Salicylates in Foods

It was recently suggested that the intake of salicylates from food may have contributed to the decline in cardiovascular mortality in the United States. However, a normal mixed diet provides far too few salicylates to have an effect on disease risk.

Acetylsalicylic acid (2-acetoxybenzoic acid [Figure 1]) is the chemical name of the drug commonly known as aspirin. Acetylsalicylic acid (ASA) is effective as an antithrombotic drug in doses as low as 30 mg/day.[1-3] Intake of ASA is also associated with a decreased risk for colon cancer.[4,5] Because foods are thought to contain acetyl- and other salicylates,[6,7] Ingster and Feinleib suggest that the intake of salicylates in foods may have contributed to the decline in cardiovascular mortality in the United States.[7] If ASA is indeed present in foods, a diet rich in ASA might have antithrombotic and possibly anticarcinogenic effects.

Adverse effects of salicylates have been described in the literature. Although hypersensitivity reactions can occur after ingesting medications containing salicylates, improvement with a salicylate-free diet is unlikely.[8] Feingold[9] suggested that eliminating artificial food colors and flavors, as well as foods containing natural salicylates, would improve behavioral disturbances in children. Although this was not substantiated in at least two properly controlled trials,[10,11] belief in the efficacy of a salicylate-free diet endures.[12] Therefore, the salicylate content of foods continues to be of interest.

Data on the salicylate content of foods are scarce and contradictory (Table 1).[13-19] Salicylic acid and other salicylates, mainly methyl esters and glucosides, have been isolated from a variety of plants.[20] These salicylates can be hydrolyzed to the parent salicylic acid.[19] Consequently, food contents of total salicylic acid published include these to various extents. Robertson and Herrmann found the salicylate contents were 0.03–3 mg/kg in fruits and vegetables, and 3–39 mg/kg in herbs and spices.[15-18] Salicylate values reported by Swain et al. were much higher: 0.8–23.9 mg/kg in fruits and vegetables and 62–2180 mg/kg in herbs and spices.[13,14] Muller and Fugelsang reported salicylic acid concentrations ranging from 11.0 to 21.5 mg/dL in California and other red and white wines. Concentrations of salicylic acid in red wines were higher than in white.[21] Venema et al.[19] found salicylate contents comparable to the data of Robertson and Herrmann[15-18]: 0.03–0.87 mg/kg in fruits and vegetables and 0.48–28.4 mg/kg in herbs and spices. They[22] also did not confirm the high salicylate content of wine reported by Muller and Fugelsang.[21]

It is important to study the ASA contents of foods because of their possible antithrombotic effects.[1-3,6,7] Data on the acetylsalicylate contents of food are meager. Qualitative analyses by Swain[13] showed the presence of ASA in 37 of 56 foods studied. Acetylsalicylic acid is spontaneously hydrolyzed to salicylic acid in aqueous solutions.[23] Venema et al.[19] subsequently developed a mild extraction method for ASA in foods that prevented hydrolysis. Subsequently, they determined acetylsalicylate quantitatively in 30 foods reported to contain salicylates. Acetylsalicylate contents were lower than the limit of detection (0.02–0.2 mg/kg) in all foods studied.[19,22]

Differences in salicylate contents found in foods by various authors might be caused by differences in origin, processing, storage, or by differences in analytic methods. Swain[13,14] found a high natural variation amounting to 10-fold differences. Venema et al.[19] reported a much smaller variation. This excludes natural variation as a possible explanation for these discrepancies. Discrepancies in salicylate contents between extraction methods may arise through differences in the extent of liberation of matrix-bound salicylates. Although Venema et al.[19] used essentially the same extraction method as Swain,[13,14] salicylate contents in foods (Table 1) were found to be much lower. There is reason to believe that high-pressure liquid chromatography (HPLC) separation and UV detection as described by Swain and coworkers[13,14] was not specific enough, and that some other components may have coeluted with salicylic acid. In contrast, Venema and coworkers[19,22] used fluorescence detection, which is more specific than UV detection.

