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Evaluation of Phenolic Compounds in Commercial Fruit Juices and Fruit Drinks

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The total phenolic content of 13 commercially available fruit juices and juice drinks, selected to represent the most popular juice flavors in the United Kingdom, were analyzed using the Folin−Ciocalteu assay. Individual phenolic compounds were identified and quantified using HPLC-PDA-MS^2. The catechin content and degree of polymerization of proanthocyanidins were also analyzed. Purple grape juice contained the largest number of individual phenolic compounds and also the highest concentration of total phenolics. The main components were flavan-3-ols, anthocyanins, and hydroxycinnamates, which accounted for 93% of the total phenolic content. In contrast, white grape juice, which contained principally hydroxycinnamates, had the lowest total phenolic content. Antioxidant activity was measured using the ORAC and FRAP assays, and the data obtained were in broad agreement with total phenol content. In view of the recent findings of the *Kame* project indicating that long-term fruit juice consumption can provide protection against Alzheimer's disease (Dai et al. *Am. J. Med.* **2006**, *379*, 464−475), it is suggested that the protective effects may be enhanced by consumption of a combination of juices rich in phenolics and containing a diverse variety of individual phenolic compounds, namely, juices derived from purple grapes, grapefruit, cranberries, and apples.

KEYWORDS: Fruit juices; phenolics; antioxidant capacity; HPLC−tandem mass spectrometry

INTRODUCTION

There is epidemiological evidence linking a diet rich in fruits and vegetables with reduced incidences of coronary heart disease, cancer, and various chronic diseases (*1*). Historically, several fruits, vegetables, and beverages have had specific health claims associated with their consumption. Centuries ago it was established that sailors could prevent the onset of scurvy by eating vitamin C-rich citrus fruit. More recently, cranberries have been recommended for the treatment of urinary tract infection, an effect arguably attributed to proanthocyanidins (*2*). The Zutphen Elderly Study linked the consumption of flavonol-rich apples, onions, and tea to a decreased incidence of the risk of stroke and heart disease (*3*). Moderate consumption of red wine is widely believed to reduce the incidence of heart disease, an effect known as the French paradox (*4*). Although a large number of epidemiological studies indicate that moderate consumption of alcoholic beverages is associated with reduced mortality and heart disease, other studies report that red wine can offer greater protection than white wine, beers, or spirits (*5*, *6*). Red wine contains high concentrations of a large number of phenolic compounds that originate from the grapes and also, in some instances, from oak when the wines are matured in wood barrels (*7*). The wide range of phytochemicals in red wine has made it very difficult to ascribe the protective effects to specific compounds, although a recent study has linked oligomeric proanthocyanidins to improved vascular health (*8*).

Fruits and vegetables contain several health-promoting factors including fiber and high concentrations of phenolic acids, flavonoids, vitamins, and minerals. Phenolic acids and flavonoids, although not essential for survival, may over the long term provide protection against a number of chronic diseases. The phenolic acids potentially involved in these beneficial effects include gallic acid, hydroxycinnamates including coumaric acid, caffeic acid, and derivatives such as chlorogenic acid (*9*). The main flavonoids of interest are anthocyanins, flavan-3-ols, and their polymeric condensation products, flavanones, flavonols, and flavones (*9*). To varying degrees these compounds are potent antioxidants in vitro (*10*), being able to inhibit lipid peroxidation (*11*) and protect low-density lipoproteins against oxidation (*12*). They can also reduce platelet aggregation (*4*) and enhance vasodilation (*13*). However, the protective effects of these compounds may not be due exclusively to their antioxidant properties and other mechanisms may also operate.

Extracts and supplements derived from various fruits and vegetables have so far failed to recreate the effects of the whole foods (*14*). Despite this, the market in the United States for supplements with putative health benefits is in the region of $23 billion per year (*15*). Although there is an abundance of low-cost fruits and vegetables available in shops and super-

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Table 1. Properties of Fruit Juices and Fruit Drinks

sample	type[a]	retail location	kcal/ 100 mL[b]	g of sugar/100 mL
Ocean Spray Classic Cranberry	D[c]	A	49	11.7
Welch's Purple Grape	J	R	68	16.5
Tesco Pure Pressed Red Grape	J	A	65	15.6
Pomegreat Pomegranate	D[d]	A	44	10.6
Tesco Pure Apple (clear)	J	A	46	11.1
Copella Apple (cloudy)	D[e]	R	44	10.3
Tesco Pure Grapefruit	J	R	41	9.0
Tesco Value Pure Orange (concentrate)	J	A	47	10.5
Tropicana Pure Premium Smooth Orange (squeezed)	J	R	43	9.0
Tropicana Pure Premium Tropical Fruit	J	R	45	10.6
Tesco Pure Pressed White Grape	J	A	65	15.6
Tesco Pure Pineapple	J	R	55	12.4
Del Monte Premium Tomato	J	A	17	4.3

[a] J, fruit juice; D, fruit drink; R, refrigerated; A, ambient. [b] Calories attributable to carbohydrates, principally sugars. [c] Twenty-five percent juice; ascorbic acid is added at 30 mg/100 mL. [d] Thirty-seven percent juice; ascorbic acid is added at 12 mg/100 mL, vitamin A at 160 μg and vitamin E at 2 mg/100 mL. [e] One hundred percent juice; ascorbic acid is added at 30 mg/100 mL.

markets, convincing the general public to consume more fruits and vegetables has so far proved to be a difficult task. Whereas it is widely believed that a healthier diet is good for you, most people, especially those with a busy lifestyle, would rather take a quick fix in the form of a supplement or pill. Evidence is emerging, however, which suggests that fruit and vegetable juices may be a more effective alternative, and a recent review has concluded that drinking fruit and vegetable juices may well be as effective as consumption of whole fruits and vegetables in relation to a reduction in the risk of chronic disease (*16*). Furthermore, the *Kame* Project carried out with Japanese-Americans between 1992 and 2001 found that subjects with a higher intake of fruit and vegetable juices had a substantially reduced incidence of Alzheimer's disease (*17*). This relationship could not be attributed to the presence of vitamin C, vitamin E, or β-carotene; in fact, once adjusted for antioxidant vitamins, the inverse relationship between the consumption of juices rich in phenolics and Alzheimer's disease was strengthened.

Here we report on an investigation of the total phenolic content and phenolic composition of 13 fruit juices and juice drinks selected to be representative of the most popular U.K. juice flavors. In the United Kingdom pure fruit juices are 100% juice with no added ingredients, whereas juice drinks may contain less than 100% juice and may contain added ingredients such as vitamin C and sugar.

MATERIALS AND METHODS

Materials. Thirteen fruit juices and juice drinks listed in **Table 1** were obtained from Tesco Extra (Glasgow, U.K.). The juices were selected using retail sales data from Information Resources Inc. and Taylor Nelson Sofres to represent the most popular U.K. fruit juice flavors based on annual sales for the year ending September 2005. The items selected for testing were the top-selling item in each flavor segment; in addition, the most popular premium orange juice (Tropicana) and premium apple juice (Copella) were included in the sample set.

