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Critical Review

Flavanones in grapefruit, lemons, and limes: A compilation and review of the data from the analytical literature

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Abstract

In order to develop a database for flavanones, the dominant flavonoid class in the genus citrus, the relevant scientific literature on flavonoids in grapefruit, lemons, and limes was searched, abstracted, documented, standardized by taxons and units (mg/100 g) and examined for quality. Values for eight flavanones (didymin, eriocitrin, hesperidin, naringin, narirutin, neoeriocitrin, neohesperidin, poncirin) are presented. Grapefruit had a total flavanone content (summed means) of 27 mg/100 g as aglycones and a distinct flavanone profile, dominated by naringin. White grapefruit varieties tended to be slightly but not significantly higher in total flavanones than pink and red varieties. For lemons, total flavanones (summed means) were 26 mg/100 g and for limes 17 mg/100 g. The flavanone profiles of both lemons and limes were dominated by hesperidin and eriocitrin.

Keywords: Database; Flavanones; Citrus; *Citrus X paradisi*, *-limon*, and *-aurantiifolia*

1. Introduction

Currently, there is much interest in the healthfulness of citrus fruits because their intakes appear to be associated with reduced risk of certain chronic diseases (Chen et al., 2002; Feldman, 2001; Joshipura et al., 1999; Kurowska et al., 2000; Levi et al., 1999, 2000; McCullough et al., 2001; Palli et al., 2001) and increased survival (Fortes et al., 2000). One or more of the citrus flavonoids may be responsible for their possible beneficial effects, although at present such evidence is limited chiefly to in vitro and mechanistic studies (Areias et al., 2001; Bae et al., 1999; Bear and Teel, 2000a, b; Borradaile et al., 1999; de Gregorio Alapont et al., 2000; Jeon et al., 2001; Kato et al., 2000; Kim et al., 2000; Kohno et al., 2001; Lee et al., 2001; Manthey et al., 2001; Miyake et al., 2000; Wilcox et al., 2001; Zhang et al., 2000). Therefore, it is important that the flavonoid composition of citrus fruits be documented so dietary intakes can be measured and linked to disease outcomes.

This paper focuses on the flavanone content of grapefruit, lemons, and limes in the genus Citrus, each of which has several varieties (Fig. 1). A similar treatment of oranges, tangerines (mandarins), tangors, and tangelos is presented in this journal issue (Peterson et al., 2006). All grapefruit are members of the species *Citrus X paradis*; the varieties vary in the color of their flesh owing to the presence (pink/red) or absence (white) of lycopene. Although several species of citrus are called lemons or limes (such as *C. jambhiri* or *C. limettioides*, respectively), this paper focuses on the several varieties of *C. limon* for lemons, and *C. aurantiifolia* for limes as information about the consumer use of the other species was not readily available and the flavanone data was sparse.

The goals of this study were to summarize analytic data of acceptable quality from the scientific literature and present values on the flavanones in grapefruit, lemon, and lime fruits for a provisional flavonoid food composition

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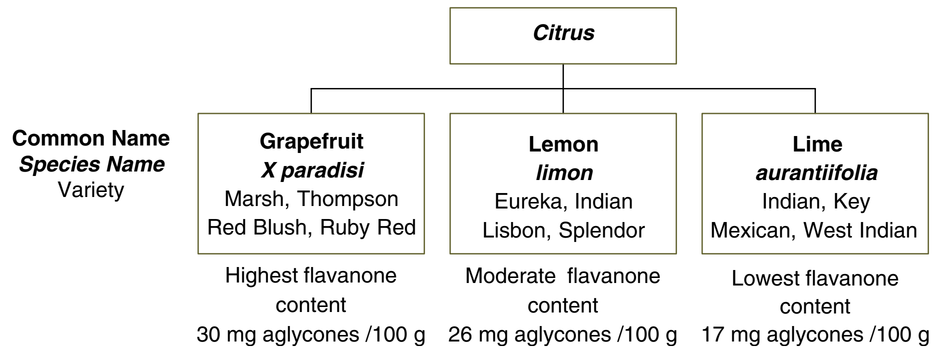

Fig. 1. Taxonomic description and flavanone content of grapefruits, lemons and limes.

table. Data on both glycosides and aglycones are summarized because these sugars affect the taste of citrus fruits and juices. We also compared the Davis spectrophotometric method and the HPLC method to determine if the flavanone values differed. In addition, the association between color and flavanone content of grapefruit was examined.