It was recently shown that urinary excretion is a valid indicator of the intake of pure salicylic and ASA.[24] Thus, urinary salicylate excretion might be an indicator of the amounts of bioavailable salicylates in the diet. Swain reported mean salicylate ex-

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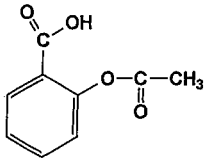
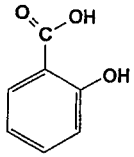


ACETYLSALICYLIC ACID



SALICYLIC ACID

Figure 1. Chemical structures of acetylsalicylic acid and salicylic acid.

cretion (±SEM) of 114 ± 6 mg/24 hours (825 ± 43 μmol/24 hours) in urines of healthy volunteers who consumed a diet providing 88 mg/day (637 μmol) of salicylates for 2 days, as recorded by food analysis. Mean salicylate excretions were 37 ± 4 mg/day (268 ± 29 μmol/24 hours) after a 2-day salicylate-free diet.[13,14] In contrast, Janssen et al.[24] found a median salicylate urinary excretion of only 1.4 mg/24 hours, with a range of 0.8–1.6 mg/24 hours (median 10 μmol, range 6–12) in 18 healthy subjects consuming a wide variety of diets. The high values noted by Swain and coworkers[13,14] may be explained by coelution of various compounds at the retention time of salicylate caused by an HPLC column that was probably too short, with a flow too high to obtain adequate separation.

Based on the urinary salicylate excretion data of the volunteers eating a wide variety of diets, their food records, and Venema's salicylate content of foods,[19,22,24] it was estimated that even purely vegetable diets provide less than 6 mg (43 μmol) of salicylates daily. If most of this was to be in the form of acetylsalicylate—which is unlikely[19,23]—these intakes would still be too low to affect disease risk. Ingster and Feinleib[7] have postulated that intake of dietary salicylates has increased over time since 1960, reaching 90 mg/day/person in 1960 and 125 mg/day/person in 1970. However, those calculations were based on salicylate contents published by Swain et al.,[14] which, in our view, overestimate dietary intake. We feel that true intakes of dietary

Table 1. Content of Salicylic and Acetylsalicylic Acid in Foods According to Various Authors[13–19]

	Content in Edible Part of Food (number of foods analyzed)*					
	Salicylic Acid (mg/kg)				Acetylsalicylic Acid (mg/kg; + = Present, − = Absent)	
Product	Swain† (333)	Hermann‡ (84)	Robertson§ (44)	Venema‖ (30)	Swain# (56)	Venema¶ (30)
Fruits, vegetables:						
Apples with peel	0.8–5.9	<1	0.04	<0.02	+	<0.02
Apricot, canned	14.2	<1	0.03	0.13		<0.02
Cucumber with peel	7.8**	<1–3		0.08	+	<0.02
Orange	23.9	<1	0.07	<0.02	+	<0.02
Herbs, spices:						
Cinnamon	152	10		23.80	+	<0.2
Curry powder, mild	2180			5.55		<0.2
Thyme	1830	11		12.8		<0.2
Beverages:						
Tea, brewed	30°°			0.42	+	<0.02
Wine, red	9			0.28–0.71	−	<0.02
Other:						
Honey	25–112			0.66	−	<0.2

* To convert values for salicylic acid from mg/kg to mmol/kg divide by 138.12; to convert values for acetylsalicylic acid from mg/kg to mmol/kg divide by 180.15.
†–¶ Methods used and their detection limits.
† HPLC with UV detection.
‡ Thin-layer chromatography preceded by hydrolysis for fruits and vegetables, detection limit 1 mg/kg; gas chromatography for herbs and spices, detection limit 1 mg/kg.
§ Spectrofluorometry.
‖–¶ HPLC with fluorescence detection, detection limit 0.02 mg/kg for fresh and 0.2 mg/kg for dried products.
Thin-layer chromatography.
** Without peel.
°° Bag.

salicylates in the United States are closer to 0–6 mg/day, and that the estimates of Ingster and Feinleib[7] are too high by almost two orders of magnitude.

It is concluded that a normal mixed diet provides only 0–6 mg of salicylates daily, and zero to almost no ASA. These amounts are probably too low to either positively affect disease risk or behavior in children.

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