5-*O*-Caffeoylquinic acid, procyanidin B2, (−)-epicatechin, and ellagic acid were purchased from Sigma-Aldrich (Poole, U.K.). Apigenin, quercetin-3-*O*-rutinoside, quercetin-3-*O*-glucoside, phloretin-2′-*O*-glucoside, neohesperidin, narirutin, ferulic acid, caffeic acid, sinapic acid, and *p*-coumaric acid were obtained from AASC Ltd. (Southampton, U.K.). Cyanidin-3-*O*-glucoside, malvidin-3-*O*-glucoside, and *trans*-resveratrol were purchased from Extransynthese (Genay, France). Methanol and acetonitrile were obtained from Rathburn Chemicals (Walkburn, Peebleshire, U.K.). Formic acid was obtained from Fisher Scientific (Loughborough, U.K.). Benzyl mercaptan was purchased from Lancaster Synthesis (Morecombe, U.K.).

trans-Resveratrol-3-*O*-glucoside was isolated from roots of *Polygonum cuspidatum*. Two kilograms of woody roots collected locally were chopped into small pieces and extracted with 80% aqueous methanol. The methanol extract was reduced to the aqueous phase kept at room temperature for 12 h. after which precipitated material was removed by filtration. Diethyl ether was added to the aqueous filtrate, which was kept at 4 °C overnight. Crude resveratrol glucoside crystallized in the aqueous layer. The light brown crystals were dissolved in methanol, and charcoal was used to remove colored impurities. Further recrystallization from aqueous methanol yielded 1.4 g of pure *trans*-resveratrol-3-*O*-glucoside as colorless needles. The structure was rigorously determined by ^{1}H and ^{13}C NMR.

HPLC with Photodiode Array and MS^2 Detection. All fruit juice samples were centrifuged at 13000*g* for 15 min at 4 °C before being passed through a 0.4 μm filter (Whatman). Samples were analyzed on a Surveyor HPLC system comprising a HPLC pump, a photodiode array (PDA) detector, scanning from 250 to 700 nm, and an autosampler cooled to 4 °C (Thermo Finnigan, San Jose, CA). Separations were carried out using a 250 × 4.6 mm i.d. 4 μm Synergi Max-RP column maintained at 40 °C (Phenomenex, Macclesfield, U.K.) and eluted with a 60 min gradient of 5−40% acetonitrile in 1% formic acid at a flow rate of 1 mL/min for all analyses except *trans*-resveratrol-3-*O*-glucoside, which used a 5−30% gradient. The PDA detector was used to monitor flavan-3-ols at 280 nm, *trans*-resveratrol-3-*O*-glucoside at 310 nm, hydroxycinnamates at 325 nm, flavonols at 365 nm, and anthocyanins at 520 nm. After passing through the flow cell of the diode array detector, the column eluate was split, and 0.3 mL/min was directed to a LCQ DecaXP ion trap mass spectrometer fitted with an electrospray interface (Thermo Finnigan). Analyses utilized the negative ion mode for hydroxycinnamates, flavan-3-ols, flavonols, and flavanones. Positive ionization was used for anthocyanins. Analyses were carried out using full-scan, data-dependent MS^2 scanning from *m*/*z* 150 to 2000. Analysis of *trans*-resveratrol-3-*O*-glucoside was with selected reaction monitoring in negative ionization mode using the *m*/*z* 389 molecular ion to confirm the identity of the absorbance peak. Capillary temperature was 350 °C, sheath gas and auxiliary gas were 60 and 10 units, respectively, and the source voltage was 4 kV for negative ionization and 1 kV for positive ionization.

Identifications are based on cochromatography with authentic standards, when available. Absorbance spectra and mass spectra, using MS^2, were used to confirm the identity of compounds previously reported in the literature. Quantitative estimates are based on calibrations generated by the PDA detector using the compound under study when a standard was available—see Materials. When this was not possible, a closely related derivative was used instead. For instance, all anthocyanins, except malvidin glycosides, were quantified by reference to cyanidin-3-glucoside, whereas hydroxycinnamate derivatives, such as 3-*O*-*p*-coumarylquinic acid and coutaric acid, were quantified by reference to the appropriate glycone. As a consequence, some of the estimates are semiquantitative. In all instances the standard curve of reference compounds ranged from 2 to 500 ng.

Procyanidin Analysis after Thiolysis. Thiolytic degradation was carried out according to the method by Alonso-Salces et al. (*18*). Freeze-dried juice aliquots (500 μL) were reacted with 400 μL of benzyl mercaptan (5% in methanol, v/v) and 200 μL of acidified methanol (3.3% HCl, v/v) at 40 °C for 30 min, vortexed every 10 min. The reaction mix was immediately cooled in an ice bath for 5 min. Samples were then filtered and stored at −80 °C prior to analysis by HPLC-MS^2, as described above but using a gradient of 1% aqueous formic acid (A) in acetonitrile (B) programmed as follows: 0 min, 3% B; 5 min, 9% B; 15 min, 16% B; 50 min, 55% B; 55 min, 55% B. The flow rate was 1 mL/min, and a fluorometric detector was also used with excitation at 280 nm and emission at 310 nm.

Total Phenolic Content. The total phenol contents of fruit juices and juice drinks were determined in triplicate in gallic acid equivalents (GAE) using the Folin−Ciocalteu method (*19*).

Antioxidant Assays. The antioxidant activity of juice was measured using two antioxidant assays. The automated oxygen radical absorbing

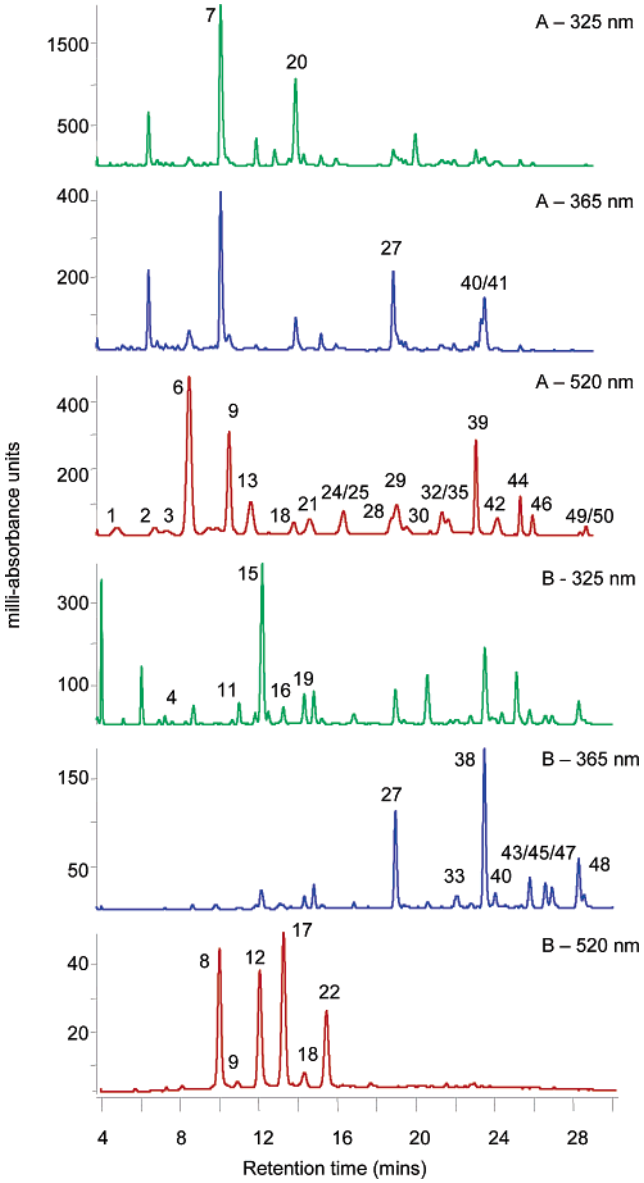

Figure 1. HPLC absorbance traces at 325, 365, and 520 nm of (**A**) purple grape juice and (**B**) a cranberry juice drink. Analysis was carried out using a 250 × 4.6 mm i.d. 4 μm Synergi RP-Max column maintained at 40 °C and eluted with a 60 min gradient of 5–40% acetonitrile in water containing 1% formic acid at a flow rate of 1 mL/min.

