spectral studies. The coordination of the ligands to the metal ion through N and O is supported by the appearance of M—N(480 cm^{-1})[8] and M—O (360 cm^{-1})[8] bands in the IR spectra. The presence of a strong band in the region of 1170–1100 cm^{-1} indicate the presence of coordinated oxine[9] molecule. The presence of new bands at 3400 cm^{-1} and 1600 cm^{-1} showing the antisymmetric and symmetric *OH* stretching and HOH bending[10] are due to coordinated water molecules. A sharp band at 1565 cm^{-1} can be correlated to the $-\overset{|}{C}=O$ stretching of the involved acid and indicates the chelation through carboxylic group.

From Table II one can see that 1:1:1, ternary complexes have been found more active to check the growth of the fungi in comparison to the free metal and involved ligands. The increased activity of these complexes is according to our earlier observations[11] which is again supported by Albert *et al.*[12] and probably depends upon the following facts: (1) due to more liposoluble nature of the ligands on being coordinated with metal ion. (2) To the combined activity effect of the involved ligands and complex. (3) To the comparatively faster diffusion of the metal complex as a whole through the cell membrane of the fungi.

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SYNTHESES OF *ANDROGRAPHIS PANICULATA* FLAVONES

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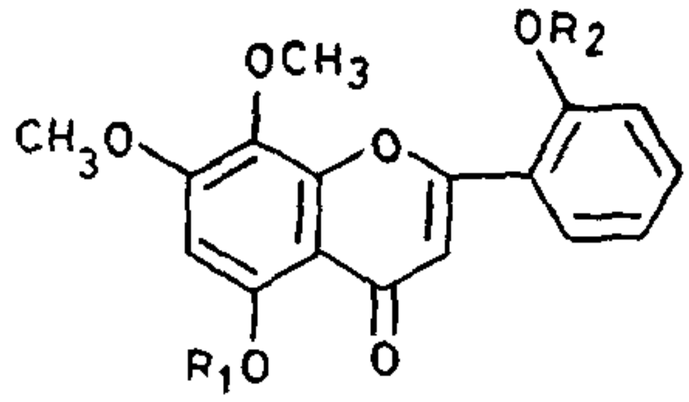
ABSTRACT

Constitutions assigned to the two flavones isolated from Andrographis paniculata as 5-hydroxy-7,8,2′-trimethoxyflavone (I) and 5,2′-dihydroxy-7,8-dimethoxyflavone (II) have been confirmed by their syntheses.

A NEW flavone ($C_{18}H_{16}O_6$, m.p. 186–87°) isolated[1,2] from *Andrographis paniculata*, on the basis of colour reactions, spectral data[1] and synthetic studies[2] was given the constitution, 5-hydroxy-7,8,2′-trimethoxyflavone (I). This paper now reports the synthesis of I by the modified[3–5] Baker–Venkataraman method which is more convenient and gives good yields. For this purpose, 2-hydroxy-3,4,6-trimethoxyacetophenone[6] (III) used as the starting material was treated with 2-methoxybenzoyl chloride in the presence of anhydrous potassium carbonate in dry acetone to obtain 2-hydroxy-3,4,6,2′-tetramethoxydibenzoylmethane (IV). Cyclodehydration of the dibenzoylmethane (IV) yielded 5,7,8,2′-tetramethoxyflavone (V) which on selective demethylation gave 5-hydroxy-7,8,2′-trimethoxyflavone (I) identical with the above compound isolated from

A. paniculata as judged by its melting point and that of its acetate, thereby confirming its proposed constitution.

Another flavone ($C_{17}H_{16}O_6$, m.p. 254–55°) also isolated from *Andrographis paniculata*, on the basis of colour reactions, spectral data and its conversion to I, indicated its constitution as 5,2′-dihydroxy-7,8-dimethoxyflavone[1,2] (II). This communication confirms the proposed structure by synthesis. The flavone (II) has been obtained using 2-(2′-benzyloxy)benzoyloxy-3,4,6-trimethoxyacetophenone (VII) obtained by the esterification of 2-hydroxy-3,4,6-trimethoxyacetophenone[6] (III) with 2-benzyloxybenzoyl chloride in the presence of pyridine. The ester (VII) underwent Baker–Venkataraman migration[7,8] to yield 2-hydroxy-3,4,6-trimethoxy-2′-benzyloxydibenzoylmethane (VIII) which on cyclodehydration gave 5,7,8-trimethoxy-2′-benzyloxyflavone (IX). The flavone (IX) was debenzylated using palladium charcoal and then selectively demethylated with aluminium chloride in acetonitrile to obtain 5,2′-dihydroxy-7,8-dimethoxyflavone (II), identical in its melting point with the second compound isolated from *A. paniculata* thereby confirming its proposed constitution.



