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Metabolism of Sinapic Acid and Related Compounds in the Rat

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1. Administration of sinapic acid to the rat results in the excretion of 3-hydroxy-5-methoxyphenylpropionic acid, dihydrosinapic acid, 3-hydroxy-5-methoxycinnamic acid and unchanged sinapic acid in the urine. The sinapic acid conjugate sinalbin is also catabolized to free sinapic acid and 3-hydroxy-5-methoxyphenylpropionic acid in the rat. 2. 3,4,5-Trimethoxycinnamic acid is metabolized in part to sinapic acid and 3-hydroxy-5-methoxyphenylpropionic acid. 3. 3,5-Dimethoxycinnamic acid is metabolized to 3-hydroxy-5-methoxycinnamic acid and 3-hydroxy-5-methoxyphenylpropionic acid. 4. The metabolic interrelationships of these compounds were studied by the administration of intermediates and a metabolic pathway is proposed. 5. The metabolism of the corresponding benzoic acids was studied, but these compounds and their metabolites were shown not to be intermediates or products of the metabolism of the related cinnamic acids.

Several psychotomimetic compounds, including mescaline, possess a 3,4,5-trimethoxyphenyl group, which is known to contribute to their pharmacological activity (de Jong, 1945). Although the 3,4,5-trimethoxyphenyl group is infrequently found in natural products, the related 4-hydroxy-3,5-dimethoxyphenyl group is known to occur widely in dietary materials of plant origin, mainly as conjugates of sinapic acid (4-hydroxy-3,5-dimethoxycinnamic acid) (Bate-Smith, 1954). In addition there is evidence (Corner, Harborne, Humphries & Ollis, 1962) that 3,4,5-trimethoxycinnamic acid is also present in certain green plants. Since dietary constituents of this type may give rise to metabolites possessing undesirable psychopharmacological properties, especially in schizophrenic individuals where some abnormality of methylation may exist (Kety, 1965), it appeared desirable to investigate the metabolism of the naturally occurring methoxy-substituted trihydric phenolic acids together with certain compounds showing structural or metabolic relationships to them. It is noteworthy that although 3,4,5-trimethoxyphenylacetic acid, a metabolite of mescaline, is pharmacologically inert (Slotta & Muller, 1936), the metabolites 3,4,5-trimethoxyphenylacetaldehyde and 3,4,5-trimethoxyphenylethanol were found to be more active than mescaline itself (Friedhoff & Goldstein, 1962).

Previous studies on the metabolic fate of naturally occurring cinnamic acids have been limited to the mono- and di-hydric acids (Booth, Emerson, Jones & DeEds, 1957; Masri, Booth & DeEds, 1962; Scheline, 1968), although the metabolic fate of certain trihydric as well as dihydric benzoic acids has been investigated (Booth *et al.* 1959; Masri *et al.* 1962; Scheline, 1966). In the present investigation not only was the metabolic fate of sinapic acid and other related cinnamic acids studied but also the fate of the corresponding benzoic acids. This was necessary to eliminate these compounds as possible intermediates in the degradation of the related cinnamic acids.

EXPERIMENTAL

Animals. Male albino rats weighing approx. 250g. were used. The animals were housed in separate metabolism cages designed to permit the collection of urine separately from faeces. The animals were fed at 24hr. intervals but unrestricted water intake was allowed throughout the experimental period.

Diet. The animals were fed on a standardized powder-type diet described by Griffiths (1964).

Administration of compounds to animals. The compounds (200mg./animal, except where otherwise stated) were administered orally in single doses in admixture with the standard diet to animals that had previously been maintained for a minimum of 2 weeks on this diet. The urine was then collected over 5 days and the phenolic metabolites were obtained by continuous ether extraction under the conditions described by Griffiths (1964). The ethereal extracts were then submitted to paper or thin-layer chromatography as described below. In each experiment the urine obtained from a similar number of control animals maintained under the same conditions but not receiving the test substance was submitted to similar examination.

