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Aluminium in tea—concentrations, speciation and bioavailability

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Abstract

Tea (*Camellia sinensis*) is one of a few plants accumulating aluminium (Al), making tea a major source of dietary Al intake. This paper reviews published studies on the concentrations, speciation and bioavailability of Al in tea. With very few exceptions, the total concentration of Al in tea infusions is in the range 1–6 mg l^{-1}. Probably more than 90% of this Al is bound to organic matter, but the nature of the organic species is unclear. Three studies using size exclusion chromatography provide evidence for Al species in the molecular mass (MM) range 4000–8500 Da, probably polyphenolic complexes. Two ultrafiltration studies indicate the presence of Al species with MMs above 10,000. The relative amount of the different organic Al species in tea infusions is unclear, and even the identity of any of these has not been demonstrated with certainty. A possible exception is Al trioxalate, which may be an important species based on evidence from two ^{27}Al-NMR studies. It seems fairly well established that drinking tea leads to measurable, but moderate increases in urinary Al excretion. However, the Al present in tea does not seem to be much more bioavailable than that from other dietary sources. Even so, it cannot be dismissed that tea infusions may contain particularly bioavailable and neurotoxic compounds such as Al maltolate, but this is at present speculative.

Keywords: Aluminium; Tea; Speciation; Bioavailability; Polyphenols; Oxalate; Maltolate; Urinary excretion

1. Introduction

Aluminium (Al) is clearly a powerful neurotoxicant, and also has a potential for skeletal and haematopoietic toxicity, especially in patients on dialysis due to chronic renal failure [1,2]. In dialysis patients, tissue accumulation of Al to levels high enough to cause toxicity is mainly due to a combination of high exposure and these patients' lack of kidney function, which is the main excretion route for Al [3,4]. Nowadays, overt dementia and osteomalacia in dialysis patients is rare due to strict control of Al intake. Although there are reports of similar neuro- and osteotoxicity also in certain patient groups without kidney failure [2], the question whether Al exposure of any kind represents a health problem for the general population remains open. The most controversial issue is whether Al exposure is causally related to Alzheimer's disease (AD), and although considerable evidence exists for such a relation, it is still open to debate whether the relation is causal [5,6].

The average total daily dietary intake of Al in most countries is a few milligrams per day; recently published

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values for adults include 3.1 mg per day in the Netherlands [7], 3.4 mg per day in the UK [8], 3.5 mg per day in Japan [9], and 7–9 mg per day in the US [10]. The reason for the higher intake in the US is probably a more widespread use of Al-containing food additives; earlier estimates of dietary Al intake in the US were generally above 10 mg per day [11]. Because typical levels of Al in tea infusions are 1–6 mg l^{-1} (see below), tea is a major source of dietary Al exposure, and heavy tea drinking may more than double an individual's intake of Al. Furthermore, Al is generally very poorly absorbed in the gastrointestinal tract; roughly in the order of 0.1% of the dietary intake is absorbed, depending on the chemical form (species) of Al [12–14]. Thus, if the species of Al present in tea are more bioavailable than the species present in other dietary items, tea could make a larger contribution to human uptake of Al than indicated from the total concentration present.

Next to water, tea is the most widely consumed beverage in the world. Global tea production in 2000 was 2.89 million tons [15], of which nearly 80% is black tea, about 20% is green tea, and some 2% is oolong tea. All these three types of tea are made from the leaves of the tea plant (*Camellia sinensis*) [16,17]. To make black tea, the leaves are air-dried (withered) before they are bruised through rolling and cutting to activate the endogenous enzyme polyphenol oxidase. This starts the fermentation process, which largely consists of oxidation of the polyphenols present in the tea leaves. When the quality is judged optimal, fermentation is arrested by drying. In contrast, green tea is not (or only very lightly) fermented, but the leaves are treated by steaming or pan firing to inactivate the polyphenol oxidase, thus avoiding oxidation. If the firing is carried out immediately after the leaves are plucked, the result is 'white' tea, if the leaves are withered (and therefore lightly fermented) before firing, the result is 'yellow' tea [17]. Oolong tea (also called 'red' tea) is an intermediate type of tea, produced employing a shorter fermentation time than for black tea.

Tea is one of the very few plants that accumulate Al [18,19]. In fact, most plants are quite sensitive to Al toxicity [20], which is a large problem in agriculture: Al toxicity is probably the major factor limiting crop productivity on acid soils, which occupy about 30% of the world's ice free land area [21]. In contrast, Al stimulates the growth of tea plants [22], possibly through improvement of the absorption and utilisation of phosphorus and perhaps other essential elements [23]. Old tea leaves may contain up to 2–3% Al (dry weight) [24,25], but the leaves are usually harvested long before they reach such levels. When plucked for human consumption, Al concentrations are typically about 300–1500 μg g^{-1} [24–31].

When discussing possible negative health effects of tea related to its Al content, it is important to realise that tea is a rich source of antioxidants, so it may potentially have positive effects on human health. There is a rapidly growing body of scientific evidence indicating that tea consumption may protect against cardiovascular diseases and several types of cancer [32,33]. In addition, tea may have a positive effect on the intestinal microflora [32] and protect against kidney stones, bacterial infections and dental cavities [33].