I , $R_1 = H$; $R_2 = CH_3$

II , $R_1 = R_2 = H$

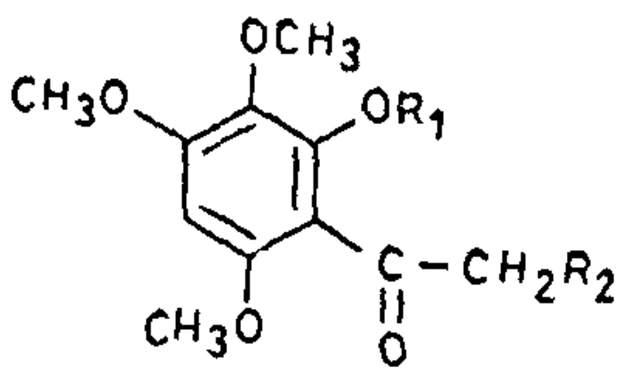
V , $R_1 = R_2 = CH_3$

VI , $R_1 = COCH_3$; $R_2 = CH_3$

IX , $R_1 = CH_3$; $R_2 = C_7H_7$

X , $R_1 = CH_3$; $R_2 = H$

XI , $R_1 = R_2 = COCH_3$



III , $R_1 = R_2 = H$

IV , $R_1 = H$; $R_2 = COC_6H_4OCH_3$ (ortho)

VII , $R_1 = COC_6H_4OC_7H_7$ (ortho) ; $R_2 = H$

VIII , $R_1 = H$; $R_2 = COC_6H_4OC_7H_7$ (ortho)

Experimental

2-Hydroxy-3,4,6,2′-tetramethoxydibenzoylmethane (IV)

A solution of 2-hydroxy-3,4,6-trimethoxyacetophenone[6] (III) (1·2 g) in dry acetone (200 ml), 2-methoxybenzoyl chloride (1·8 g) and anhydrous potassium carbonate (5 g) was heated under reflux. The progress of the reaction was monitored by T.L.C. using benzene : methanol (9 : 1) as the solvent system. The inorganic salts were filtered, washed with hot acetone and the solvent was removed from the combined filtrate and washings. The residue thus obtained crystallised from ethyl acetate-petroleum ether as yellow needles (1 g), m.p. 143–44° (Found : C, 63·10; H, 5·80. $C_{19}H_{20}O_7$ requires C, 63·33; H, 5·59%). It dissolved in aqueous sodium hydroxide (10%) and gave an olive green colouration with alcoholic ferric-chloride. N.M.R. (δ, $CDCl_3$, TMS as internal standard): 3·86 (3H, *s*, $-OCH_3$), 3·92 (9H, *s*, 3X $-OCH_3$), 6·93 (1H, *s*, C_5–H), 7·02–7·50 (3H, *m*, $C_{3'}$–H, $C_{4'}$–H and $C_{6'}$–H), 7·63 (1H, *s*, $-CO-\underline{CH}=C-OH$), 7·90 (1H, *dd*, $J = 8·0$ Hz and 2·0 Hz, $\underline{C_{6'}}$–H), 13·30 (1H, *s*, –OH), 15·70 (1H, *s*, $-CO-CH=\underline{C}-O-\underline{H}$).