Paper chromatography. Whatman no. 1 paper was employed for normal qualitative chromatography, but for

the separation of larger amounts of metabolites by band chromatography either Whatman 3MM or 17MM paper was used. The solvent mixtures were: *A*, propan-2-ol–aq. NH_3 (sp.gr. 0·88)–water (8:1:1, by vol.); *B*, benzene–acetic acid–water (6:7:3, by vol.); *C*, chloroform–acetic acid–water (2:1:1, by vol.); *D*, 20% (w/v) KCl. The detecting reagents used were diazotized *p*-nitroaniline, diazotized sulphanilic acid (Smith, 1960) and the $FeCl_3$–$K_4Fe(CN)_6$ reagent of Barton, Evans & Gardner (1952) for phenolic acids, the Mäule reagent for compounds containing a 4-hydroxy-3,5-dimethoxyphenyl grouping (Seikel, 1964), aq. 1% $KMnO_4$ for cinnamic acids lacking a free hydroxyl group, and a naphtharesorcinol reagent for the detection of glucuronides (Elliott, Parke & Williams, 1959). A Bromocresol Green reagent (Smith, 1960) was used for the detection of nonphenolic acids. A *p*-dimethylaminobenzaldehyde reagent prepared as described by Smith (1960) was used for the detection of benzoylglycines. Several compounds (Table 1) were detected by their u.v. fluorescence.

Ethereal extracts of the urines were submitted to a screening procedure based on two-dimensional chromatography with solvent *A* followed by solvent *B*. The ethereal extracts were also examined for alkali-labile metabolites with solvent *C* followed by solvent *D*. Metabolites were then isolated by band chromatography with two or more solvent systems and the appropriate bands were eluted with acetone. All identifications were based on co-chromatography with authentic compounds, allowing the solvent front to run for 35cm. The R_F values observed under these conditions are given in Table 1.

Acid hydrolysis of conjugates in urine. The conditions employed were as described by Das & Griffiths (1968).

Spectra. The u.v.-absorption spectra were determined in methanol alone and in the presence of $AlCl_3$, with which a characteristic bathochromic displacement is given by benzoic acids and cinnamic acids but not by phenylpropionic acids (Nakagawa, Shetlar & Wender, 1964). The i.r. spectra were determined in Nujol mull in a Unicam SP. 200 spectrophotometer.

Colorimetric determination of phenolic metabolites. Although quantitative recovery of individual phenolic acid metabolites of sinapic acid by band chromatography did not prove practicable, the total phenolic-metabolite excretion after the administration of sinapic acid and other cinnamic acids was determined by a modification of a procedure described by Griffiths (1964).

The test compound (100mg.) was administered to each of a group of six rats, a second group of six animals being maintained as controls. The urine from each animal was collected over a period of 4 days and the final volume adjusted to 100ml. The diluted urine was then used directly for the colorimetric determination of total phenol (Griffiths, 1964). In all cases readings were related to a standard curve obtained with 0–60μg. of sinapic acid.

Thin-layer chromatography. Glass plates coated with a layer of silica gel G (E. Merck A.-G., Darmstadt, W. Germany) 250μm. thick were used. The chromatograms were developed by the ascending method with solvent *E* (benzene–acetic acid–water, 2:3:1, by vol.). The two diazotized amine reagents and aq. 1% $KMnO_4$ were found suitable for the detection of hydroxylated and non-hydroxylated cinnamic acids respectively on silica gel, although the colours obtained with the two former reagents differed from those observed on paper.

Table 1. *R_F values of metabolites of sinapic acid and related compounds*

The solvents are described in the text. Chromatograms were run until the solvent front was 35cm. from the origin.