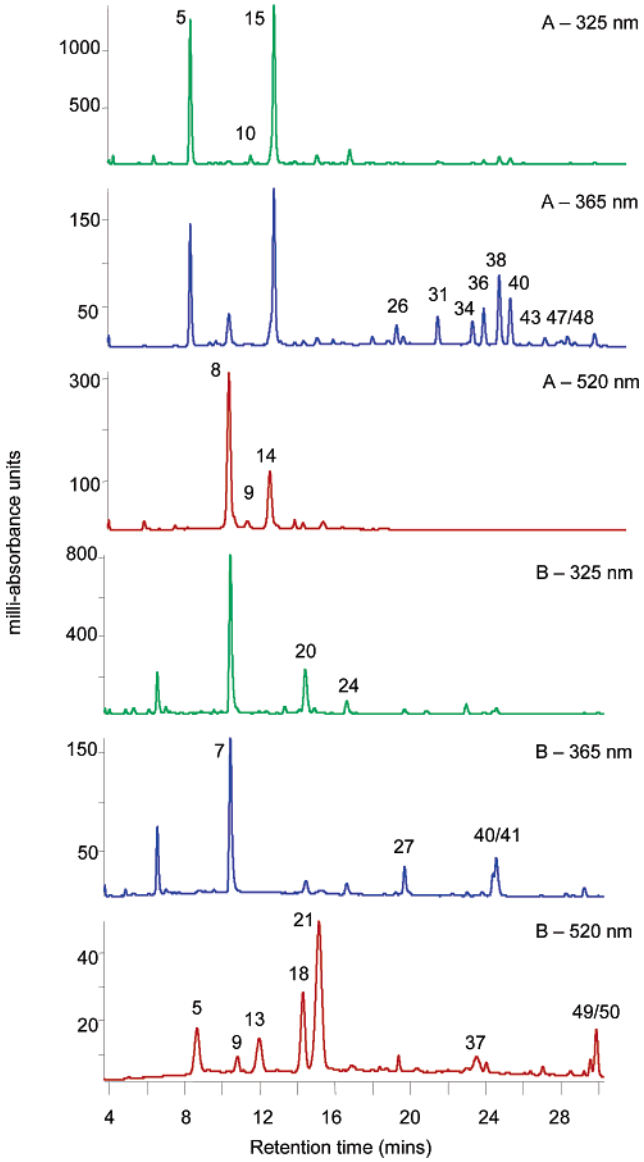

Figure 2. HPLC absorbance traces at 325, 365, and 520 nm of (**A**) a pomegranate juice drink and (**B**) red grape juice. For analysis conditions see the caption of **Figure 1**.

capacity (ORAC) assay was carried out as described by Huang et al. (*20*) with the data expressed as millimoles of Trolox equivalents (TE)-per liter of juice. The ferric reducing antioxidant power (FRAP) assay utilized the procedures of Benzie and Strain (*21*) with activity expressed as millimoles of Fe^{2+} per liter of juice.

RESULTS

HPLC-PDA-MS^2 Analysis. The wide range of compounds found in the different juice samples as determined by HPLC-PDA-MS^2 is illustrated in **Figures 1**−**5**. To simplify the analysis, only peaks that represented >3% of the main compound were quantified. For comparison, the analyses of the juice samples have been separated into three groups.

Anthocyanin-Containing Products. The anthocyanin-containing products were the purple grape, cranberry, pomegranate, and red grape samples. Purple grape juice contained a large number of anthocyanins, which prevented many of the flavan-3-ols detected by MS^2 from being quantified using the response of the PDA detector. This was due to the absorbance spectrum of the anthocyanins obscuring any peaks being quantified using the absorbance trace at 280 nm. However, the flavan-3-ols were quantified using a method based on thiolysis degradation (*18*).

The compounds with retention times ranging from 4 to 30 min are shown in **Figures 1** and **2**, and the 53 compounds identified and quantified are listed in **Table 2**. For structures, see Crozier et al. (*9*). The identities of the anthocyanins were based on cochromatography with authentic standards, elution profile, their absorbance spectra, mass spectrometric information, and published data. The six anthocyanins identified in the cranberry drink were in agreement with a previous paper (*22*). The pomegranate sample contained only three anthocyanins in quantifiable amounts (**Figure 2A**, 520 nm), clearly different from the juices analyzed by Gil et al. (*23*), which contained delphinidin anthocyanins and substantial amounts of the ellagitannins including punicalagin. None of these compounds were detected in the Pomegreat pomegranate drink used in the present study. The red grape juice contained many of the documented anthocyanins reported in red wine (*24*). The purple grape juice was made from Concord grapes, and the anthocyanin content

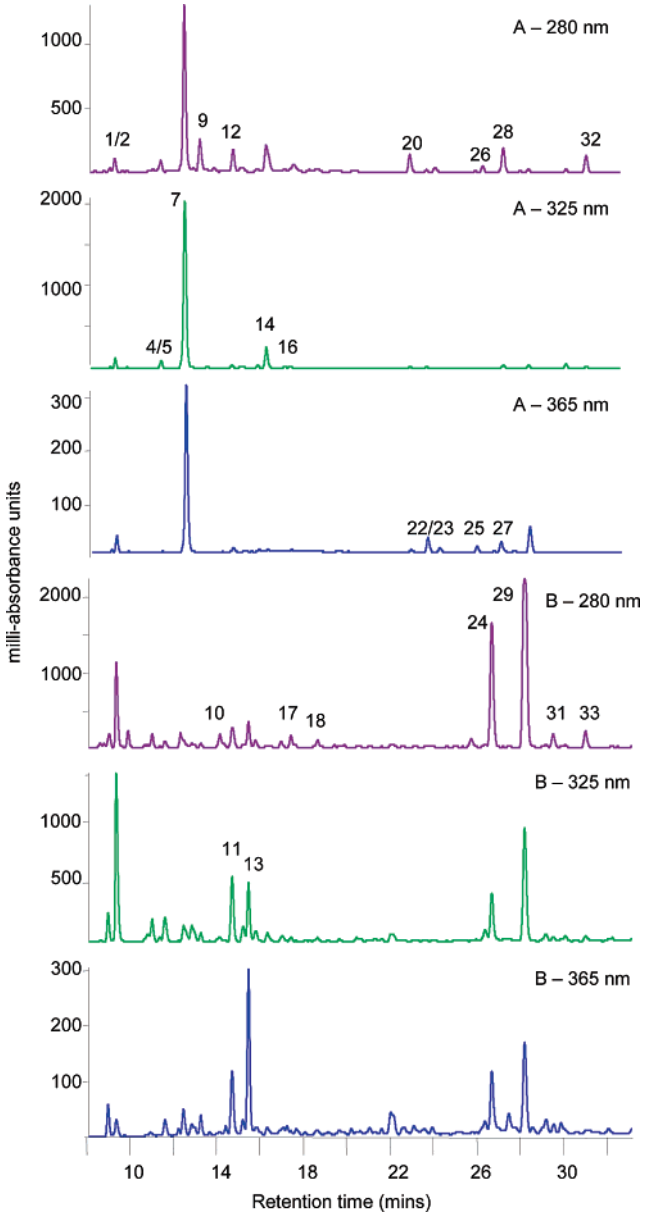

Figure 3. HPLC absorbance traces at 280, 325, and 365 nm of (**A**) apple juice and (**B**) grapefruit juice. For analysis conditions see the caption of **Figure 1**.

