Chlorogenic Acid Bioavailability Largely Depends on Its Metabolism by the Gut Microflora in Rats[1]

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ABSTRACT Chlorogenic acid, the ester of caffeic acid with quinic acid, is one of the most abundant polyphenols in the human diet with coffee, fruits and vegetables as its major sources. Its antioxidant and anticarcinogenic properties have been well established in animal studies. However, little is known about its gut absorption and metabolism. In the present work, four groups of rats ($n = 8$) were fed a diet supplemented with chlorogenic, caffeic or quinic acids (250 μmol/d) or an unsupplemented diet for 8 d. Parent compounds and their metabolites were estimated in urine (24-h collection) and plasma by HPLC-electrospray ionization-tandem mass spectrometry. Significant differences in their levels were observed among the groups. The recovery of chlorogenic acid in urine was low (0.8%, mol/mol), and the total urinary excretion of caffeic acid liberated by hydrolysis of chlorogenic acid and its tissular methylated metabolites (ferulic and isoferulic acids) did not account for >0.5% (mol/mol) of the dose ingested. On the other hand, the metabolites of microbial origin, namely, *m*-coumaric acid and derivatives of phenylpropionic, benzoic and hippuric acids, represented the major compounds in both urine and plasma. Hippuric acid largely originated from the transformation of the quinic acid moiety, and all other metabolites from the caffeic acid moiety. These microbial metabolites accounted for 57.4% (mol/mol) of the chlorogenic acid intake. Such a high abundance of microbial metabolites shows that the bioavailability of chlorogenic acid depends largely on its metabolism by the gut microflora. Their potential importance in explaining the biological effects of dietary polyphenols is emphasized. J. Nutr. 133: 1853–1859, 2003.

KEY WORDS: • *chlorogenic acid* • *polyphenols* • *bioavailability* • *gut microflora* • *microbial metabolites* • *rats*

Hydroxycinnamic acids such as caffeic, ferulic, sinapic and *p*-coumaric acids are present in a large variety of fruits and vegetables including blueberries, grapes, apples, cereal brans, broccoli, spinach and lettuce (1). The most abundant hydroxycinnamic acid in food is chlorogenic acid, the ester of caffeic acid with quinic acid. Coffee, one of the most widely consumed beverages in the world, also contains high amounts of chlorogenic acid and provides 0.5–1 g/d hydroxycinnamic acids to coffee drinkers (1). Like other dietary polyphenols, chlorogenic acid is an antioxidant. In vitro, it scavenges radicals generated in the aqueous phase (2,3), increases the resistance of LDL to lipid peroxidation (4–6) and inhibits DNA damage (7,8). In vivo, when added to the diet, it inhibits chemically induced carcinogenesis of the large intestine, liver and tongue in rats and hamsters (9–12).

The biological properties of chlorogenic acid depend on its absorption in the gut and on its metabolism. Although the bioavailabilities of caffeic and ferulic acids have been investigated in several studies (13–21), little is known about the bioavailability of chlorogenic acid. In rats and humans, chlorogenic acid ingested as a pure compound or in coffee has not been detected (22,23) or found only as traces in urine (24,25). This was attributed to a poor absorption of chlorogenic acid through the small intestine barrier. Chlorogenic acid was also shown to be metabolized by the gut microflora into various aromatic acid metabolites including *m*-coumaric acid and derivatives of phenylpropionic and benzoic acids (26–28). These microbial metabolites may contribute to explaining the biological properties of polyphenols poorly absorbed in the gut such as chlorogenic acid. However, their importance has seldom been assessed in vivo (29,30).

In the present work, we studied the bioavailability of chlorogenic acid and compared it with that of caffeic and quinic acids in rats fed diets supplemented with pure compounds for 8 d. The relative abundance of microbial metabolites in urine and plasma was compared with that of their intact parent compounds.

