REVIEW

A systematic review of salicylates in foods: Estimated daily intake of a Scottish population

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Several studies suggest that natural salicylates in plant-based foods may benefit health. However, large variation in published values of the salicylate content of foods means that relating dietary intakes to disease risk is problematical. Consequently, we have systematically reviewed the available literature using prescribed selection criteria. By combining these literature values with in-house analysis, we have constructed a food composition database describing median salicylate values for 27 different types of fruits, 21 vegetables, 28 herbs, spices and condiments, 2 soups and 11 beverages. Application of a validated food frequency questionnaire estimated median dietary intakes of 4.42 (range 2.90–6.27) and 3.16 (2.35–4.89) mg/day for Scottish males and females, respectively. Major dietary sources of salicylates were alcoholic beverages (22%), herbs and spices (17%), fruits (16%), non-alcoholic beverages including fruit juices (13%), tomato-based sauces (12%) and vegetables (9%). Application of the database to populations with differing dietary habits and disease risk profiles may provide further evidence for the role of dietary salicylates in the prevention of chronic diseases.

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1 Introduction

Associations between human dietary patterns and risk of chronic diseases are well documented. For example, high dietary intakes of fruits and vegetables are associated with reduced risk of developing heart disease and several common types of cancer [1, 2]. Numerous epidemiological and laboratory studies have suggested protective effects for a variety of nutritionally essential plant-based dietary components, such as fibre, antioxidant vitamins and trace elements [3]. However, plants also contain more than 100 000 secondary metabolites ranging from structurally simple alkaloids to more complex polyphenols and steroids. Many such non-nutritive compounds exert biological activities in mammalian systems that may have impact on health and disease risk [4].

There is a growing interest in the role of salicylic acid (2-hydroxybenzoic acid) (Fig. 1) as a dietary component with beneficial effects on human health. Potential anti-inflammatory, anti-atherogenic and anti-neoplastic mechanisms in human cells include the inhibition of cyclo-oxygenase 2 transcription, the stimulation of apoptosis, moderation of DNA mismatch repair and stimulation of antioxidant activity [5]. Moreover, several intervention studies indicate that regular intake of acetylsalicylic acid (aspirin) decreases the risk of developing cancer [6], rapid deacetylation following consumption indicating that salicylic acid is the biologically active component [7]. Salicylic acid and its salts and esters are abundant in the plant kingdom functioning as hormonal mediators of local and systemically acquired resistance to pathogens and environmental stress [8]. They are therefore likely to be present in plant products of dietary relevance such as fruits, vegetables, herbs and spices [9]. This has led to the suggestion that the recognised

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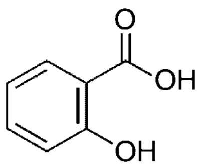

Figure 1. Molecular structure of salicylic acid.

effects of plant-based diets on lowering disease risk may be attributable, at least in part, to their salicylic acid content [10, 11].

It is unclear whether sufficient salicylic acid can be obtained from dietary sources to exert disease preventative activity, estimated daily intakes ranging from 0.4 to 200 mg/day have been reported [9, 12, 13]. Such a difference may be ascribed to the disparate information available on the salicylic acid content of foods confounding estimation of dietary intakes. Consequently, we set out to (i) construct a comprehensive database on salicylate levels in plant-based foods through both in-house analytical determinations and rigorous systematic examination of available literature and (ii) estimate dietary salicylate intake in a healthy Scottish population. It is intended that the food composition database can be used in population studies exploring dietary salicylate intakes and disease risk.

2 Materials and methods

To ensure as comprehensive a database as possible, data from the literature were critically and systematically evaluated and then augmented with additional values from in-house analyses of foods commonly consumed in the UK.