5,7,8,2′-Tetramethoxyflavone (V)

A solution of the above dibenzoylmethane (IV) (0·9 g) in glacial acetic acid (15 ml) was treated with fused sodium acetate (1 g) and then heated under reflux for 4 hr. The reaction mixture, when worked out, gave flavone (V) which crystallised from ethyl acetate-petroleum ether as colourless needles (0·8 g), m.p. 177–78° (Found: C, 66·30; H, 5·50. $C_{19}H_{18}O_6$ requires C, 66·66; H, 5·30%). It did not give any colouration with alcoholic ferric chloride. N.M.R. (δ, $CDCl_3$, TMS as internal standard): 3·91 (6H, *s*, 2X-OCH_3), 3·98 (6H, *s*, 2X $-OCH_3$), 6·44 (1H, *s*, C_3–H), 7·0 (1H, *s*, C_6–H), 7·06–7·52 (3H, *m*, $C_{3'}$–H, $C_{4'}$–H and $C_{5'}$–H), 7·84 (1H, *dd*, $J = 8·0$ Hz and 2·0 Hz, $C_{6'}$–H).

5-Hydroxy-7-8,2′-trimethoxyflavone (I)

A solution of the above flavone (V) (0·5 g) in acetonitrile (120 ml) was treated with anhydrous aluminium chloride (0·5 g) and then heated under reflux for 2 hr. The solvent was distilled off under reduced pressure and the residue was acidified with hydrochloric acid. The reaction product thus obtained was filtered, washed with water and dried. It crystallised from ethyl acetate to give the flavone (I) as light yellow

reedles (0·35 g). m.p. 186–87° (Found: C, 65·50; H, 4 80. $C_{18}H_{16}O_6$ requires C, 65·85; H, 4·91%). It gave an olive-green colouration with alcoholic ferric chloride. UV (MeOH): 275, 340 nm; + $AlCl_3$: 280, 295 (*sh*). 340, 405 nm; + $AlCl_3$ + HCl: 280, 297, 345, 410 nm.

On acetylation (acetic anhydride/pyridine), the flavone (I) gave the acetate (VI). It crystallised from chloroform-petroleum ether as colourless needles (0 04 g), m.p. 151-52° (Found: C, 64·50; H, 5·0 $C_{20}H_{18}O_7$ requires C, 64 86; H, 4·90%). NMR (δ, $CDCl_3$, TMS as internal standard): 2·42 (3H, *s*, $-OCOCH_3$), 3 90 (3H, *s*, $-OCH_3$), 3 96 (6H, *s*, 2X OCH_3), 6·64 (1H, *s*, C_3–H), 6·93–7·45 (4H, *m*, $C_{3'}$–H, $C_{4'}$–H, $C_{5'}$–H and $C_{6'}$–H), 7·90 (1H, *dd*, $J = 8·0$ Hz and 2·0 Hz, $C_{6'}$–H).

2-(2'-Benzyloxy)benzoyloxy-3,4,6-trimethoxyacetophenone (VII)

2-Hydroxy-3,4,6--trimethoxyacetophenone[6] (III) (2 g) in dry pyridine (15 ml) was treated with 2-benzyloxybenzoyl chloride (3 g) and then heated on a boiling water-bath for an hour. The reaction mixture was cooled and treated with ice and hydrochloric acid. The ester (VII) thus obtained was filtered, washed with aqueous sodium bicarbonate (5%) to remove any 2-benzyloxybenzoic acid and then with water. It crystallised from alcohol-acetone as colourless prisms (3 g), m.p. 114° (Found: C, 68·70; H, 5·50. $C_{25}H_{24}O_7$ requires C, 68 80; H, 5·54%). It was insoluble in cold aqueous sodium hydroxide (10%) and did not give any colouration with alcoholic ferric chloride. NMR (δ, $CDCl_3$, TMS as internal standard): 2·40 (3H, *s*, $-COCH_3$), 3·73 (3H, *s*, OCH_3), 3·80 (3H, *s*, $-OCH_3$), 3·86 (3H, s, $-OCH_3$), 5·10 (2H, *s*, $-\underline{OCH_2}C_6H_5$), 6·34 (1H, *s*, C_6–H), 6 92–7·36 (8H, *m*, $-OCH_2\underline{C_6H_5}$, $C_{3'}$–H, $C_{4'}$–H and $C_{5'}$–H), 7·90 (1H, *dd*, $J = 8·0$ Hz and 2·0 Hz, $C_{6'}$–H).

