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REVIEW

Flavanols from green tea and phenolic acids from coffee: Critical quantitative evaluation of the pharmacokinetic data in humans after consumption of single doses of beverages

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Coffee contains a complex mixture of chlorogenic acids, which are mainly ferulic and caffeic acids ester-linked to quinic acid. Green tea contains flavanols, mainly (−)-epigallocatechin gallate (EGCG), (−)-epigallocatechin (EGC) and (−)-epicatechin (EC). For healthy humans, we identified seven studies on green tea in liquid form and five on coffee beverage reporting single-dose plasma pharmacokinetics. Weighted averages, based on the number of subjects, and elimination of outliers, allowed estimation of some pharmacokinetic parameters. After consumption of an ''average'' cup of green tea containing 112 mg of (−)-epigallocatechin gallate, 51 mg of EGC and 15 mg of EC in 200 mL, the predicted C_{max} values (total free and sulfate/glucuronide conjugates) in plasma are 125, 181 and 76 nM, respectively, together with 94 nM methyl-EGC and 51 nM methyl-EC (standard deviation $<20\%$). After consumption of an ''average'' cup of coffee (160 mg total chlorogenic acids (0.46 mmol)/200 mL), predicted C_{max} values of caffeic, ferulic, isoferulic, dihydrocaffeic and dihydroferulic acids are 114, 96, 50, 384 and 594 nM, respectively (too few studies to calculate standard deviation). Most studies report a very low amount of intact chlorogenic acids in plasma, with one exception. More studies on absorption of chlorogenic acids from coffee are required, including dose–response studies.

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1 Introduction

Coffee is one of the World's most popular beverages, and green tea is extensively drunk in many Eastern countries with increasing popularity in the West. Both beverages deliver these bioactive compounds in a water-soluble form, which contain various amounts of caffeine, depending on the brewing method. Coffee and green tea contribute extensively to the total intake of phenolics [1]. Coffee consumption may reduce the risk of diabetes [2]; both coffee and green tea may reduce the risk of cardiovascular diseases and of certain cancers [3–5]. Green tea contains five main catechins, (−)-epigallocatechin gallate (EGCG), (−)-epigallocatechin (EGC), (–)-epicatechin gallate (ECG), (−)-epicatechin (EC) and (+)-catechin. The amount varies from one tea preparation to another, but generally EGCG and EGC are present at the highest concentration, EC intermediate, and (+)-catechin and ECG lowest (www.phenol-explorer.eu). Intact green tea flavanols are absorbed in the small intestine. In coffee, chlorogenic acids are the major antioxidants. They are a family of esters formed between *trans*-cinnamic acids, mainly caffeic or ferulic acid, and quinic acid [6]. They can be ester-linked through several positions, and there can be one or two phenolic acids per quinic acid

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Abbreviations: CQA, caffeoyl quinic acid; **EC,** (–)-epicatechin; **ECG,** (–)-epicatechin gallate; **EGC,** (–)-epigallocatechin; **EGCG,** (–)-epigallocatechin gallate; **FQA,** feruloyl quinic acid

moiety, making a complex pattern, which depends on variety, location, roasting and processing. The nine main isomers in green coffee beans are as follows: 5-CQA (5-caffeoyl quinic acid), 4-CQA, 3-CQA, 3,5-diCQA, 4, 5-diCQA, 3,4-diCQA, 5-FQA (5-feruloyl quinic acid), 4-FQA and 3-FQA [6]. Coffee phenolics are absorbed mainly in the colon after cleavage of the ester bond and further metabolism, which is dependent on the microbiota. Although the pathways of metabolism are partially understood for the flavanols from green tea and the phenolic acids from coffee, there are still some discrepancies in the literature on the amount that is absorbed. In this respect, there is more information on green tea than there is on coffee. The former has been studied by many groups, but only a few groups have so far published quantitative data on the uptake of phenolic acids from coffee. This review will evaluate the quantitative data and present a weighted and judged average as a guide for use in future studies.