2.1 Critical appraisal of available literature

The method of systematic review and subsequent acceptance or rejection of data followed the procedures previously employed in the construction of a flavonoid food database [14] using the selection criteria based on the Royal Society of Chemistry food composition tables [15–18]. In brief, these were (i) food items had to be randomly selected and purchased from various commercial outlets during different seasons of the year, (ii) food samples were prepared using normal domestic practices, (iii) optimized sample extraction and hydrolysis conditions were clearly described or cited and (iv) salicylate determination was based on modern techniques of high-pressure liquid chromatography and MS with validation and quality assurance measures summarised. Using this approach, the bibliography databases CAB abstracts, BIDS and Medline were searched using the keywords "salicylic acid, salicylates, food and diet." Data from nine publications [9, 12, 13, 19–23] satisfied the selection criteria and were used in the construction of the salicylate food composition database.

2.2 Analysis of salicylate in foods

Information on commonly consumed food items in northeast Scotland was obtained from a previous survey [18]. The total salicylate content of the edible portions of 19 fruits, 20 vegetables, 7 spices and 6 juices purchased from local supermarkets were determined using high-performance liquid chromatography (HPLC) with electrochemical detection as previously described [19, 20]. Six items of the same food were homogenised together to minimise individual variation within each food type. Duplicate portions (1.0 g fruit and vegetables, 0.05 g spices and 0.5 mL liquids) of homogenised foods were suspended in 3 mL of 2.5 mol/L sodium hydroxide for 24 h at room temperature. Hydrochloric acid (1 mL of 5.3 mol/L) was then used to adjust the mixtures so that they contained a final concentration of 0.1 mol/L HCl. Following addition of EDTA (final concentration 100 μmol/L), 4-methyl salicylic acid (internal standard, final concentration of 2.0 μmol/L), vortexing (15 min) and centrifugation (3000 rpm, 10 min, 4°C), the organic phases were dried under oxygen free nitrogen and reconstituted in 0.5 mL of 30 mmol/L citrate (pH 3.8) containing 5% methanol. Eluted substances were detected electrochemically at an oxidation potential of +1.1 V using a previously described four-step program [19]. The presence of salicylic acid was confirmed by peak disappearance following addition of salicylate hydroxylase and by MS [19]. Intra-assay and inter-assay coefficients of variation (CV) were 3 and 4% respectively.

2.3 Database construction

Data for total salicylates from the literature and the in-house analysis were combined and total salicylates for 27 different types of fruits, 21 vegetables, 28 herbs, spices and condiments, 2 soups and 11 beverages were calculated as median values to accommodate non-normal distribution of the range of values available for each food item.

2.4 Estimating dietary salicylate intake

Dietary intake was assessed by applying the salicylate database to the Scottish Collaborative Group (SCG) semi-quantitative Food Frequency Questionnaire (FFQ) version 6.5 [18], consisting of a list of 170 food items, and a supplemental questionnaire of similar format incorporating spices and recipes. One hundred and sixteen healthy men, mean age 31 years (range 19–72) and 121 healthy women, mean age 31 years (range 17–64) from Aberdeen, Scotland, UK completed the questionnaires. For each item, participants were asked to report their average use over the preceding three months for a specified serving size of each food and beverage. Nine pre-specified frequency responses were possible, ranging from rarely or never eaten to eaten every day. Individual salicylate intakes were calculated by multiplying the frequency of each food or beverage consumed by the salicylate content of the specified portion size and then summing the contributions from all foods and beverages. The salicylate contents of 19 composite dishes (e.g. pizzas and spaghetti bolognaise) were also calculated from standard recipes using the values for individual ingredients from the database with adjustment for weight lost through cooking [24–32]. Median daily total salicylic acid intakes were adjusted for energy intake. Dietary investigations were approved by the local research ethics committee and informed consent was obtained.

3 Results

3.1 Total salicylate content of foods

Electrochemical determination following separation by HPLC confirmed the presence of salicylates in a range of plant-based food items readily available to the UK consumer (Table 1). Herbs and spices were particularly rich sources whereas salicylates were absent in some vegetables such as aubergines, broccoli and courgettes.