MATERIALS AND METHODS

Chemicals. Chlorogenic acid, quinic acid, caffeic acid, ferulic acid, isoferulic acid, *p*-coumaric acid, *m*-coumaric acid, 3-hydroxybenzoic acid, 4-hydroxybenzoic acid, hippuric acid, 3-hydroxyphe-

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nylacetic acid, 3,4- dihydroxyphenylacetic acid and syringic acid were purchased from Sigma Chemical (St. Louis, MO); 3-hydroxyphenylpropionic acid and 3,4-dihydroxyphenylpropionic acid were from Apin Chemicals (Abingdon, UK). 3-Hydroxyhippuric acid and 4-hydroxyhippuric acid were kindly provided by P.C.H. Hollman (RIKILT, Wageningen University, The Netherlands) and R.R. Scheline (University of Bergen, Norway), respectively.

Animals and diets. Male Wistar rats (n = 32; Iffa Credo, L'Arbresle, Lyon, France) weighing 153.8 ± 0.3 g at the beginning of the experiment were housed singly in metabolic cages in a temperature-controlled room (22°C) and maintained in a normal light:dark cycle (dark period from 2000 to 0800 h) with free access to food from 1600 to 0800 h. After 14 d of adaptation to a nutritionally complete semipurified diet (**Table 1**) (31,32), rats were randomly divided into four groups of 8 rats and given four different diets for 8 d, i.e., the control semipurified diet (20 g/d) or the same diet supplemented with chlorogenic, caffeic or quinic acid (250 μmol in 20 g diet/d). This dose would represent an intake of ~2 g chlorogenic acid for humans ingesting 0.5 kg/d diet (dry matter). This quantity is equal to that found in 1.5–2 L of coffee (1). Animals were handled according to the recommendations of the Institutional Ethic Committee (INRA), in accordance with the decree N° 87–848.

Sampling procedures. Urine samples were collected for 24 h during the 8 d of the experimental diet in bottles containing sodium azide (1 g/L) and stored at –20°C. For plasma sampling, rats were anesthetized with pentobarbital (40 mg/kg body, intraperitoneal) 12 h after the beginning of the last meal. Blood was drawn from the abdominal aorta into heparinized tubes. Plasma obtained by centrifugation (10,000 × g for 2 min) was immediately acidified with 10 mmol/L acetic acid and aliquots kept at −20°C until analysis.

HPLC-electrospray ionization-tandem mass spectrometry (HPLC-ESI-MS-MS) analysis of metabolites. Urine samples (diluted in 0.1 mol/L sodium acetate buffer, pH 5, 175 μL) containing syringic acid (3 μmol/L) as an internal standard, were acidified to pH 4.9 with 20 μL of 0.58 mol/L acetic acid and incubated at 37°C for 45 min in the presence of 1100 U β-glucuronidase and 42 U sulfatase (*Helix pomatia* extract, Sigma Chemical). After acidification to pH 2 with 6 mol/L HCl, the urine was extracted twice with ethyl acetate and centrifuged at 2400 × g for 10 min. The resulting supernatant was dried under nitrogen, redissolved in 500 μL of 25% aqueous methanol and filtered (PTFE membrane, 0.45 μm, Millipore, Bedford, MA). Then a 40-μL aliquot of the filtrate was injected directly into the HPLC-ESI-MS-MS system. HPLC-ESI-MS-MS analyses were performed on a Hewlett-Packard HPLC system equipped with MS-MS detection (API 2000, Applied Biosystem, Toronto, Canada) according to a method recently described (30,33). Aromatic acid metabolites and syringic acid were detected according to the respective m/z values of their parent and product ions as follows: chlorogenic acid (353/190), caffeic acid (179/135), ferulic acid (193/134), isoferulic acid (193/134), *p*-coumaric acid (163/119), *m*-coumaric acid (163/119), 3,4-dihydroxyphenylpropionic acid (181/59), 3-hydroxyphenylpropionic acid (165/121), 3,4-dihydroxyphenylacetic acid (167/123), 3-hydroxyphenylacetic acid (151/107), 3-hydroxybenzoic acid (137/93), 4-hydroxybenzoic acid (137/93), 3-hydroxyhippuric acid (194/150), 4-hydroxyhippuric acid (194/100) and syringic acid (197/123).

