloridzin and 3--hydroxy-phloridzin. All the compounds showed strong antioxidant activities, and their DPPH-scavenging activities were 2-3 times and superoxide anion radical--scavenging activities were 10-30 times better than those of the antioxidant vitamins C and E. The antiradical activity of apple pomace was tested by measuring their ability to scavenge DPPH and hydroxyl radicals by ESR spectroscopy. The highest DPPH (EC_{50}^{DPPH} = 6.33 mg/ml) and hydroxyl (EC_{50}^{OH} = 26.11 mg/ml) radical scavenging activities were obtained in the case of Reinders pomace (Table 3). The total phenolics, total flavonoids, total flavan-3-ols, and some individual phenolic compounds contributed significantly to the antiradical activities of apple pomace [12,18-21].

Furthermore, tumour-cell proliferation has strongly inhibited *in vitro* by apple extracts, and these effects have been attributed to phenolic acids and flavonoids [22]. The phenolic components of apples have been linked with the inhibition of colon cancer *in vitro* [22,23]. Eberhardt *et al.* [22] reported that apple extracts (both with and without skin) inhibited the proliferation of CaCo-2 cells in a dose-dependent manner, the inhibitory effect was greater in extracts containing apple skins. Veeriah *et al.* [23] found that a flavonoid mixture from apples inhibited the proliferation of HT-29 (colon adenocarcinoma) cells. The antiproliferative activities of different apples (Pinova, Reinders, Jonagold, Iduna, Braeburn and Granny Smith) pomace, as well as apple pomace from a fruit juice industry (D.O.O. "Nectar", Bačka Palanka, Serbia), were assessed by measurement of the growth inhibition of three histologically