	Ultraviolet fluorescence	Colour with diazotized *p*-nitroaniline	Colour with diazotized sulphanilic acid	Mäule reagent	$FeCl_3$+ $K_4Fe(CN)_6$	R_F values in solvents: *A*	*B*	*C*	*D*	*E*
Dihydrosinapic acid	Weak blue	White	Pink	+	+	0·55	0·73	0·94	0·64	0·52
3,5-Dihydroxycinnamic acid		Brown	Brown		+ +	0·32	0	0	0·13	—
3,5-Dihydroxybenzoic acid		Brown	Brown		+ +	0·33	0	0	0·48	—
3,5-Dimethoxycinnamic acid†	Blue	—	—		—	—	0·99	—	0	—
5-Hydroxy-3,4-dimethoxybenzoic acid		Red	Orange		+	0·39	0·63	0·84	0·62	—
p-Hydroxybenzoic acid		Pink	Yellow		+ +	0·36	0·40	0·44	0·60	—
3-Hydroxy-5-methoxybenzoic acid		Red–brown	Orange		+ +	0·30	0·40	0·52	0·48	—
3-Hydroxy-5-methoxycinnamic acid	Blue*	Orange	Yellow		+ +	0·55	0·58	0·60	0·25	0·55
3-Hydroxy-5-methoxyphenyl-propionic acid		Red–brown	Red–brown		+ +	0·60	0·56	0·63	0·63	0·47
3-*O*-Methylgallic acid		Red	Red		+	—	0·12	0·30	0·47	—
Sinapic acid	Blue	Grey–blue	Grey–pink	+	+ +	0·18	0·75	0·91	0·24	0·60
Syringic acid		Blue–yellow	Red	+	+	0·16	0·75	0·90	0·42	—
3,4,5-Trimethoxycinnamic acid	Blue	—	—		—	0·77	0·95	0·97	0·48	—

* After the paper was sprayed with diazotized *p*-nitroaniline the compound showed a characteristic yellow fluorescence. † Detected by the $KMnO_4$ reagent.

MATERIALS

Sinapic acid, 3,5-dimethoxycinnamic acid, sinalbin (sinapine 4-hydroxybenzylglucosinolate), 3,4,5-trimethoxycinnamic acid, syringic acid (4-hydroxy-3,5-dimethoxybenzoic acid), 3,5-dimethoxybenzoic acid and 3,4,5-trimethoxybenzoic acid were purchased from commercial sources and where necessary recrystallized before use.

3,5-Dihydroxycinnamic acid was prepared from 3,5-dimethoxycinnamic acid by the demethylation method of Blakley & Simpson (1964). The product had m.p. 245°, in agreement with that reported by Mauthner (1925).

3-Hydroxy-5-methoxycinnamic acid, m.p. 198°, was obtained by a modification of the latter procedure. 3,5-Dimethoxycinnamic acid (3g.) was heated under reflux with pyridinium chloride (1·5g.) for 30min. and the residue extracted with aq. 10% $NaHCO_3$. After a washing with diethyl ether the aqueous solution was adjusted to pH3 and re-extracted with ether. The second ether extract was evaporated to dryness and the residue heated under reflux with benzene (10ml.). The benzene-extracted residue was dissolved in hot water (15ml.), a small amount of insoluble material being discarded. On cooling the solution, an orange–yellow solid was deposited, which by paper chromatography in solvent *B* was shown to contain two phenolic components. One of these, the minor component, was shown to have an R_F identical with that of 3,5-dihydroxycinnamic acid (Table 1); the other possessed R_F 0·30. Repeated recrystallization from hot water, after treatment with activated charcoal, gave a crystalline solid, m.p. 198°, in agreement with that reported by Mauthner (1927).

3-Hydroxy-5-methoxybenzoic acid, m.p. 202°, was prepared from 3,5-dihydroxybenzoic acid by the method of Mauthner (1927).

Dihydrosinapic acid was prepared by treatment of sinapic acid (200mg.) in water (20ml.) with 10% sodium amalgam (10g.). The sodium amalgam was added slowly to the cooled solution over 1hr. Immediately evolution of hydrogen ceased, the aqueous solution was decanted, acidified with HCl to pH2 and submitted to continuous extraction with diethyl ether for 12hr. The ether extract was then evaporated to dryness and the residue recrystallized from dry diethyl ether, when dihydrosinapic acid was obtained as white crystalline needles, m.p. 103°, in agreement with that reported by Pearl (1959).