For plasma samples, metabolites were hydrolyzed with glucuronidase/sulfatase, extracted by adding methanol/HCl 200 mmol/L (34) and analyzed by the same HPLC-ESI-MS-MS method.

HPLC-diode array detection (DAD) analysis of hippuric acid. Urine and plasma samples were hydrolyzed and extracted as described above. Hippuric acid was quantified by reversed-phase HPLC with diode array detection (Kontron, Milan, Italy) as previously described (30).

Data analysis. Data were entered into the Instat statistical analysis program (Instat, San Diego, CA). Comparisons of results were done by the Kruskal-Wallis test (nonparametric ANOVA). Significant differences were determined by post-hoc analysis using Dunn's Multiple Comparison Test. Differences with $P < 0.05$ were considered significant. Numerical values are expressed as means ± SEM.

TABLE 1

Composition of the semipurified diet

	g/kg dry feed
Ingredient	
Wheat starch	755
Casein	150
Peanut oil	50
Mineral mixture[1]	35
Vitamin mixture[2]	10

[1] Mineral mixture AIN-93M (per kg of diet): $CaHPO_4$, 18 g; K_2HPO_4, 3 g; KCl, 6 g; NaCl, 5 g; $MgCl^2$, 2.5 g; Fe_2O_3, 3 mg, $MnSO_4$, 150 mg; $CuSO_4$, 125 mg; $ZnSO_4 \cdot 7H_2O$, 120 mg; KI, 0.48 mg (31).

[2] Vitamin mixture AIN-76A supplemented in choline (mg/kg of diet): thiamin, 15; riboflavin, 20; pyridoxine, 10; nicotinamide, 100; pantothenate, 70; folic acid, 5; biotin, 0.3; cyanocobalamin, 0.05; retinyl palmitate, 1.5; *dl*-α-tocopheryl acetate, 125; cholecalciferol, 0.15; menadione, 1.5; ascorbic acid, 50; myo-inositol, 100; choline, 1360 (32).

RESULTS

Food intake and weight gain (4.4 ± 0.2 g/d) of rats were not different among the groups fed the control diet or diets supplemented with chlorogenic, caffeic or quinic acid. Rats consumed 17.1 ± 0.1 g/d of the control semipurified diet, 16.7 ± 0.1 g/d of the chlorogenic acid diet, 16.3 ± 0.1 g/d of the caffeic acid diet and 16.9 ± 0.2 g/d of the quinic acid diet. Chlorogenic, caffeic and quinic acid intakes were 208.7 ± 1.1, 203.7 ± 1.9 and 211.2 ± 2.2 μmol/d per rat, respectively.

Metabolites excreted in urine. Parent compounds and all their metabolites were analyzed in urine and plasma after deconjugation by glucuronidase/sulfatase. The chlorogenic acid diet affected the urinary excretion of chlorogenic acid itself and that of several of its metabolites, i.e., caffeic acid and its methylated forms (ferulic and isoferulic acids), *m*-coumaric acid, 3,4-dihydroxyphenylpropionic acid, 3-hydroxyphenylpropionic acid, 3-hydroxybenzoic acid, 3-hydroxyhippuric acid and hippuric acid (**Table 2**). The most abundant metabolites were hippuric acid, followed by 3-hydroxyphenylpropionic acid and *m*-coumaric acid. In contrast to the high urinary concentrations of these metabolites of microbial origin, the levels of urinary excretion of intact chlorogenic acid, caffeic acid and its derivatives ferulic and isoferulic acids, were much lower.

For rats fed the caffeic acid diet, all of the same metabolites described above were identified (Table 2). Hippuric acid was again the most abundant metabolite. In contrast to the chlorogenic acid and caffeic acid diets, the quinic acid diet affected the urinary excretion only of hippuric acid.