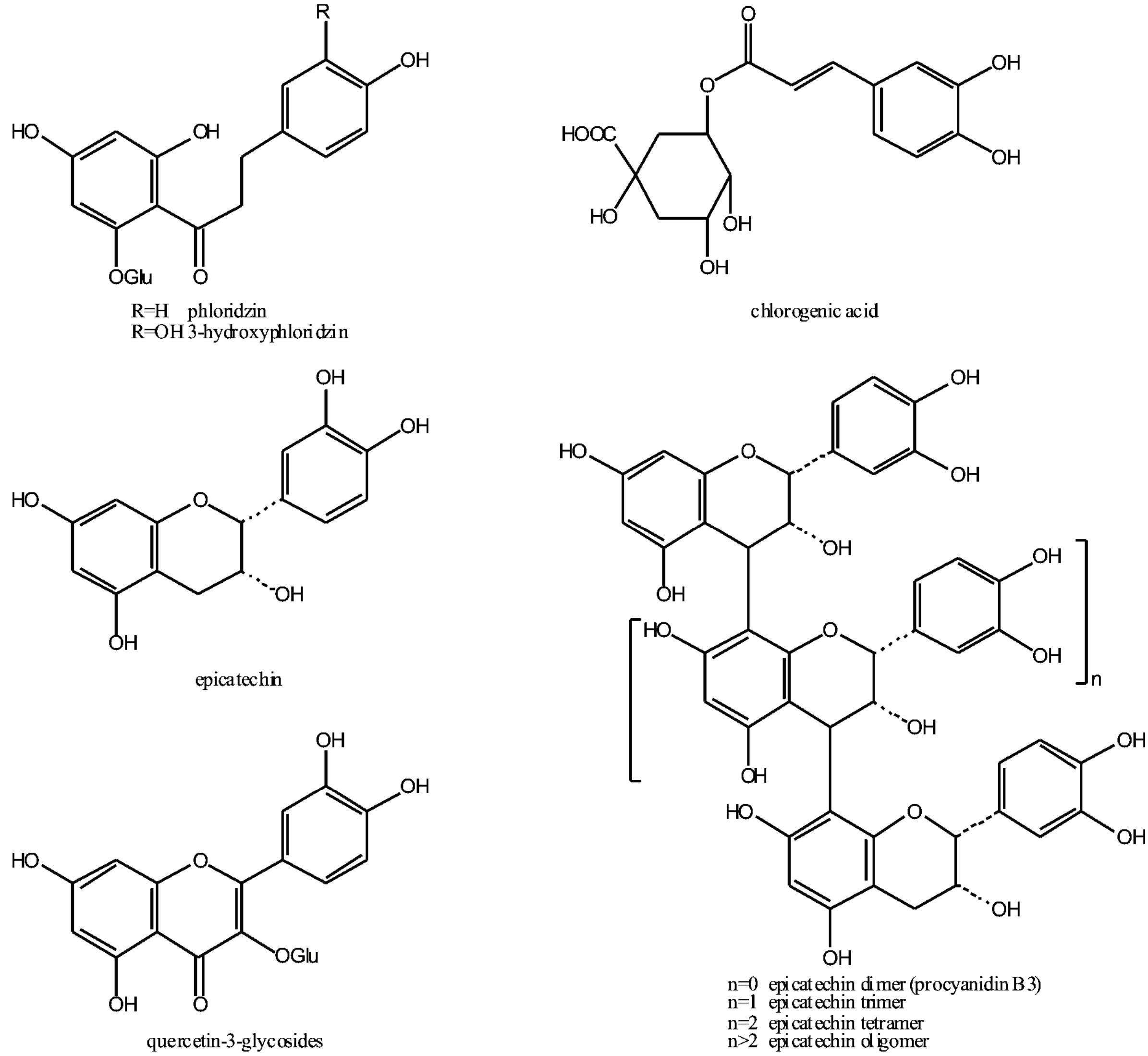

Figure 4. Chemical structures of polyphenols from apple pomace.

Table 3. $EC_{50}^{DPPH\bullet}$ and $EC_{50}^{\bullet OH}$ values of apple pomace

Apple pomace	$EC_{50}^{DPPH\bullet}$ / mg ml^{-1}	$EC_{50}^{\bullet OH}$ / mg ml^{-1}
Pinova	9.22 ± 0.45	33.75 ± 1.68
Reinders	6.33 ± 0.31	26.11 ± 1.30
Jonagold	9.50 ± 0.47	31.17 ± 1.55
Iduna	12.22 ± 0.61	32.01 ± 1.60
Braeburn	7.95 ± 0.39	34.47 ± 1.82
Granny Smith	9.51 ± 0.47	29.17 ± 1.45
Nectar[a]	15.72 ± 0.78	52.83 ± 2.63

[a]Industrial apple pomace obtained from factory "Nectar"

different human cancer cell lines: HT-29, HeLa and MCF-7. The apple pomace extracts influenced the cell growth depending on the cell line and dose (Figure 5). Pinova, Iduna and Braeburn pomace extracts showed the strongest antiproliferative activity against the investigated human cell lines, as well as HeLa cells were found to be the most sensitive to all extracts [24,25].

Grape

Grapes (Vitis sp., Vitaceae) and products obtained therefore, such as wine, grape juice, jams and raisins constitute an economically important factor. Grapes are the world's largest fruit crop with more than 60 million tons produced annually. About 80% of the total crop is used in wine making [26,27], and pomace represents approximately 20% of the weight of grapes