2 Qualitative analysis of bioavailability data for tea

After ingestion of green tea, ECG and (+)-catechin are generally absent from plasma. EGCG, EGC and EC are found in various forms, free or conjugated with glucuronide, sulfate or methyl groups. Many studies on blood and urine have been performed after enzymatic deconjugation, which removes the sulfate and glucuronide groups. When analysis is done without hydrolysis, up to ~90% of EGCG is present in the blood as the unconjugated form [7–9]. The proportion of EGCG that was conjugated was mostly as sulfated forms with less glucuronides [8]. In contrast, EGC and EC were present predominantly in plasma as conjugates [7, 8, 10]. EC was present as two-thirds sulfate and one-third glucuronide, while EGC was mostly as glucuronide with less sulfates [8]. Methylated forms are also present: 4′-*O*-methyl-EGC [10], 4′,4″-*O*-dimethyl-EGCG [11] and 3′ and 4′-*O*-methyl-EC [12] have been reported in plasma. There is considerable inter-individual variation in the amount of these forms in plasma following green tea consumption [10, 11, 13]. However, it is difficult to quantify the conjugates owing to the absence of appropriate standards. A simplified summary of the pathways of absorption of green tea catechins are shown in Fig. 1.

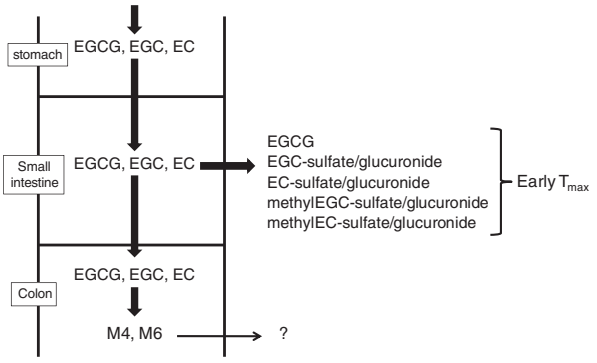

Figure 1. Absorption and metabolism of green tea catechins.

3 Quantitative analysis of bioavailability data for tea

Since beverage consumption may show some differences in bioavailability when compared to consumption of extracts or capsules, we have considered only consumption of green tea in liquid form when quantifying plasma concentrations. Table 1 summarises the data for EGCG after single-dose consumption of green tea beverages in healthy humans. Since the quantities given in each study are different, we have normalised the data to a 50-mg dose of each compound. This assumes linearity with dose, which is supported by evidence from dose–response studies: administration of a wide range of doses of pure EGCG to volunteers showed that the C_{max} in plasma was linearly proportional to the amount given [14]. There is some variability in the data, with a range of C_{max} from 19 to

Table 1. Pharmacokinetic data for EGCG after consumption of green tea beverage derived directly from the references indicated

Number of subjects	Dose of EGCG (mg)	C_{max} (nM)	T_{max} (hr)	AUC (μmol/h/L)	Urine (%)	C_{max}/dose (nM/50 mg)	Reference
6	109.5	260	1.6	1.95	0	119	[50]
6	219	711	2.4	4.85	0	162	[50]
6	328.5	700	2.7	5.37	0	107	[50]
8	67[a)]	170	1.45	1.11	nd	127	[10]
30	213.6	80	1.3	0.27	0.06	19	[51]
12	134	80	nd	nd	nd	30	[52]
2	63	330	2	1.06	nd	262	[53]
20	75	80	1.4	nd	0	53	[54]
10	105	55	1.9	0.17	nd	26	[55]

Data from [50] have been averaged with $n = 18$ for the weighted average calculation. nd, not determined in that publication.
a) Dose calculated assuming 70 kg body weight.

Table 2. Summary of evaluated data on green tea beverages

	T_{max} (h)	Urine (% of dose)	C_{max}/dose (L^{-1})	Half-life ($T_{1/2}$)
EGCG	1.7±0.4	0±0	$0.51 \times 10^{-3} \pm 0.08 \times 10^{-3}$	3.2±2.1
EGC	1.6±0.3	1.6±1.3	$1.08 \times 10^{-3} \pm 0.14 \times 10^{-3}$	2.0±0.6
EC	1.6±0.3	4.3±4.3	$1.46 \times 10^{-3} \pm 0.12 \times 10^{-3}$	2.6±1.3
Methyl-EGC	2.2	nd	0.56×10^{-3}	nd
Methyl-EC	1.5	nd	0.98×10^{-3}	nd

Values are shown as mean±standard deviation (for metabolites where there are sufficient studies). nd, not determined in that publication.

