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Swertisin dihydrate

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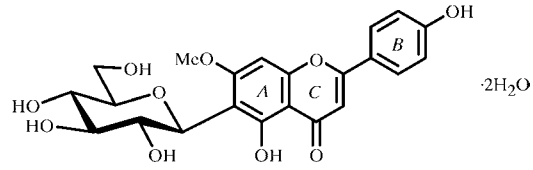
The title compound, 6-*C*-glucopyranosyl-7-*O*-methylapigenin dihydrate, $C_{22}H_{22}O_{10}\cdot 2H_2O$, is a natural *C*-glucosylflavone. The flavone skeleton is almost planar, the dihedral angle between the pyran moiety and the 4-hydroxyphenyl ring being 9.8 (3)°. The basal plane of the pyranosyl ring of the glucose moiety is almost perpendicular to the benzopyran ring system. The flavone skeletons are stacked along the *a* axis, forming layers parallel to (001). Between these hydrophobic layers, the glucose groups and water molecules of crystallization are connected *via* O—H···O hydrogen bonds, forming hydrophilic layers.

Comment

Flavonoid compounds make up a large group of secondary plant metabolites. Some of them exist as glycosides and show various biological functions, such as co-pigment effects on flower pigmentation, screening effects from solar UV radiation, signaling between micro-organisms and chemo-attraction between insects (Harborne & Williams, 2000). Swertisin (7-*O*-methylisovitexin) is a *C*-glucosylflavone isolated from the whole herb of *Swertia japonica* (Komatsu & Tomimori, 1966; Komatsu *et al.*, 1967) and from the seeds of *Ziziphus jujuba* Mill var. spinosa (Cheng *et al.*, 2000), *Piper elongatum* (Masuoka *et al.*, 2003) and other plants. This compound has also been obtained by acid hydrolysis of flavocommelin, which was isolated from the blue petals of *Commelina communis* (Takeda *et al.*, 1966).



(I)

In the supramolecular metal complex pigment (commelinin) of the blue flowers of *C. communis* (Kondo *et al.*, 1992), six molecules of anthocyanin (malonylawobanin) and six molecules of flavone (flavocommelin) form a flattened spherical cluster with two metal atoms and chiral π–π stacking interactions inside the cluster. Chiral self-association of flavocommelin in aqueous solution was also deduced on the basis of CD (circular dichroism; Goto *et al.*, 1990). In these chiral molecular stacking phenomena, the conformation of the glucosyl moieties and intermolecular hydrogen bonding involving the sugar groups must play very important roles (Kondo *et al.*, 2001). The octaacetate derivative of flavocommelin does not show any π–π stacking in the crystal (Ohsawa *et al.*, 1994), possibly as a result of there being no intermolecular hydrogen bonding. The crystal structures of flavone glycosides may give some features of the self-association. However, X-ray structural analyses of flavone glycosides are very rare (Jin, Yamagata & Tomita, 1990; Jin, Fujii & Tomita, 1990; Hirakura *et al.*, 1997). We report here the crystal structure of the title compound, (I).