2. Concentrations of Al in tea infusions

A considerable number of studies have reported the total concentration of Al in tea infusions (Table 1). The concentration varies with many factors [22], primarily the age of the tea leaves when they are harvested, but also with the genetics of the plant, soil conditions, rainfall, altitude, and the conditions used when preparing the infusions (amount of tea relative to water, infusion time and temperature, etc.).

Despite the wide variation in infusion conditions (Table 1, column 1), the reported concentrations of Al in tea infusions are remarkably consistent. With few exceptions, values are in the range of 1–6 mg l^{-1}. The most notable exception is the data of Coriat and Gillard of 40–100 mg Al l^{-1} [34], published as a letter in Nature in 1986. These data have not been fully published reporting analytical methods and quality control procedures, so the results may have been in error. Also, a concentration of 100 mg Al l^{-1} in the infusion necessitates a concentration of 5 mg Al g^{-1} in the tea leaves, assuming that 2 g of tea leaves is used in 100 ml of water, and that 100% of the Al present in tea leaves is eluted during infusion (which is unrealistic). Commercial tea leaves rarely contain much more than 1 mg Al g^{-1}. Of the 36 studies listed in Table 1, two others reported comparatively high concentrations, but one used a very high amount of tea relative to water [35], and the other also used a fairly high amount of tea combined with a long infusion time [36]. Finally, one study reported much lower concentrations than the others, but here, about five times less tea relative to water was used than in most other studies [37].

3. Speciation of aluminium in tea infusions

The physicochemical form of an element, that is, the actual species found in the exposure media and in the different body compartments, is often determinant in evaluating its bioavailability and toxicity. In most aquatic systems, only a tiny fraction of Al is found as the simple Al^{3+} aquo ion [38], so Al absorption and biokinetics strongly depend on the properties of the

Table 1
Published concentrations of aluminium in tea (*C. sinensis*) infusions, sorted by year of publication

Reference	Infusion conditions	No. of brands or samples analysed	Mean (mg Al l^{-1})	Range (mg Al l^{-1})	Analytical procedure *
[72]	'Steeped'	1 (orange pekoe, bag)	2.8	–	AES
[26]	2 g/100 ml deionised water, simmered for 5 min and decanted	4 brands (leaves, probably black teas)	3	2–4	F-AAS
[73]	–	1 black, 1 oolong	2.9	1.9–3.9	AAS
[74]	1.5 g/100 ml hot water, 5 min	31 green teas	5.1	–	ICP-AES
[75]	'Steeped'	–	4.6	–	–
[34]	Infused in teapots with soft tap water	–	–	40–100 ('typically')	AAS
[27]	1 g/100 ml boiling water, 5 min	12 brands (leaves, 9 black teas, 3 green teas)	3.9	2.7–4.9	GF-AAS
[56]	2 g/150 ml tap water	–	–	4.5–6.0 ('typically')	–
[42]	1 g/100 ml distilled water, infused for 5 min and decanted	5 brands (2 bags, 3 leaves, all black teas)	3.3	2.0–6.2	ICP-AES
[45]	2 g/200 ml hard tap water, 10 min	9 brands, probably black tea leaves	–	1.8–3.9	–
[76]	'1% extract' for tea leaves, no conditions given for tea bags	23 brands (9 leaves, 14 bags, all black teas)	1.3	0.6–2.9	GF-AAS
[28]	0.5 g/45 ml 'Al-free' water, infused for 5 min at 95 °C	10 brands (9 leaves, 1 bag, all black teas)	2.3	0.9–5.0	
[77]	3 g/150 ml boiling deionised distilled water, infused for 4 min, filtered and made up to 400 ml with water	12 brands (black tea leaves, Indian, Ceylonese and Chinese)	3.6	2.2–4.5	GF-AAS
[78]	9 g/375 ml boiling water	12 clones of Kenyan black tea, leaves	3.7	2.8–4.8	F-AAS
[35]	2 g/40 ml 'Al-free' water, infused for 20 min at 95 °C	2 brands (1 tea bag, 1 tea leaves)	9.9	7.2–12.9	ICP-AES, ^{27}Al-NMR
[79]	2 g/100 ml boiling water, infused for 5 min	5 grades of black Indian tea leaves	4.4	–	ICP-AES
[80]	–	5 samples	1.3	1.1–1.5	GF-AAS
[47]	3 g/200 ml boiling ultraclean water, infused for 5 min	1 brand, black tea leaves	3.6	–	ICP-MS
[81]	10 g/1000 ml boiling tap water, infused for 2 min	2 brands (Ceylon orange pekoe black tea leaves)	1.35	1.15–1.54	GF-AAS
[29]	–	Several	–	0.6–5.6	–
[48]	1 bag/250 ml boiled deionised water, infused for 3 min	1 black tea, Tetley bags	2.9	–	ICP-AES
[82]	1 g/100 ml boiling deionised water, infused for 5 min	5 samples	1.2	0.47–1.7	GF-AAS
[83]	Ready-to drink infusions in cans or cardboard containers, internally plasticised	–	1.3	0.4–2.2	GF-AAS, ICP-AES
[84]	2 g/150 ml boiling water, 10 min	6 brands (1 jasmine, 3 green, 1 oolong, 1 black)	1.9	0.6–3.2	
[37]	2 g/1000 ml water, boiled for 5 min	6 brands of 'commercial tea powders'	0.065	–	ICP-AES
[85]	0.5 g/50 ml deionised water, boiled for 5 min	11 brands (leaves, 1 green and 10 black teas)	2.8	1.0–8.4	ICP-AES
[52]	2.5 g/100 ml water, infused at 90 °C for 2 min	7 brands (2 green, 2 black, 1 oolong, all leaves, and 2 canned oolong teas)	3.2	0.9–6.4	GF-AAS
[53]	1 g/100 ml boiling deionised distilled water, 20 min	4 brands (leaves, 1 green and 3 black teas)	2.7	1.3–4.1	GF-AAS
[86]	2 g/200 ml boiling distilled water, 10 min	2 (bags, black teas)	4.5	4–5	GF-AAS
[30]	1 bag/100 ml boiled water, infused in cups for 5 min	12 samples (bags, black tea)	4.2	–	GF-AAS
[53]	1 g/100 ml boiling deionised distilled water, 20 min	4 brands (leaves, 1 green and 3 black teas)	2.7	1.3–4.1	GF-AAS
[31]	1 bag/200 ml boiling distilled deionised water, 5 min	1 (Lipton Yellow Label bags)	3.2	–	ICP-MS
[54]	2 g/200 ml boiling distilled deionised water, 3 min	4 black tea leaves of 4 different nationalities, Twinings Earl Grey bags	3.2	1.0–6.3	ICP-AES
[87]	2 g/200 ml boiling distilled water, 5 min	4 (green, black, oolong and puerh tea leaves)	2.3	–	AAS
[36]	2 g/100 ml cold deionised water, heated to boiling and left to infuse for 10 min	1 Turkish black tea, leaves	12.0	11.0–13.0	F-AAS
[88]	0.5 g/50 ml boiling water, 5 min	Black and green teas, number not given	2.5	–	GF-AAS

