

CONSTITUTION OF *Teucrium nuchense* FLAVONE :  
A SYNTHETIC STUDY

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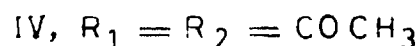
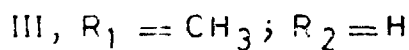
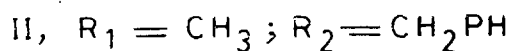
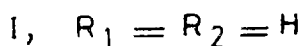
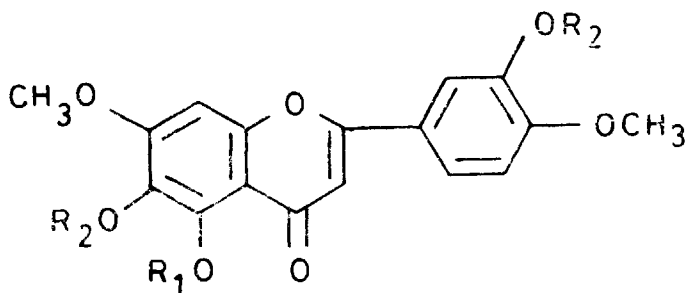
Two flavones isolated from two different sources : *Teucrium nuchense* and *Eupatorium inulaefolium* having different melting points and also different spectral data, were given the same constitution as 5,6,3'-trihydroxy-7,4'-dimethoxyflavone (I). In view of this discrepancy and the absence of any synthetic evidence in the literature, this flavone (I) has been now synthesised. Since the synthetic compound (I) agreed with the sample isolated from *Eupatorium inulaefolium* but not with that isolated from *Teucrium nuchense*, the constitution of the flavone isolated from the latter plant needs revision.

**Keywords :** *Teucrium Nuchense* and *Eupatorium inulaefolium*: Flavones;  
Constitution of Nuchensein 5,6,3'-Trihydroxy-7,4'-dimethoxy-  
flavone (I)

INTRODUCTION

NUCHENSEIN, a new flavone (m.p. 258-59 °C) isolated from *Teucrium nuchense* (Slyun' kova *et al.*, 1978) and the flavone (m.p. 245-47 °C) isolated from *Eupatorium inulaefolium* (Ferraro *et al.*, 1977) which also had different spectral data were given the same constitution as 5,6,3'-trihydroxy-7,4'-dimethoxyflavone (I). In view of the different melting points and spectral data reported for the two different samples of the compound having the same constitution, it was considered necessary to synthesise 5,6,3'-trihydroxy-7,4'-dimethoxyflavone (I) in order to settle this discrepancy. This paper reports the synthesis of 5,6,3'-trihydroxy-7,4'-dimethoxyflavone (I) using 2'-hydroxy-3,5'-dibenzoyloxy-4,4',6'-trimethoxychalkone as the essential intermediate. This chalkone was obtained by the condensation of 2-hydroxy-4,6-dimethoxy-5-benzoyloxyacetophenone (Stout *et al.*, 1964) and O-benzyl iso-vanillin (Robinson & Sugasawa, 1931). Selenium dioxide oxidation (Mahal & Venkataraman, 1936 ; and Bhardwaj *et al.*, 1977, 1978) of the above chalkone gave 5,7,4'-trimethoxy-6,3'-dibenzoyloxyflavone (II) which on catalytic debenylation and subsequent selective demethylation of the resulting 5,7,4'-trimethoxy-6,3'-dihydroxyflavone (III) gave the required 5,6,3'-trihydroxy-7,4'-dimethoxyflavone (I). On acetylation, the flavone (I) yielded its triacetate (IV). However, it has been now observed that the properties for the synthetic trihydroxydimethoxyflavone (I) [m.p. 246-47 °C ; UV (MeOH) : 240(sh), 285, 340nm ; + NaOAc : 242(sh), 285, 340nm ; + NaOAc + H<sub>3</sub>BO<sub>3</sub> : 242(sh), 285, 340nm ; + AlCl<sub>3</sub> : 240(sh), 260(sh), 295, 372nm ; + AlCl<sub>3</sub> + HCl : 240(sh), 262(sh), 300, 370nm ; + NaOMe : 260, 320(sh), 370nm] are different from the natural sample

