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Hydrogen bonding and π–π stacking in 6-hydroxybiochanin A monohydrate

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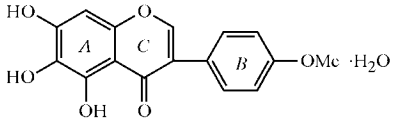
In the lattice of the title compound (systematic name: 5,6,7-trihydroxy-4′-methoxyisoflavone monohydrate), $C_{16}H_{12}O_6\cdot H_2O$, the isoflavone molecules are linked into chains through $R_4^3(17)$ motifs composed *via* O—H···O and C—H···O hydrogen bonds. Centrosymmetric $R_4^2(14)$ motifs assemble the chains into sheets. Hydrogen-bonding and aromatic π–π stacking interactions lead to the formation of a three-dimensional network structure.

Comment

Irisolidone (5,7-dihydroxy-6,4′-dimethoxyisoflavone), a type of isoflavonoid, as one of the effective components in the flowers of *Pueraia lobata*, possesses potential inhibitory activity against *Helicobacter pylori* (HP), which is a risk factor for gastric cancer (Kim *et al.*, 1998; Bae *et al.*, 2001). Furthermore, various animal studies have indicated that irisolidone greatly reduces ethanol-induced mortality, as well as serum alanine aminotransferase (ALT) and aspartate aminotransferase (AST) activities. Both pre- and post-treatment with irisolidone have been found to reduce blood ethanol levels (Han *et al.*, 2003; Yamazaki *et al.*, 1997, 2002). In this paper, using irisolidone as a starting compound, 6-hydroxybiochanin A (4′-methoxy-5,6,7-trihydroxyisoflavone), (II), was synthesized by demethylation. It has been reported that (II) was isolated from *Serratula strangulata* (Dai *et al.*, 2001).



(I)

Klus & Barz (1998) found that tempe-derived bacterial strains identified as *Micrococcus* or *Arthrobacter* species were shown to transform biochanin A to (II) by a hydroxylation reaction at position C6. Additionally, compound (II) is one of the main extrahepatic metabolism constituents of biochanin A through recombinant human CYP1A1 or CYP1B1 (Roberts *et al.*, 2004). Compound (II) has potential medical applications and we report here the crystal structure of 6-hydroxybiochanin A monohydrate, (I).

Compound (I) is composed of a benzopyranone moiety, a benzene ring, three hydroxyl groups, a methoxy group and a solvent water molecule (Fig. 1). The bond lengths and angles of the isoflavone skeleton of (I) are similar to those in both 7-methoxy-4′-hydroxyisoflavone and 4′,7-diethoxy-5-hydroxyisoflavone (Zhang & Wang, 2005) and in 5-hydroxy-7,4′-dimethoxyisoflavone (Zhang *et al.*, 2005). The atoms of the benzopyranone moiety, including ring *A* (C1–C6) and ring *C* (O4/C5–C9), are nearly coplanar, the dihedral angle between the rings being 2.6 (1)°. To avoid steric conflicts, the two rigid ring systems, *viz*. benzene ring *B* (C10–C15) and the benzopyranone moiety, are rotated by 44.2 (1)° with respect to each other. The methoxy group at C13 is nearly coplanar with its attached ring *B*, as revealed by the C16—O6—C13—C12 torsion angle of 5.1 (4)°. Furthermore, an independent intramolecular O1—H1···O5 hydrogen bond forms a characteristic intramolecular *S*(6) motif (Bernstein *et al.*, 1995).

As shown in Fig. 2, an $R_4^3(17)$ motif is formed by atoms O5, O6^{ii} [symmetry code: (ii) $\frac{1}{2}+x, \frac{3}{2}-y, -\frac{1}{2}+z$] and O7, involving C—H···O (entry 6 in Table 1) and O—H···O (entries 2 and 4 in Table 1) hydrogen bonds. These $R_4^3(17)$ motifs are generated *via* C—H···O and O—H···O hydrogen bonds and link the isoflavone molecules into chains. In addition, a centrosymmetric $R_4^2(14)$ motif is defined by paired O2—H2···O7 and O3—H3···O7^{iii} interactions [symmetry code: (iii) $1-x, -y, 1-z$; entries 4 and 5 in Table 1]. Atom O7 interacts with atoms H2 and H3^{iii} to form a three-centred hydrogen bond. The isoflavone skeletons of (I) are assembled into (101) sheets *via* $R_4^3(17)$and $R_4^2(14)$ motifs. The solvent water molecules are involved in the formation of four O—H···O hydrogen bonds (entries 1, 2, 4 and 5 in Table 1).