Yields of urinary metabolites. In rats fed the chlorogenic acid diet, the urinary excretion of intact chlorogenic acid, caffeic acid and its two methylated forms, ferulic and isoferulic acids, accounted for 1.3 ± 0.2% (mol/mol) of the dose of chlorogenic acid ingested (**Table 3**). On the other hand, the total urinary excretion of the metabolites of microbial origin, namely, *m*-coumaric acid and derivatives of phenylpropionic, benzoic and hippuric acids, accounted for 57.4 ± 8.8% (mol/mol) of chlorogenic acid intake. We assumed for this calculation that both caffeic and quinic acid moieties may form hippuric acid and that two molecules of hippuric acid may thus derive from each molecule of chlorogenic acid.

TABLE 2

Metabolite urinary excretion of rats fed diets supplemented with chlorogenic, caffeic or quinic acids for 8 d[1]

Metabolite	Control diet	Chlorogenic acid diet[2]	Caffeic acid diet[2]	Quinic acid diet[2]
		μmol/d		
Chlorogenic acid	ND[3]	1.8 ± 0.3	ND	ND
Caffeic acid	ND	0.4 ± 0.1[b]	18.10 ± 3.01[a]	ND
Ferulic acid	ND	0.51 ± 0.05[b]	6.5 ± 1.1[a]	ND
Isoferulic acid	ND	0.100 ± 0.003[b]	1.4 ± 0.2[a]	ND
p-Coumaric acid	0.030 ± 0.008	0.020 ± 0.003	0.010 ± 0.003	0.01 ± 0.02
m-Coumaric acid	ND	3.30 ± 1.05[a]	2.2 ± 0.7[a]	ND
3,4-Dihydroxyphenylpropionic acid	0.014 ± 0.005[b]	0.32 ± 0.06[a]	0.16 ± 0.03[a]	0.021 ± 0.001[b]
3-Hydroxyphenylpropionic acid	0.020 ± 0.002[c]	39.17 ± 9.02[a]	7.9 ± 1.2[b]	0.030 ± 0.009[c]
3,4-Dihydroxyphenylacetic acid	0.05 ± 0.01	0.035 ± 0.003	0.036 ± 0.007	0.06 ± 0.01
3-Hydroxyphenylacetic acid	0.06 ± 0.01	0.045 ± 0.007	0.054 ± 0.007	0.043 ± 0.005
3-Hydroxybenzoic acid	ND	0.20 ± 0.04[a]	0.18 ± 0.03[a]	ND
4-Hydroxybenzoic acid	0.7 ± 0.1	0.5 ± 0.1	0.4 ± 0.1	0.4 ± 0.1
3-Hydroxyhippuric acid	ND	0.7 ± 0.1[a]	0.1 ± 0.03[b]	ND
4-Hydroxyhippuric acid	0.31 ± 0.01	0.27 ± 0.05	0.22 ± 0.04	0.31 ± 0.05
Hippuric acid	6.8 ± 1.1[c]	158.8 ± 18.6[a]	53.5 ± 8.9[b]	123.6 ± 11.3[a]

[1] Values are means ± SEM, $n = 8$. Means in a row without a common letter differ, $P < 0.05$.
[2] Doses ingested [μmol/(d · rat)]: chlorogenic acid, 208.7 ± 1.1; caffeic acid, 203.7 ± 1.9; quinic acid, 211.2 ± 2.2.
[3] ND, not detected (limits of quantification for chlorogenic acid: 35 nmol; caffeic acid: 20 nmol; ferulic and isoferulic acids: 5 nmol; *m*-coumaric, 3-hydroxybenzoic and 3-hydroxyhippuric acids: 15 nmol).

Such a low yield of intact chlorogenic acid and caffeic acid derivatives and a high yield of microbial metabolites were continuously observed during the 8 d of the chlorogenic acid diet period with a transient peak of excretion after 1–3 d for some of the metabolites (**Fig. 1**).