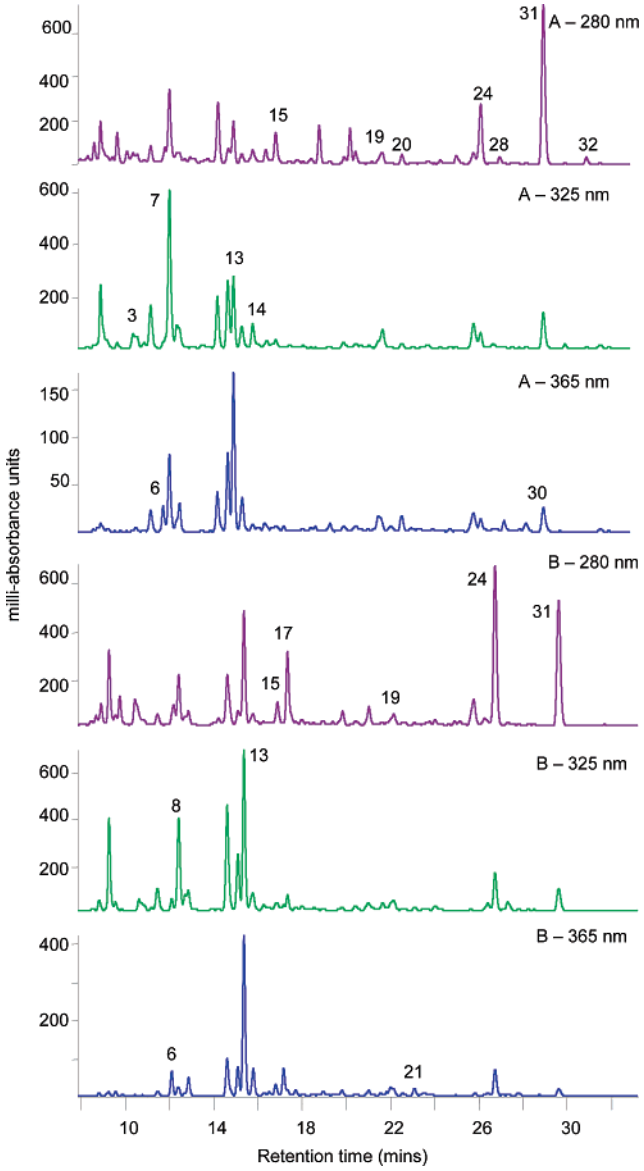

Figure 4. HPLC absorbance traces at 280, 325, and 365 nm of (**A**) tropical juice and (**B**) orange juice. For analysis conditions see the caption of **Figure 1**.

is in good agreement with a previously published paper (*25*). The other major group of phenolics found in these juices comprised the hydroxycinnamates, flavonols, and flavan-3-ols, and their identification by MS^2 and retention profiles (**Table 2**) are similar to those described in detail by Monagas et al. (*26*).

Apple- and Citrus-Derived Juices. The absorbance HPLC traces obtained in the apple- and citrus-derived juices are illustrated in **Figures 3** and **4**, and the 36 compounds identified and quantified are listed in **Table 3**. Two types of apple juice were analyzed, clear and cloudy. The traces illustrated in **Figure 3A** were obtained with the cloudy juice. For reasons of space, the 520 nm trace showing the presence of cyanidin-3-*O*-galactoside (peak 2 in **Table 3**), the sole anthocyanin, is not illustrated. Two types of orange juice were analyzed. One was made from a concentrate and the other from pressed fruit. The traces in **Figure 4B** were obtained with the juice prepared from a concentrate.

The main phenolic compounds in apple juice were the hydroxycinnamate 5-*O*-caffeoylquinic acid (peak 7, **Figure 3A**, 325 nm), which was also a significant component of tropical juice (**Figure 3B**, 325 nm; **Table 3**). The phenolic profiles of both apple juices were similar to those found by Marks et al. (*27*) in an investigation of phenolics in cider apples. Orange juice contained high levels of the flavone apigenin-6,8-*C*-diglucoside (peak 13) and two flavanones, naringenin-7-*O*-rutinoside (narirutin) (peak 24) and hesperetin-7-*O*-rutinoside (hesperidin) (peak 31) (**Figure 4B**, 280 nm; **Table 2**). These three compounds were also major components of tropical juice (**Figure 4A**, 280 nm; **Table 2**), confirming the manufacturer's claim that it was made from apple and orange juices. Grapefruit juice also contained apigenin-6,8-*C*-diglucoside (peak 13) and naringenin-7-*O*-rutinoside (peak 24) in significant amounts (**Figure 3B**, 280 nm; **Table 2**). However, the main compound was another flavanone, naringenin-7-*O*-neohesperidoside (naringin) (peak 29, **Figure 3B**, 280 nm), which is responsible for the bitter taste of this fruit. Mass spectrometric data were of great importance in the identification of these and other flavones and flavanones in the juices, with a study of the flavonoid

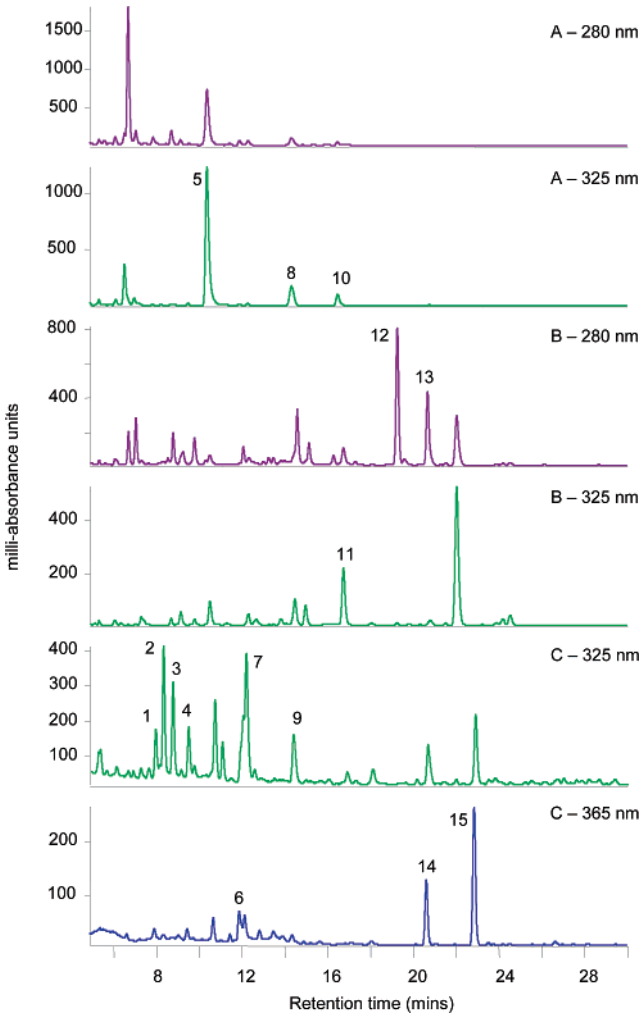

Figure 5. HPLC absorbance traces at 280 and 365 nm of (**A**) white grape juice, (**B**) pineapple juice, and (**C**) tomato juice. For analysis conditions see the caption of **Figure 1**.

glycosides in bergamot juice by Gattuso et al. (*28*) being an important reference source.