The isoflavone skeletons of (I) are arranged in a parallel fashion and π–π stacking interactions exist between them (Fig. 3). Ring *A* of the isoflavone skeleton stacks with those of neighbouring isoflavone skeletons, with $CgA\cdots CgA^{v}$ =

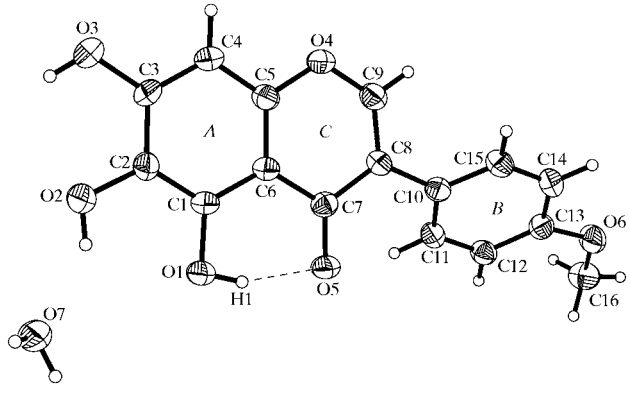


Figure 1
A view of the molecule of (I), showing the atom-numbering scheme and displacement ellipsoids at the 50% probability level. The thin dashed line represents the intramolecular hydrogen bond.

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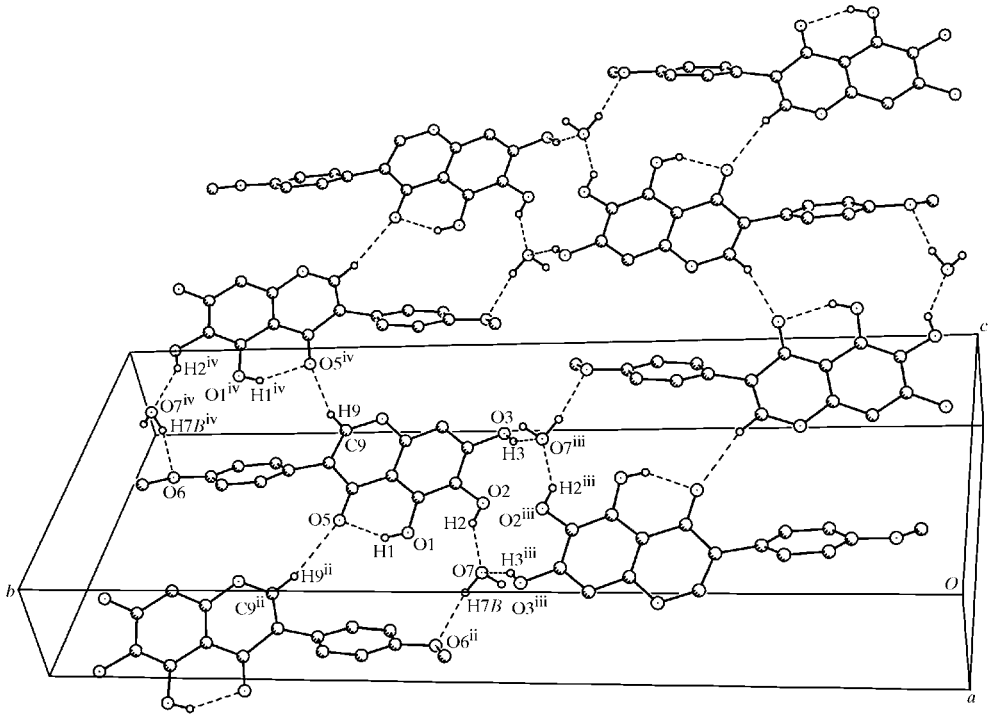

Figure 2
Part of the crystal structure of (I), showing the formation of the (101) sheets *via* $R_4^3(17)$ and $R_4^2(14)$ motifs. For clarity, some H atoms have been omitted. Thin dashed lines indicate the hydrogen-bonding interactions. (See Table 1 for symmetry codes.)