In rats fed the caffeic acid diet, the total urinary excretion of intact caffeic, ferulic and isoferulic acids was 26-fold higher than that measured after the chlorogenic acid diet, and the total excretion of microbial metabolites accounted for only 28.1 ± 4.4% (mol/mol) of caffeic acid intake (Table 3). In rats fed quinic acid, the increase in the urinary excretion of hippuric acid represented half of the dose of quinic acid ingested (Table 3).

Metabolites in plasma. Only ferulic, *m*-coumaric, 3-hydroxyphenylpropionic and hippuric acids were detected in the plasma of rats fed the chlorogenic acid diet (**Table 4**). The metabolites of microbial origin (hippuric acid, 3-hydroxyphenylpropionic acid and *m*-coumaric acid) were the most abundant, as was observed for urine.

3-Hydroxyphenylpropionic acid was also detected in the plasma of rats fed caffeic acid, together with caffeic acid itself, ferulic acid and isoferulic acid. However, in this group of rats, the plasma concentration of 3-hydroxyphenylpropionic acid was much lower than those of caffeic acid and its two methylated derivatives.

DISCUSSION

Dietary polyphenols when tested in animals or humans affect various physiologic and physiopathologic processes, but the exact nature of the active compounds is still unknown. To understand how polyphenols affect these processes, it is necessary to determine the polyphenols and their metabolites that effectively reach the target tissues. In the present work, we identified and quantified the main metabolites formed in rats fed a diet supplemented with chlorogenic acid, one of the most common polyphenols in food. Both intact chlorogenic acid and a variety of metabolites were detected in the urine and plasma.

The detection of intact chlorogenic acid in urine shows that it has been absorbed in its native form. Several authors failed to detect chlorogenic acid in either plasma or urine of rats and humans fed pure chlorogenic acid or chlorogenic acid–containing foods (18,22,23,26,28,35). However, in

TABLE 3

Yields of metabolites in urine of rats fed diets supplemented with chlorogenic, caffeic or quinic acids for 8 d[1]

Metabolite	Urinary excretion, *% of intake, mol/mol*		
	Chlorogenic acid diet	Caffeic acid diet	Quinic acid diet
Chlorogenic acid	0.86 ± 0.12	—	—
Caffeic + ferulic + isoferulic acids	0.48 ± 0.07	12.8 ± 1.9	—
m-Coumaric acid	1.6 ± 0.5	1.1 ± 0.3	—
Hydroxyphenylpropionic acids	18.9 ± 4.2	4.0 ± 0.5	—
Hydroxybenzoic + hydroxyhippuric acids	0.43 ± 0.07	0.10 ± 0.03	—
Hippuric acid	36.5 ± 3.9	22.9 ± 3.6	55.3 ± 4.2

[1] Values are means ± SEM, $n = 8$.