3-Hydroxy-5-methoxyphenylpropionic acid, obtained by sodium amalgam reduction of 3-hydroxy-5-methoxycinnamic acid under the conditions employed in the preparation of dihydrosinapic acid, crystallized as colourless platelets, m.p. 127°, in agreement with that reported by Salway (1910).

RESULTS

Sinapic acid. Ethereal extracts of the urine of six rats, each given sinapic acid (200mg.), contained compounds showing chromatographic properties and i.r. and u.v. characteristics identical with those of 3-hydroxy-5-methoxycinnamic acid, dihydrosinapic acid, 3-hydroxy-5-methoxyphenylpropionic acid and sinapic acid (Tables 1 and 2). Comparison of the chromatograms obtained on successive days showed that sinapic acid excretion was maximal on the first day and it was accompanied by 3-hydroxy-5-methoxyphenylpropionic acid. On the second and third days excretion of 3-hydroxy-5-methoxyphenylpropionic acid and 3-hydroxy-5-methoxycinnamic acid was maximal. Dihydrosinapic acid was present only in trace amounts on the first day but larger amounts were excreted on the second day. A control group of rats maintained under the same conditions but fed on a sinapic acid-free diet gave none of these metabolites.

Table 2. *Ultraviolet-absorption maxima of substituted cinnamic acid and benzoic acid metabolites*

	Absorption maxima (nm.)	
	In methanol	In methanol + $AlCl_3$
Dihydrosinapic acid	273	273
3,5-Dimethoxycinnamic acid	227, 281	230, 293
5-Hydroxy-3,4-dimethoxybenzoic acid	258	271
p-Hydroxybenzoic acid	253	262
3-Hydroxy-5-methoxybenzoic acid	250, 305	260, 315
3-Hydroxy-5-methoxycinnamic acid	282	294
3-Hydroxy-5-methoxyphenylpropionic acid	274, 280	274, 280
Sinapic acid	232, 315	242, 337
Syringic acid	270	290
3,4,5-Trimethoxycinnamic acid	228, 294	235, 313

3,4,5-Trimethoxycinnamic acid, 5-hydroxyferulic acid (3,4-dihydroxy-5-methoxycinnamic acid), 3,5-dimethoxycinnamic acid and syringic acid were not detected in the urine nor were any benzoylglycines detected other than those found in control urines.

On acid hydrolysis, under the standard conditions, of the urine of rats given sinapic acid the only additional compound detected was shown to be 2,6-dimethoxyphenol, an artifact produced by the action of hot acid on unchanged sinapic acid, but increase in the amounts of 3-hydroxy-5-methoxyphenylpropionic acid and 3-hydroxy-5-methoxycinnamic acid indicated that these compounds are in part present as acid-labile conjugates.

By the colorimetric method, it was shown that 26·5% of the sinapic acid administered was excreted as phenolic compounds in the urine (Table 3).

3,5-Dimethoxycinnamic acid. Ethereal extracts of the urine of six rats, which had each received 3,5-dimethoxycinnamic acid (200mg.), were found to contain two major metabolites showing chromatographic and spectral characteristics identical with those of 3-hydroxy-5-methoxyphenylpropionic acid and 3-hydroxy-5-methoxycinnamic acid. The corresponding benzoic acid, 3-hydroxy-5-methoxybenzoic acid, was not detected. Trace amounts of

Table 3. *Excretion of phenolic metabolites after administration of substituted cinnamic acids*

Phenolic metabolites are expressed as mg. of total phenol (measured as sinapic acid) and the values are the means of six experiments with the ranges in parentheses.