* AES, atomic emission spectrometry; F-AAS, flame atomic absorption spectrometry; GF-AAS, graphite furnace atomic absorption spectrometry; ICP-AES, inductively coupled plasma atomic emission spectrometry; ICP-MS, inductively coupled plasma mass spectrometry; NMR, nuclear magnetic resonance spectrometry.

Al^{3+} complexes formed with different ligands. Aluminium is a metal with very strong 'A-type' or 'hard' properties [39], so it strongly prefers oxygen-donor ligands, notably with phosphate, carboxylate and phenolate functional groups. Of course, particularly strong chelate-type complexes may be formed with molecules containing several oxygen-donor functional groups arranged in a close geometrical environment. Many different potential Al-binding ligands are available in the environment and in biological systems, and sorting out which ligands are relevant under different conditions has proved a very difficult task. Tea contains a large number of compounds that are able to complex Al (Table 2). It has often been assumed that the polyphenols, which make up about 40% of the dry matter present in tea infusions, are the most important Al-complexing compounds in tea due to their many phenolic hydroxyl groups that provide a large number of potential complexation sites. Infusions of green and black tea differ chemically mainly within the polyphenolic fraction (Table 2). This difference results from the fermentation, the main result of which is the oxidation of simple polyphenols to more complex condensed polyphenols that give oolong and black teas their red–brown colours and brisk astringent flavour. A large fraction of the black tea polyphenols has resisted chemical identification, and these compounds are often referred to as thearubigens. One recent nice and comprehensive review of the basic chemistry of tea was given by Harbowy and Balentine [17], cf. Table 2, who also present the chemical structures of most of the compounds.

Table 2
Chemical composition of typical tea infusions, in wt.% of the dry matter (based on Harbowy and Balentine [17])

	Green tea (%)	Black tea (%)
Polyphenols		
Catechins	30	9
Theaflavins		4
Simple polyphenols	2	3
Flavonols	2	1
Other polyphenols	6	23
Nitrogenous compounds		
Caffeine	3	3
Other methylxanthines	< 1	< 1
Theanine	3	3
Amino acids	3	3
Peptides and proteins	6	6
Organic acids *	2	2
Sugars	7	7
Other carbohydrates	4	4
Lipids	3	3
Potassium	5	5
Other minerals/ash	5	5
Aroma	Trace	Trace

The dry matter content of tea infusions is about 0.35%.
* The most common organic acids are oxalic and malic acids, followed by citric, isocitric and succinic acids.

Nagata et al. [40] studied Al forms in intact tea leaves by ^{27}Al-NMR spectroscopy. In young leaves, one single Al signal dominated the NMR spectrum. This signal was in good accordance with the signal from a model Al–catechin complex. The authors therefore suggested that most of the Al in young tea leaves is bound to catechins (a group of polyphenolic compounds containing the bichelating cathecolate groups). For older tea leaves, there were additional small peaks in the spectra that were attributed to Al complexes with phenolic and organic acids. In addition, evidence of complexation between Al and fluoride was found in one single spectrum of mature tea leaves. Tea is a rich source of fluoride; tea infusions may contain several mg l^{-1} of fluoride [41].