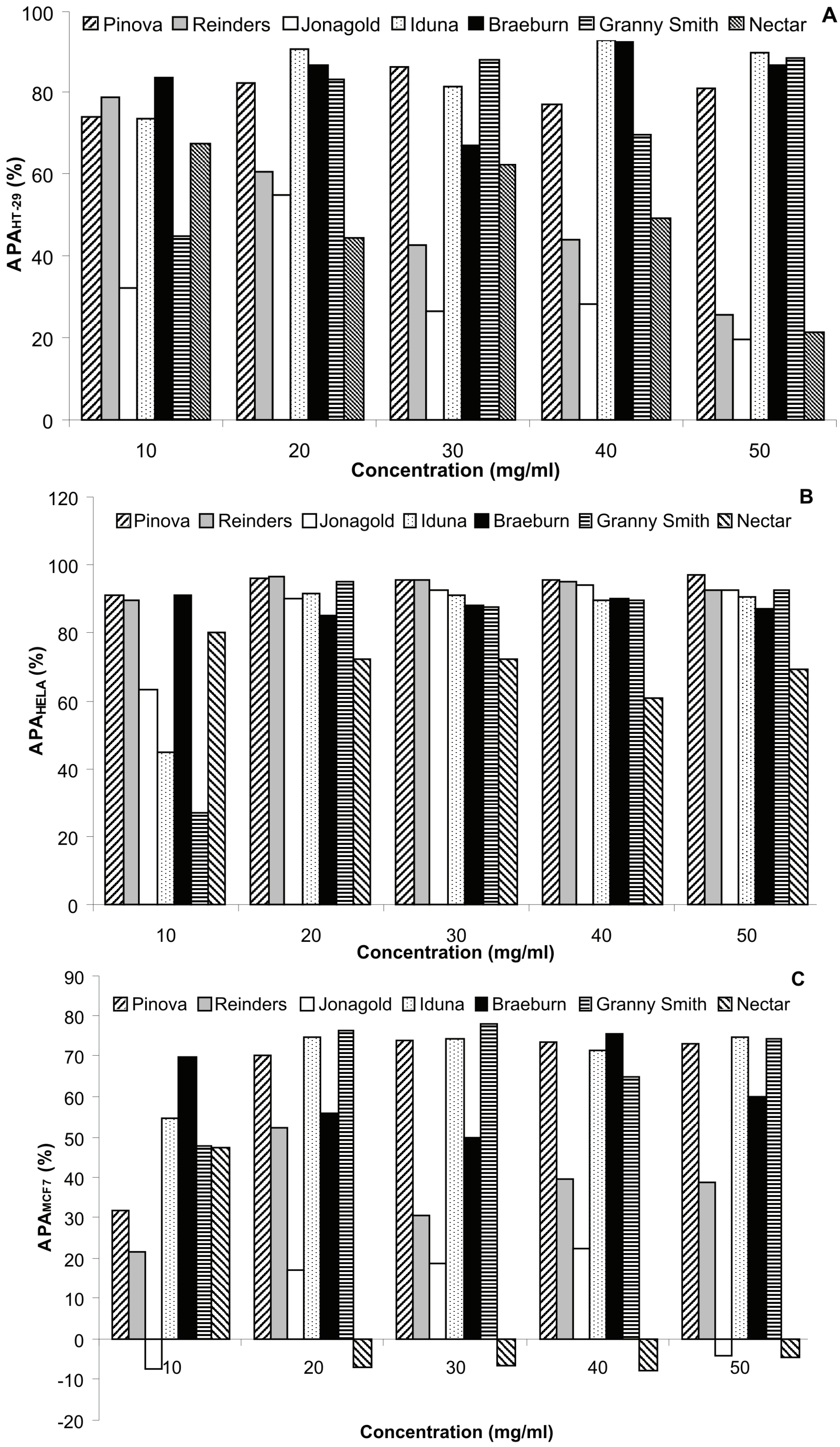

Figure 5. Antiproliferative activities of apple pomace extracts against HT-29 (A), HeLa (B) and MCF-7 (C) cells.

processed. Its composition varies considerably, depending on grape variety and technology of wine making.

However, wine making leads to the generation of large quantities of wastes (around 5-9 million tonnes per year, worldwide), which considerably increase the chemical oxygen demand (*COD*) and the biochemical oxygen demand (*BOD*) due to a high pollution load (high content of organic substances such as sugars, tannins, polyphenols, polyalcohols, pectins and lipids) with detrimental effects on the flora and fauna of discharged zones [26,27]. Therefore, the treatment and disposal of winery waste is a serious environmental problem and winery waste must find another use other than as animal feed or as fertilizers.

Beginning with the „French Paradox“ observations numerous studies have been initiated dealing with the antioxidative and health-promoting effects to the plant secondary metabolites in grapes, revealing the inhibition of LDL oxidation by grape phenolics. As a consequence, grape pomace is considered as a valuable source of phenolic compounds which could be recovered as functional food ingredients.