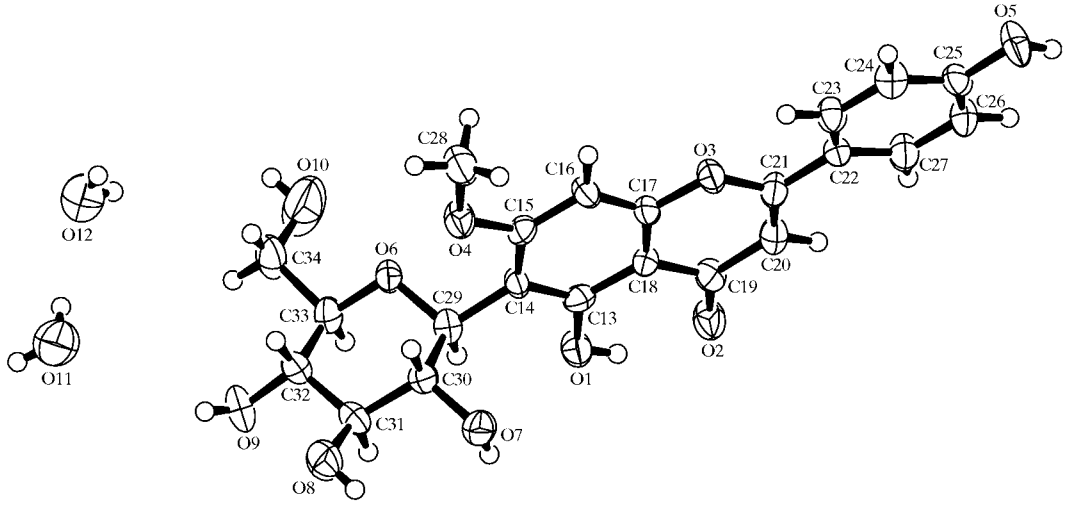


Figure 1
The molecular structure of (I), showing displacement ellipsoids at the 50% probability level. H atoms bonded to atoms O8, O11 and O12 show positional disorder, and atoms H8*B*, H11*C* and H12*B* have been omitted for clarity.

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The molecular structure of (I) is shown in Fig. 1. The basal plane of the hexopyranosyl glucose ring (defined by atoms O6, C33, C31 and C30) is almost perpendicular to the plane of benzene ring *A* (atoms C13–C18), the dihedral angle being 87.3 (3)°. Cheng *et al.* (2000) reported the existence of rotamers of (I) on the basis of the temperature dependence of ^{1}H and ^{13}C NMR spectra in DMSO-d_6 solution, and described the contribution of the methyl group (atom C28) to the rotational energy barrier around the *C*-glucopyranosyl bond (C14—C29 bond) on the basis of conformational analysis. The nearly perpendicular arrangement of the basal plane of the glucose moiety and ring *A* may be the result of non-bonded interatomic repulsions around the *C*-glucopyranosyl bond.

Phenyl ring *B* (atoms C22–C27) is slightly rotated out of the plane of the pyran ring (ring *C*; atoms O3/C17–C21), the O3—C21—C22—C23 torsion angle being 8.3 (9)° (Table 1). In addition, there is a slight bending of ring *B* with respect to ring *C*, as measured by the 0.24 (1) Å shift of the center of phenyl ring *B* from the plane of pyran ring *C*. Similar bending has been observed in flavocommelin octaacetate and other flavone crystals (Ohsawa *et al.*, 1994). The dihedral angles between the planes of rings *A* and *C*, and between the planes of rings *B* and *C* are 3.0 (2) and 9.8 (3)°, respectively.

The roughly planar 4-hydroxyphenylbenzopyranone skeletons are stacked along the *a* axis, forming hydrophobic layers (Fig. 2). Fig. 3 shows the π–π stacking in detail by illustrating the neighboring π systems below and above the molecule at (x, y, z), where $0 < x < \frac{1}{4}$. There are two π systems above (related by the 2_1 screw axis parallel to *b*) and one π system below the flavone plane (related by the twofold axis parallel to *b*). The shortest intermolecular distances between the flavone skeletons are 3.263 (9) (for O2···C21^{vii}) and 3.399 (10) Å for (C19···C20^{ix}) [symmetry codes: (vii) $\frac{1}{2}-x$, $y-\frac{1}{2}$, $1-z$; (ix) $-x$, y, $1-z$].

The glucose groups and water molecules of crystallization are connected *via* O—H···O hydrogen bonds (Table 2), forming hydrophilic layers parallel to (001) (Fig. 2). There is positional disorder of the H atoms in a hydroxy group (O8) and the water molecules (O11 and O12), resulting in two possible hydrogen-bond linkages. In Fig. 4, one of two possible linkages is shown, *i.e.* O8^{iii}—H8*A*^{iii}···O11—H11*B*···O12—H12*C*···O12^{iv}—H12*B*^{iv} (for symmetry codes, see Table 2). The other possible linkage is H8*B*^{iii}—O8^{iii}···H11*C*—O11···H12*B*—O12···H12*C*^{iv}—O12^{iv}.