Before any speciation studies of tea infusions had been reported it seemed reasonable to assume that most of the Al would be complexed with organic molecules, and that large complexes are less bioavailable than smaller ones [42]. Published studies of speciation of Al in tea infusions before and after gastrointestinal digestion are listed in Tables 3 and 4, respectively. The studies are discussed below in chronological order. It should be emphasised that many techniques used for speciation in solution change the physicochemical conditions of the surroundings of the metal; what is measured is therefore not always what was in the original solution. For chromatography, the species present in the original solution may dissociate when passing through size-exclusion or cation-exchange columns, and complexes may form with the eluent buffer. For ultrafiltration, a serious potential problem is that low molecular mass (MM) species may adsorb to the filters and filtration apparatus, leading to an underestimation of the low-MM fraction. In addition, Al contamination from the environment is always a potential problem. In general, it is important to realise that many published values for Al concentrations in biological samples are too high because of sample contamination and analytical errors [43,44].

The first preliminary speciation study was reported by French et al. in 1989 [45]. Employing the Barnes–Driscoll kinetic cation-exchange procedure [46], widely used for estimating the extent of organic complexation in natural waters, they found that 91–100% of the filterable (0.45 μm filter) Al in tea infusions passed through a strong cation-exchange resin column, which suggests that the Al was almost totally bound to organic matter. For tea infusions incubated for 2 h at 37 °C and pH 2 (a crude simulation of stomach conditions), 70–99% of the Al passed through the column, indicating that organic complexes dominate Al speciation even at stomach pH. Ultrafiltration studies showed that as much as 86% of the 0.45-μm filterable Al in tea infusions

Table 3
Studies of the speciation of aluminium in tea infusions, sorted by year of publication

Reference	Methods	Main findings
[45]	Cation-exchange and ultrafiltration	91–100% of Al bound to organic matter
		86% of Al > 20,000 Da, 4% < 5000 Da
[47]	Size exclusion chromatography	14% of Al as 'stable', high MM species, 86% as 'labile' species with MM ≤ 2100
[48]	Ultrafiltration	15% of Al > 30,000 Da, 70% < 3000 Da
[50]	^{27}Al-NMR	Two detectable species: $[Al(C_2O_4)_3]^{3-}$ and probably a mixed ligand chelate containing oxalate and another organic acid
[51]	^{27}Al-NMR	Two detectable species: $[Al(C_2O_4)_3]^{3-}$ and possibly a mixed complex of Al, oxalate and fluoride
[52]	Chrome azurol S complexation	11–27% of the Al present in oolong tea was 'free', as defined by binding to this Al complexing agent; 0% in green and black tea
[53]	Filtration and lumogallion complexation	Particulate Al (> 0.45 μm): 4% in black tea, 14% in oolong tea, 43% in green tea
		Fractions of Al so strongly bound in tea infusions that treatment with the complexing agent lumogallion could not decomplex it: 52% in black tea, 71% in oolong tea, 91–94% in green tea
[31]	Size exclusion chromatography	Two Al-containing peaks, at 4000–6000 and 6500–8500 Da, respectively
[54]	Size exclusion chromatography	One Al-containing peak at 4000–6500 Da

was retained by a 20,000 Da molecular-mass cut-off (MMCO) filter, and 96% by 10,000 and 5000 Da MMCO filters. This indicates that the bulk of Al in tea infusions exists as large organic complexes. However, for the pH 2 tea infusions only 33% of the Al was retained by the 20,000 Da MMCO filter, 51% by the 10,000 and 54% by the 5000 Da MMCO filter. Therefore, with acidification of tea infusions there seems to be a shift towards organic complexes of lower MM, which can be rationalised in terms of lower MM of the ligands or a lower complex stoichiometry (ligand to metal molecular ratio). This could result in a higher bioavailability but also a partial release of free Al ions.

Owen et al. [47] used size exclusion chromatography coupled to inductively coupled plasma mass spectrometry to study the behaviour of Al in tea infusions before and after simulated gastrointestinal digestion (Tables 3 and 4). For tea infusions in a 0.12 M Tris buffer at pH 5.5, Al recovery was only 24% (76% of the Al present in the tea infusion was retained on the column), and this Al eluted from the column as a single peak at a retention time corresponding to a MM of about 6100 Da. Adding 5 mM NaF to the Tris buffer resulted in nearly 100% recovery of Al from the column; 13% of the Al present in the tea infusion eluted at about 5800 Da and 83% at 2060 Da. Using a lower concentration of Tris (0.02 M) and 5 mM NaF, 12% of the Al eluted at 12,800 Da and 75% at 3000 Da. Obviously, eluent conditions had a profound influence on the speciation results. The authors' interpretation of the results was that about 14% of the Al in the tea infusion existed as 'stable' species ('Al associated with high-MM species which eluted in 0.12 M Tris, pH 5.5, in the presence or absence of 5 mM NaF'), and 86% as 'labile' species ('Al associated with low-MM (≤2100 Da) species which only eluted when 5 mM NaF was added').