262 nM per 50 mg dose. Each study used a different number of volunteers, and so we have calculated a simple weighted average from the data, where the weighting is based on the number of volunteers (Fig. 2). The average data are shown in Table 2, including the expected C_{max} for a given dose, the half-life and the T_{max}. The data for EGC are shown in Table 3. When normalised to dose, the data vary about fivefold, with the exception of one study. We consider the value from this study to be an outlier (Fig. 2) and it was discarded from the weighted averages shown in Table 2. The data for EC are shown in Table 4. Most studies cluster together quite well with the exception of Lee et al. [10], which we regard as an outlier (Fig. 2). This is the same study that was discarded for EGC. The weighted averages are shown in Table 2.

From the weighted average data shown in Table 2, it can be seen that the trihydroxy substitution in the B ring (i.e. EGC) is less well absorbed than the dihydroxy catechol group (i.e. EC). EC and EGC are better absorbed than EGCG. This shows that galloylation reduces uptake of the parent compound in its native form.

Methylated forms were also reported but only in a very restricted number of studies owing to the absence of standards (Table 5). Methyl-EC was reported in two studies (the others did not look for it). Although there is some discrepancy in the C_{max} (Fig. 2), the average values were calculated (Table 2). For methyl-EGC, several studies are in good agreement, but one is clearly an outlier. This has been discarded and is not included in the estimation shown in Table 2.

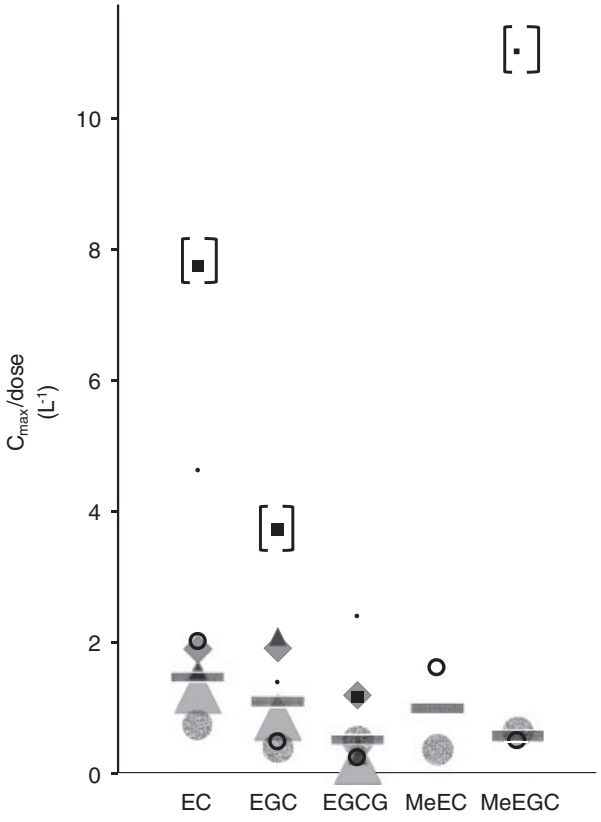

Figure 2. Maximum concentration (C_{max}) data for green tea beverages normalised to dose. The data are taken from the following publications in which the investigators gave green tea beverages to normal, healthy humans and measured the appearance of the stated compounds in plasma: grey diamonds [50]; black squares [10]; grey triangles [51]; black triangles [52]; black dots [53]; grey circles [54]; open circles [55]. Only one contribution per paper was allowed; if multiple doses were given, then these were averaged. The size of the data point is proportional to the number of subjects in the study. Weighted averages (shown as black bars) are calculated from the data accounting for the number of volunteers in the study, with study [10] excluded (see text), and is expressed in μM C_{max} values per μmol dose (of each flavanol). All studies used HPLC with electrochemical detection after enzymatic hydrolysis with β-glucuronidase and sulfatase, except for [54] and [55], which used HPLC with mass spectrometric detection and no enzymatic hydrolysis. We assume C_{max} is proportional to dose as shown [14] for EGCG. Excluded data points are shown in square brackets.