2. Methods

Using methods previously described (Peterson et al., 2006, in this journal issue), the relevant food composition analytical literature was searched for articles dealing with grapefruit, lemons, and limes using Food Science and Technology Abstracts from 1968 to 1998 with a follow up search of Commonwealth Agriculture Bureau 1973–2002 and abstracted. All flavanone compounds in citrus were listed in the search and fifteen articles were found for this study.

There were 10 useful articles on grapefruit, 5 articles on lemons, and 4 articles on limes. There were some studies on grapefruit for flavonols (Berhow et al., 1998; Hertog et al., 1993; Justesen et al., 1998) and hydroxyflavones (Berhow et al., 1998; Hertog et al., 1993; Hsu et al., 1998), on lemons for flavonols (Berhow et al., 1998; Hertog et al., 1993; Justesen et al., 1998; Vandercook and Tisserat, 1989) and for hydroxyflavones (Berhow et al., 1998; Justesen et al., 1998) and on limes for flavonols (Berhow et al., 1998; Justesen et al., 1998) and for hydroxyflavones (Berhow et al., 1998; Justesen et al., 1998) and no studies on anthocyanins, flavan-3-ols, or isoflavonoids for these fruits. Using preliminary data, we estimated that grapefruits' flavonoid content was 24 mg aglycones/100 g edible fruit or juice, lemons contained 30 mg aglycones/100 g edible fruit or juice and limes contained 18 mg aglycones/100 g edible fruit or juice. Flavanones constituted virtually all of the total flavonoids present (e.g., 98% in grapefruit, 90% lemons and 96% limes) and, therefore, they were the focus of our study. Although citrus flavonoid data on flavanones, flavones, flavonols and anthocyanins were compiled, this article will focus on the flavanones as they are the major class of flavonoids present in citrus. Articles on the other compounds are planned for the future.

Following our earlier methods (Peterson et al., 2006, in this journal issue) we focused on the 4 major aglycones—hesperetin, naringenin, eriodictyol, and isosakuranetin—with their rutinose or neohesperidose glycosides for a total of 8 separate compounds (didymin, eriocitrin, hesperidin, narirutin, naringin, neoeriocitrin, neohesperidin, and poncirin) (Fig. 2). Data on four other glycosides of naringenin [naringin-4′-glucoside, naringin-6″-malonate (closed form), naringin-6″-malonate (open form), narirutin-4′-glucoside] were excluded because only one study (Berhow et al., 1998) was available.

The quality of the flavanone analytical data was assessed using the criteria for evaluating food composition data that were originally developed and used in compiling United States Department of Agriculture (USDA) food composition tables (Holden et al., 2002; Mangels et al., 1993). This system was adapted for evaluation of citrus flavonoids in consultation with collaborators familiar with the chemistry and food science of citrus. The five quality assessment criteria (number of samples, sample handling, sampling plan, analytical method, and analytical quality control) were utilized and applied to each citrus datapoint in the analytical literature that could be identified for flavanones in these citrus. Only data meeting these criteria were utilized in the calculation of descriptive statistics for the food composition tables.

With respect to the evaluation of the number of samples, a "datapoint" was taken to be whatever analytical value was reported, usually a mean of duplicate or triplicate analytical values but occasionally a single analytical value. Each datapoint was conservatively treated as an N of 1 and no weighting factor was applied to adjust if a greater number of samples were included. Datapoints described as "not detected" were assigned a value of zero. "Trace" values were assigned to be 71% of the limit of quantification for the method used based on calculations described previously (Mangels et al., 1993).