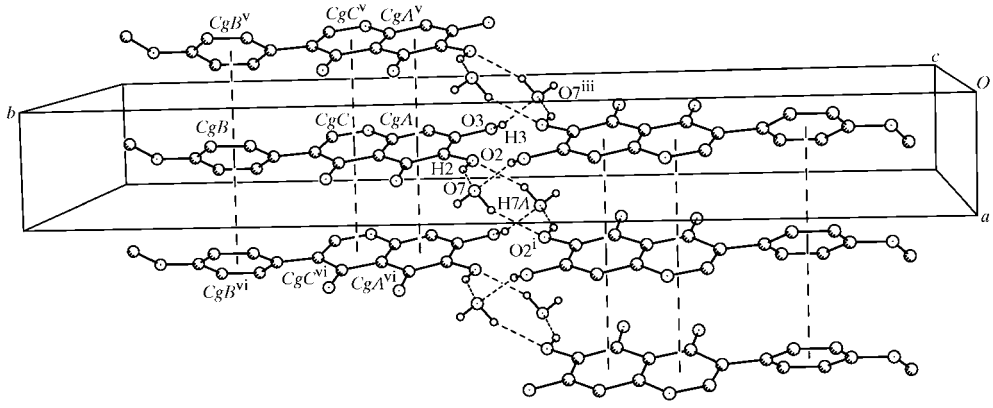

Figure 3
Part of the crystal structure of (I), showing some of the hydrogen-bonding and π–π stacking interactions and the $R_4^4(8)$ motif. For clarity, some H atoms have been omitted. Thin dashed lines indicate the hydrogen bonding and π–π stacking interactions. *CgA*, *CgB* and *CgC* are the centroids of rings *A*, *B* and *C*, respectively, as defined in Fig. 1. [See Table 1 for symmetry codes; additionally, (v) $-1+x, y, z$; (vi) $1+x, y, z$.]

$CgA\cdots CgA^{vi}$ = 3.773 (2) Å, where *CgA* is the centroid of ring *A* [symmetry codes: (v) $-1+x, y, z$; (vi) $1+x, y, z$], as do rings *B* and *C*. The offset distances of rings *A* and A^v, rings *B* and B^v, and rings *C* and C^v are 1.438, 1.424 and 1.430 Å, respectively. The centriod-to-centroid distances lie in the normal range of 3.3–3.8 Å (Janiak, 2000), indicative of π–π stacking interactions. These π–π stacking interactions result in the isoflavone skeletons forming columns along the *a* axis. These columns propagate *via* paired O2—H2$\cdots$O7 and O7—H7*A*$\cdots$O2^i [symmetry code: (i) $-x+2, -y+1, -z+1$] hydrogen bonds (entries 1 and 4 in Table 1), which form centrosymmetric $R_4^4(8)$ motifs (Fig. 3). Hydrogen-bonding and aromatic π–π stacking interactions play a key role in the assembly of the three-dimensional network structure.

Experimental

Irisolidone (1.0 g, 3.185 mmol) and anhydrous pyridine (15 ml) were placed into a 50 ml flask and dissolved by stirring at 313 K. Anhydrous aluminium chloride (3.0 g, 22.472 mmol) was added to the solution in three batches in order to control the reaction temperature. The mixture was stirred for 8 h at 353 K and excess pyridine was removed using a rotary evaporator under reduced-pressure distillation. The residue was cooled, hydrolyzed with 5% hydrochloric acid solution and extracted with ethyl acetate. The ethyl acetate layer was

washed with water until the pH was 7 and finally dried overnight over anhydrous sodium sulfate. Evaporation of the ethyl acetate gave 6-hydroxybiochanin A (0.85 g, yield 88.5%) as a pale-yellow powder, which was purified by 50% ethanol–water and recrystallized from 95% alcohol to give pale-yellow needles of (I) (m.p. 532 K).

Crystal data

$C_{16}H_{12}O_6\cdot H_2O$
$M_r = 318.27$
Monoclinic, $P2_1/n$
$a = 3.7734$ (5) Å
$b = 30.030$ (4) Å
$c = 12.0750$ (16) Å
$\beta = 93.894$ (2)°
$V = 1365.1$ (3) Å^3
$Z = 4$
$D_x = 1.549$ Mg m^{-3}
Mo $K\alpha$ radiation
$\mu = 0.12$ mm^{-1}
$T = 296$ (2) K
Needle, yellow
0.20 × 0.18 × 0.12 mm

Data collection

Bruker SMART CCD area-detector diffractometer
φ and ω scans
Absorption correction: multi-scan (*SADABS*; Bruker, 1999)
$T_{min} = 0.976$, $T_{max} = 0.985$
6841 measured reflections
2432 independent reflections
1460 reflections with $I > 2\sigma(I)$
$R_{int} = 0.046$
$\theta_{max} = 25.1°$

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)] = 0.046$
$wR(F^2) = 0.122$
$S = 1.09$
2422 reflections
219 parameters
H atoms treated by a mixture of independent and constrained refinement
$w = 1/[\sigma^2(F_o^2) + (0.0493P)^2 +]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} < 0.001$
$\Delta\rho_{max} = 0.22$ e Å^{-3}
$\Delta\rho_{min} = -0.19$ e Å^{-3}
Extinction correction: *SHELXL97* (Sheldrick, 1997*a*)
Extinction coefficient: 0.0077 (16)

Table 1
Hydrogen-bond geometry (Å, °).