4 Urinary excretion of green tea flavanols

Following green tea ingestion, a range of compounds are found in urine, including parent compounds (Tables 1 and 3–5). EGCG is present at very low levels, if at all (summarised in Table 2). EGC and EC are present at significant levels (Table 2). The urinary forms of EGC and of EC appear to be mainly as conjugates, such as monoglucuronides and monosulfates of EGC and EC, and glucuronide and sulfates of methyl-EGC [15] and 4′,4″-dimethyl-EGCG [13]. The urinary excretion of both 4′,4″-dimethyl-EGCG and EGCG did not exceed 0.1% of the

Table 3. Pharmacokinetic data for EGC after consumption of green tea beverage derived directly from the references indicated

Number of subjects	Dose (mg)	C_{max} (nM)	T_{max} (h)	AUC (μmol/h/L)	Urine (%)	C_{max}/dose (nM/50 mg)	Reference
6	102	483	1.4	2.01	2.9	237	[50]
6	204	1660	1.8	8.14	1.9	407	[50]
6	306	1791	1.3	10.7	1.4	293	[50]
8	60[a)]	728	nd	3.1		607	[10]
30	270	740	1.3	2.6	0.19	137	[51]
12	81	550	nd	nd	nd	340	[52]
2	53	240	2	0.97	nd	226	[53]
20	32	40	2	nd	1.1	62	[54][b)]
10	79	126	2.2	0.56	3.1	80	[55][b)]

Data from [50] have been averaged with $n = 18$ for the weighted average calculation. nd, not determined in that publication.
a) Dose calculated assuming 70 kg body weight.
b) EGC-glucuronide in plasma, EGC-glucuronide+EGC-sulfate in urine.

Table 4. Pharmacokinetic data for EC after consumption of green tea beverage derived directly from the references indicated

Number of subjects	Dose (mg)	C_{max} (nM)	T_{max} (h)	AUC (μmol/h/L)	Urine (%)	C_{max}/dose (nM/50 mg)	Reference
6	38	190	1.4	2.0	4.8	253	[50]
6	75	651	1.8	3.7	5	434	[50]
6	113	655	1.8	4.1	2.6	291	[50]
8	16[a)]	427	1.5	1.8		1334	[10]
30	77	330	1.2	1.0	0.5	216	[51]
12	37	200	nd	nd	nd	270	[52]
2	16	255	2	0.9	nd	797	[53]
20	12	29	1.6	nd	0.73	125	[54][b)]
10	17	118	1.6	0.6	12.2	347	[55][c)]

Data from [50] have been averaged with $n = 18$ for the weighted average calculation. nd, not determined in that publication.
a) dose calculated assuming 70 kg body weight.
b) EC-glucuronide in plasma, EC-glucuronide and EC-sulfate in plasma.
c) EC-sulfate+EC-glucuronide

Table 5. Pharmacokinetic data for methylated catechins after consumption of green tea beverage derived directly from the references indicated

Compound	Number of subjects	Dose of flavanol (mg)	C_{max} (nM)	T_{max} (hour)	AUC (μmol/h/L)	Urine (%)	C_{max}/dose (nM/50 mg)	Reference
Methyl-EGC	10	79	125	2.2	0.76	8.3	79	[55]
Methyl-EGC[a)]	20	32	62	2.3	nd	1.13	97	[54]
Methyl-EGC	4	154	5300	2	nd	nd	1721	[10]
Methyl-EC-sulfate	10	17	90	1.7	0.42	16.2	265	[55]
Methyl-EC-sulfate	20	12	14	1.3	nd	0.49	58	[54]

nd, not determined in that publication.
a) Me-EGC-sulfate+Me-EGC-glucuronide.

ingested dose. After EC consumption, conjugates in human urine were EC-3′-*O*-glucuronide, 4′-*O*-methyl-EC-3′-*O*-glucuronide and 4′-*O*-methyl-EC-5 or 7-*O*-glucuronide [16]. Amounts in urine can be used to compare only between the absorption of single compounds (intra-individual or between treatment variation) and cannot be used to compare between different compounds (inter-compound comparison). Percentage urinary excretion only indicates the *minimum* amount of a compound that was absorbed in a given study. For some compounds, such as quercetin, which is predominantly excreted in the bile [17], the amount in urine is much less than the actual total amount absorbed.