The seeds constitute a considerable proportion of the pomace, amounting to 38-52% on a dry matter basis. Their oil is rich in unsaturated fatty acids, linoleic acid in particular [28]. Grape seed oil is mainly produced in Italy, France and Spain; however, the demand for this oil has also increased in the rest of Europe [29]. Apart from being a rich source of high-value fatty oil, grape seeds have also been appreciated because of their content of phenolic compounds such as gallic acid, catechin and epicatechin, and a wide variety of procyanidins.

Thus, fractionation, isolation, and structural identification of grape seed proanthocyanidins have been extensively studied. Only procyanidin-type of proanthocyanidins, with partial galloylation, was detected in grape seeds [30]. The degree of polymerization may be reached around 30 [31,32]. Several individual dimer and trimer procyanidins were successfully isolated from grape seeds [33].

Also, a great range of products such as ethanol, tartrates, citric acid, grape seed oil, hydrocolloids, and dietary fibre are recovered from grape pomace [34-36]. Anthocyanins have been considered the most valuable components, and methods for their extraction have been reported [37]. Enzymatic treatment of grape pomace enhanced a release of phenolic compounds, as determined by the Folin-Ciocalteu assay [38]. However, the effects of this treatment on individual phenolics were not investigated. Gamma irradiation extended the shelf life of grape pomace and improved anthocyanin yields [39]. The extraction of crushed grape pomace with a mixture of ethyl acetate and water yielded phenolic compounds displaying antioxidant activities comparable to BHT in the Rancimat test. Catechin, epicatechin, epicatechin gallate and epigallocatechin were the major constitutive units of grape skin tannins [40]. A new class of compounds, aminoethylthio-flavan-3-ol conjugates, has been obtained from grape pomace by thiolysis of polymeric proanthocyanidins in the presence of cysteamine [41].

The antioxidant activity of the extracts obtained from grape by-products was analyzed by different in vitro tests: scavenging of the stable DPPH radical, reactive $^{\bullet}OH$, $O_2^{\bullet -}$ and of authentic peroxynitrite ($ONOO^-$). For example, Lacopini *et al.* [37] evaluated the extracts obtained from skin and seeds of 10 native Tuscan and international *Vitis vinifera* varieties for their antioxidant activity and subjected to HPLC-UV analysis to quantify the content of five phenolic constituents of biological interest: catechin and epicatechin in seeds and quercetin, rutin and resveratrol in skin extracts. All the five phenols investigated possessed strong antiradical activity. Quercetin, catechin and epicatechin showed maximum activity (respectively, $IC_{50}^{DPPH\bullet}$ 5.5, 6.7 and 6.8 M, and $IC_{50}^{ONOO^-}$ 48.8, 55.7 and 56.7 M).

Mandić *et al.* [42] obtained grape seed extracts (GSEs,) from Italian and Rhine Rieslings and examined their antioxidant activities using ESR spectrometry (Figure 6). IC_{50} values were between 0.1016 and 0.0445 mg/ml for the stable DPPH radicals in ethanol and ethyl acetate extracts of Italian (I-i and II-i) and Rhine (I-r and II-r) Rieslings, and for the very reactive OH radicals they were between 0.2759 and 0.0352 mg/ml.

Recent reports indicate a wide range of biological activities, *e.g.* radioprotective effects [43], the prevention of cataract [44] antihyperglycemic effects [45] the enhancement of postprandial lipemia [46], the modulation of the expression of antioxidant enzyme systems [47], the inhibition of the protein kinease activity of the epidermal growth factor receptor, protective effects against oxidative damage in mouse brain cells [48], and anti-inflammatory effects [49].

The high efficiency of natural phenolic extracts obtained from grape seeds as potent antioxidants was confirmed, by the fact which encourages the prospect of their commercialization as natural powerful antioxidants in foods in order to increase the shelf life of food by preventing lipid peroxidation and protecting from oxidative damage. Many of the grape seed products are commercially available [50].