For gastric digestion, tea infusions were mixed with simulated gastric juice (1% pepsin in 0.15 M NaCl acidified to pH 1.8 with HCl), and the mixture was adjusted to pH 2.2 with HCl before incubation at 37 °C

Table 4
Studies of the speciation of aluminium in tea under gastrointestinal conditions, sorted by year of publication

Reference	Methods	Main findings
[45]	Cation-exchange and ultrafiltration	Stomach conditions (acid only): 70–99% of Al bound to organic matter; 33% of Al > 20,000 Da, 54% > 5000 Da
[47]	Size exclusion chromatography	Stomach conditions (simulated gastric juice): practically all Al soluble and present as < 2100 Da species
		Intestinal conditions (simulated gastric juice + simulated intestinal juice): 17% of Al soluble, of which 90% < 2100 Da species
[48]	Ultrafiltration	Stomach conditions (human gastric juice): > 90% of Al < 3000 Da
		Intestinal conditions (human gastric juice adjusted to pH 6.5): < 5% of Al < 3000 Da, but no precipitation
[52]	Chrome azurol S complexation	Stomach conditions (acid only): 16–37% of the Al present in oolong tea was 'free', as defined by binding to this Al complexing agent; 0% in green and black tea

for 1 h. Practically all the Al present in the tea infusions was soluble, and was present as low-MM (<2100 Da) species. Part of the tea/gastric juice mixture was then adjusted to pH 6.3 with $NaHCO_3$ before addition of simulated intestinal juice (1.5% pancreatin, 0.5% amylase and 0.15% bile salts in 0.15 M NaCl) and incubation at 37 °C for 1 h. After this treatment, only 17% of the Al from the tea infusion was soluble. Of this soluble fraction, 10% was interpreted as 'stable' and 90% as 'labile', as defined above.

Powell et al. [48] employed ultrafiltration in centrifuged microconcentrators for black tea infusions before and after addition of human gastric juice, collected from patients undergoing routine gastroscopy (Tables 3 and 4). In contrast to the ultrafiltration study by French et al. described above [45], only 15% of the Al present in the tea infusions was retained by a 30,000 Da MMCO filter, and about 30% was retained by both 10,000 and 3000 Da MMCO filters. Thus, the results of Powell et al. indicate that 30% of the Al in tea exists as species larger than 10,000 Da, while those of French et al. indicate that 96% of the Al species are larger than this. Powell et al. suggest [48] that this discrepancy may be partly explained by the fact that they used deionised water for tea infusions, while French et al. used (soft) tap water, and that the resulting slightly lower pH in the tea infusions could explain the difference. However, the large discrepancies would seem hard to explain by differences in tea pH of a few tenths of a pH unit. An alternative explanation may be that in the study by French et al., a larger fraction of low-MM species may have been adsorbed on the filters or filtration apparatus instead of passing through the filters. This is a well-known problem in ultrafiltration studies.

After the tea infusion had been incubated with human gastric juice for 1 h at 37 °C, more than 90% of the Al passed through all three ultrafilters (30,000, 10,000 and 3000 Da MMCO) [48]. However, when the pH in the tea/gastric juice mixture was adjusted to 6.5 (to simulate passage from the stomach into the small intestine), only 5% of the Al passed through the 3000 Da MMCO ultrafilter. This percentage was the same when the pH-adjusted tea was incubated for 24 h at 37 °C before ultrafiltration, so the reactions from low- to high-MM species upon pH increase were rapid. These findings indicate that after passing from the stomach into the small intestine, where most Al absorption occurs [49], little Al will remain associated with low-MM ligands (probably mainly citrate and fluoride), and most Al is therefore probably of low bioavailability. Powell et al. [48] argued that it was unlikely that precipitation of Al was the reason for the increase in MM after pH adjustment; because adjusting digested tea to neutral pH followed by centrifugation did not alter the total Al in solution. Rather, this Al may be associated with gut endogenous gastroferrin or other compounds that stabilise polyvalent metals in solution.

As discussed above, it is likely that a considerable part of the Al in tea infusions is present as complexes with polyphenolic compounds. If these polyphenols are degraded in the gut, it could make the Al more bioavailable, by release from the large MM polyphenolic ligands, or by shifting to the smaller phenolic breakdown products. Powell et al. [48] investigated this possibility by sampling gut effluents from ileostomy patients after drinking tea. The ileostomy effluent supernatant was analysed by ^{1}H-NMR, but no evidence was found of significant breakdown of tea-derived polyphenols to low-MM phenols during the transit of tea through the intestine.