Other Products. The third group comprised white grape juice, pineapple juice, and tomato juice, which are linked only in that they contained the fewest phenolic compounds and the lowest overall concentration of total phenolics (**Table 4**). The major peaks in the 280 nm trace obtained with pineapple juice (**Figure 5B**) are sinapyl-glutathione and glutamyl-*S*-sinapyl-cysteine conjugates (peaks 12 and 13) (*29*), whereas a caffeoylquinic acid (peak 11) appears in the 325 nm trace (**Figure 5B**). The lack of information on the quantities of phenolics in pineapples and juice has been commented on in a review paper (*30*). The tomato juice contained a range of hydroxycinnamates, the major one being 5-*O*-caffeoylquinic acid (peak 7) (**Figure 5C**, 325 nm). The main flavonol in tomato juice was quercetin-3-rutinoside (peak 13) (**Figure 5C**, 365 nm). The major compounds in white grape juice were the hydroxycinnamate tartaric acid conjugates and caftaric, coutaric, and fertaric acids (peaks 5, 8, and 10) (**Figure 5A**, 325 nm).

Stilbene Analysis. The only stilbene to be detected was *trans*-resveratrol-3-*O*-glucoside, which was present in low concentrations in purple grape juice (0.31 ± 0.01 μmol/L) and red grape juice (0.29 ± 0.01 μmol/L).

Proanthocyanidin Analysis. The analysis involved acid-catalyzed depolymerization with benzyl mercaptan, a procedure known as thiolysis, which releases the terminal unit of the proanthocyanidins as free flavan-3-ols and the extension unit as benzyl thioether adducts. These products were identified and quantified using reversed phase HPLC with fluorescence detection. By calculating the ratio between total units (terminal units plus extension units) and terminal units, the mean degree of polymerization can be derived. This method can also be used to calculate the mass of total procyanidins present in the sample by summing all catechin equivalents detected after thiolysis and subtracting the amount of native catechins derived by HPLC prior to thiolysis. Only the samples in which (+)-catechin and (−)-epicatechin were present were analyzed by this method (see **Tables 2** and **3**). Again, the products that had the highest levels were purple grape juice and cloudy apple juice, with 434 ± 13 and 445 ± 3 μmol/L and respective degrees of polymerization of 2.3 and 3.9.

Total Phenolics and Antioxidant Activity. The total phenolics were measured in two ways; with the Folin−Ciocalteu assay and by combining the estimates of the individual phenolics obtained by HPLC-PDA (**Figure 6**). The Folin−Ciocalteu assay revealed that purple grape juice with 7.5 ± 0.15 mmol/L contained the highest concentration of phenolics, with cloudy apple juice, which contained 6.0 ± 0.08 mmol/L, ranked second. The lowest concentrations were detected in white grape juice (0.9 ± 0.05 mmol/L) and clear apple juice (1.7 ± 0.02 mmol/L). As in an earlier study with red wines (*7*), the Folin−Ciocalteu-based estimates were substantially higher than the HPLC-derived measurements of phenolic compounds. Nevertheless, the two estimates for the different juices correlated well ($p < 0.001$, $r_s = -0.87$).

There was broad agreement between the data obtained with the FRAP and ORAC antioxidant assays ($p < 0.004$, $r_s = -0.74$), which showed that the purple grape juice contained the most antioxidant activity and the white grape, clear apple, pineapple, and tomato juices the least. Relative to the other samples the cloudy apple and tropical juice exhibited enhanced activity in the FRAP compared to the ORAC assay (**Figure 6**).

DISCUSSION

The 13 juices and juice drinks had widely different phenolic contents as revealed in the data presented in **Tables 2**−**5**. Total phenolics measured by the Folin−Ciocalteu assay varied 8.6-fold, and 19-fold when measured by HPLC, whereas there was a 15.2-fold difference in ORAC antioxidant capacity and a 7-fold difference in FRAP antioxidant activity. The purple grape juice contained the highest levels of phenolics and antioxidants. Other high-ranking juice samples in this regard included the cloudy apple juice, pomegranate juice drink, and cranberry juice drink. Products low in phenolics and antioxidants were the clear apple, white grape, pineapple, and tomato juices.

The purple grape juice, which is made from Concord grapes (*Vitis labrusca*) that have a thicker skin and larger seeds than the grapes of *Vitis vinifera*, is of interest because it not only had high overall levels of phenolics and antioxidants, but also it contained the largest number of individual phenolic compounds—26 were identified, with 12 being present in concentrations of >10 μmol/L. In contrast, red grape juice contained 16 identifiable peaks with only 2, caftaric acid and malvidin-3-*O*-glucoside attaining levels >10 μmol/L (**Table 2**). At the other end of the scale only three phenolics were identified in white grape juice with caftaric acid being the sole component present in excess of 10 μmol/L (**Table 4**). Contrary to these white grape juice findings, our laboratory has analyzed methanolic extracts of *V. labrusca* white grapes, variety Niagara, using the same techniques as employed in thecurrent study, and, with the

Table 2. HPLC-MS^2-Based Identifications of Phenolics in Cranberry, Purple Grape, Red Grape, and Pomegranate Juices[a]

