*Phytochemistry*, Vol. 28, No. 1, pp. 243–244, 1989.
Printed in Great Britain.

0031-9422/89 $3.00+0.00


# A REASSESSMENT OF THE DATA SUPPORTING THE STRUCTURES OF *BLUMEA MALCOLMII* FLAVONOLS

KENNETH R. MARKHAM

Chemistry Division, DSIR, Private Bag, Petone, New Zealand

(*Received* 21 *June* 1988)

**Key Word Index**—*Blumea malcolmii*; Compositae, flavonols; revised structures; quercetagetin methyl ethers.

**Abstract**—The data previously presented in support of the structures of four new flavonols from *Blumea malcolmii*, are shown to have been misinterpreted. A reassessment indicates that the four flavonols earlier defined as 6-hydroxy-3,5,7,4′-tetramethoxyflavone, 6,2′,5′-trihydroxy-3,5,7-trimethoxyflavone, and its 2′- and 2′,5′-methyl ethers, are most probably 5-hydroxy-3,6,7,4′-tetramethoxyflavone and the 3,6,7-, 3,6,7,3′- and 3,6,7,3′,4′-methyl ethers of quercetagetin respectively.

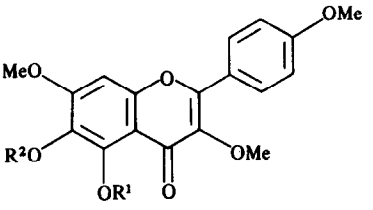
## INTRODUCTION

In a recent paper [1], the isolation and structure elucidation of four flavonols, 6-hydroxy-3,5,7,4′-tetramethoxyflavone (**1**), 6,2′,5′-trihydroxy-3,5,7-trimethoxyflavone (**2**), 6,5′-dihydroxy-3,5,7,2′-tetramethoxyflavone (**3**) and 6-hydroxy-3,5,7,2′,5′-pentamethoxyflavone (**4**), from *Blumea malcolmii* were described. All four are new and highly unusual biosynthetically, **1**–**4** because of their substituted 5-hydroxyl functions and **2**–**4** because of the 2′,5′-dioxygenation patterns which have been encountered only rarely before in flavones/flavonols [2]. For these reasons the flavonols are of particular interest, and the present communication describes a critical re-examination of the data cited in support of the proposed structures.

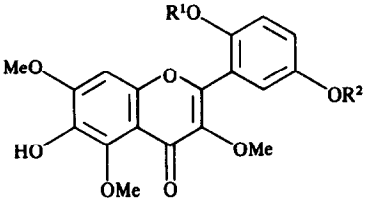
## DISCUSSION

The structure of the single pentaoxygenated flavonol (**1**) is supported by chromatographic spot colour, absorption spectra, an $^1$H NMR spectrum and a mass spectrum. Permethylation gave the same pentamethyl ether as is produced from penduletin, so confirming the 3,5,6,7,4′-oxygenation pattern. This permethyl ether appeared blue fluorescent in UV light as expected for a flavonol-3,5-dimethyl ether [3]. In contrast, the parent flavonol (**1**) produces a dark (brown) UV-absorbing spot which is indicative of a flavonoid with a free 5-hydroxyl [3]. The presence of a free 5-hydroxyl is also evident from the absorption spectrum in $AlCl_3$/HCl which exhibits a band I shift of *ca* 15 nm relative to the spectrum in methanol alone [4]. The size of this shift is consistent with the additional presence of a 6-methoxyl group [4] and would not occur at all if the 5-hydroxyl group was methylated. The proposed structure **1** is therefore incorrect and indeed the literature m.p. cited by the authors for this compound at 199–200° [5] does not compare well with that reported for **1** (178–180°) [1]. The only structure consistent with all of the presented data is 5-hydroxy-3,6,7,4′-tetramethoxyflavone (**1a**), a known compound with a reported mp of 173–174° [6].

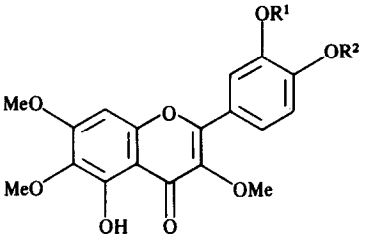
The three hexaoxygenated flavonols, **2**–**4**, are all related by methylation, **2** producing **4**, and **3** and **4** produc-



**1** $R^1$ = Me; $R^2$ = H
**1a** $R^1$ = H; $R^2$ = Me



**2** $R^1$ = $R^2$ = H
**3** $R^1$ = Me; $R^2$ = H
**4** $R^1$ = $R^2$ = Me



**2a** $R^1$ = $R^2$ = H
**3a** $R^1$ = Me; $R^2$ = H
**4a** $R^1$ = $R^2$ = Me

ing the same permethyl ether, mp 138–139°. This permethyl ether is described as appearing blue fluorescent on a chromatogram, as expected for a flavonol-3,5-dimethyl ether [3]. Again, as with **1** above, compounds **2–4** which are proposed to be flavonol-3,5-dimethyl ethers, appear dark (brown) and not blue fluorescent, and exhibit $AlCl_3$/HCl induced shifts in their absorption spectra. All three therefore possess underivatized 5-hydroxyl groups and methylated 3-hydroxyl groups, and thus must possess structures different from those proposed.