Combining the values from the in-house analysis with those from the systematic assessment of the literature resulted in a dietary database containing the median salicylate content of 27 different types of fruits, 21 vegetables, 28 herbs, spices and condiments, 2 soups and 11 beverages (Table 2). The salicylate content ranged from 0 to 33.59 mg/kg in fruits, 0 to 6.01 mg/kg in vegetables, 5.74 to 450 mg/kg in spices and 0.10 to 4.06 mg/kg in juices. Estimated salicylate contents of standard recipes [24–32] (Table 3) ranged from 0 mg/kg (oil and lemon dressing) to 8.5 mg/kg (tomato chutney). Raisins were particularly rich sources of salicylates (0.98–66.2 mg/kg), a likely relative concentration effect of water loss by the drying process.

Table 1. Total salicylate content of foods purchased from local Scottish retailers as determined by HPLC with electrochemical detection

Food item	Salicylates (mg/kg)	Food item	Salicylates (mg/kg)
Fruits		*Vegetables*	
Banana	0.34	Asparagus	1.29
Blackberries	0.81	Aubergine	0.0
Blueberries	0.57	Broccoli	0.0
Gala melon	0.62	Cabbage green	0.0
Grapefruit	0.44	Carrots	0.16
Green apple	0.55	Cauliflower	0.01
Kiwi fruit	0.31	Celery	0.04
Lime	0.0	Courgette	0.0
Mango	0.03	Cucumber	0.02
Nectarine	3.29	Green bean	0.07
Orange	0.11	Green pepper	0.01
Peach	0.12	Lettuce (iceberg)	0.05
Pear	0.23	Mange tout	0.20
Plum	0.01	Mushroom (button)	0.13
Raspberry	0.09	Onion (white)	0.80
Red grape	0.02	Potato	0.02
Strawberry	0.61	Red pepper	0.09
White grape	0.02	Swede	0.07
Yellow melon	0.11	Tomato	0.13
		Yellow pepper	0.09
Juices		*Spices*	
Apple	0.83	Black cumin	25.05
Cranberry	0.99	Cumin	29.76
Grapefruit	0.10	Chat masala	5.74
Orange	0.68	Cinnamon	0.78
Pineapple	4.06	Garam masala	12.85
Tomato	1.32	Paprika	28.25
		Turmeric	20.88

3.2 Estimated daily intakes and main food sources

Estimated medial total salicylate intakes were 4.42 and 3.16 mg/day for males and females, respectively. Following adjustment for energy, this gender difference was no longer apparent (Table 4). Primary food sources of salicylates (Fig. 2) were alcoholic beverages (22%), herbs and spices (17%), fruits (16%), non-alcoholic beverages including fruit juices (13%), tomato-based sauces (12%) and vegetables (9%). Salicylate intake was significantly and positively associated ($p<0.01$) with intakes of fibre, potassium, vitamin C and alcohol (data not shown).

4 Discussion

Food composition databases provide essential information for research on the health effects of nutrients, nutritional surveillance, clinical dietetic practice and food formulation and processing. Compositional information on potentially bioactive phytochemicals in foods is generally lacking although several databases for polyphenols in foods are now under construction [33]. The present study provides the first comprehensive and systematic assessment of the salicylate content of commonly consumed foods and is the first estimation of the dietary intake of salicylates by a Scottish population. The database can be updated and estimates of intake improved as further literature that satisfies the systematic selection criteria becomes available.

A particular strength of the database is only accepting salicylate values obtained using gas or LC with alkaline or acid hydrolysis, compound validation by MS and stated quality assurance procedures. Values obtained by older, less specific and colorimetric procedures were excluded as being potentially artefactually high. However, a limitation is the

Table 2. The total salicylate database: median values calculated from combining in-house determinations with systematically reviewed literature values