5 Microbial metabolism of green tea flavanols

Hippuric acid is a major metabolite (~18% of green tea flavanols) after green tea ingestion in healthy volunteers [18, 19]. (−)-5-(3,4,5-trihydroxyphenyl)-γ-valerolactone (M4) and (−)-5-(3′,4′-dihydroxyphenyl)-γ-valerolactone (M6) were identified after green tea consumption in urine [13, 20]. M4, derived from microbial metabolism of EGC or EGCG, was detected only in urine, whereas M6, derived from microbial metabolism mostly of EC, was present in both plasma and urine [10]. The colonic microflora does not play a role in the methylation, sulfation or glucuronidation of the parent flavanols, since the pharmacokinetic parameters are similar in healthy and ileostomist subjects [21]. After microbial metabolism of green tea flavanols, several metabolites are found in urine such as 4-hydroxyphenylacetic acid, hippuric acid and pyrogallol [22], but these are common after consumption of many polyphenols [23].

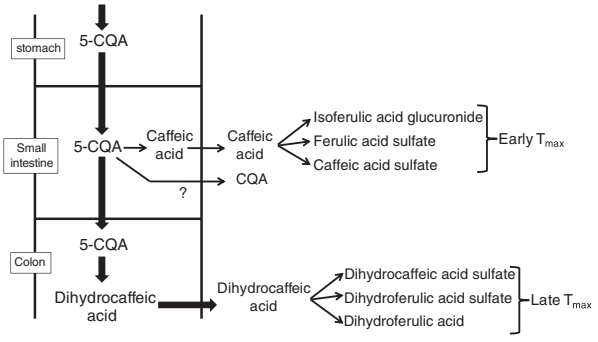

Figure 3. Absorption and metabolism of chlorogenic acids. The pathway is shown for 5-CQA, but would be equivalent for other CQA isomers, for FQAs and for diCQAs. Note also that there can be some isomerisation between different isomers of CQA and of FQA under physiological conditions.

6 Qualitative analysis of bioavailability data for coffee

There are far fewer studies on the bioavailability of phenolic acids from coffee. How much absorption occurs of intact chlorogenic acids, the parent compounds in coffee, is still unresolved. Large amounts of intact 3-CQA, 4-CQA and 5-CQA as well as 3,4-di-CQA, 3,5-di-CQA and 4,5-di-CQA in plasma have been reported by one group [24, 25]. In this study, samples were hydrolysed (to remove glucuronide and sulfate groups) using the *Helix pomatia* enzyme mixture, which has been reported to contain some chlorogenic acid esterase activity [26], but whether this activity was present or how this affected the intact chlorogenic acid was not explained. 3-, 4- and 5-CQA have been noted as absent after coffee consumption by other studies [27, 28]. In a study that measured intact chlorogenic acids in plasma 1 and 3 h after coffee consumption (~150 mg aglycone equivalents), low amounts of 3-CQA, 4-CQA, 5-CQA, 3-FQA, 4-FQA, 5-FQA and free ferulic acids were detected. Although the values are not reported at the T_{max} (which was not measured), the values at 1 h are between ~10 and 40 nM [29], which agrees with studies reporting a low level of intact chlorogenic acids in plasma. Studies on a different source of chlorogenic acid, artichoke, also qualitatively support the presence of only very low levels of intact chlorogenic acids in plasma. After consumption of artichoke, containing 154 mg caffeic acid equivalents (≈300 mg chlorogenic acids), there were no intact chlorogenic acids in human plasma [30]. After consumption of a meal including artichokes containing ≈470 mg chlorogenic acids, ≈20 nM chlorogenic acid (exact isomer not defined but presumably 5-CQA) was present at the C_{max} in plasma [31]. These values are very low and would support the studies showing very low levels of CQA in plasma after consumption of coffee. It would be useful to conduct an inter-laboratory investigation into the presence of CQA and diCQA in human plasma to solve this issue. Small amounts (<30 nM) of 3-FQA, 4-FQA and

Table 6. Pharmacokinetic data for phenolic acids after consumption of coffee beverage (dose calculated from total chlorogenic acid content derived directly from the references indicated