In the supramolecular blue pigment, commelinin (Kondo *et al.*, 1992), the *C*-glucosyl moiety of flavocommelin is a rotamer of (I), suggesting the flexibility of the relative orientation of the glucose moiety. In commelinin, two molecules of flavocommelin are stacked anticlockwise, the torsion angle between the C═O bond axes of the flavone moieties being *ca* −100°. The C═O bond direction is roughly the direction of electric transition moment of the main absorption band of the flavone compound, and the chiral arrangement of the exciton coupling will cause the CD activity (Nakanishi & Berova, 1994). On the other hand, in (I), the C═O bond axes are approximately parallel to one other. This configuration may be the result of the two-dimensional arrangement of the flavone

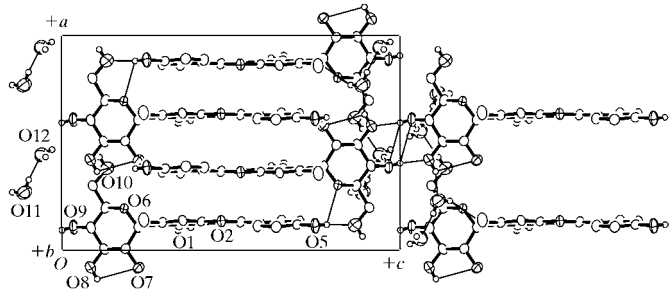

Figure 2
The crystal structure of (I), projected along the *b* axis. Thin lines indicate hydrogen bonds. H atoms bonded to C atoms and atoms H8*B*, H11*C* and H12*B* have been omitted for clarity.

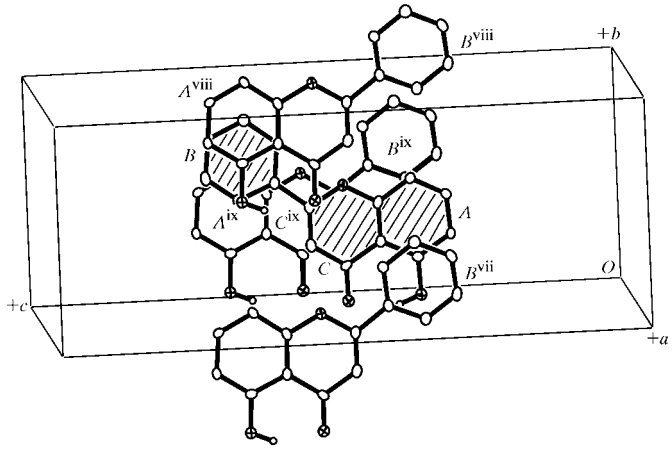

Figure 3
The π–π stacking between the flavone moiety at (x, y, z) ($0 < x < \frac{1}{4}$; hatched) and those of the neighboring molecules above ($\frac{1}{4} < x < \frac{1}{2}$) and below ($-\frac{1}{4} < x < 0$). The substituents, such as glucose groups, have been omitted for clarity. Rings, *A*, *B* and *C* are labeled. [Symmetry codes: (vii) $\frac{1}{2}-x$, $y-\frac{1}{2}$, $1-z$; (viii) $\frac{1}{2}-x$, $y+\frac{1}{2}$, $1-z$; (ix) $-x$, y, $1-z$.]

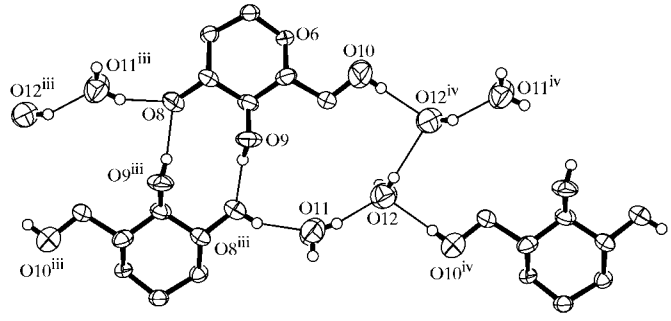

Figure 4
The hydrogen-bond network of glucose groups and water molecules. The flavone moieties, some atoms bonded to the sugar rings and some of the disordered H atoms have been omitted for clarity. [Symmetry codes: (iii) $-x$, y, $-z$; (iv) $1-x$, y, $-z$.]

skeletons in (I), which is supported by a two-dimensional hydrogen-bonding network of the sugar groups and water molecules.