Compound administered	Phenolic metabolites: Total (mg.)	Phenolic metabolites: Increase over controls (mg.)
Control	13·3 (10–15·5)	—
Sinapic acid (100 mg.)	39·8 (34–42·5)	26·5
3,5-Dimethoxycinnamic acid (100 mg.)	18·0 (15–22)	4·7
3,4,5-Trimethoxycinnamic acid (100 mg.)	24·8 (21–30)	11·5

3,5-dimethoxycinnamic acid and sinapic acid were also present (Tables 1 and 2). These compounds were absent in urines of the control group. No benzoylglycines were detected other than those present in the control group. An ether-soluble glucuronide of low R_F in solvents *A* and *B* was detected but not identified. Acid hydrolysis of the urine of rats given 3,5-dimethoxycinnamic acid gave rise to increased amounts of 3-hydroxy-5-methoxyphenylpropionic acid and 3-hydroxy-5-methoxycinnamic acid.

Colorimetric measurement showed that 4·7% of the 3,5-dimethoxycinnamic acid administered is excreted as phenolic compounds in the urine (Table 3).

3-Hydroxy-5-methoxycinnamic acid. Administration of 3-hydroxy-5-methoxycinnamic acid (50 mg.) to six rats resulted in the excretion of 3-hydroxy-5-methoxyphenylpropionic acid accompanied by unchanged 3-hydroxy-5-methoxycinnamic acid. 3-Hydroxy-5-methoxybenzoic acid was not detected.

Dihydrosinapic acid. Administration of dihydrosinapic acid (200 mg.) to six rats resulted in the excretion of small amounts of 3-hydroxy-5-methoxyphenylpropionic acid accompanied by unchanged dihydrosinapic acid.

3,4,5-Trimethoxycinnamic acid. After the administration of 3,4,5-trimethoxycinnamic acid (200 mg.) to each of six rats, the presence of metabolites chromatographically and spectrally identical with sinapic acid and 3-hydroxy-5-methoxyphenylpropionic acid was shown (Tables 1 and 2). Two further metabolites were detected but not identified. Compound A gave a red–brown colour with diazotized *p*-nitroaniline, and had a similar R_F value to that of 3-hydroxy-5-methoxyphenylpropionic acid in solvent *A*, but a higher R_F than it in solvent *B*. Compound B resembled 3-hydroxy-5-methoxycinnamic acid in its colour reaction with diazotized *p*-nitroaniline and in having a similar R_F in solvent *A*, but had a higher R_F than it in solvent *B*. Both compounds could be detected on the chromatograms in increased amounts after acid hydrolysis of the urine. The presence of trace amounts of 3,4,5-trimethoxycinnamic acid on the chromatograms was detected by its blue fluorescence and by the use of the Bromocresol Blue spray reagent (Tables 1 and 2). It was shown that 11·5% of the 3,4,5-trimethoxycinnamic acid administered is excreted as phenolic metabolites in the urine (Table 3).

Sinalbin. Sinalbin (100 mg.) was administered to each of six rats by stomach tube. Examination of the urine collected over the first 24 hr. revealed the presence of metabolites that had chromatographic and spectral characteristics identical with those of sinapic acid, dihydrosinapic acid and *p*-hydroxybenzoic acid (Tables 1 and 2). On the second day a further metabolite was excreted that was shown by similar means to be identical with 3-hydroxy-5-methoxyphenylpropionic acid.