	Number of subjects	Dose (mg)	C_{max} (nM)	T_{max} (h)	AUC (μmol/h/L)	Urine (%)	C_{max}/50 mg dose	Reference
Caffeic acid	10	96	426	~1	nd	nd	222	[27]
	6	1236	1560	1.42	2.81	nd	63	[25]
	11	145	92	1	0.3	1.7	32	[28]
	11	335	81	1.6	nd	nd	12	[36, 37]
Caffeoyl quinic acid	10	96	0	nd	nd	nd	0	[27]
	6	1033	4890	2.3	11.5	nd	237	[25]
	11	145	50	0.6 to 1	0.06	0.5	17	[28]
Ferulic acid	11	145	76	0.6	0.467	3.9	26	[28]
	11	335	139.4	0.6 and 6.0[a)]	nd	nd	21	[36, 37]
Isoferulic acid	11	335	97.6	1.8	nd	nd	15	[36, 37]

a) Two peaks of ferulic acid are seen. nd, not determined in that publication.

5-FQA, and of 3- and 4-CQA-lactone sulfates have been reported in plasma after coffee consumption by healthy volunteers in one study, with ≈1% of the dose in urine (3-FQA+4-FQA+5-FQA+3-CQA-lactone sulfate+4-CQA-lactone sulfate) [28]. This was unaffected by the absence of the colon in ileostomists [32].

Studies on rats have shown that some chlorogenic acids are absorbed in the stomach [33] but that the majority is absorbed as phenolic acids after hydrolysis by microbial enzymes [34]. The pattern of esterase activity distribution in humans is consistent with this observation and leads to much more extensive hydrolysis in the colon compared to the small intestine [35]. Multiple pathways of metabolism operate in humans, leading to the circulation in plasma of dihydroferulic acid, dihydroferulic acid-4-*O*-sulfate, dihydrocaffeic acid-3-*O*-sulfate, all with a late T_{max}, and lower levels of ferulic and caffeic acid sulfates, which appear in plasma much earlier [28, 36, 37]. The pathways of absorption are summarised in Fig. 3.

7 Quantitative analysis of bioavailability data for coffee

Tables 6 and 7 show data on the absorption and excretion of phenolic acids after consumption of a single dose of coffee beverages by healthy humans. There are far fewer data points and numbers of volunteers compared to comparable studies on green tea. As above, the amount in the plasma has been normalised to the dose of the total chlorogenic acids calculated as aglycone (caffeic and ferulic acids) equivalents. However, there are no dose–response studies on metabolism and so we can only assume that the C_{max} is proportional to dose, which remains to be proven. For caffeic acid, the C_{max} values vary by ~19-fold between the four studies. One of these is very high [27] and was the first to be reported in humans. Since only two time points were measured, and the methodology was pioneering, this study has been excluded, since the other three more recent studies are in closer agreement (Fig. 4). A weighted average, based on the number of volunteers, was calculated for caffeic acid (Table 8). For intact chlorogenic acids, the values are too diverse to enable an average value to be estimated. For isoferulic acid, only one study has quantified this compound. For ferulic acid, only two studies have reported this, but they agree well. Only two studies have reported C_{max} values for dihydroferulic and dihydrocaffeic acids (Table 7). One of these studies reported values using LC-MS and chemically synthesised standards, whereas the second