To evaluate the sampling plan, the data were placed in a standardized format with respect to taxons (genus, species). All varieties were verified using Germplasm Resources Information Network (GRIN),[2] Evaluer Gérer,

[2]http://www.ars-grin.gov/cgi-bin/npgs/html/taxgenform.pl

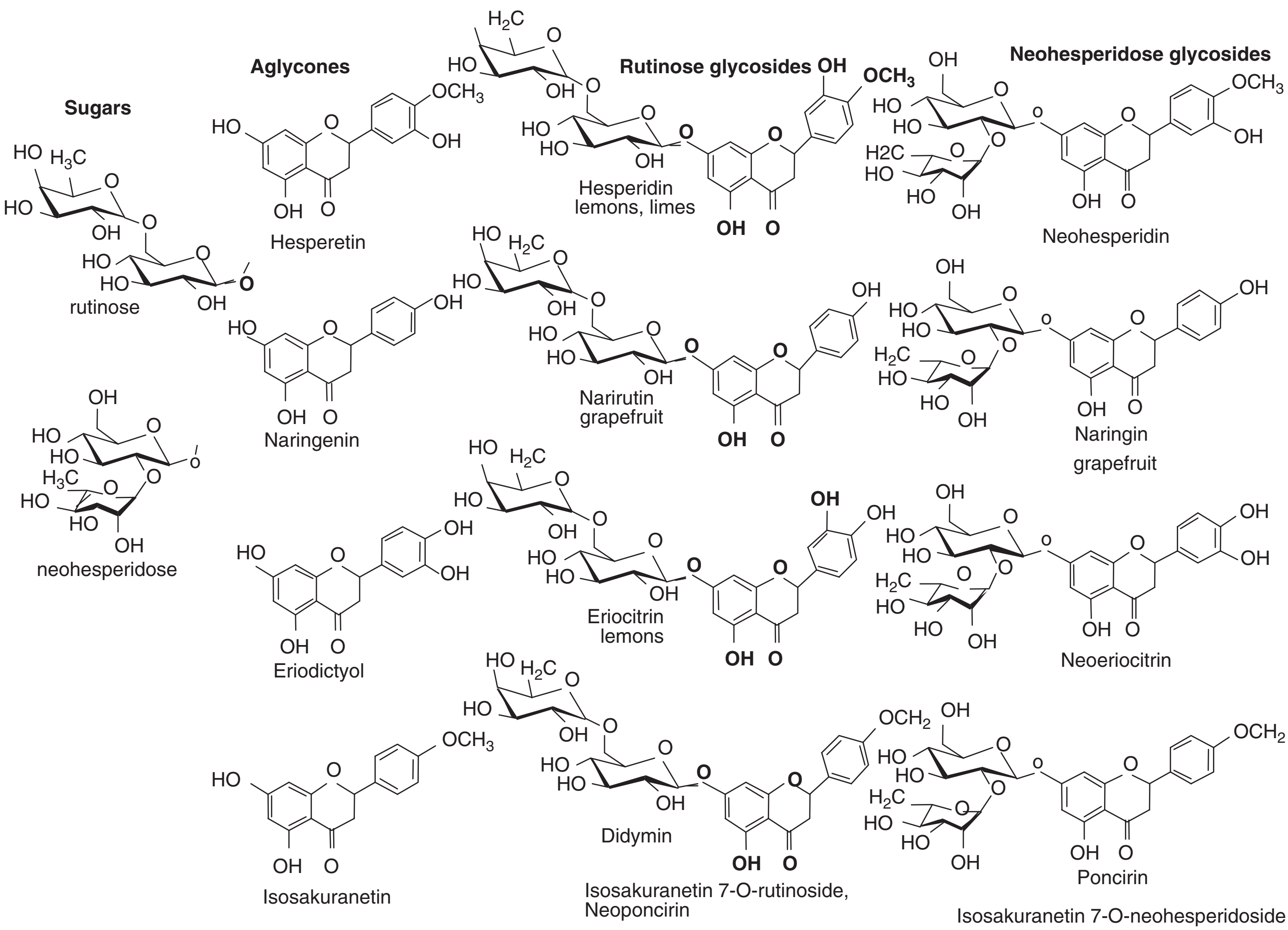

Fig. 2. Citrus flavanone aglycones and glycosides. Structures from Harborne and Baxter (1999). Structure numbers for glycosides are didymin—1123, eriocitrin—1200, hesperidin—1207, narirutin—1111, naringin –1112, neoeriocitrin—1201, neohesperidin—1208, and poncirin—1124.

Informatiser, Diffuser (EGID),[3] and other taxonomic sources (Purdue,[4] USDA,[5] and Australia[6]). In addition, lists of commercial cultivars and varieties were obtained using two sources, *Fresh Citrus Fruits* (Wardowski et al., 1986) and *Florida Citrus Varieties* (Tucker et al., 1998). Information was insufficient to classify the citronelle (rough lemon, *C. jambhiri*), a near relative of lemons with *C. limon* or the Bearss (*C. latifolia*) and sweet limes (*C. limettoides*) with *C. aurantiifolia*; therefore, data on them were not included.

For the evaluation of sample handling, data on juice and fruit were separated from values provided for the peel or other citrus products. All citrus flavonoid data were converted from their original units to mg/100 g by using either Brix data to obtain density or by employing a standard density of 1.044 for freshly squeezed and 1.057 for commercially processed that is used by the USDA for grapefruit juice as needed and a standard density of 1.031 and 1.040 for lemon and lime juices fresh or commercial, respectively. All glycosides were converted to mg aglycones/100 g edible fruit or juice.

The analytic methodology used in generating these data was all high performance liquid chromatography (HPLC). The Davis method, a quick semiquantitative spectrophotometric method that measures total flavanones and is used to determine potential taste characteristics, was commonly used for grapefruit. It was compared to the results of HPLC methods for individual compounds. The Davis method data were compiled but were not used in preparing these tables since chemically analyzed values for specific flavanones were available which could be summed to obtain more valid estimates of total flavanones. Data for each of the 8 flavanone glycoside compounds in each citrus group were reviewed and descriptive statistics were calculated.