Citrus fruits

Citrus is the largest fruit crop worldwide, with approximately 100 million metric tons produced an-

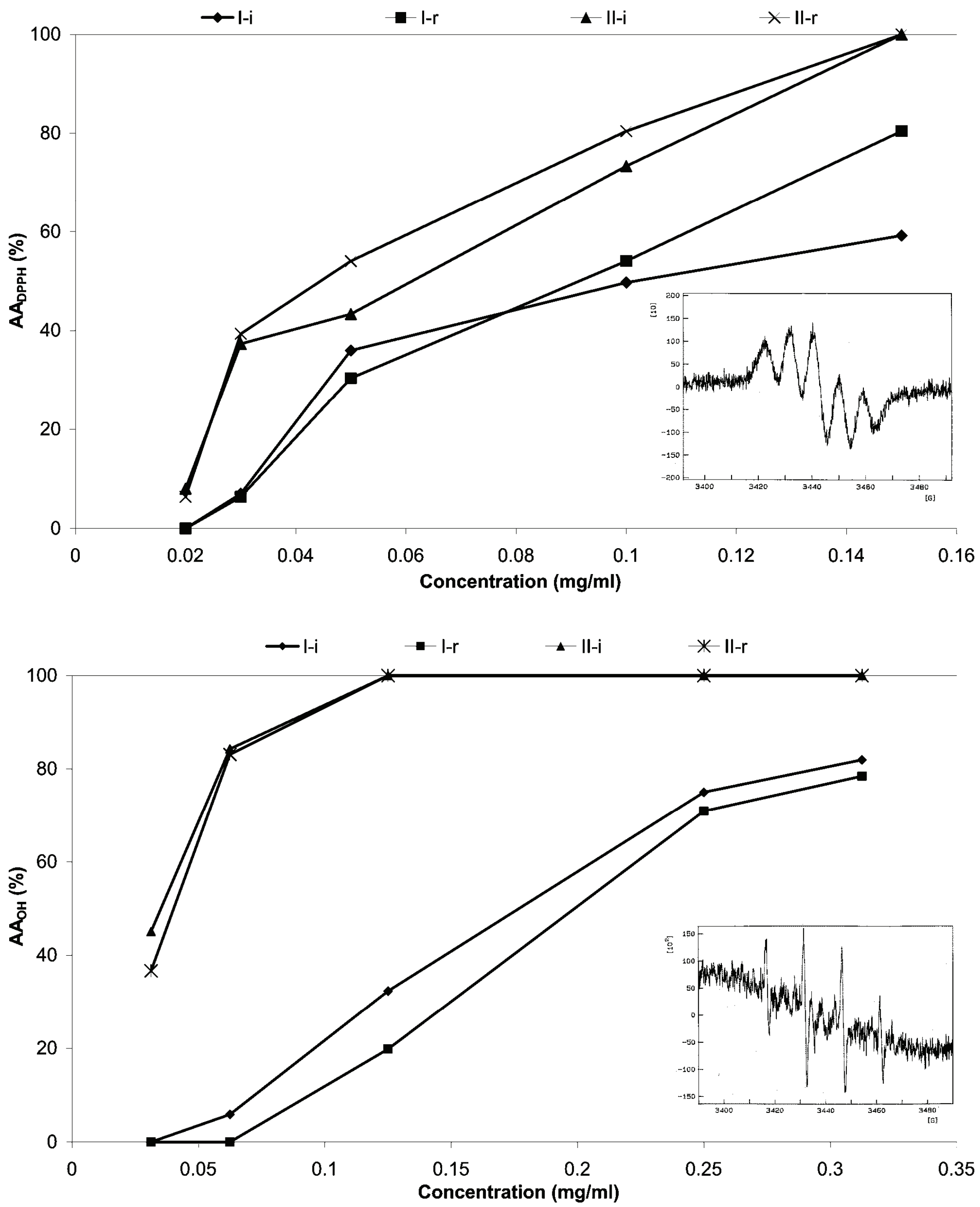

Figure 6. Antioxidant activities of different concentrations of grape seed extracts on DPPH• and hydroxyl radicals. ESR spectra of the DPPH• radical and DMPO-OH adduct are shown in the insert.

nually [5]. Brazil and the United States are the major producers; they grow around 60% of the world oranges and process 85% of their production [51]. The Mediterranean countries also present a significant production and processing. The EU countries more specifically produce approximately 10 million metric tons a year.