2-Hydroxy-2'-benzyloxy-3,4,6-trimethoxydibenzoylmethane (VIII)

A solution of the above ester (VII) (2·5 g) in pyridine (20 ml) was treated with powdered potassium hydroxide (3 g) and the reaction mixture was throughly shaken with occasional warming on a water-bath for about 45 min. On acidification with hydrochloric acid, β-diketone (VIII) was obtained as yellow solid. It crystallised from ethyl acetate–petroleum ether as yellow needles (2 g), m.p. 115° (Found: C, 68·60; H, 5·70. $C_{25}H_{24}O_7$ requires C, 68·80; H, 5·54%). It dissolved in aqueous sodium hydroxide (10%) and gave an olive-green colouration with alcoholic ferric chloride. NMR (δ, $CDCl_3$ TMS as internal standard): 3 83 (3H, *s*, $-OCH_3$), 3·90 (3H, *s*, $-OCH_3$), 3 98 (3H, *s*, $-OCH_3$), 5·20 (2H, *s*, $-\underline{OCH_2}C_6H_5$), 6·98 (1H, *s*, C_6–H), 7·04–7·40 (8H, *m*, $-OCH_2\underline{C_6H_5}$, $C_{3'}$–H, $C_{4'}$–H and $C_{5'}$–H), 7·68 (1H, *s*, $-CO-\underline{CH}=\underline{C}-OH$), 7·90 (1H, *dd*, $J = 8·0$ Hz and 2·0 Hz, $C_{6'}$–H), 13·20 (1H, s, –OH), 15·80 (1H, *s*, $-CO-CH=\underline{C}-O\underline{H}$).

5,7,8-Trimethoxy-2'-benzyloxyflavone (IX)

A solution of the above β-diketone (VIII) (1·8 g) in glacial acetic acid (30 ml) was treated with fused sodium acetate (2 g) and then heated under reflux for 4 hr. The reaction mixture, when worked out, gave flavone (IX) which crystallised from ethyl acetate-petroleum ether as colourless needles (1·6 g), m.p. 141–42° (Found: C, 71·3; H, 5·50. $C_{25}H_{22}O_6$ requires C, 71·76; H, 5·30%). It did not give any colouration with alcoholic ferric chloride. NMR (δ, $CDCl_3$, TMS as internal standard): 3·86 (3H, *s*, $-OCH_3$), 3·96 (6H, *s*, 2X $-OCH_3$), 5·18 (2H, *s*, $-\underline{OCH_2}C_6H_5$), 6·40 (1H, *s*, C_3–H), 6·94 (1H, *s*, C_6–H), 7·06–7·35 (8H, *m*, $-OCH_2\underline{C_6H_5}$, $C_{3'}$–H, $C_{4'}$–H and $C_{5'}$–H) 7·86 (1H, *dd*, $J = 8·0$ Hz and 2 0 Hz, $C_{6'}$–H).

5,7,8-Trimethoxy-2'-hydroxyflavone (X)

A solution of the above flavone (IX) (0·5 g) in ethyl acetate (200 ml) was treated with palladium charcoal (0·2 g; 10%) and then stirred in an atmosphere of hydrogen till absorption completed. The catalyst was filtered and washed with ethyl acetate. Removal of the solvent from the combined filtrate gave the flavone (X) which crystallised from benzene as colourless needles (0·3 g), m.p. 278–79° (Found: C, 66·10; H, 5·10. $C_{18}H_{16}O_6$ requires C, 65·85; H. 4·91%).

5,2'-Dihydroxy-7,8-dimethoxyflavone (II)

A solution of the above flavone (X) (0·2 g) in acetonitrile (60 ml) was treated with anhydrous aluminium chloride (0·2 g) and then heated under reflux for 2 hr. The solvent was distilled off under reduced pressure and the residue was acidified with hydrochloric acid. The reaction product thus obtained was filtered, washed with water and dried. The flavone (II) crystallised from ethyl acetate as light yellow needles (0·15 g), m.p. 254–55° (Found: C, 64·50; H, 4·80. $C_{17}H_{14}O_6$ requires C, 64·96; H, 4·49%). It gave an olive-green colouration with alcoholic ferric chloride. UV (MeOH): 275, 335 nm; + $AlCl_3$: 285, 295 (*sh*), 345, 400 nm; + $AlCl_3$ + HCl: 285, 297, 355, 405 nm.