The absorption spectra of all three compounds resemble those of quercetagetin (3,5,6,7,3′,4′-hexahydroxyflavone) methyl ethers and their derivatives. For example, the absorption spectra of **2–4** approximate to those of 5,3′,4′-trihydroxy-3,6,7-trimethoxyflavone, **2a** [7], jacein (5,7,4′-trihydroxy-3,6,3′-trimethoxyflavone 7-*O*-glucoside) [8] and artemetin (5-hydroxy-3,6,7,3′,4′-pentamethoxyflavone, **4a**) [8] respectively. There are also strong similarities between the $^1$H NMR spectra of compounds **2–4** and quercetagetin derivatives. Apart from the H-8 singlet at *ca* 6.5 ppm, quercetagetin derivatives show two protons (H-2′ and 6′) resonating at low field and one (H-3′) at higher field [7, 8], as is seen in the spectra of compounds **2–4**. However, in the spectra of 2′,5′-dioxygenated flavones the reverse is observed, with only one proton (H-6′) resonating at low field and two (H-3′ and 4′) at higher field (e.g. see [9]). In particular, the spectra presented for compound **4** and for the permethyl ether derived from **2–4** are indistinguishable from those in the literature for artemetin (**4a**) and quercetagetin hexamethyl ether respectively [8]. Certain features of the mass spectra too are inconsistent with the proposed structures **2–4**. For example the presence of 2′-hydroxyl and 2′-methoxyl groups should be evidenced by the production of major ions representing [M − 17] or [M − 31] [10], but these are not seen in the spectra of **2–4**.

From the above, it is evident that the physical evidence strongly favours quercetagetin-related structures for compounds **2–4**. These structures find further support in that the permethyl ether of **2–4** has a mp of 138–139° compared with a reported mp of 142–143° for quercetagetin hexamethyl ether [11], and that their $^1$H NMR spectra are identical. The equivalent gossypetin structures are seemingly excluded since the mp of gossypetin hexamethyl ether is markedly different at 171–172.5° [12].

Proposed structures which account for all published data on compounds **2–4** are as follows. Compound **2** is assigned the structure, 5,3′,4′-trihydroxy-3,6,7-trimethoxyflavone (**2a**) since it must possess a 5-hydroxyl and an *ortho*-dihydroxyl system based on the observed $AlCl_3$ and $AlCl_3$/HCl induced shifts in the absorption spectrum. Further, reported mps of 237–238° [13] and 249–250° ([14], product of Wessely–Moser rearrangement) for **2a** are in general accord with the value of 252° recorded for compound **2**. Compound **3** with only two free hydroxyls, one of which is at C-5, is assigned the structure 5,4′-dihydroxy-3,6,7,3′-tetrahydroxyflavone (**3a**), the 4′-hydroxyl being evidenced [4] by the 45 nm bathochromic shift in band I of the absorption spectrum with NaOMe (accompanied by no significant decrease in intensity). Authentic **3a** is reported to have a mp of 181–182° [11] which is close to the 189–191° quoted for compound **3**. The 8-methoxy equivalent is clearly excluded as a possible alternative as it possesses a much higher mp (210–212.5° [12]). Finally, compound **4** is almost certainly 5-hydroxy-3,6,7,3′,4′-pentamethoxyflavone (artemetin, **4a**), since it possesses an identical $^1$H NMR spectrum and its single hydroxyl group must be at C-5 to account for the chromatographic appearance. Artemetin has reported mps of 163–164° and 173–175° [12] both values being close to the 166–168° recorded for **4**.

In conclusion, it is considered on the basis of the reported physical data, that the structures of all four 3-methoxyflavones from *Blumea malcolmii* have been incorrectly assigned, and are best represented instead by structures **1a**, **2a**, **3a** and **4a**. These new structures represent commonly co-occurring 4′- and 3′,4′-oxygenated analogues with the same A-ring oxygenation. In this respect they provide a more rational biosynthetic relationship between the penta- and hexa-oxygenated flavones of *B. malcolmii* than did those originally proposed.

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