The family of citrus fruits consists of Oranges, Kinnow, Khatta, Lime, Lemon, Grapefruit, Malta, Sweet orange etc. The large quantities of processed citrus fruits result in large amounts of by-products. The industrial utilization of these by-products was encountered before 1920 and has increased significantly since the 1980s.

Citrus peel, remaining after juice extraction, is the primary waste fraction amounting to almost 50% of the fruit mass [51]. It is processed to dried pulp cattle feed and molasses, the latter being incorporated into the cattle feed or fermented for the production of valuable products like biogas, ethanol, citric acid, various enzymes, volatile flavouring compounds, fatty acids and microbial biomass. Pectin is also produced from the peel by acid extraction, dietary fibres by mechanical processing, while the recovery of flavonoids and carotenoids are new potential applications. The juice pulp from the finishing process and the essences recovered from the juice and the peel press liquor amounting to approximately 5% of the fruit mass, are also by-products that find industrial utilization. Citrus seeds amount to 0.1-5% of the fruit mass depending on the variety. They can be used for oil extraction and the recovery of terpenoids while the meal remaining from the extraction is a good source of proteins.

Citrus by-products, if utilized fully, could be major sources of phenolic compounds. The peels, in particular, are an abundant source of natural flavonoids, and contain higher amount of phenolics compared to the edible portions. Gorinstein *et al.* [52] reported that the contents of total phenolics in peels of lemons, oranges, and grapefruit were 15% higher than those in the peeled fruits. The ability of a number of methods to extract phenolics compounds from citrus peels have been evaluated, such as γ-irradiation assisted extraction, solvent extraction, enzyme-assisted extraction, and heat treatment. However, these extraction methods have drawbacks to some degree. For example, γ-irradiation assisted extraction is still unknown to safety; solvent extraction has low efficiency and consuming time; heat treatment results in pyrolysis, and enzyme in enzyme-assisted extraction is easy to denature [53].

Flavonoids in citrus are a major class of secondary metabolites. The peel contains the highest amount of flavonoids than other parts [54] and those flavonoids present in citrus fruits belong to six peculiar classes according to their structure. They are: flavones; flavanones; flavonols; isoflavones; anthocyanidins and flavanols [55]. The chemical structures of main flavonoids found in citrus species are shown in Figure 7.

Flavonoids from citrus that have been extensively studied for antioxidative, anti-cancer, anti-viral, and anti-inflammatory activities, effects on capillary fragility, and an observed inhibition of human platelet aggregation [56].

Recent research suggests that citrus fruits possess another health benefit phytochemicals called limonoids, highly oxygenated triterpenoid. Citrus limonoids appear in large amounts in citrus juice and citrus tissues as water soluble limonoid glucosides or in seeds as water insoluble limonoid aglycones. The limonoid aglycones are responsible for the development