of nuchensein [m.p. 258–59 °C ; *UV* (*MeOH*) : 257(sh), 272, 348nm ; + NaOAc : 268, 353nm ; + NaOAc +  $H_3BO_3$  : 265, 378nm ; +  $AlCl_3$  : 282, 367nm ; +  $AlCl_3$  + HCl : 263(sh), 282, 365nm ; + NaOMe : 273, 393nm] but identical with the compound isolated by Ferraro *et al.*, (1977) from *Eupatorium inulaefolium*. Hence, the constitution assigned to nuchensein by Slyun'kova *et al.*, (1978) needs revision whereas the constitution of the compound isolated by Ferraro *et al.*, (1977) is confirmed as 5,6,3'-trihydroxy-7,4'-dimethoxyflavone (I).



#### EXPERIMENTAL

##### 2-Hydroxy-4,4',6'-trimethoxy-3,5'-dibenzylloxychalkone

A solution of 2-hydroxy-4,6-dimethoxy-5-benzyloxyacetophenone (1g) in ethanol (15ml) and 0-benzyl iso-vanillin (1.5g) was treated with aqueous-ethanolic solution of potassium hydroxide (2g), left at room temperature for 48 hours and then acidified with hydrochloric acid. The chalkone thus obtained was filtered, washed and dried. It crystallised from ethanol as yellow needles (1.1g), m.p. 146–47 °C (*Found* : C, 72.5 ; H, 5.5.  $C_{32}H_{30}O_7$  requires C, 72.99 ; H, 5.74 per cent). It gave positive ferric reaction.

*NMR* ( $\delta$ ,  $CDCl_3$ , TMS as Internal Standard) : 3.82 (3H, s,  $-OCH_3$ ), 3.84 (3H, s,  $-OCH_3$ ), 3.92 (3H, s,  $-OCH_3$ ), 4.97 (2H, s,  $-OCH_2C_6H_5$ ), 5.20 (2H, s,  $-OCH_2C_6H_5$ ), 6.28 (1H, s,  $C_3-H$ ), 6.90 (1H, d,  $J = 9Hz$ ,  $C_5-H$ ), 7.18 (2H, s,  $C_2-H$  &  $C_6-H$ ), 7.24–7.58 (10H, m, 2 X  $-OCH_2C_6H_5$ ), 7.74 (2H, s,  $C_\alpha-H$  &  $C_\beta-H$ ).

##### 5,7,4'-Trimethoxy-6,3'-dibenzyloxyflavone (II)

A mixture of the above chalkone (1.0g), selenium dioxide (1.7g) and iso-amyl alcohol (40ml) was refluxed for 24 hours and then filtered to remove selenium metal and its dioxide. Removal of the solvent from the filtrate gave the flavone (II) that

crystallised from ethyl acetate-petroleum ether as colourless needles (0.8g), m.p. 134–35 °C (*Found* : C, 72.9 ; H, 5.1.  $C_{32}H_{28}O_7$  requires C, 73.27 ; H, 5.38 per cent). It did not give ferric reaction.

*NMR* ( $\delta$ ,  $CDCl_3$ , TMS as Internal Standard) : 3.89 (6H, s, 2X —  $OCH_3$ ), 3.95 (3H, s, — $OCH_3$ ), 5.01 (2H, s, — $OCH_2C_6H_5$ ), 5.14 (2H, s, — $OCH_2C_6H_5$ ), 6.46 (1H, s,  $C_3$ -H), 6.67 (1H, s,  $C_8$ -H), 6.90 (1H, *d*,  $J = 9\text{Hz}$ ,  $C_5'$ -H), 7.20–7.54 (12H, m,  $C_2'$ -H,  $C_6'$ -H & 2X — $OCH_2C_6H_5$ ).