D—H···A	D—H	H···A	D···A	D—H···A
O7—H7A···O2^{i}	0.85 (3)	2.06 (3)	2.873 (3)	159 (4)
O7—H7B···O6^{ii}	0.86 (3)	2.02 (3)	2.860 (3)	165 (3)
O1—H1···O5	0.82	1.90	2.617 (3)	146
O2—H2···O7	0.82	1.99	2.707 (3)	145
O3—H3···O7^{iii}	0.82	2.03	2.808 (3)	159
C9—H9···O5^{iv}	0.93	2.54	3.439 (3)	163

Symmetry codes: (i) $-x+2, -y+1, -z+1$; (ii) $x+\frac{1}{2}, -y+\frac{3}{2}, z-\frac{1}{2}$; (iii) $-x+1, -y+1, -z+1$; (iv) $x-\frac{1}{2}, -y+\frac{3}{2}, z+\frac{1}{2}$.

Water H atoms were located in a difference Fourier map and refined with O—H distances restrained to 0.85 (1) Å, with U_{iso}(H) = 1.5U_{eq}(O). Hydroxyl H atoms were placed in calculated positions, with O—H = 0.82 Å, and refined using a riding model, with U_{iso}(H) = 1.5U_{eq}(O). H atoms bonded to C atoms were placed in calculated positions, with C—H = 0.93 and 0.96 Å, and refined as riding, allowing free rotation of the rigid methyl groups; U_{iso}(H) = 1.2U_{eq}(C) or 1.5U_{eq}(methyl C).

Data collection: *SMART* (Bruker, 1999); cell refinement: *SMART*; data reduction: *SMART*; program(s) used to solve structure: *SHELXS97* (Sheldrick, 1997*a*); program(s) used to refine structure: *SHELXL97* (Sheldrick, 1997*a*); molecular graphics: *SHELXTL* (Sheldrick, 1997*b*); software used to prepare material for publication: *SHELXTL*.

Supplementary data for this paper are available from the IUCr electronic archives (Reference: GZ3040). Services for accessing these data are described at the back of the journal.

References

Bae, E. A., Han, M. J. & Kim, D. H. (2001). *Planta Med.* **67**, 161–163.
Bernstein, J., Davis, R. E., Shimoni, L. & Chang, N.-L. (1995). *Angew. Chem. Int. Ed. Engl.* **34**, 1555–1573.
Bruker (1999). *SMART* (Version 5.624), *SAINT-Plus* (Version 6.02a) and *SADABS*. Bruker AXS Inc., Madison, Wisconsin, USA.
Dai, J. Q., Hou, Z. F., Zhu, Q. X., Yang, L. & Li, Y. (2001). *J. Chin. Chem. Soc. (Taipei)*, **48**, 249–252.
Han, Y. O., Han, M. J., Park, S. H. & Kim, D. H. (2003). *J. Pharmacol. Sci.* **93**, 331–336.
Janiak, C. (2000). *J. Chem. Soc. Dalton Trans.* pp. 3885–3896.
Kim, D. H., Yu, K. H., Bae, E. A. & Han, M. J. (1998). *Biol. Pharm. Bull.* **21**, 628–630.
Klus, K. & Barz, W. (1998). *Phytochemistry*, **47**, 1045–1048.
Roberts, D. W., Doerge, D. R., Churchwell, M. I., Gamboa da Costa, G., Marques, M. M. & Tolleson, W. H. (2004). *J. Agric. Food Chem.* **52**, 6623–6632.
Sheldrick, G. M. (1997*a*). *SHELXS97* and *SHELXL97*. University of Göttingen, Germany.
Sheldrick, G. M. (1997*b*). *SHELXTL*. Version 5.10. Bruker AXS Inc., Madison, Wisconsin, USA.
Yamazaki, T., Hosono, T., Matsushita, Y., Kawashima, K., Someya, M., Nakajima, Y., Narui, K., Hibi, Y., Ishizaki, M., Kinjo, J. & Nohara, T. (2002). *Int. J. Clin. Pharmacol. Res.* **22**, 23–28.
Yamazaki, T., Nakajima, Y., Niho, Y., Hosono, T., Kurashige, T., Kinjo, J. & Nohara, T. (1997). *J. Pharm. Pharmacol.* **49**, 831–833.
Zhang, Z. T. & Wang, Q. Y. (2005). *J. Chem. Crystallogr.* **35**, 679–686.
Zhang, Z.-T., Wang, X.-B., Liu, Q.-G., Zheng, J.-B. & Yu, K.-B. (2005). *Acta Cryst.* C**61**, o29–o31.