Food item (*n*)	State	Median (mg/kg)	Range (mg/kg)	References
Fruits				
Apple (5)	Fresh	0.55	<0.02–5.9	[9, 12, 21, 22], Table 1
Apricot (3)	Tinned	0.10	0.03–25.8	[9, 12, 22]
Banana (3)	Fresh	0.40	0.34–18.6	[9, 21], Table 1
Blackberry (3)	Fresh	0.81	0.07–18.6	[9, 23], Table 1
Black chokeberry (1)	Fresh	1.20	1.2	[23]
Blueberry (3)	Fresh	0.57	0.33–27.80	[9, 23], Table 1
Bramble (1)	Fresh	8.30	8.3	[23]
Cherry (2)	Fresh	4.43	0.36–8.5	[9, 12]
Crowberry (1)	Fresh	2.80	2.8	[23]
Grapes red (2)	Fresh	4.71	0.02–9.4	[9], Table 1
Grapes white (4)	Fresh	0.04	0.02–0.6	[12, 21, 22], Table 1
Grapefruit (3)	Fresh	0.44	0.2–6.8	[9, 21], Table 1
Kiwi fruit (3)	Fresh	0.31	<0.2–3.2	[9, 21], Table 1
Lemon (2)	Fresh	2.50	1.8–3.2	[9, 21]
Lime (1)	Fresh	0	0	Table 1
Mango (2)	Fresh	0.57	0.03–1.1	[9], Table 1
Melon gala (1)	Fresh	0.62	0.62	Table 1
Melon honeydew (1)	Fresh	0.11	0.11	Table 1
Nectarine (5)	Fresh	0.87	0.04–4.9	[9, 12, 21, 22], Table 1
Orange (5)	Fresh	0.11	<0.02–23.9	[9, 12, 21, 22], Table 1
Peach (2)	Fresh	2.96	0.12–5.8	[9], Table 1
Pear (3)	Fresh	1.46	<0.2–2.7	[9, 21], Table 1
Plum (3)	Fresh	0.50	0.01–2.1	[9, 21], Table 1
Raspberries (3)	Fresh	0.90	0.09–51.4	[9, 23], Table 1
Raisins (2)	Fresh	33.59	0.98–66.2	[9, 12]
Sorbus (1)	Fresh	0.28	0.28	[22]
Strawberry (4)	Fresh	0.63	0.04–13.6	[9, 12, 22], Table 1
Vegetables				
Asparagus (2)	Fresh	1.35	1.29–1.4	[9], Table 1
Aubergine (2)	Fresh	4.40	0–8.8	[9], Table 1
Broccoli (2)	Fresh	3.25	0–6.5	[9], Table 1
Cabbage-green (2)	Fresh	0	0	[9], Table 1
Carrot (3)	Fresh	0.50	0.16–2.3	[9, 21], Table 1
Cauliflower (2)	Fresh	0.80	0.01–1.6	[23], Table 1
Celery (2)	Fresh	0.02	0–0.04	[9], Table1
Courgette (1)	Fresh	0	0	Table 1
Cucumber (4)	Fresh	0.24	0.02–7.8	[9, 12, 21], Table 1
Green beans (2)	Fresh	0.59	0.07–1.1	[9], Table 1
Lettuce (2)	Fresh	0.02	0–0.05	[9], Table 1
Mange tout (1)	Fresh	0.20	0.2	Table 1
Mushroom (2)	Fresh	1.27	0.13–2.4	[9], Table 1
Onion (2)	Fresh	1.20	0.8–1.6	[9], Table 1
Peas frozen (2)	Fresh	0.35	0.3–0.4	[9, 21]
Peppers-green (2)	Fresh	6.01	0.01–12	[9], Table 1
Peppers-red (1)	Fresh	0.1	0.1	Table 1
Pepper-yellow (1)	Fresh	0.1	0.1	Table 1
Potato (2)	Fresh	0.01	0–0.02	[9], Table 1
Swede (2)	Fresh	0.04	0–0.07	[9], Table 1
Tomato (5)	Fresh	0.36	0.05-1.3	[9, 12, 21, 23], Table 1
Herbs, spices and condiments				
Asafoetida (1)	Dried	38	38	[20]
Black cumin (1)	Dried	25.05	25.05	Table 1
Cardamom black (2)	Dried	173.5	77–270	[9, 20]
Cardamom green (1)	Dried	132	132	[20]
Chat masala (1)	Dried	5.74	5.74	Table 1
Chilli powder (3)	Dried	13	<0.2–1466	[9, 20]