Analytical quality control was also assessed. Older articles tended to be less explicit in the mention of these details in part perhaps because at the time they were written such details were understood as standard

[3]http://www.corse.inra.fr/sra/egide.htm
[4]http://www.hort.purdue.edu/newcrop/morton/
[5]http://www.ars.usda.gov/ls/np/phenolics/ap1/ca-I.htm
[6]http://www.sardi.sa.gov.au/hort/cit_page/cit_var.htm

laboratory operating procedures. Newer articles were more detailed.

Descriptive statistics were calculated as aglycones. The means of all flavanone aglycones measured were summed for grapefruits, lemons and limes, and box plots on each type were produced and reviewed by a statistician with expertise in food composition (W Rand, Ph.D.). Outlying values were examined and all were judged to be within the normal limits of environmental variability and included in the analysis. The flavanone data for red (and pink) and white grapefruits were also examined separately to determine the degree to which these citrus fruits had similar flavanone levels.

3. Results

Tables 1 and 2 provide a provisional table of total flavanone content and individual flavanone compounds for grapefruits, lemons, and limes. Grapefruit, lemons and limes differed both in the amount of total flavanones provided and in their individual flavanone profiles.

Grapefruit contained 27 mg total flavanone aglycones/100 g edible fruit or juice (summed means) and the flavanone glycoside pattern consisted predominantly of naringin. Grapefruits averaged 17 mg ($\pm$9.6 SD) aglycone/100 g edible fruit or juice for naringin and 3 and 5 mg aglycone/100 g edible fruit or juice for hesperidin ($\pm$5.4 SD) and narirutin ($\pm$3.4 SD), respectively. Red (and pink) grapefruit was lower in total flavanone content than white grapefruit but the individual glycosides were not significantly different between white and red (and pink) grapefruit by Kruskal–Wallis analysis.