On acetylation (acetic anhydride/pyridine), the flavone (II) gave the acetate (XI). It crystallised from chloroform-petroleum ether as colourless needles (0·03 g), m.p. 133-34° (Found: C, 63·20; H, 4·70 $C_{21}H_{18}O_8$ requires C, 63·31; H, 4·55%). NMR (δ, $CDCl_3$, TMS as internal standard): 2·30 (3H, *s*, $-OCOCH_3$), 2·40 (3H, *s*, $-OCOCH_3$), 3·85 (3H, *s*,

$-OCH_3$), 3·90 (3H, *s*, $-OCH_3$), 6·62 (1H, *s*, C_3–H), 7·08 (1H, *s*, C_6–H), 7·10–7·50 (3H, *m*, $C_{3'}$–H, $C_{4'}$–H and $C_{5'}$–H), 7·84 (1H, *dd*, $J = 8·0$ Hz and 2·0 Hz, $C_{6'}$–H).

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GIANT CELLS IN THE PLACENTA OF THE INDIAN SHEATH-TAILED BAT *TAPHOZOUS LONGIMANUS* (HARDWICKE)

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PLACENTAL giant cells have been described by several workers in many mammals, specially in the rodents[1–7], ruminants[8–10], carnivores[11], primates[12,13], and recently in some bats[14]. With regard to their origin they have been shown to be endometrial in some species, trophoblastic in some, endothelial in a few species and from all the three sources in some. There is considerable controversy regarding their function. Most earlier authors attributed to these cells the function of glycogen storage[12,13]. They are also believed to aid in the transformation of the trophoblast during the process of implantation of the blastocyst[15]. Endometrial giant cells are supposed to act as an effective barrier between the mother and the developing embryo and aid in the maternal tolerance of the embryonic homograft providing protection in the nature of an immune reaction[15]. Giant cells have been shown to be important sites of synthesis of chorionic gonadotrophins[8,13,16] and also assist in the invasion of maternal tissues by phagocytic activity[17]. Endothelial giant cells have been attributed a function of transport of iron and ascorbic acid from the mother to the foetus[8,18].

In *Taphozous longimanus* the giant cells were first noticed at an early stage of pregnancy after the invasion of the trophoblast into the uterine endometrium. At this stage they occur as large cells at the peripheral border of the invading trophoblastic zone, and are continuous with the layer of cytotrophoblastic cells (Figs. 1 and 2). There is a progressive increase in the size of these cells from the foetal surface towards the deeper regions of the trophoblastic shell, and it is possible to trace the progressive transformation of the cytotrophoblastic cells into the large giant cells. The endometrial tissue immediately bordering the zone of giant cells appears to be undergoing destruction as evidenced by the fact that the endometrial cells have lost their distinctive shapes, their nuclei have become pycnotic, and, in many of the cells, the nuclei are fragmented. Consequently, this region of the endometrium is loose and often tears off during fixation and processing of the tissue. Hence, in many stained sections there appears to be a space between the zone of giant cells and the necrotic zone of the endometrium. The fully formed giant cells at this stage have numerous stained granules most of which are located in the pole towards the foetal border of the cells and the clear cytoplasm towards the endometrium. At this stage while most of the giant cells are mononucleate a few have two to three nuclei.

At a slightly more advanced stage of gestation, when the embryo reaches the primitive streak stage, the thickness of the placental shell increases considerably, and there is a concomitant increase in the number and size of the giant cells (Figs. 3 and 4). Many of the giant cells are binucleate and trinucleate and they are located mostly near the utero-placental junction. Their shape and cytological picture are as in the previous stage. The giant cells reach their maximum development at the early neural groove stage of development of the embryo when they occur as a distinct band of large cells immediately below the endometrial stroma (Figs. 5 and 6). They are very large and most of them are multinucleate. It is noteworthy that there was not a single mitotic stage in any of these cells at any stage of pregnancy. The polarity of the localization of stainable cytoplasmic inclusions