peak	t_R (min)	[M − H]$^-$ (*m*/*z*)	MS^2 (*m*/*z*)	compound	cranberry	purple grape	red grape	pomegranate
1	4.9	627$^+$	303	delphinidin-3,5-*O*-diglucoside	nd	7.0	nd	nd
2	7.0	611$^+$	287	cyanidin-3,5-*O*-diglucoside	nd	5.3	nd	nd
3	7.5	641$^+$	317	petunidin-3,5-*O*-diglucoside	nd	3.4	nd	nd
4	8.5	465$^+$	303	delphinidin-3-*O*-glucoside	nd	84.3	3.6	nd
5	8.8	325	163	coumaric acid hexose conjugate	4.5	nd	nd	nd
6	8.9	353	191	3-*O*-caffeoylquinic acid	nd	nd	nd	38.3
7	10.4	311	179	caftaric acid	nd	65.2	24.6	nd
8	10.5	449	287	cyanidin-3-*O*-galacoside	6.2	nd	nd	50.1
9	10.9	449$^+$	287	cyanidin-3-*O*-glucoside	0.9	45.1	1.3	3.4
10	11.1	337	163	3-*O*-*p*-coumaroylquinic acid	nd	nd	nd	3.4
11	11.2	341	179	caffeic acid hexose conjugate	2.6	nd	nd	nd
12	12.0	435	287	cyanidin-3-*O*-arabinoside	6.7	nd	nd	nd
13	12.1	479$^+$	317	petunidin-3-*O*-glucoside	nd	17.4	2.8	nd
14	12.2	419	287	cyanidin pentose conjugate	nd	nd	nd	21.5
15	12.3	353	191	5-*O*-caffeoylquinic acid	25.4	nd	nd	88.1
16	12.7	865	577	procyanidin trimer	1.8	nd	nd	nd
17	14.2	463	301	peonidin-3-*O*-galactoside	8.4	nd	nd	nd
18	14.4	463$^+$	301	peonidin-3-*O*-glucoside	1.3	7.6	5.2	nd
19	14.5	289	245	(−)-epicatechin	36.3	nd	nd	nd
20	14.6	295	163	coutaric acid	nd	96.3	6.9	nd
21	15.1	493$^+$	331	malvidin-3-*O*-glucoside	nd	11.5	12.4	nd
22	15.5	433	301	peonidin-3-*O*-arabinoside	4.9	nd	nd	nd
23	16.7	507	303	delphinidin-3-*O*-acetylglucoside	nd	13.4	nd	nd
24	16.9	325	193	fertaric acid	nd	nd	1.7	nd
25	17.1	773$^+$	303	delphinidin-*p*-coumaroyl diglucoside	nd	8.8	nd	nd
26	18.6	625	301	quercetin dihexose conjugate	nd	nd	nd	2.6
27	19.2	479	317	myricetin-hexose conjugate	17.5	39.8	5.3	nd
28	19.6	491$^+$	287	cyanidin-3-*O*-acetyl glucoside	nd	7.2	nd	nd
29	19.9	773$^+$	303	delphinidin-3-*O*-*p*-coumaroyl-5-*O*-diglucoside	nd	20.1	nd	nd
30	20.4	521$^+$	317	petunidin-3-*O*-acetylglucoside	nd	4.9	nd	nd
31	20.7	595	301	quercetin hexose pentose conjugate	nd	nd	nd	4.0
32	22.3	757$^+$	287	cyanidin-3-*O*-*p*-coumaroyl-5-*O*-diglucoside	nd	7.4	nd	nd
33	22.4	449	317	myricetin-3-*O*-xyloside	3.3	nd	nd	nd
34	22.5	609	301	quercetin rutinoside conjugate	nd	nd	nd	3.5
35	22.7	787$^+$	317	petunidin-3-*O*-*p*-coumaroyl-5-*O*-diglucoside	nd	4.5	nd	nd
36	23.1	609	301	quercetin-3-*O*-rutinoside	nd	nd	nd	5.1
37	23.7	535	331	malvidin-3-*O*-acetylglucoside	nd	nd	1.7	nd
38	23.9	463	301	quercetin-3-*O*-galactoside	30.1	nd	nd	13.6
39	24.2	611$^+$	303	delphinidin-3-*O*-*p*-coumaroylglucoside	nd	15.4	nd	nd
40	24.4	463	301	quercetin-3-*O*-glucoside	3.0	11.7	3.3	9.0
41	24.6	477	301	quercetin-3-*O*-glucuronide	nd	25.0	7.9	nd
42	25.3	771$^+$	301	peonidin-3-*O*-*p*-coumaroylglucoside	nd	6.4	nd	nd
43	26.2	433	301	quercetin-3-*O*-xyloside	6.0	nd	nd	1.4
44	26.5	595$^+$	287	cyanidin-3-*O*-*p*-coumaroylglucoside	nd	6.9	nd	nd
45	26.9	433	301	quercetin-3-*O*-arabinoside	5.4	nd	nd	nd
46	27.2	625$^+$	317	petunidin-3-*O*-*p*-coumaroylglucoside	nd	3.9	0.7	nd
47	27.4	433	301	quercetin pentose conjugate	4.8	nd	nd	1.9
48	28.8	447	301	quercetin rhamnoside	10.8	nd	nd	2.4
49	29.6	609$^+$	301	peonidin-3-*O*-*p*-coumaroylglucoside	nd	1.1	0.7	nd
50	30.0	639$^+$	331	malvidin-3-*O*-*p*-coumaroylglucoside	nd	2.6	1.9	nd
51	30.6	317		myricetin	16.1	nd	nd	nd
52	31.5	435	273	phloretin-2′-*O*-glucoside	nd	nd	nd	11.0
	39.7	301	179	quercetin	30.6	nd	1.8	4.6
				subtotal (HPLC-PDA)	226.6	522.2	81.8	263.9
				flavan-3-ols by thiolysis	134	434	10	172
				total, including thiolysis[b]	325 ±3	968 ± 11	92 ± 1	436 ± 5

[a] Quantifications based on HPLC-PDA data (see **Figures 1** and **2**). Data expressed as mean values in μmol/L ($n = 3$). Standard deviations were typically <5% of the mean; [M − H]$^-$ negatively charged molecular ion; $^+$ indicates positively charged molecular ion; nd, not detected. [b] For total, including thiolysis–HPLC-PDA measurements of flavan-3-ols were not incorporated into the value.

exception of being devoid of anthocyanins, found them to have a phenolic content similar to that of purple Concord grapes (data not shown). White grape juice made from Niagara grapes is not available commercially in the United Kingdom.

The overall concentration of phenolics in the purple grape juice measured by Folin−Ciocalteu assay was 7.5 ± 0.15 mmol/L (**Figure 6**). Values obtained for red wines in an earlier study with this assay ranged from 18.6 ± 0.10 mmol/L for a Bulgarian Cabernet Sauvignon to 7.7 ± 0.09 mmol/L for a Valpolicella and 6.5 ± 0.03 mmol/L for a Beaujolais (*7*). Purple grape juice has also been shown to have a vasodilation capacity (*31*) similar to that of red wines investigated by Burns et al. (*7*). The purple grape juice, therefore, in terms of both the number of phenolics it contains and the overall level of phenolics, broadly equates with a light red wine. This is not the case with either the red grape juice or the white grape juice, both of which contained fewer phenolics (see **Table 2**) and had a lower concentration of total phenolics at 2.7 ± 0.09 and 0.9 ± 0.05 mmol/L, respectively (**Figure 6**).

Table 3. HPLC-MS^2-Based Identifications of Phenolics in Cloudy (1) and Clear (2) Apple Juice, Grapefruit Juice, Orange Juices Prepared from Concentrate (1) and Squeezed Fruit (2), and Tropical Fruit Juice[a]