Mhatre et al. [50] and Horie et al. [51] studied Al forms in black, green and oolong tea infusions by ^{27}Al-NMR spectroscopy (Table 3). Both reported two detectable narrow resonance peaks, at 16.15 [50] and 16.2 ppm [51], and at 9.85 [50] and 10.7 ppm [51], respectively. Comparisons with the spectra of model ligands strongly indicated that the resonances in the spectra of the tea infusions could not be assigned to Al complexes with the major polyphenolic constituents in tea [50]. Instead, both author groups presented strong evidence that the species at 16.15/16.2 ppm was an anionic complex of Al with three oxalate anions, $[Al(C_2O_4)_3]^{3-}$. The other Al signal was more difficult to identify. Mhatre et al. [50] argued that it was probably a mixed ligand chelate containing oxalate and another organic acid, Horie et al. [51] suggested that it was a mixed complex of Al, oxalate and fluoride. However, predicting speciation based on ^{27}Al-NMR in solutions containing several potential organic species is a difficult task, because the Al complexes produce broad peaks due to the complicated multiplets associated to the high nuclear spin of the ^{27}Al isotope, namely in low symmetry complexes as expected with mixed hydroxo species.

Fukushima and Tanimura [52] analysed total Al and 'free' Al ions (as determined by the Al complexing dye chrome azurol S) in tea infusions before and after incubation for 1 or 3 h at 37 °C and pH 1.8 (Tables 3 and 4). Al was not detectable by chrome azurol S spectrophotometry in any of the infusions of green or black teas, but in oolong teas, the percentage of 'free' Al ions was 11–27% in the untreated tea infusions, and 16–37% after acid incubation.

Zhou et al. [53] reported that the fraction of Al passing a 0.45 μm filter was only 54 and 57% for two green teas, 86% for an oolong tea and 96% for a black tea (Table 3). These percentages were virtually identical for a 0.20 μm filter, indicating that very little of the Al species present were in the size range 0.20–0.45 μm. These results would indicate that a considerable fraction of the Al present in green tea, but not in black tea

infusions may be in particulate form. These authors also determined the fraction of Al that reacted with the Al complexation agent lumogallion during 1.5 h at 85 °C. Again, the fractions varied between the different tea types, from 6 and 9% in the two green tea types to 48% in the black tea and 69% in the oolong tea. Thus, Al seems to be more tightly bound to the ligands in green tea than in black tea, since this harsh treatment with the fairly strong Al complexing agent lumogallion was only able to decomplex less than 10% of the Al present in green tea.

Lund and co-workers published two studies (Table 3) on Al speciation in tea infusions by size exclusion chromatography [31,54]. In one of the studies, the eluent was 0.1 M ammonium acetate buffer at a pH of 5.5: two Al peaks were observed, corresponding to estimated MM ranges of 4000–6000 and 6500–8500 Da, respectively [31]. The recovery of Al from the tea infusions was about 60%. In the other study, the eluent was 0.12 M Tris buffer at a pH of 5.5; here, a single Al-containing peak was found at about 4000–6500 Da [54], and the average recovery from newly cleaned columns was 24%, similar to that reported in the study by Owen et al. discussed above [47].

Erdemoglu et al. [55] used two different ion-exchange resins to study Al fractions in Turkish black tea. This and the other study by the same authors described below are not listed in Table 3. Tea infusions were fed into a non-ionic sorbent Amberlite XAD-7 resin column, and the effluent from this column was fed into a Chelex-100 weak acidic cation-exchange resin. The main result of this study was that 28–33% of the Al present in the tea infusion was sorbed to the XAD-7 resin, and 10–19% to the Chelex-100 resin. Thus, more than 50% of the total Al present in the tea infusions was unaccounted for by these two fractions. The XAD-7 resin is commonly used for separation of organic species of trace elements in natural waters. The authors' conclusion, however, that this fraction consists of 'hydrolysable polyphenols bound Al' (implicating that non-hydrolysable polyphenols and other organic forms of Al are not adsorbed to this resin) seems weakly founded. The 10–19% fraction bound to the Chelex-100 resin will almost exclusively consist of cations, and may include Al^{3+} and its hydrolysis products, Al–fluoride and cationic organic complexes. Fluoride complexation was specifically investigated in another study by the same authors [36]. Using a fluoride ion selective electrode, they estimated that about 10% of the Al present in the Turkish tea infusions was complexed with fluoride. However, 10% is a maximum estimate, because this fraction may also include complexes of fluoride with iron, manganese and magnesium, although the authors argue that this was probably not the case.

4. Bioavailability of aluminium from tea infusions

4.1. Human studies

Published studies of the bioavailability of Al from tea in humans are listed in Table 5, in chronological order. The first study was reported by Koch et al. in 1988 [56]. Six healthy male volunteers consumed standardised meals with 1.2 l (distributed over four meals) of tea, coffee or tap water on separate days. Urine was collected for 12 h, and urinary Al excretion was about 60% higher when drinking tea than tap water, indicating that 'at least some of the Al present in tea is absorbed'. However, the high concentrations of Al in urine (25–90 μg Al l^{-1} when not consuming tea) reported in this study could indicate analytical errors; presently accepted values in individuals with normal kidney function are in the range of 3–10 μg Al l^{-1}, corresponding to an excretion of about 5–15 μg per day [44]. In general, measurement of low Al levels is prone to errors particularly due to contamination of samples during collection, storage, handling and analysis. This is a problem common to all elements that occur at low levels in tissues and body fluids but at the same time are environmentally ubiquitous [43,44]. Thus, when interpreting the biological significance of studies relying on measured Al concentrations in tissues and body fluids, it is very important to compare with accepted levels and to assure that the authors have adhered to good laboratory practice and analytical quality control.