Experimental

Compound (I) was obtained by acid hydrolysis of the *O*-glucopyranosyloxy group bonded to ring *B* of flavocommelin isolated from *C. communis*. To flavocommelin (500 mg) was added 10% HCl–methanol (500 ml) and the mixture was warmed at 333 K for 12 h. The reaction mixture was concentrated *in vacuo* and the resulting syrup was recrystallized from an aqueous methanol solution [yield of (I): 140 mg, 38%]. The powder of (I) (280 mg) was dissolved in an aqueous methanol solution (500 ml) at room temperature and left to stand for slow evaporation of the solvent for five months. At the bottom of the beaker, spherical micelle-like particles were obtained on a curved thin film of (I). Inside the spherical particles were found very thin plate-like crystals of (I) with well developed (001) faces.

Crystal data

$C_{22}H_{22}O_{10}\cdot 2H_2O$
$M_r = 482.44$
Monoclinic, $C2$
$a = 12.950\ (3)$ Å
$b = 8.036\ (3)$ Å
$c = 20.436\ (6)$ Å
$\beta = 90.14\ (2)^\circ$
$V = 2126.7\ (11)$ Å^3
$Z = 4$
$D_x = 1.507$ Mg m^{-3}
Mo $K\alpha$ radiation
Cell parameters from 25 reflections
$\theta = 10.0$–13.5°
$\mu = 0.12$ mm^{-1}
$T = 296$ K
Plate, pale yellow
0.40 × 0.20 × 0.03 mm

Data collection

Rigaku AFC-7*R* diffractometer
ω scans
Absorption correction: by integration (*ABSCOR*; Higashi, 1999)
$T_{min} = 0.980$, $T_{max} = 0.997$
2235 measured reflections
2017 independent reflections
1063 reflections with $I > 2\sigma(I)$
$R_{int} = 0.014$
$\theta_{max} = 25.0^\circ$
$h = -6 \rightarrow 15$
$k = 0 \rightarrow 9$
$l = -24 \rightarrow 24$
3 standard reflections
every 150 reflections
intensity decay: 0.7%

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)] = 0.045$
$wR(F^2) = 0.135$
$S = 1.01$
2017 reflections
330 parameters
H-atom parameters constrained
$w = 1/[\sigma^2(F_o^2) + (0.0633P)^2 + 0.191P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} = 0.007$
$\Delta\rho_{max} = 0.21$ e Å^{-3}
$\Delta\rho_{min} = -0.29$ e Å^{-3}

Table 1
Selected geometric parameters (Å, °).

O1—C13	1.345 (11)	C14—C15	1.404 (11)
O2—C19	1.249 (11)	C14—C29	1.518 (9)
O3—C17	1.372 (8)	C15—C16	1.385 (9)
O3—C21	1.375 (9)	C16—C17	1.383 (10)
O4—C15	1.349 (8)	C17—C18	1.377 (12)
O5—C25	1.381 (9)	C18—C19	1.456 (10)
C13—C14	1.394 (9)	C19—C20	1.426 (10)
C13—C18	1.413 (9)	C20—C21	1.337 (13)
C13—C14—C29	118.0 (7)	O4—C15—C14	114.4 (6)
C15—C14—C29	124.0 (6)	O4—C15—C16	123.3 (7)
O3—C21—C22—C23	8.3 (9)	C15—C14—C29—C30	−64.5 (9)
O6—C29—C14—C15	58.1 (8)	C16—C15—O4—C28	−0.4 (9)

Table 2
Hydrogen-bonding geometry (Å, °).