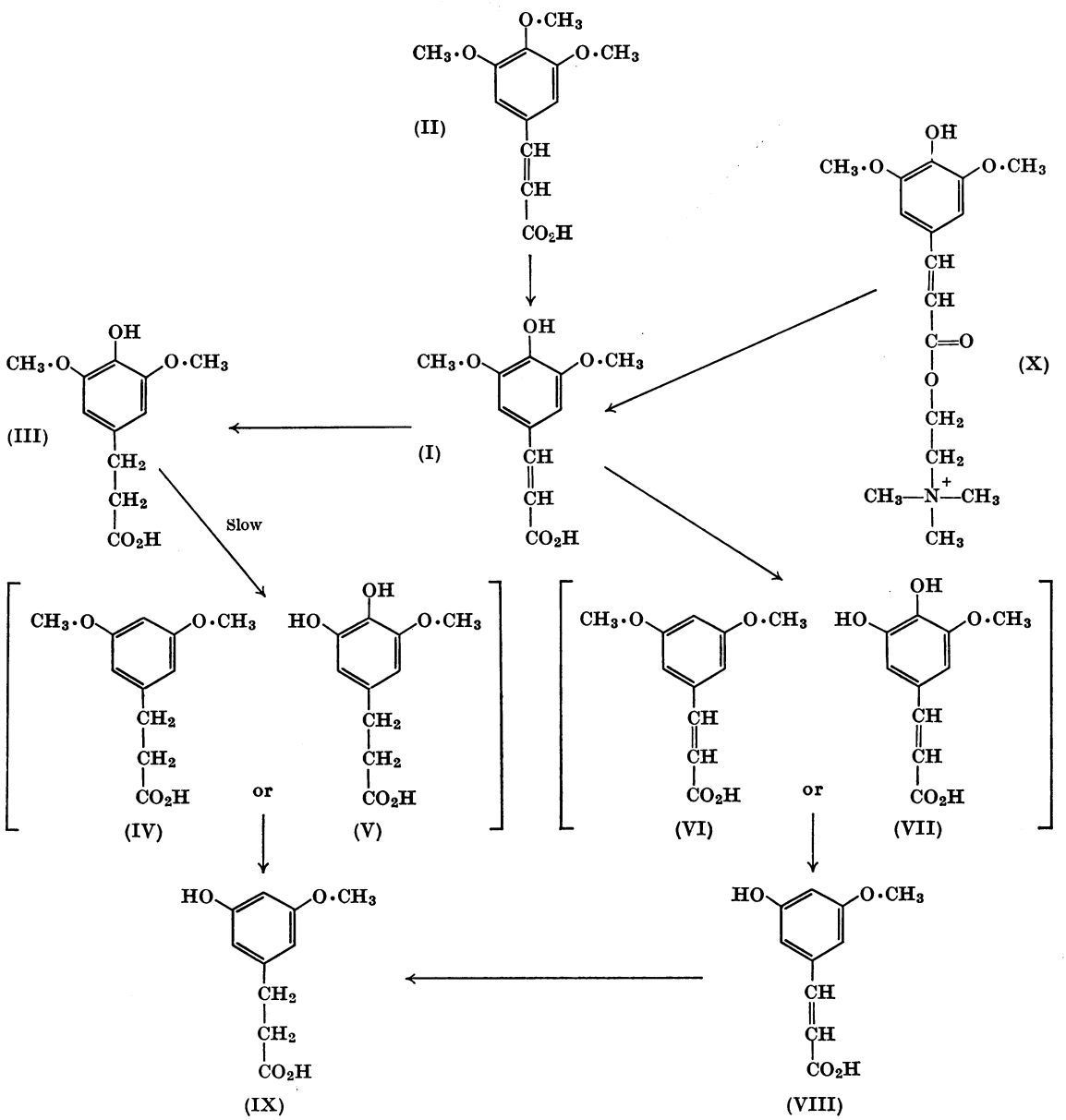
3,4,5-Trimethoxybenzoic acid. 3,4,5-Trimethoxybenzoic acid (200 mg.) was administered orally to each of six rats. Examination of the urine showed that the major metabolite possessed chromatographic and spectral properties identical with those of 5-hydroxy-3,4-dimethoxybenzoic acid. A second metabolite detected in small amounts was shown to be syringic acid (Tables 1 and 2). 3-*O*-Methylgallic acid was not detected.