A comparison of the older and less precise Davis spectrophotometric method with HPLC data for individual compounds found the HPLC values for naringin were slightly but not significantly lower than the Davis method values for white grapefruit. The total flavanone (summed means) from HPLC values for white grapefruit was consistent with the Davis method values. However, for pink grapefruit Davis method data was significantly lower than the HPLC data, possibly indicating that the pigment lycopene affects the Davis test.

Lemons provided 26 mg total flavanone aglycones (summed means)/100 g edible fruit or juice and limes 17 mg total flavanone aglycones/100 g edible fruit or juice (summed means). In lemons, eriocitrin and hesperidin glycosides predominated, and in limes hesperidin. Lemons and limes averaged the same amount of the glycoside

Table 1
Flavanones in grapefruit

Citrus type	Compound	Mean	SD	Median	Range	n	Refs.
Grapefruit	Didymin	0.07	0.21	0.0	0.0–0.62	9	1
	Eriocitrin	0.45	1.30	0.0	0.0–4.97	15	1,5,6,
	Hesperidin	2.78	5.37	0.4	0.0–18.06	22	1,5,6,8,10
	Naringin	16.60	9.61	17.9	0.0–48.89	44	1,2,3,4,5,6,7,8,9,10
	Narirutin	4.90	3.41	4.8	0.0–11.98	29	1,2,4,5,6,8,
	Neoeriocitrin	0.35	1.39	0.0	0.0–6.39	21	1,4,5,6,
	Neohesperidin	1.4	5.87	0.2	0.0–31.29	28	1,4,5,6,8,9
	Poncirin	0.17	0.22	0.0	0.0–0.46	15	1,4
	Total	26.72					
Grapefruit White	Didymin	0.09	0.23	0.0	0.0–0.62	7	1
	Eriocitrin	0.16	0.39	0.0	0.0–1.30	11	1,5,6
	Hesperidin	3.95	6.46	0.5	0.0–18.06	14	1,5,6
	Naringin	16.90	8.26	18.5	0.0–43.22	36	1,2,3,4,5,6,7,8,9
	Narirutin	5.36	3.47	5.4	0.0–11.98	22	1,2,4,5,6,8
	Neoeriocitrin	0.05	0.10	0.1	0.0–0.27	17	1,4,5,6,
	Neohesperidin	0.25	0.20	0.2	0.0–0.63	21	1,4,5,6,8,9
	Poncirin	0.20	0.22	0.0	0.0–0.46	13	1,4
	Total	26.96					
Grapefruit Red and Pink	Didymin	0.00			0.0	1	1
	Eriocitrin	0.00	0.00	0.0	0.0	3	1,6
	Hesperidin	0.27	0.26	0.2	0.0–0.76	6	1,6,8
	Naringin	13.87	17.42	6.56	3.28–48.89	6	1,6,8
	Narirutin	3.34	3.26	2.11	1.03–9.78	6	1,6,8
	Neoeriocitrin	0.00	0.00	0.0	0.00	3	1,6
	Neohesperidin	0.42	0.47	0.23	0.19–1.38	6	1,6,8
	Poncirin	0.00			0.00	1	1
	Total	17.90					

All amounts are mg aglycone/100 g fresh fruit or juice.
[1]Berhow et al. (1998), [2]Bronner and Beecher (1995), [3]Dougherty and Fisher (1977), [4]Hsu et al. (1998), [5]Mouly et al. (1993), [6]Mouly et al. (1994), [7]Rouseff et al. (1980), [8]Rouseff et al. (1987), [9]Rouseff (1988), [10]Wallrauch (1995).