D—H···A	D—H	H···A	D···A	D—H···A
O1—H1···O2	0.82	1.81	2.542 (6)	148
O5—H5···O10^{i}	0.82	2.07	2.886 (9)	175
O7—H7···O5^{ii}	0.82	2.10	2.907 (9)	170
O8—H8*A*···O11^{iii}	0.82	2.00	2.728 (7)	148
O9—H9···O8^{iii}	0.82	1.96	2.771 (7)	173
O10—H10···O12^{iv}	0.82	1.91	2.732 (8)	179
O11—H11*A*···O4^{v}	0.82	2.32	2.945 (6)	133
O11—H11*A*···O6^{v}	0.82	2.37	3.023 (8)	137
O11—H11*B*···O12	0.82	2.03	2.751 (7)	146
O11—H11*C*···O8^{iii}	0.82	2.10	2.728 (7)	133
O12—H12*A*···O9^{vi}	0.82	1.98	2.787 (7)	168
O12—H12*B*···O11	0.82	1.98	2.751 (7)	156
O12—H12*C*···O12^{iv}	0.82	2.16	2.837 (10)	140

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

H atoms bonded to C atoms were positioned geometrically, with C—H distances of 0.96 (methyl group) and 0.95 Å (other H atoms), and fixed with U_{iso}(H) values of $1.2U_{eq}$(C) [U_{eq}(C) for the methyl group]. The positions of these H atoms were recalculated after each set of refinement cycles, except for the last. About half of the H atoms bonded to O atoms were located from difference syntheses, and positional disorder of the water H atoms was observed, suggesting two possible hydrogen-bond patterns, *viz*. O11—H11*B*···O12 and O11···H12*B*—O12. The positions of the remaining hydroxy and water H atoms were calculated by assuming an intermolecular hydrogen-bond network, with O—H distances of 0.82 Å. The site-occupancy factors of atoms H8*A*, H8*B*, H11*B*, H11*C*, H12*B* and H12*C* are 50% each. Atom H11*C* was introduced at one of two possible positions, assuming sp^3 hybridization of atom O11, on the basis of the positions of atoms H11*A* and H11*B*; the other position was rejected because of a short contact (1.86 Å) to atom H34*A*($\frac{1}{2}-x$, $y-\frac{1}{2}$, $-z$). In order to account for the disorder of the hydrogen bond, O8—H8*A*···O11^{iii} [symmetry code: (iii) $-x$, y, $-z$] and O8···H11*C*^{iii}—O11*C*^{iii}, two geometrically possible positions were calculated, assuming sp^3 hybridization of atom O8, on the basis of the positions of atoms C31 and H8*A*. The position close to atom H9^{iii} was rejected; the other position, which was assigned to atom H8*B*, has no H···H short contact, although there is no hydrogen-bond acceptor. Atoms H1, H5, H7 and H9 were refined as riding on their parent O atoms, with U_{iso}(H) values of U_{eq}(O). The positions of atoms H10, H11*A* and H12*A* were refined for several cycles and then fixed to maintain a reasonable hydrogen-bonding geometry. Restraints were applied for the C31···H8*A*/H8*B* (1.88 Å), H11*A*···H11*B*/H11*C* (1.31 Å) and H12*A*···H12*B*/H12*C* (1.31 Å) distances. Friedel pairs were merged before the final refinement, since anomalous scattering effects were negligible. The absolute structure was assigned on the basis of the absolute configuration of D-(+)-glucose.

Data collection: *WinAFC Diffractometer Control Software* (Rigaku, 1999); cell refinement: *WinAFC Diffractometer Control Software*; data reduction: *TEXSAN* (Molecular Structure Corporation, 2001); program(s) used to solve structure: *SIR*92 (Altomare *et al.*, 1994); program(s) used to refine structure: *SHELXL*97 (Sheldrick, 1997); molecular graphics: *ORTEP*II (Johnson, 1976); software used to prepare material for publication: *TEXSAN*.

Supplementary data for this paper are available from the IUCr electronic archives (Reference: SX1162). Services for accessing these data are described at the back of the journal.

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