Drewitt et al. [57] studied blood plasma Al in 12 healthy volunteers, six men and six women. Together with an identical low-Al diet, each subject consumed on different days either mineral water or a tea infusion (500 ml/70 kg body weight) with either milk or lemon juice (which contains citric acid, known to markedly enhance Al absorption) as additives. Blood plasma samples were collected immediately before tea drinking and 10 times during the 24 h after tea drinking. The mean total amounts of Al ingested during the three 24-h periods were: diet plus mineral water, 1.23 mg; diet plus tea with milk, 2.33 mg; and diet plus tea with lemon, 2.81 mg. Plasma Al concentrations were identical between the three exposure conditions and stable between 4 and 5 μg l^{-1} throughout the study.

Powell et al. [48] studied urinary Al excretion in one healthy male volunteer during two following 24-h periods. The subject drank 2 l of tea (ca. 6 mg Al) over 4 h while commencing the first 24-h urine collection. Deionised water was allowed ad libitum, and food was taken as required during both 24-h periods. The total urinary Al excretion was five times higher when drinking tea than water (Table 5). However, the total urinary volume was also almost five times higher (ca. 3000 vs. 700 ml/24 h). There was little difference in the concentrations of Al in urine in the two 24-h collection

Table 5
Studies of the bioavailability of aluminium from tea in humans, sorted by year of publication

Reference	No. of subjects	Urinary Al excretion after water consumption	Urinary Al excretion after tea consumption	Blood Al after water consumption ($\mu g\ l^{-1}$)	Blood Al after tea consumption ($\mu g\ l^{-1}$)
[56]	6	45 (25–90) $\mu g\ l^{-1}$	73 (60–95) $\mu g\ l^{-1}$		
[57]	12			4–5	4–5
[48]	1	4 μg per day	20 μg per day		
[58]	4	0.17 (0.07–0.31) $\mu g\ h^{-1}$ (2–7 μg per day)	0.55 (0.24–1.19) $\mu g\ h^{-1}$ (6–29 μg per day)		
[59]	4	43 (25–70) μg per day	86 (70–105) μg per day (green tea); 114 (95–165) μg per day (oolong tea)		

All studies used crossover designs in which the same subjects drank tea and other fluids on separate days. See text for details of study designs.

periods (1–12 $\mu g\ Al\ l^{-1}$, 13 samples when drinking tea and six samples when drinking water). Tea drinking is known to enhance urinary volume, and Powell et al. suggested that it might be misleading to estimate systemic Al absorption from tea drinking simply from total urinary Al excretion [48].

Gardner and Gunn [58] studied urinary Al excretion in four healthy volunteers, three men and one woman. On separate days, the subjects drank 2 l of either tea containing ca. 4 mg $Al\ l^{-1}$, or a soft mineral water. Over the next 7 h, no other food or drink was consumed, and all urine produced was collected. The mean Al excretion rate was about three times higher after drinking tea than water (Table 5). Even so, the total excretion of Al in the 7 h after drinking tea was only 2–8 μg, that is, 0.025–0.1% of the total Al ingested from tea. This is very close to the presently accepted absorption rate of Al in healthy individuals [12–14], indicating that the Al present in tea is not much more bioavailable than that from other dietary sources.

Wu et al. [59] studied 24-h urinary Al excretion in four healthy male volunteers. During separate 24-h periods, each subject consumed a 'required diet' (Al concentrations not determined) after ingesting either 900 ml of oolong tea, 900 ml of green tea (Long-Jin) or deionised water. The average amounts of Al excreted were 43 μg per day when drinking water, 86 μg per day for green tea and 114 μg per day for oolong tea.

Determining whether Al from tea is absorbed to any appreciable degree by determining total Al concentrations in urine and especially blood is difficult, due to the low levels present and problems with contamination and analysis. During the last decade, a number of studies employing the long-lived ^{26}Al isotope and accelerator mass spectrometry have considerably improved our understanding of Al absorption, metabolism and biokinetics [12–14]. However, the high cost of the isotope and low equipment availability hinder the widespread use of this methodology. In addition, adding the ^{26}Al isotope to tea either before or after making tea infusions would probably not be very helpful, because the speciation of ^{26}Al in the infusion would be different from that of the Al endogenous in the tea. Therefore, the concentrations (and speciation) of ^{26}Al in blood and urine after ingesting such isotope-labelled tea infusions would probably not be representative of the Al naturally present in tea.

4.2. Animal studies

Fairweather-Tait et al. [60] fed weanling rats for 28 days on a semi-synthetic diet. Relative to control rats, no increase in blood or liver Al was found in rats either drinking tea infusion instead of water, or consuming tea leaves incorporated into the diet, regardless of whether the diet was low in iron or not. Urine was not analysed in this study.