Table 2. Continued

Food item (*n*)	State	Median (mg/kg)	Range (mg/kg)	References
Cinnamon (5)	Dried	23.8	0.78–642	[9, 12, 20, 21], Table 1
Cloves (2)	Dried	41.2	25–57.4	[9, 20]
Coriander (2)	Fresh	14.5	2–27	[9, 20]
Cumin (3)	Dried	450	29.8–16 294	[9, 20], Table 1
Curry powder (3)	Dried	15.2	5.55–2180	[9, 12, 21]
Fennel (2)	Dried	14	8–20	[9, 20]
Fenugreek (2)	Dried	61.5	1–122	[9, 20]
Garam masala (2)	Dried	340.42	12.85–668	[9], Table 1
Garlic (3)	Fresh	1	<0.2–56	[9, 19, 20]
Ginger (3)	Fresh	35	<0.2–45	[9, 20, 21]
Honey (3)	Liquid	0.66	<0.2–39	[9, 12, 21]
Mint (2)	Fresh	54.2	14.4–94	[9, 21]
Mixed herbs (2)	Dried	289.15	22.3–556	[9, 21]
Nutmeg (2)	Dried	26.09	24–28.18	[9], Table 1
Oregano (3)	Dried	26	19.9–660	[9, 12, 21]
Paprika – hot (5)	Dried	28.25	2.98–2030	[9, 12, 20, 21], Table1
Pepper – black (4)	Dried	33.85	3.05–90	[9, 12, 20, 21]
Tamarind (1)	Fresh	96	96	[20]
Turmeric (4)	Dried	392.44	17–3505	[9, 12, 20], Table 1
Thyme (3)	Dried	28.6	12.8–1830	[9, 12, 21]
Malt vinegar (2)	Liquid	0.03	0–0.05	[9, 21]
White vinegar (2)	Liquid	6.73	0.15–13.3	[9, 21]
Soups				
Lentil (2)	Tinned, liquid	0.21	0.12–0.3	[19]
Tomato (3)	Tinned, liquid	0.022	0.005–0.034	[19]
Drinks				
Coffee-instant (3)	Freeze dried, liquid	1.8	0.37–6.8	[9, 12, 21]
Tea (3)	Tea bag, liquid	1.06	0.42–34.5	[9, 12, 21]
Beer (2)	Liquid	1.63	0.06–3.2	[9, 21]
White wine (8)	Liquid	0.44	0.01–12.9	[21, 23]
Red wine (13)	Liquid	0.50	0–2.58	[12, 21, 23]
Apple juice (3)	Liquid	0.83	0.73–3.81	Table 1
Cranberry juice (2)	Liquid	0.99	0.91–1.07	Table 1
Grapefruit juice (1)	Liquid	0.10		Table 1
Orange juice (5)	Liquid	0.68	0.47–3.01	Table 1
Pineapple juice (1)	Liquid	4.06		Table 1
Tomato juice (1)	Liquid	1.32		Table 1

lack of information on how locality, varietal and growing conditions and the effects of processing and storage affect the salicylate content of foods. For example, the salicylate content of five brands of orange juice ranged from 0.47 to 3.01 mg/L. Such potential confounding affects have been minimised by the computation of single, median salicylate values for each food item. This may more likely reflect the intake of a population exposed to a diverse range of products over the longer term. In addition to seasonal and varietal influences on salicylate contents of primary products, the database would benefit from direct analysis of commonly consumed meals. Calculated daily intakes included standard recipes but no information is available on the salicylate content of processed foods where some forms may be used as flavouring agents or preservatives [34].