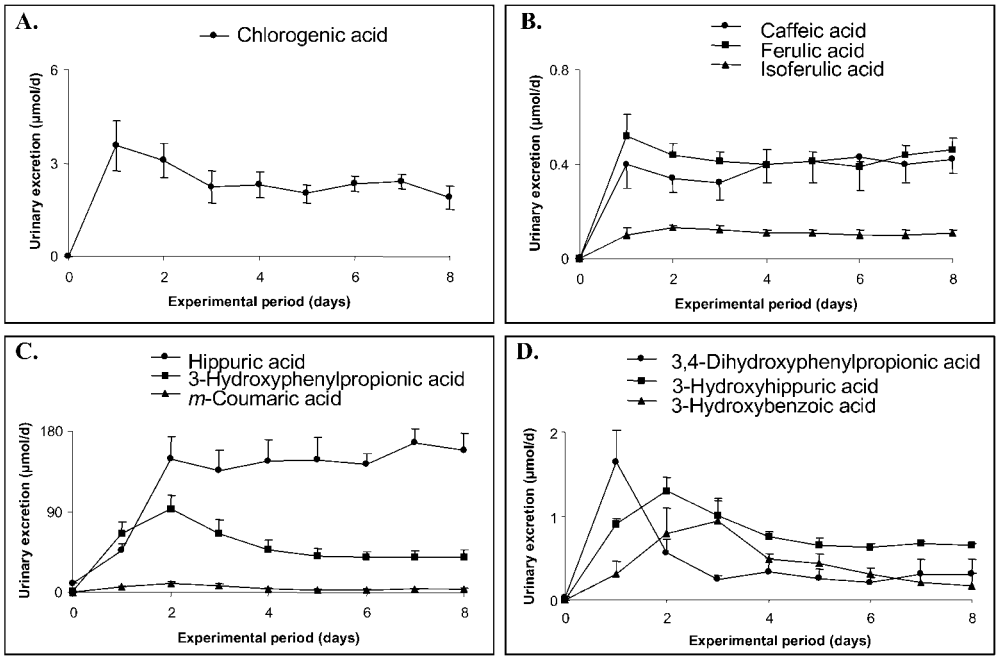

FIGURE 1 Kinetics of the urinary excretion of chlorogenic acid (*A*), caffeic acid and its derivatives ferulic and isoferulic acids (*B*) and the various microbial metabolites (*C*, *D*) formed in rats fed the chlorogenic acid diet for 8 d. Values (means ± SEM, $n = 8$) represent concentrations of chlorogenic acid and metabolites in 24-h urine collections in rats.

agreement with the present results, other authors detected traces of chlorogenic acid in urine of volunteers after intake of pure chlorogenic acid or prunes (24,25). A low absorption of chlorogenic acid (90–95% lower than that of caffeic acid) was also demonstrated in a perfusion experiment with rat jejunum (36). In a study with ileostomized volunteers, the recovery of chlorogenic acid in urine accounted for 0.29% of the dose ingested (25), a value close to that determined here (0.86%). Thus the gut absorption of chlorogenic acid appears weak compared with various other polyphenols (37).

A gut absorption of 33% of chlorogenic acid has been calculated by measuring its recovery in ileostomy effluents (25). The difference between this figure and the low recovery of chlorogenic acid in urine could be explained by its hydrolysis in the body. Accordingly, a rapid disappearance of chlorogenic acid in plasma associated with the appearance of caffeic acid conjugates was observed 0.5 h after intravenous administration of chlorogenic acid to rats (22). The rapid detection of caffeic acid and ferulic acid, 0.5–1 h after the ingestion of chlorogenic acid by rats or humans (22,23), and the absence of degradation of chlorogenic acid in the upper part of the intestinal tract (22,25) also support the hypothesis of hydrolysis in inner tissues. The corresponding mechanisms remain unclear because no esterase activity was found in the human small intestine, plasma or liver (38). Biliary excretion of chlorogenic acid could also explain its low recovery in urine.

The major part of chlorogenic acid is thus not absorbed in the proximal part of the gut and reaches the large intestine where it is hydrolyzed by the microflora, which exhibits esterase activities (38,39). Caffeic acid and quinic acid are liberated and further metabolized (40,41). The metabolism of both caffeic and quinic acids was explored in this work by supplementation of the diet of rats. The only metabolite derived from quinic acid, recognized by a significant increase in urinary excretion, is hippuric acid formed by aromatization of quinic acid into benzoic acid by the microflora and subsequent conjugation with glycine in the liver and kidney (41,42). Hippuric acid was also the major metabolite observed in the urine and plasma of rats fed the chlorogenic acid diet. The level of its urinary excretion was similar to that observed upon quinic acid intake. This clearly establishes for the first time that the quinic acid moiety in chlorogenic acid is the major precursor of hippuric acid. However the urinary excretion of hippuric acid

TABLE 4

Plasma metabolite concentrations in plasma of rats fed chlorogenic, caffeic or quinic acids for 8 d[1]