Syringic acid. Oral administration of syringic acid (200 mg.) to each of six rats resulted in the excretion of large amounts of unchanged syringic acid. In addition two minor metabolites were detected. The first of these was unstable in solvent, *A* but had similar R_F values to those of 3-*O*-methylgallic acid in solvents *B*, *C* and *D*. The second showed similar chromatographic and spectral properties to 5-hydroxy-3,4-dimethoxybenzoic acid (Tables 1 and 2).

3,5-Dimethoxybenzoic acid. Administration of 3,5-dimethoxybenzoic acid (200 mg.) to six rats gave rise to metabolites that were shown to have similar chromatographic and spectral properties to those of 3-hydroxy-5-methoxybenzoic acid and syringic acid respectively (Tables 1 and 2). A third metabolite giving a red colour with *p*-nitroaniline, of R_F 0·26 in solvent *A* and R_F 0·20 in solvent *B*, was not identified. Trace amounts of 3,5-dihydroxybenzoic acid were also detected (Table 1).

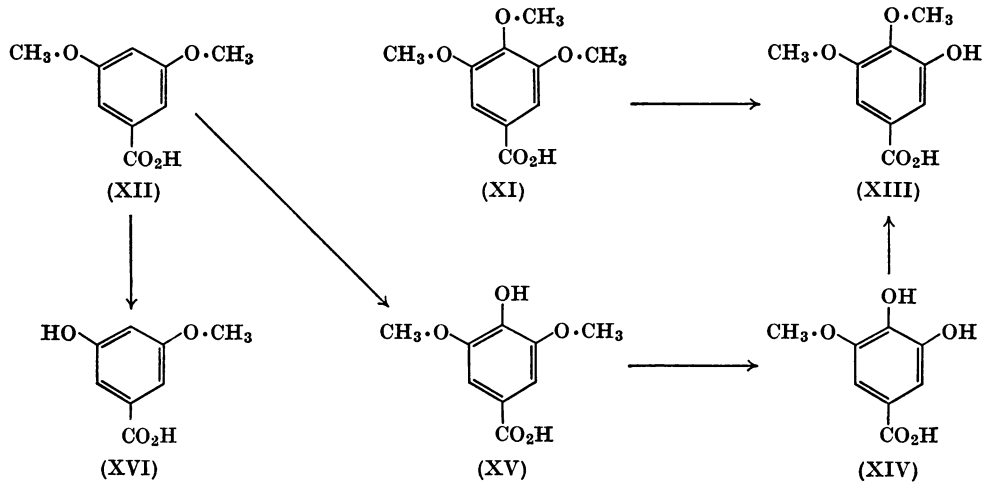
DISCUSSION

The metabolic pathway of sinapic acid and some related compounds in the rat is shown in Scheme 1. The interconversions shown involve mainly *p*-dehydroxylation, demethylation and reduction of the double bond in the cinnamic acid side chain. It



Scheme 1. Metabolic pathways of sinapic acid and related compounds in the rat: (I) sinapic acid; (II) 3,4,5-trimethoxycinnamic acid; (III) dihydrosinapic acid; (IV) 3,5-dimethoxyphenylpropionic acid; (V) 3,4-dihydroxy-5-methoxyphenylpropionic acid; (VI) 3,5-dimethoxycinnamic acid; (VII) 5-hydroxyferulic acid; (VIII) 3-hydroxy-5-methoxycinnamic acid; (IX) 3-hydroxy-5-methoxyphenylpropionic acid; (X) sinapine moiety of sinalbin. The compounds shown in square brackets are postulated intermediates in the conversion of compound (III) into compound (IX) and of compound (I) into compound (VIII).

is notable that none of the 3,4,5- or 3,5-substituted cinnamic acids and phenylpropionic acids are converted into the corresponding benzoic acids or their metabolites (Scheme 2), although certain mono- and 3,4-substituted cinnamic acids and phenylpropionic acids are readily converted into the corresponding benzoic acid derivatives (Booth *et al.* 1957; Das & Griffiths, 1968).