Estimated medial salicylate intakes of 4.42 and 3.16 mg/day for males and females respectively are comparable with

Table 3. Estimated total salicylate content of some standard recipe dishes

Recipe dish	Total salicylates (mg/kg)
Bolognaise sauce	3.2
Pizza, tomato	0.7
Flan, cheese onion and potato	0.5
Flan, cheese and mushroom	0.2
Pancakes, savoury, stuffed with vegetables	4.2
Nut roast	3.2
Dressing, oil and lemon	0.0
Chutney, tomato	8.5
Cornish pastie	4.9
Vegetable korma	7.3

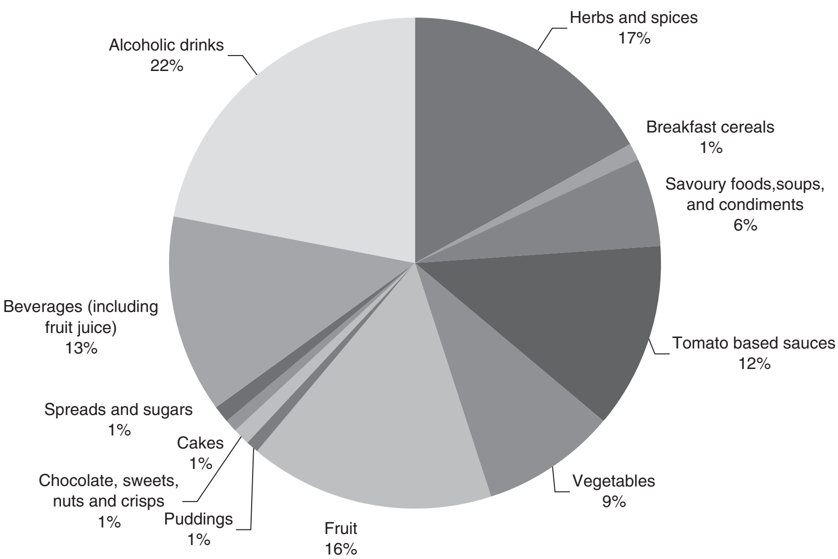

Figure 2. Relative contribution of different food groups to total salicylate intake of a Scottish population.

Table 4. Median and interquartile ranges (IQR) of total daily salicylate intake of Scottish men ($n = 116$) and women ($n = 121$) unadjusted and adjusted for energy intake

	Males		Females	
	Median	IQR	Median	IQR
Total salicylate (mg)	4.42	2.9–6.27	3.16	2.35–4.89
Total salicylate (mg/10 000 kJ)	3.41	2.72–5.22	3.62	2.64–4.75
Energy (kJ)	11 199	8532–14 971	8858	7181–11 600

estimated intakes in a Scottish population of other phenolic compounds including types of flavonols, flavones, flavonones and proanthocyanins [35]. Fruits and vegetables are major sources of salicylates accounting for approximately 25% of total intake. Fruits and vegetables are also rich sources of fibre, vitamin C and potassium and, therefore, significant associations between intakes of these nutrients and salicylates are not unexpected. Spices also account for a considerable proportion of total salicylate intake (14% in males and 10% in females). Consequently, populations that incorporate substantial amounts of spices in foods may have markedly higher daily intakes of salicylates. Indeed, it has been suggested that the low incidence of colorectal cancer among Indian populations may be ascribed in part to high exposure to dietary salicylates throughout life from spice consumption [36]. In contrast, any potential cancer preventative affects of dietary salicylates [37] in Scots may be negated by the substantial proportion derived from beverages containing alcohol (22%), a recognised pro-carcinogenic risk factor [38].

Serum and urinary salicylate concentrations of vegetarians are higher than omnivores and overlap with individuals who regularly take low-dose aspirin [39, 40]; this suggests substantial absorption of salicylates from ingested plant-based foods. Such serum concentrations are sufficient to inhibit PGHS-2 mRNA synthesis and promoter activity in vitro [41, 42] thus preventing the conversion of arachidonic acid to potentially tumour-promoting cyclic prostanoids. The Scottish population has a habitually low intake of fruits and vegetables [43] and salicylate intakes in the present study, therefore, may be insufficient to exert disease preventative effects. Application of the database to populations with differing dietary habits and disease risk profiles may provide further evidence for the role of dietary salicylates in the prevention of chronic diseases.

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