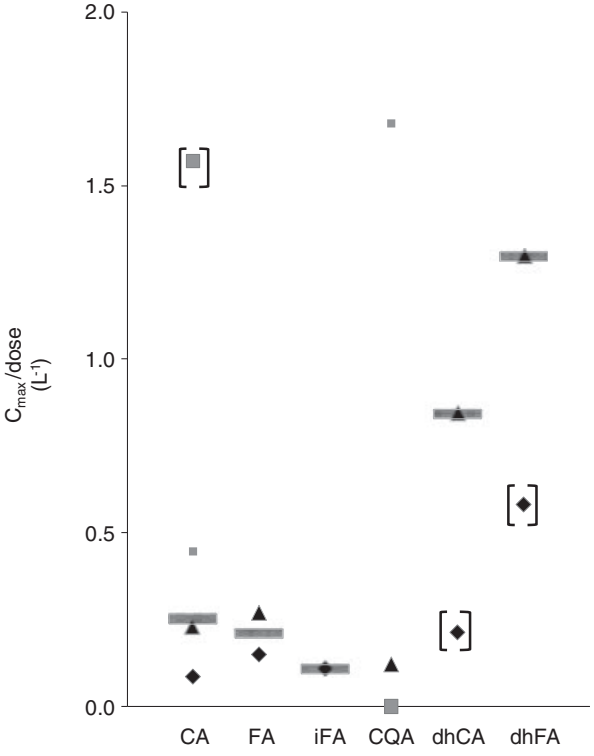

Figure 4. Maximum concentration (C_{max}) data for coffee beverages normalised to dose. The data are taken from the following publications, which gave coffee beverages to normal, healthy humans and measured the appearance of the stated compounds in plasma: larger squares [27]; smaller squares [25]; triangles [28]; black diamonds [37]. The size of the data point is proportional to the number of subjects in the study. Averages (shown as dark grey bars) are calculated from the data and are expressed in μM C_{max} values per μmol dose (total chlorogenic acids), assuming a linear dose response. Excluded data points (see text) are shown in square brackets.

Table 7. Pharmacokinetic data for dihydrocinnamic acids after consumption of coffee beverage (dose calculated from total chlorogenic acid content derived directly from the references indicated

	Number of subjects	Dose (mg)	C_{max} (nM)	T_{max} (h)	AUC (μmol/h/L)	Urine (%)	C_{max}/50 mg dose	Reference
Dihydrocaffeic	11	145	346	5	2.79	9.1	119	[28]
acid	11	335	200	10	nd	nd	30	[37]
Dihydroferulic	11	145	530	4.8	3.5	8	183	[28]
acid	11	335	550	10	nd	nd	82	[37]

nd, not determined in that publication.

study used enzymatic hydrolysis with β-glucuronidase, sulfatase and esterase to quantify free phenolic acids. However, it was subsequently shown that the predominant conjugates, sulfates, were incompletely hydrolysed by the sulfatase enzyme [38]. Consequently, the second study underestimated the level of dihydroferulic and dihydrocaffeic acids in the blood, and the values are excluded. CQA-lactones and FQA are also present in plasma at low levels. However, in healthy volunteers, these have only been reported in one study [28], since other studies did not consider the presence of these compounds.

8 Urinary excretion of coffee phenolic acids

A comprehensive profile of metabolites has been reported in healthy volunteers [28]. The main metabolites in urine are dihydrocaffeic acid-3-*O*-sulfate, feruloylglycine, ferulic acid-4-*O*-sulfate, dihydroferulic acid, dihydroferulic acid-4-*O*-glucuronide, caffeic acid-3-*O*-sulfate and isoferulic acid-4-*O*-glucuronide. The total amount of metabolites in urine is equivalent to ~27% of the consumed chlorogenic acid on a molar basis, showing that at least 27% of the chlorogenic acid is absorbed, but mostly in the form of a wide range of metabolites [28].

Table 8. Summary of evaluated data on coffee beverages

	T_{max} (h)	C_{max}/dose (L^{-1})
Caffeic acid	1.6±0.6	$0.25 \times 10^{-3} \pm 0.2 \times 10^{-3}$
Ferulic acid[a)]	0.6[b)]	0.21×10^{-3}
Isoferulic acid[c)]	1.8	0.11×10^{-3}
Dihydrocaffeic acid[a)]	7.5	0.84×10^{-3}
Dihydroferulic acid[a)]	7.4	1.3×10^{-3}

Values are shown as mean±standard deviation.
a) Data from two publications so no standard deviation shown.
b) First peak of a double peak, second peak (smaller) at ~6 h.
c) Data from one publication so no standard deviation shown.