Deng et al. [61] fed 12-month-old rats for 2 months on a controlled diet with different levels of tea leaves or infusions of green and black tea added. Compared with the control group, all experimental groups had increased Al contents in the brain (30–135% increase) and in the tibia bone (10–55% increase). However, the reported concentrations were extremely high (80 $\mu g\ Al\ g^{-1}$ dry weight in the control brains), indicating serious analytical problems.

5. Epidemiological studies of tea consumption and Alzheimer's disease

Tea consumption has been investigated in at least four epidemiological case-control studies of AD. In a study of 109 AD cases <65 years of age in northern England [62], Forster et al. reported an odds ratio (OR) of 1.4 (95% confidence interval (CI) 0.8–2.6) for consuming >4 cups of tea per day. In a study of 258 AD cases in Canada [63], the OR for consuming tea (amount not specified) was 1.40 (95% CI 0.86–2.28). In a study of 170 AD cases in Australia [64], the OR for drinking >4 cups of tea daily sometime in life was 1.42 (95% CI 0.93–2.17). Finally, in a pilot study of only 23 AD cases in the USA, the OR for tea consumption was 0.7 ($P = 0.69$). Thus, the three full-scale case-control studies all

reported slight but non-significant increase in risk of about 40%, and although the studies therefore provide evidence that tea consumption is not a *strong* risk factor for AD, the possibility of a weaker relationship cannot be dismissed on the epidemiological evidence.

6. Discussion and conclusion

It is well documented that in tea infusions as prepared for human consumption, the total concentration of Al rarely falls outside the range 1–6 mg l^{-1}. Thus, for the majority of heavy tea drinkers around the world, tea is likely to be the largest single source of Al intake. The most important exceptions are individuals regularly consuming Al-containing antacids, and individuals with a diet rich in Al-containing food additives.

It is difficult to form a consistent picture of the speciation of Al in tea infusions from the studies published to date (Table 3). What does seem undisputed, however, is that more than 90% of the Al is bound to organic matter [45], but the nature of the organic species is unclear. The three studies employing size exclusion chromatography indicate that the main species detected by this method have MMs in the region 4000–8500 Da, and the species eluted as one [47,54] or two [31] sharp peaks, indicating well-defined species. From the MMs, it would seem reasonable to assume that these species are polyphenolic compounds. However, the two studies using ^{27}Al-NMR did not detect any polyphenolic Al complexes at all [50,51], but instead provided strong evidence for Al–oxalate complexes, which have MMs of about 300. One of the two studies employing ultrafiltration reported that 86% of the Al species had MMs $>20{,}000$ Da [45], the other that 70% of the Al species had MMs <3000 Da [48]. Some of the discrepancies are certainly related to problems inherent in the different speciation methods (see above). Clearly, much work remains to be done before we have satisfactory knowledge of the speciation of Al in tea.

All four studies investigating urinary excretion in human volunteers (Table 5) reported that tea consumption considerably increased Al excretion relative to water consumption, indicating measurable absorption of Al from drinking tea infusions. However, two of the studies [56,59] must be interpreted with caution because the concentrations of Al in urine are high relative to the presently accepted normal values of about 3–10 μg Al l^{-1} [44]. One of the studies reporting acceptably low Al concentrations indicated that the increased Al excretion when drinking tea could be at least partly explained by increased urinary volume [48]. The one study of Al in blood [57] reported no differences when drinking tea or water. In conclusion, it would seem that drinking tea leads to measurable, but moderate increases in urinary Al excretion, and that the Al present in tea is not much more bioavailable than that from other dietary sources [58].

In general, the speciation of an element may change several times from its dietary source on its way through different compartments of the organism to the final target site. After uptake from the gastrointestinal tract, Al probably largely follows the iron pathway in being bound to transferrin in blood and extracellularly [49], while the slightly more acid intracellular environment favours binding to phosphate-containing ligands like inositol or membrane phosphate groups. Because Al is very poorly absorbed (in the order of 0.1%) in the gastrointestinal tract [12–14,49], a dietary source of Al with high bioavailability could greatly increase the uptake of Al, even if the total concentration of Al in this source is not particularly high. Intuitively, one could expect [65] that the actual speciation of ingested Al would be of minor importance for bioavailability, since in the acid environment of the stomach, low-solubility Al compounds would largely pass into solution and a complete re-speciation of Al could be expected to take place. All three major studies [45,47,48] investigating the speciation of Al in tea infusions before and after stomach condition treatment clearly indicated a shift to lower-molecular-mass species under stomach conditions (Tables 3 and 4). When shifting from stomach to intestinal conditions (pH 6.3–6.5), a new dramatic re-speciation took place, either to high-molecular-weight soluble species [48] or to insoluble species [47].

It is perfectly conceivable, however, that certain species of Al could be stable enough to pass the gastrointestinal tract unchanged. For certain organic complexes of Al, differences in lipophilicity, hydrophilicity and hydrolytical stability are associated with remarkable differences in the biological effects [66]. An especially interesting compound is Al maltolate [67], which is very stable to hydrolysis and seems to be an unusually potent neurotoxin [68]. Maltol has been identified in green tea [69,70], and tea could also contain other organic Al complexes with properties similar to those of Al maltolate, stable enough to pass through the stomach and accumulate in brain and bone [71].

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