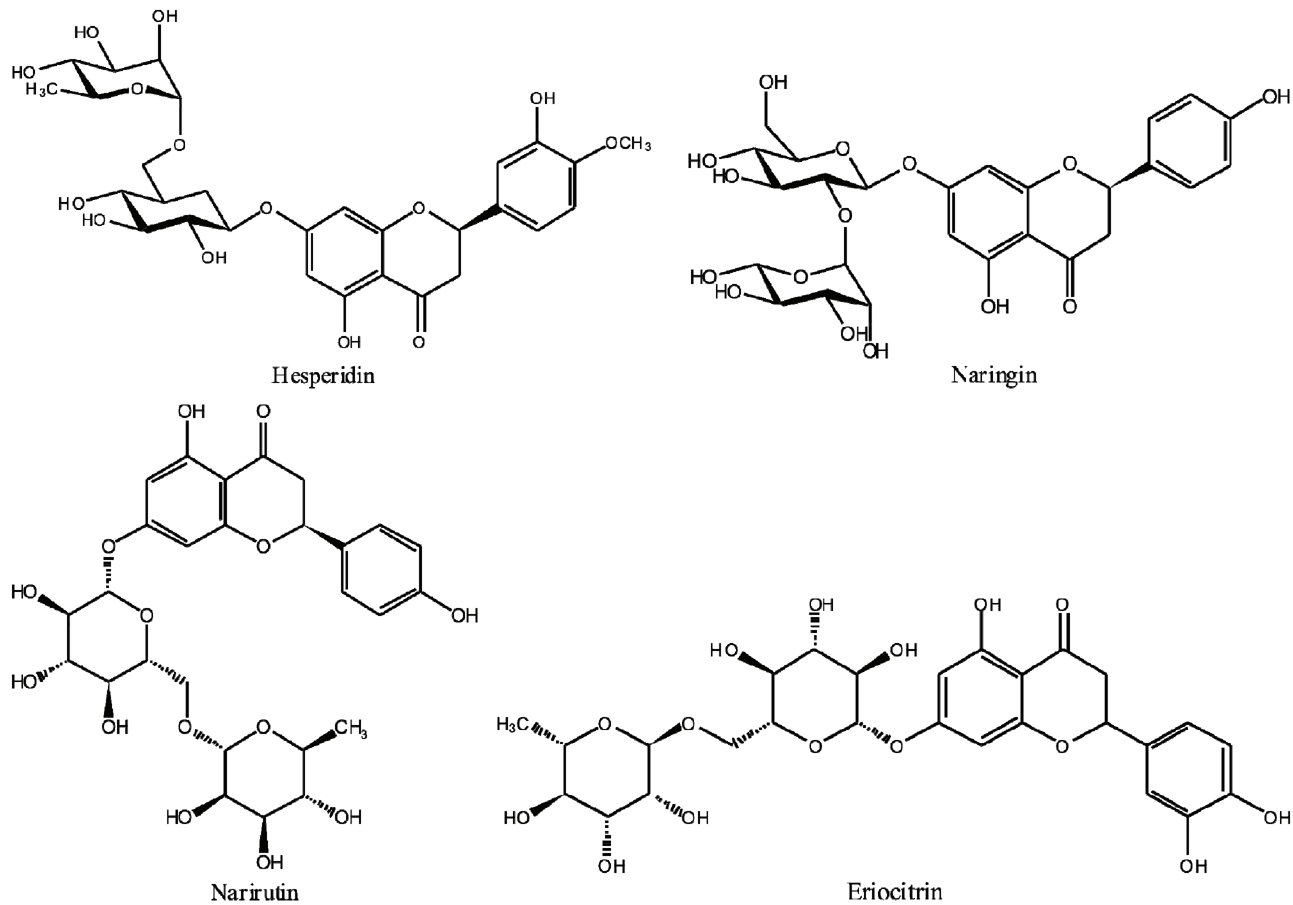

Figure 7. The main flavonoids found in citrus fruits.

of delayed bitterness in citrus and are converted to the non-bitter limonoid glucosides during fruit maturation [57]. Citrus fruits contain the limonoids limonin, nomilin and nomilinic acid, while both neem seeds and leaves contain the limonoid azadirachtin (Figure 8).

Currently limonoids are under investigation for a wide variety of therapeutic effects such as antiviral, antifungal, antibacterial, antineoplastic and antimalarial. Certain limonoids are insecticides such as azadirachtin from the neem tree. Most recently several limonoid aglycones and a mixture of limonoid glucosides were administered in vitro to estrogen dependent and estrogen independent human breast cancer cell lines [53,57].

FUTURE TRENDS

The exploitation of by-products of fruit processing as a source of functional compounds and their application in food is a promising field which requires interdisciplinary research of food technologists, food chemists, nutritionists and toxicologists. In the near future, we are challenged to respond to the following research needs. Furthermore, investigations on stability and interactions of phytochemicals with other food ingredients during processing and storage need to be initiated. Since functional foods are on the boundary between foods and drugs, their regulation still proves to be difficult. In any case, a consumer protection must have priority over economic interests.