Metabolite	Control diet	Chlorogenic acid diet	Caffeic acid diet	Quinic acid diet
		μmol/L		
Caffeic acid	ND[2]	ND	41.3 ± 6.1	ND
Ferulic acid	ND	0.4 ± 0.1[b]	7.3 ± 0.7[a]	ND
Isoferulic acid	ND	ND	4.5 ± 0.4	ND
m-Coumaric acid	ND	1.9 ± 0.3	ND	ND
3-Hydroxyphenylpropionic acid	ND	12.9 ± 2.9[a]	1.4 ± 0.6[b]	ND
Hippuric acid	44.7 ± 5.3[b]	98.2 ± 15.8[a]	54.2 ± 9.3[b]	41.1 ± 4.8[b]

[1] Values are means ± SEM, $n = 8$. Means in a row without a common letter differ, $P < 0.05$.
[2] ND, not detected.

was also increased by supplementation of the diet with caffeic acid. Thus, the caffeic acid moiety in chlorogenic acid also contributes, although to a lesser extent, to the formation of this metabolite.

The other metabolites formed from chlorogenic acid were similar to those observed after caffeic acid intake and thus derive from the metabolism of the caffeic acid moiety. Caffeic acid is the direct product of chlorogenic acid hydrolysis, and ferulic and isoferulic acids are tissular metabolites formed by methylation of caffeic acid (14,43). *m*-Coumaric acid and hydroxylated derivatives of phenylpropionic, benzoic and hippuric acids derive from the metabolism of caffeic acid by the microflora. *m*-Coumaric acid is formed by dehydroxylation, and 3,4-dihydroxyphenylpropionic and 3-hydroxyphenylpropionic acids by hydrogenation and dehydroxylation (40,44,45). Their microbial origin was clearly established by suppression of their formation in rats treated with antibiotics (46,47) and in germ-free rats (48–50). 3-Hydroxyphenylpropionic acid is further dehydroxylated in part by the microflora and β-oxidized in tissue to form benzoic acid or directly β-oxidized once absorbed, yielding 3-hydroxybenzoic acid (17,47,51–53). Subsequent tissular conjugation of benzoic acid metabolites with glycine leads to the formation of 3-hydroxyhippuric and hippuric acids (42). The general pathway of chlorogenic acid metabolism in rats is shown in **Figure 2**.

The present results allow us to compare the relative abundance of the different metabolites. The total urinary recovery of caffeic acid and its tissular methylated derivatives did not exceed 0.5% of the dose of chlorogenic acid ingested. This contrasts with the higher yield of the total microbial metabolites (57.4%). Those derived from the caffeic moiety accounted altogether for a minimum of 20% of the chlorogenic acid ingested, hippuric acid excluded. Hippuric acid itself, deriving from both caffeic and quinic acids moieties accounted for 36.5% of the chlorogenic acid intake. The low recovery of intact chlorogenic acid, caffeic acid and its tissular methylated metabolites and the high yields of the microbial metabolites in rats fed chlorogenic acid clearly suggest that chlorogenic acid, poorly absorbed through the small intestine, largely reaches the cecum of rats where it is extensively degraded by the microflora.

In contrast, intake of pure caffeic acid, better absorbed in the small intestine, is associated with a higher plasma concentration and urinary excretion of intact caffeic acid and its