Table 2
Flavanones in lemons and limes

Citrus type	Compound	Mean	SD	Median	Range	*n*	Refs.
Lemons	Didymin	0.17	0.51	0.0	0.0–1.5	9	1
	Eriocitrin	9.46	5.54	8.3	0.0–25.1	40	1,11,13
	Hesperidin	15.78	21.72	13.3	1.9–142.2	41	1,11,12,13
	Naringin	0.18	0.53	0.0	0.0–1.6	9	1
	Narirutin	0.80	1.24	0.0	0.0–3.2	9	1
	Neoeriocitrin	0.00			0.0	9	1
	Neohesperidin	0.00			0.0	9	1
	Poncirin	0.00			0.0	9	1
	Total	26.58					
Limes	Didymin	0.00			0.0	7	1
	Eriocitrin	1.38	1.26	1.2	0.0–3.5	9	1,6
	Hesperidin	15.64	11.15	13.2	5.2–43.0	10	1,6,13
	Naringin	0.00			0.0	8	1,15
	Narirutin	0.23	0.37	0.0	0.0–1.0	9	1,6
	Neoeriocitrin	0.04	0.07	0.0	0.0–1.8	9	1,6
	Neohesperidin	0.00			0.0	7	1
	Poncirin	0.00			0.0	7	1
	Total	17.29					

All amounts are mg aglycone/100 g fresh fruit or juice.
[1]Berhow et al. (1998), [6]Mouly et al. (1994), [11]Grandi et al. (1994), [12]Justesen et al. (1998), [13]Vandercook and Tisserat (1989), [14]Yusof et al. (1990).

hesperidin (16 mg aglycone/100 g edible fruit or juice, SD for lemons 21.7, SD for limes 11.2) but lemons also averaged 9 mg (±5.5 SD) aglycone/100 g edible fruit or juice for eriocitrin (limes 1.4 mg aglycone/100 g edible fruit or juice for eriocitrin, SD 1.3).

4. Discussion

Compared to our previous paper on orange type citrus (Peterson et al., 2006, in this journal issue), we have fewer studies and a smaller number of datapoints for grapefruit, lemons and limes.

The flavanones in lemons and limes were mostly rutinose glycosides of eriodictyol and hesperetin, whereas in grapefruit neohesperidose glycosides were predominant (Fig. 2). The dominant flavanone glycoside in grapefruit (*C. X paradisi*) is naringin. The sugar neohesperidose (2-*O*-α-L-rhamnosyl-*β*-D-glucose), which is high in grapefruits, imparts the tangy or bitter taste to the glycoside naringin. In lemons (*C. limon*) the flavanone profile is dominated by two specific flavanone glycosides—hesperidin and eriocitrin. In limes (*C. aurantiifolia*), only one flavanone, hesperidin, is dominant. The sugar rutinose (6-*O*-α-L-rhamnosyl-D-glucose) which is relatively high in lemons and limes, and its flavanone glycosides, hesperidin and eriocitrin, have a neutral taste.

Grapefruit, lemons, and limes had statistically similar total flavanone content, primarily because of somewhat lower values observed for red and pink grapefruit (limes had similar lower flavanone values). Lemons and limes had flavanone profiles more like sweet oranges, whereas grapefruits had a flavanone pattern similar to sour oranges (Peterson et al., 2006, in this journal issue). The flavanone content and profiles of each of these fruits was distinct. In provisional tables of food flavanone composition grapefruits, lemons and limes should be listed separately.

5. Conclusion

Grapefruit had a total flavanone content (summed means) of 27 mg aglycones/100 g edible fruit or juice and a distinct flavanone profile, dominated by naringin and similar to sour oranges. White grapefruit varieties tended to be slightly but not significantly higher in total flavanones (27 mg) than pink and red varieties (18 mg). For lemons, total flavanone content (summed means) were 26 mg aglycones/100 g edible fruit or juice and for limes 17 mg aglycones/100 g edible fruit or juice. The flavanone profiles of both lemons and limes were dominated by hesperidin and eriocitrin and similar to sweet oranges.

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