Scheme 2. Metabolic pathways of substituted benzoic acids in the rat: (XI) 3,4,5-trimethoxybenzoic acid; (XII) 3,5-dimethoxybenzoic acid; (XIII) 5-hydroxy-3,4-dimethoxybenzoic acid; (XIV) 3-*O*-methylgallic acid; (XV) syringic acid; (XVI) 3-hydroxy-5-methoxybenzoic acid.

The isolation of 3-hydroxy-5-methoxycinnamic acid and 3-hydroxy-5-methoxyphenylpropionic acid from the urine of rats given sinapic acid and of 3-hydroxy-5-methoxyphenylpropionic acid from the urine of rats given dihydrosinapic acid provides evidence for the *p*-dehydroxylation of 4-hydroxy-3,5-dimethoxycinnamic acid and 4-hydroxy-3,5-dimethoxyphenylpropionic acid. Whether this *p*-dehydroxylation occurs directly with sinapic acid or with a demethylated intermediate, i.e. 5-hydroxyferulic acid (Scheme 1), was not established as neither of the expected intermediates, 3,5-dimethoxycinnamic acid and 5-hydroxyferulic acid, was excreted in the urine. Since, however, the direct administration of 3,5-dimethoxycinnamic acid to the rat, although giving rise to 3-hydroxy-5-methoxycinnamic acid and 3-hydroxy-5-methoxyphenylpropionic acid, resulted in the excretion of only trace amounts of the unchanged compound, it is evident that, if 3,5-dimethoxycinnamic acid were formed as an intermediate, its excretion would not be expected. Similar *p*-dehydroxylation has been reported with 3,4-dihydroxycinnamic acid and 4-hydroxy-3-methoxycinnamic acid (Booth *et al.* 1957; Booth & Williams, 1963; Scheline, 1968). However, no evidence was found in the present investigation of *p*-dehydroxylation of 3,5-disubstituted 4-hydroxybenzoic acids. This is in agreement with the finding of Booth *et al.* (1959) that the related compound, gallic acid, was not dehydroxylated when given to the rat, but methylated to give 4-*O*-methylgallic acid. The formation of 5-hydroxy-3,4-dimethoxybenzoic acid from syringic acid (Scheme 2) also involves methylation in the 4-position, but no evidence was found for the 4-methylation of sinapic acid, although 3,4,5-trimethoxycinnamic acid would, if formed, be readily detectable on the chromatograms under u.v. light. Moreover, since 3,4,5-trimethoxycinnamic acid is readily converted into sinapic acid and its metabolites (Scheme 1), a pathway for its degradation is available.

Although Indahl & Scheline (1968) reported that decarboxylation of certain 4-hydroxycinnamic acids to the corresponding vinylphenol is carried out *in vitro* by strains of *Bacillus* isolated from rat intestine, no neutral phenolic compounds were detected in rat urine after the administration of sinapic acid. This may be a consequence of the presence of methoxyl groups adjacent to the 4-hydroxyl group, as Scheline (1966) noted that such substitution decreased or abolished the decarboxylation of 4-hydroxybenzoic acids. Sinalbin, a sinapic acid conjugate present in mustard (Remson & Coale, 1884; Bauer & Holle, 1937), is metabolized by the rat to free sinapic acid and 3-hydroxy-5-methoxyphenylpropionic acid. The *p*-hydroxybenzoic acid detected is thought to have arisen from the 4-hydroxybenzylglucosinolate moiety.

The known ability of the intestinal microflora of the rat to effect *p*-dehydroxylation of 3,4-dihydroxycinnamic acid (Booth & Williams, 1963) and of metabolites derived from flavonoids possessing adjacent hydroxyl groups in the 3′,4′-positions (Griffiths, 1964; Das & Griffiths, 1968) suggests a similar microbial involvement in the *p*-dehydroxylation of either the postulated intermediates, 5-hydroxyferulic acid and 3,4-dihydroxy-5-

methoxyphenylpropionic acid, or of sinapic acid and dihydrosinapic acid (Scheme 1).

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