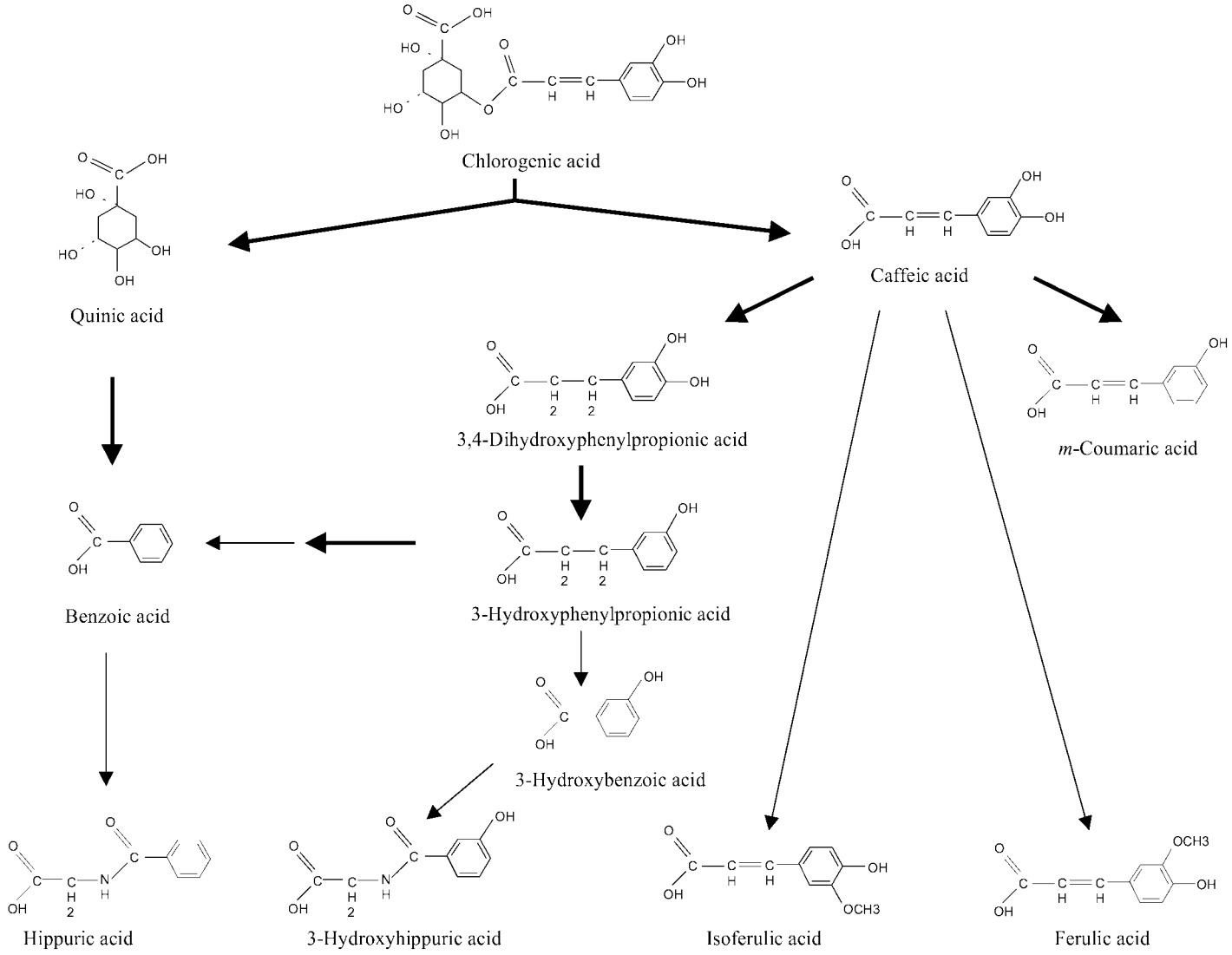

FIGURE 2 General pathway of chlorogenic acid metabolism in rats. Bold arrows indicate reactions carried out by the gut microflora.

tissular metabolites. They accounted altogether for 12.8% of the dose of caffeic acid ingested. Similar figures were previously reported in humans and rats (25,54). The yield of microbial metabolites is as a consequence lower (28.1%) than that observed for chlorogenic acid.

Therefore, polyphenols poorly absorbed in the small intestine such as chlorogenic acid, appear to provide higher yields of microbial metabolites. Similar conclusions were made for wine polyphenols compared with catechin when supplemented to the diet of rats (30) and for the flavonoids ingested by humans given a diet rich in fruits and vegetables (29). This raises questions about the nature of the active compounds responsible for the biological properties attributed to dietary polyphenols. The microbial metabolites still bearing a free phenolic group could act as antioxidants (2,55). Some of them were also shown to inhibit platelet aggregation in vitro (56). Thus more emphasis should be given in the future to the microbial metabolites to gain a fuller understanding of the health benefits of chlorogenic acid and other poorly absorbed dietary polyphenols.

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