peak	t_R (min)	$[M-H]^-$ (*m*/*z*)	MS^2 (*m*/*z*)	identity	apple (1)	apple (2)	grapefruit	orange (1)	orange (2)	tropical
1	9.0	577	451, 425, 407	procyanidin dimer	17.4	nd	nd	nd	nd	nd
2	9.3	449$^+$	287	cyanidin-3-*O*-galactoside	1.2	nd	nd	nd	nd	nd
3	10.8	355	193	ferulic acid conjugate	nd	nd	8.3	nd	nd	nd
4	11.1	337	163	3-*O*-*p*-coumaroylquinic acid	nd	1.7	nd	nd	nd	nd
5	11.3	341	179	caffeic acid hexose conjugate	7.7	nd	nd	nd	nd	nd
6	11.8	771	609, 463, 301	quercetin glucosyl-rutinoside	n.d	nd	n.d	5.4	2.0	0.9
7	12.1	353	191,179	5-*O*-caffeoylquinic acid	140.4	117.7	nd	n.d	n.d	39.0
8	12.8	609	519, 489, 399	luteolin-6,8-*C*-diglucoside	n.d	nd	nd	3.5	3.5	4.0
9	13.1	577	451, 425, 407	procyanidin dimer B2	3.9	nd	nd	nd	nd	nd
10	14.0	595	287	eriodictyol-7-*O*-rutinoside	n.d	nd	5.7	n.d	n.d	nd
11	14.5	355	193	ferulic acid conjugate	n.d	nd	31.0	nd	nd	nd
12	14.7	289	245,205	(–)-epicatechin	81.7	56.1	nd	nd	nd	nd
13	15.0	593	503, 473, 383	apigenin-6,8-*C*-diglucoside	n.d	nd	13.5	18.6	17.4	7.1
14	15.9	337	173	4-*O*-*p*-coumaroylquinic acid	15.1	20.2	nd	n.d	n.d	4.6
13	16.5	623	533, 503, 413	chrysoeriol-6,8-*C*-diglucoside	nd	nd	nd	2.4	3.4	1.3
14	17.0	337	173	*p*-coumaroylquinic acid	nd	3.0	n.d	n.d	n.d	nd
15	17.3	741	579	narirutin hexose conjugate	nd	nd	4.8	1.3	1.0	nd
16	18.5	741	579	narirutin hexose conjugate	nd	nd	2.9	n.d	n.d	nd
17	21.8	595	287	eriodictyol-7-*O*-neohesperidoside	nd	nd	nd	2.0	4.4	3.1
18	22.7	583	289, 245, 205	catechin conjugate	38.2	nd	nd	nd	nd	8.6
19	23.0	609	301	quercetin-3-*O*-rutinoside	nd	nd	nd	0.9	2.1	nd
20	23.9	463	301	quercetin-3-*O*-galactoside	6.2	5.2	nd	nd	nd	nd
21	24.2	463	301	quercetin-3-*O*-glucoside	1.4	1.3	nd	nd	nd	nd
22	26.3	579	271	naringenin-7-*O*-rutinoside	nd	nd	66.0	24.6	6	10.6
23	26.5	433	301	quercetin pentose conjugate	2.0	1.5	nd	nd	nd	nd
24	27.3	583	289, 245, 205	catechin conjugate	13.7	nd	n.d	nd	nd	nd
25	27.4	433	301	quercetin pentose conjugate	4.7	2.6	n.d	nd	nd	nd
26	27.6	567	273	phloretin -2′-*O*-(2″-*O*-xylosyl)glucoside	16.7	13.5	nd	nd	nd	2.1
27	28.2	579	459, 313, 271	naringenin-7-*O*-neohesperidoside	nd	nd	138	nd	nd	nd
28	28.4	447	301	quercetin rhamnoside	9.0	3.3	nd	nd	nd	1.8
29	29.5	609	301	hesperetin-7-*O*-rutinoside	n.d	nd	9.0	18.6	45.8	26.2
30	31.2	435	273	phloretin-2′-*O*-glucoside	25.8	33.5	nd	nd	nd	2.6
31	31.5	609	301	hesperetin-7-*O*-neohesperidoside	nd	nd	7.4	nd	nd	nd
32	36	301	301	ellagic acid	nd	nd	2.1	nd	nd	nd
33	39.6	593	285	isosakuranetin-7-*O*-rutinoside	nd	nd	3.2	3.3	3.3	1.4
34	41.0	593	285	isosakuranetin-7-*O*-neohesperidoside	nd	nd	10.9	nd	nd	nd
				subtotal HPLC-PDA	385	260	303	81	89	113
				flavan-3-ols by thiolysis	445					11
				total, including thiolysis[b]	675 ± 4	260 ± 3	303 ± 2	81 ± 1	89 ± 1	115 ± 1

[a] Quantifications based on HPLC-PDA data (see **Figures 3** and **4**). Data are expressed as mean values in μmol/L ($n = 3$). Standard deviations were typically <5% of the mean; $[M-H]^-$ negatively charged molecular ion; $^+$ indicates positively charged molecular ion; nd, not detected. [b] For total, including thiolysis, if flavan-3-ols were measured by thiolysis, the HPLC-PDA values for flavan-3-ols were not incorporated into the value.

Table 4. HPLC-MS^2-Based Identifications of Phenolics in White Grape, Pineapple, and Tomato Juices[a]

peak	t_R (min)	$[M-H]^-$ (*m*/*z*)	MS^2 (*m*/*z*)	compound	white grape juice	pineapple juice	tomato juice
1	8.0	353	191, 179	3-*O*-caffeoylquinic acid	nd	nd	2.5
2	8.4	341	179	caffeic acid hexose conjugate	nd	nd	7.6
3	8.8	325	163	coumaric acid hexose conjugate	nd	nd	4.7
4	9.5	341	179	caffeic acid hexose conjugate	nd	nd	2.8
5	10.5	311	179, 149	caftaric acid	41.2	nd	nd
6	11.8	771	609, 301	quercetin glucosyl-rutinoside	nd	nd	2.1
7	12.1	353	191, 179	5-*O*-caffeoylquinic acid	nd	nd	13.5
8	14.4	295	163	coutaric acid	8.0	nd	nd
9	14.5	179	135	caffeic acid	nd	nd	7.4
10	16.6	325	193	fertaric acid	3.6	nd	nd
11	17.0	353	173	4-*O*-caffeoylquinic acid	nd	11.4	nd
12	19.8	498	306	*S*-sinapylglutathione	nd	23.7	nd
13	20.6	441	249	*N*-L-glutamyl-*S*-sinapyl-L-cysteine	nd	16.1	nd
14	20.7	743	609,301	quercetin pentose rutinoside	nd	nd	4.6
15	22.9	609	301	quercetin-3-*O*-rutinoside	nd	nd	12.2
				total	53 ± 1	51 ± 1	57 ± 1

[a] Quantifications based on HPLC-PDA data (see **Figure 5**). Data are expressed as mean values in μmol/L ($n = 3$). Standard deviations were typically <5% of the mean; $[M-H]^-$ negatively charged molecular ion; nd, not detected.

Only the purple and red grape juices contained *trans*-resveratrol-3-*O*-glucoside, albeit at very low concentrations of 0.31 and 0.29 μmol/L, respectively. This compares with a combined concentration of the glucoside and the *cis*- and *trans*-isomers of the aglycone in red wines, which range from 4.3 to 88 μmol/L (*7*). In vitro studies suggest that resveratrol has a