#### 5,7,4'-Trimethoxy-6,3'-dihydroxyflavone (III)

A solution of the dibenzyloxytrimethoxyflavone (II) (0.7g) in ethyl acetate (80ml) was treated with palladium-charcoal (0.5g ; 10 per cent) and then stirred in an atmosphere of hydrogen till absorption completed. The catalyst was filtered and removal of the solvent from the filtrate gave dihydroxytrimethoxyflavone (III) which crystallised from ethanol as colourless needles (0.4g), m.p. 192–93 °C (*Found* : C, 62.5; H, 4.3.  $C_{18}H_{16}O_7$  requires C, 62.79; H, 4.68 per cent).

*NMR* ( $\delta$ ,  $Me_2CO$ ) : 3.85 (3H, s, — $OCH_3$ ), 3.91 (3H, s, — $OCH_3$ ), 3.99 (3H, s, — $OCH_3$ ), 6.50 (1H, s,  $C_3$ -H), 7.0–7.1 (2H, m,  $C_8$ -H &  $C_5'$ -H), 7.42 (2H, s,  $C_2'$ -H &  $C_6'$ -H).

#### 5,6,3'-Trihydroxy-7,4'-dimethoxyflavone (I)

A solution of the dihydroxytrimethoxyflavone (III) (0.3g) in acetonitrile (20ml) was treated with anhydrous aluminium chloride (0.3g) and then refluxed for 4 hours. The solvent was distilled off under reduced pressure and on acidification with hydrochloric acid, the demethylation product (I) was obtained as yellow solid. It was filtered, washed with water and dried. It crystallised from ethanol as light yellow needles (0.2g), m.p. 246–47 °C (*Found* : C, 61.5; H, 4.2.  $C_{17}H_{14}O_7$  requires C, 61.82; H, 4.27 per cent). It gave an olive-green ferric reaction.

*UV* ( $MeOH$ ) : 240(sh), 285, 340nm; +  $CH_3COONa$  : 242(sh), 285, 340nm; +  $CH_3COONa$  +  $H_3BO_3$  : 242(sh), 285, 340nm; +  $AlCl_3$  : 240(sh), 260(sh), 295, 372nm; +  $AlCl_3$  +  $HCl$  : 240(sh), 262(sh), 300, 370nm; +  $NaOMe$  : 260, 320(sh), 370nm.

#### 5,6,3'-Triacetoxy-7,4'-dimethoxyflavone (IV)

The above trihydroxydimethoxyflavone (I) (0.05g) was treated with acetic anhydride (0.40ml) and pyridine (0.50ml), warmed on a water-bath to obtain a clear solution and then left overnight. It was treated with ice and the acetate (IV) thus obtained was filtered, washed and dried. The acetate (IV) crystallised from chloroform-petroleum ether as colourless needles (0.04g), m.p. 218–20 °C (*Found* : C, 60.2 ; H, 4.3.  $C_{23}H_{20}O_{10}$  requires C, 60.52; H, 4.42 per cent). It did not give ferric reaction.

*NMR* ( $\delta$ ,  $CDCl_3$ , TMS as Internal Standard) : 2.33 (6H, s, 2X — $OCOCH_3$ ), 2.41 (3H, s, — $OCOCH_3$ ), 3.88 (3H, s, — $OCH_3$ ), 3.92 (3H, s, — $OCH_3$ ), 6.45 (1H, s,  $C_3$ -H), 6.90 (1H, s,  $C_8$ -H), 7.02 (1H, *d*,  $J = 9\text{Hz}$ ,  $C_5'$ -H), 7.54–7.70 (2H, m,  $C_2'$ -H &  $C_6'$ -H).

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