9 Microbiota metabolism of coffee phenolic acids

Maximal uptake of chlorogenic acids from coffee depends on the presence of gut microbiota. Esterases necessary to hydrolyse the ester bond of chlorogenic acids are not present in human tissues, but are present in the colonic microbiota [35] and possibly in some digestive fluids or small intestinal microbiota [39]. Bifidobacterium and Lactobacillus, both species constituting the colonic microbiota, can hydrolyse chlorogenic acids [40]. When 5-CQA was incubated in vitro with human colonic microbiota, it disappeared rapidly within 2 h with the production of 3-hydroxyphenylpropionic acid and benzoic acid [41]. Hippuric acid is a major breakdown product of 5-CQA in rats [34]. In ileostomy volunteers, caffeic acid and ferulic acid, but only traces of 5-CQA, were found in the urine after consumption of pure 5-CQA [42]. A comprehensive profile of metabolites has been reported, both in healthy volunteers and in ileostomists [28, 32], illustrating the important role of the colon microbiota in absorption and distribution of metabolites. In ileostomists, the main metabolites were ferulic acid-4-*O*-sulfate and caffeic acid-3-*O*-sulfate, with lower amounts of feruloyl glycine and dihydrocaffeic acid-3-*O*-sulfate [32]. The total metabolites from coffee were only 8% of the dose, compared to 27% in healthy volunteers. This shows that the microbiota is responsible for the metabolism to dihydroferulic and dihydrocaffeic derivatives and that these constitute the majority of the metabolites so far found in healthy humans.

Table 9. Predicted absorption from typical green tea and coffee beverages

Parent, present in beverage (if it will not directly give indicated metabolite, then in brackets)	Measured metabolite	Typical dose in 200 mL beverage (mg)	Typical dose in 200 mL beverage (mmol)	Predicted C_{max} from Tables 2 and 8 (nM)
EGCG	EGCG	112	0.245	125
EGC	EGC	51	0.168	181
EC	EC	15	0.052	76
EGC	Methyl-EGC	51	0.168	94
EC	Methyl-EC	15	0.052	51
	Sum of flavanols	178	0.464	526
CQA+diCQA (+FQA)	Caffeic acid	160	0.457	114
CQA+diCQA+FQA	Ferulic acid	160	0.457	96
CQA+diCQA (+FQA)	Isoferulic acid	160	0.457	50
CQA+diCQA (+FQA)	Dihydrocaffeic acid	160	0.457	384
CQA+diCQA+FQA	Dihydroferulic acid	160	0.457	594
	Sum of phenolic acids	160	0.457	1239

10 Typical composition of green tea and coffee beverages and absorption of their component polyphenols

The compositions of eight different tisanes from commercially available green tea bags have been reported [43]. Based on a 200-mL beverage, the average content of EGCG+EGC+EC from these teas was 178 mg (Table 9). For coffee, a typical beverage is difficult to define since there are so many different ways to make coffee. Based on eight studies where coffee was administered, the average amount of chlorogenic acids per 200-mL cup was 160 mg total chlorogenic acids (~0.46 mmol) [24, 26, 28, 32, 36, 44–46], which is composed of various ratios of the isomers of CQA, FQA and di-CQA. Based on these typical values, the predicted C_{max} values are shown in Table 9 for each of the metabolites using the values calculated from published studies and presented in Tables 2 and 8. From these data, the predicted C_{max} for all the major phenolic acids from coffee and the major flavanols from green tea can be seen.

11 Concluding remarks and future work

When consumed by healthy volunteers, phenolic acids from coffee and flavanols from green tea are absorbed and metabolised by complex pathways involving reduction, hydrolysis, methylation, sulfation and glucuronidation. Green tea flavanols are absorbed predominantly in the small intestine, whereas phenolic acids from coffee are partially absorbed in the small intestine, but mostly after microbial catabolism in the colon. Quantification is generally performed using HPLC with coulometric detection (especially for green tea flavanols) or HPLC with mass spectrometric detection. Standards are only available for a limited number of compounds, although this has improved recently with a full set of metabolites from coffee being synthesised [47] allowing improved analysis. There are several gaps that need to be filled in the future. More studies on chlorogenic acid bioavailability are needed on healthy humans after consumption of coffee, including dose–response studies. The esterase activity of various tissues and gut microbiota have been tested [35, 48, 49] but it is still not clear how much hydrolysis of chlorogenic acids by digestive fluids and small intestinal microbiota occurs in vivo. For green tea, it is important that more standards are synthesised, especially the methylated, sulfated and glucuronidated derivatives of green tea catechins and also the valerolactones, which are major products of microbial metabolism but have not been extensively studied.

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