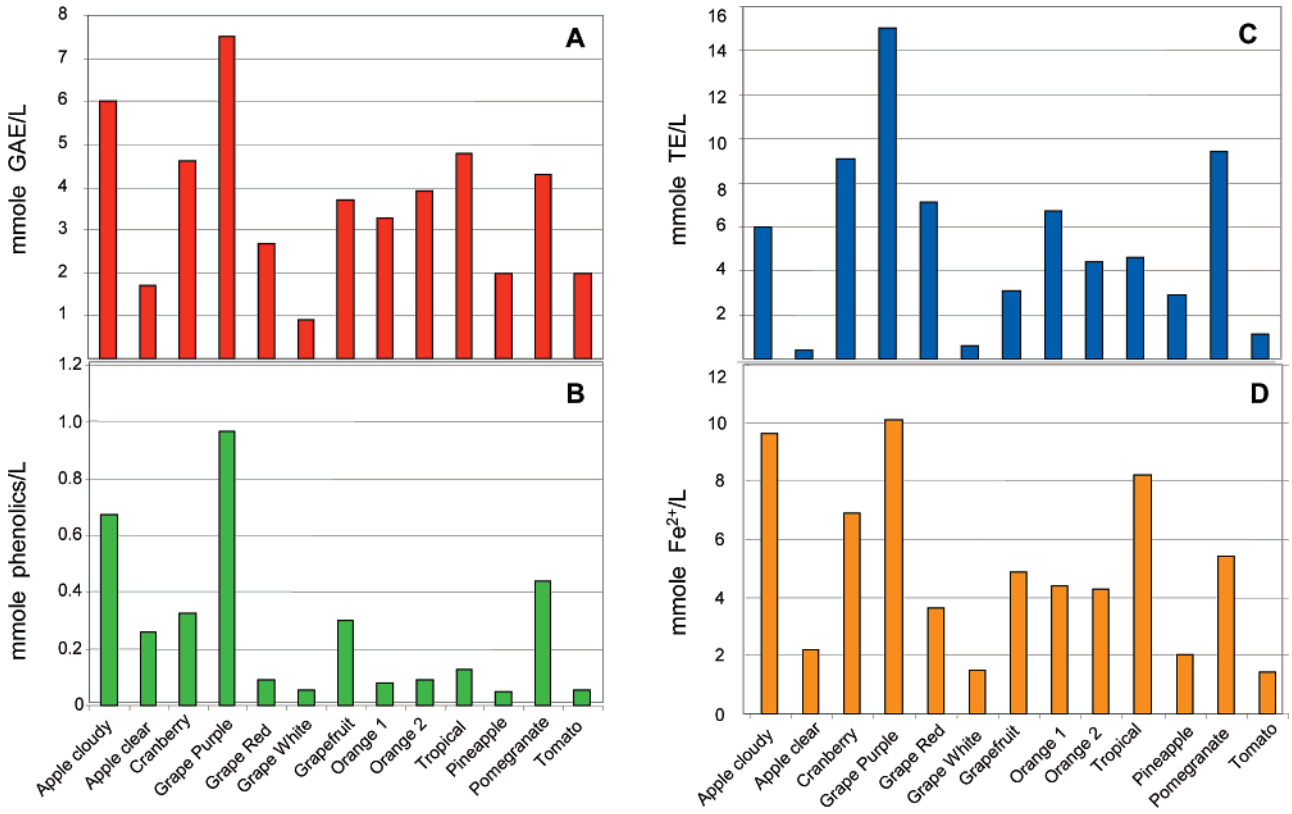

Figure 6. Estimates of total level of phenolics by (**A**) Folin–Ciocalteu and (**B**) HPLC and antioxidant activity measured with (**C**) ORAC and (**D**) FRAP assays.

Table 5. Summary of the Concentration of the Different Types of Flavonoids and Phenolics in 13 Commercial Fruit Juices[a]

juice	hydroxy-cinnamates	flavonols	flavan-3-ols	antho-cyanins	flavanones and flavones	hydroxy-chalcones
Ocean Spray Classic Cranberry	33 (***20***)	130 (***100***)	134 (***30***)	28 (***9***)	nd (***0***)	nd (***0***)
Welch's Purple Grape	162 (***99***)	76 (***58***)	434 (***98***)	296 (***100***)	nd (***0***)	nd (***0***)
Tesco Pure Pressed Red Grape	33 (***20***)	18 (***14***)	10 (***2***)	30 (***10***)	nd (***0***)	nd (***0***)
Pomegreat Pomegranate	130 (***80***)	48 (***37***)	172 (***39***)	75 (***25***)	nd (***0***)	11 (***23***)
Tesco Pure apple (clear)	143 (***88***)	14 (***11***)	56[b] (***13***)	nd (***0***)	nd (***0***)	47 (***100***)
Copella Apple (cloudy)	163 (***100***)	23 (***18***)	445 (***100***)	1.2 (***0.4***)	nd (***0***)	43 (***91***)
Tesco Pure Grapefruit	39 (***24***)	2.1 (***2***)	nd (***0***)	nd (***0***)	242 (***100***)	19 (***40***)
Tesco Value Pure Orange (concentrate)	nd (***0***)	6.2 (***5***)	nd (***0***)	nd (***0***)	52 (***21***)	22 (***47***)
Tropicana Pure Premium Smooth Orange (squeezed)	nd (***0***)	4.1 (***3***)	nd (***0***)	nd (***0***)	64 (***26***)	21 (***45***)
Tropicana Pure Premium Tropical Fruit	44 (***27***)	2.7 (***2***)	11 (***2***)	nd (***0***)	53 (***22***)	4.7 (***10***)
Tesco Pure Pressed White Grape	53 (***33***)	nd (***0***)	nd (***0***)	nd (***0***)	nd (***0***)	nd (***0***)
Tesco Pure Pineapple	51 (***31***)	nd (***0***)	nd (***0***)	nd (***0***)	nd (***0***)	nd (***0***)
Del Monte Premium Tomato	38 (***23***)	19 (***15***)	nd (***0***)	nd (***0***)	nd (***0***)	nd (***0***)

[a] Data are expressed as μmol/L with figures in bold italic in parentheses representing values as a percent of the highest concentration for each class of compound. nd, not detected. [b] No thiolysis, calculated by HPLC-PDA only.

wide range of biological properties including cardioprotection, anticancer activity, anti-inflammatory effects, estrogenic/anti-estrogenic properties, and modulation of cellular signal transduction pathways (*32*, *33*), and there is much speculation that it is the active agent responsible for the reported reduction in the incidence of heart disease associated with red wine consumption. This is unlikely for a number of reasons (*34*). Resveratrol and its glucoside represent 0.4−6.6% of the total phenolics in red wine and are very minor constituents compared to other potentially protective components such as flavonols, anthocyanins, flavan-3-ols, gallic acid, and hydroxycinnamates (*7*). For humans to ingest stilbenes in amounts that are required to induce protective effects in animal models, they would have to consume >1000 L of red wine daily—not a practical proposition.

In view of the findings and of the *Kame* project indicating that long-term fruit and vegetable juice consumption provides protection against the onset of Alzheimer's disease (*17*), it is possible that the beneficial effects will be enhanced by the consumption of phenolic-rich juices containing an array of individual phenolic compounds. In this regard, examination of the summary of phenolic levels in **Table 5** suggests that this could best be achieved by regular consumption of a variety of juices, namely, purple grape juice, which contains the highest levels of flavan-3-ols and procyanidins, anthocyanins, and hydroxycinnamates, a flavonol-rich cranberry juice drink, grapefruit juice, which contains flavanones in high levels, and cloudy apple juice, which is a good source of hydroxychalcones and flavan-3-ols. The volume of juices that should be consumed on a daily basis will be limited by one's total caloric needs and

total sugar intake, and in this regard the grape juices are a richer source than the other juice products sampled (**Table 1**). In the United Kingdom, the Department of Health recommends a daily calorie intake of ca. 2000 kcal for women and 2500 kcal for men, of which total sugars should comprise no more than 11% of the total (220−275 kcal) (*35*). Drinking 200 mL per day of any of the juices should be well within these limits provided there is not an excessive sugar intake from other dietary constituents. Consumption of juices as part of the meal may improve digestion and reduce the impact of sugars on dental health.

It should always be borne in mind that a full understanding of the role of dietary phenolics in disease prevention will remain unclear until their bioavailability is established. Further research is required to establish which of the flavonoids and phenolic compounds and their related metabolites gain access to appropriate cellular sites within the body to exert their biological effects. In the case of Alzheimer's disease this is likely to involve access through the blood−brain barrier. An investigation with rats has detected methyl and glucuronide metabolites in the brain of rats after acute ingestion of a high dose of (−)-epicatechin (*36*). Other studies have detected anthocyanins in rat brains after supplementation with berry and grape extracts. Rats fed a daily a blueberry extract for 8−10 weeks exhibited enhanced special learning and memory in the Morris water maze test, and trace levels of anthocyanins, which could not be quantified, were detected in the cerebellum, cortex, and hippocampus, regions of the brain important for learning and memory (*37*). Extremely low concentrations of anthocyanins were also detected in rat brains after the consumption of a blackberry extract for 15 days (*38*). It has also been reported that within 10 min of the feeding of a red grape extract to rats, unmetabolized trace quantities anthocyanins were detected in the brain (*39*). However, in the only study to date with humans, glucurono-, sulfo-, and methylated flavan-3-ol metabolites were identified in plasma, but they were not present in cerebrospinal fluid 3 h after the ingestion of 300 mL of green tea (*40*).

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