Acknowledgement

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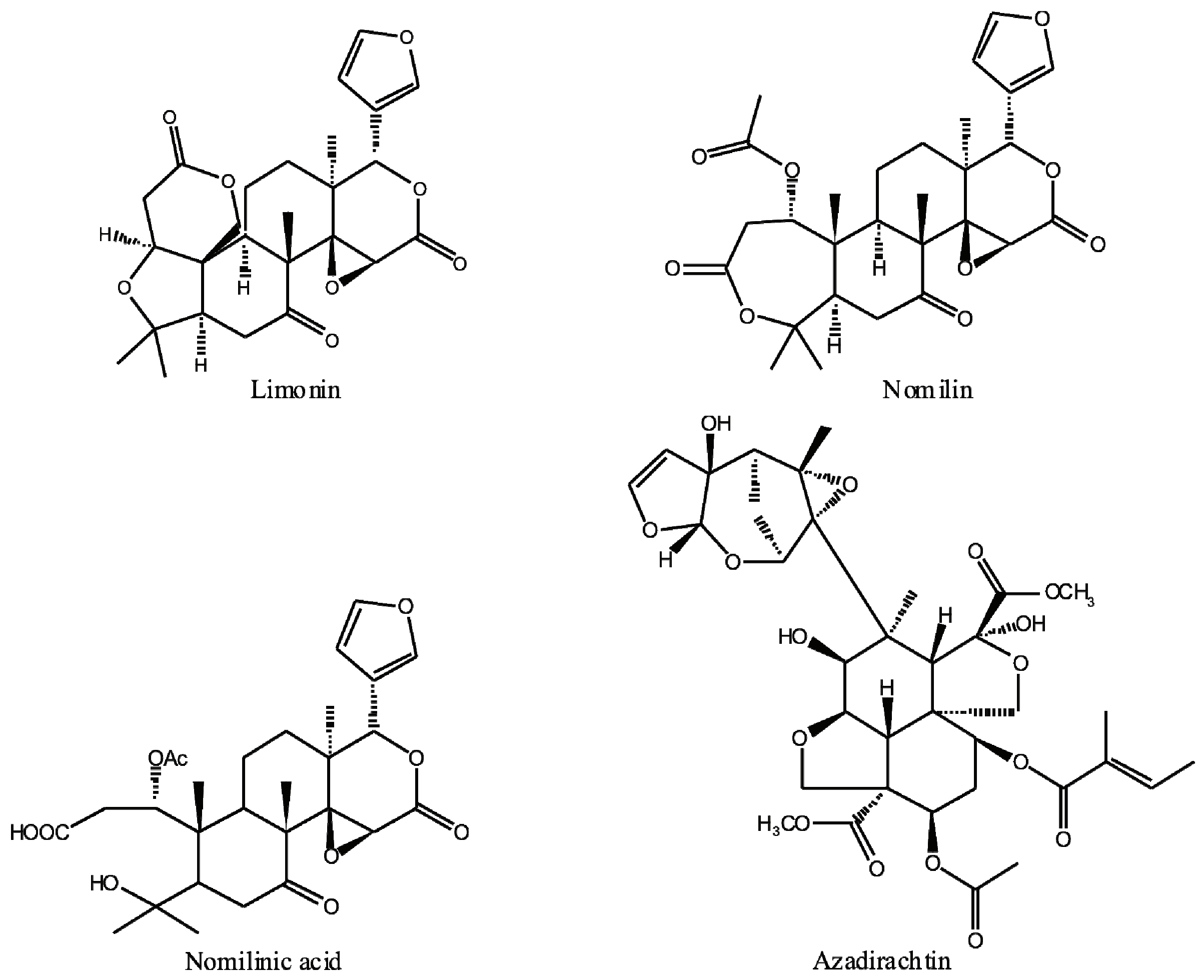

Figure 8. The main limonoids found in citrus fruits.

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