A Major Diplotaxis harra-Derived Bioflavonoid Glycoside as a Protective Agent against Chemically Induced Neurotoxicity and Parkinson's Models; In Silico Target Prediction; and Biphasic HPTLC-Based Quantification

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1. TLCs and a bioautographic TLC of F3

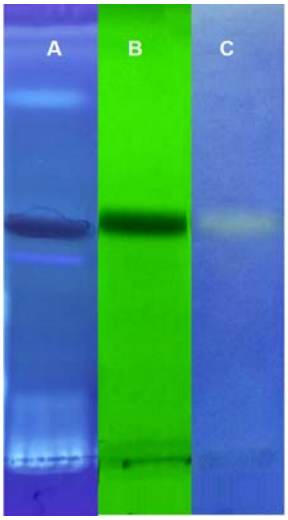

Figure S1. Silica gel TLC chromatograms of EtOAc fraction (F3) as visualized under UV light at 366 nm (A), at 254 nm (B) and after exposure to 0.5 % w/v methanolic DPPH spray reagent under white light (C). Solvent system: EtOAc – MeOH – H_2O (10:1.5:1).

2. X ray diffraction analysis

The isolated Isorhamnetin-3-O-β-D-glucoside (IR3G) was obtained as single crystals by slow evaporation from ethanol solution of the pure compound at room temperature. Data were collected on a Bruker APEX-II D8 Venture area diffractometer, equipped with graphite monochromatic Cu *Kα* radiation, λ = 1.54178 Å at 293 Cell refinement and data reduction were carried out by Bruker SAINT. The SHELXT [1, 2] was used to solve structure. The final refinement was carried out by full-matrix least-squares techniques with anisotropic thermal data for nonhydrogen atoms on *F*. CCDC 1545557 contains the supplementary crystallographic data for this compound can be obtained free of charge from the Cambridge Crystallographic Data Centre *via* www.ccdc.cam.ac.uk/data_request/cif. The molecular structure of IR3G, $C_{22}H_{22}O_{12}\cdot 2(H_2O)$, was crystallized in the Monoclinic, *C*2, a = 24.2571 (7) Å, b = 11.5984 (3) Å, c = 9.3161 (3) Å, β = 107.456 (1)°, V = 2500.32 (13) Å^3, Z = 4.

The crystallographic data and refinement information are summarized in Table S1. The selected bond lengths and bond angles are listed in Table S2. The asymmetric unit is containing of one independent molecule as shown in Figure 1. All the bond lengths and angles are in normal ranges [3]. In the crystal packing, molecules are linked *via* intermolecular hydrogen bonds (Figure 1 and Table S3).

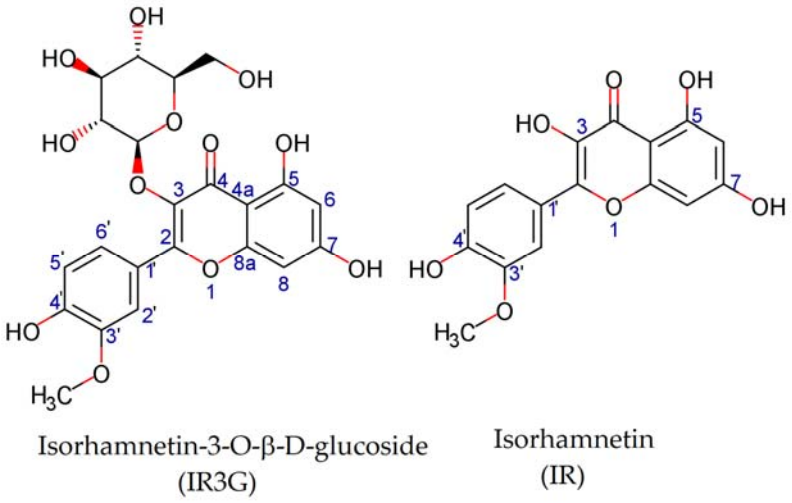

Figure S2. The 2D **s**tructures of IR3G and IR

Table S1. Experimental details of the X ray diffraction analysis

Crystal data	
Chemical formula	$C_{22}H_{22}O_{14}$
Mr	510.40
Crystal system, space group	Monoclinic, *C*2
Temperature (K)	293
a, *b*, *c* (Å)	24.2571 (7), 11.5984 (3), 9.3161 (3)
β (°)	107.456 (1)
V (Å^3)	2500.32 (13)
Z	4
Radiation type	Cu *Kα*
Crystal size (mm)	0.54 × 0.25 × 0.12
Data collection	
Diffractometer	Bruker APEX-II D8 venture diffractometer
Absorption correction	Multi-scan SADABS Bruker 2014
Tmin, Tmax	0.774, 0.810
No. of measured, independent and observed [I > 2σ(I)] reflections	32484, 4933, 4596
R_{int}	0.056
Refinement	
R[F^2 > 2σ(F^2)], wR(F^2), S	0.062, 0.193, 1.11
No. of reflections	4933
No. of parameters	343
No. of restraints	1
H-atom treatment	H atoms treated by a mixture of independent and constrained refinement
$\Delta\rho_{max}$, $\Delta\rho_{min}$ (e Å^{-3})	0.86, −0.27

Table S2. Selected geometric parameters (Å, °)

O1—C1	1.362 (3)	O6—C22	1.425 (5)
O1—C9	1.355 (3)	O7—C13	1.354 (4)
O2—C3	1.351 (4)	O8—C17	1.406 (4)
O3—C5	1.346 (4)	O9—C18	1.426 (4)
O4—C7	1.255 (3)	O10—C19	1.426 (4)
O5—C8	1.376 (3)	O11—C21	1.398 (6)
O5—C16	1.419 (3)	O12—C16	1.418 (3)
O6—C12	1.349 (4)	O12—C20	1.445 (4)
C1—O1—C9	122.3 (2)	O6—C12—C13	115.3 (2)
C8—O5—C16	118.1 (2)	O6—C12—C11	124.4 (2)
C12—O6—C22	117.9 (3)	O7—C13—C12	117.0 (3)
C16—O12—C20	112.0 (2)	O7—C13—C14	123.5 (2)
O1—C1—C6	120.0 (3)	O5—C16—O12	106.68 (19)
O1—C1—C2	116.8 (3)	O5—C16—C17	105.0 (2)
O2—C3—C2	121.6 (3)	O12—C16—C17	111.6 (2)
O2—C3—C4	116.6 (3)	O8—C17—C16	110.9 (2)
O3—C5—C6	120.3 (3)	O8—C17—C18	107.3 (2)
O3—C5—C4	119.2 (3)	O9—C18—C19	111.2 (2)
O4—C7—C8	122.9 (2)	O9—C18—C17	111.0 (2)
O4—C7—C6	121.4 (3)	O10—C19—C18	109.7 (2)
O5—C8—C9	120.4 (2)	O10—C19—C20	107.6 (3)
O5—C8—C7	117.6 (2)	O12—C20—C19	109.0 (3)
O1—C9—C10	110.2 (2)	O12—C20—C21	107.5 (3)
O1—C9—C8	120.5 (2)	O11—C21—C20	112.8 (3)

Table S3. Hydrogen-bond geometry (Å, °)

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
O8—H1O8···O4^{i}	1.05 (6)	1.83 (6)	2.850 (3)	163 (5)
O9—H1O9···O2W	0.72 (4)	2.01 (5)	2.710 (4)	167 (5)
O2—H2B···O1W	0.8200	1.8000	2.581 (7)	158.00
O7—H1O7···O9^{ii}	0.76 (5)	1.99 (5)	2.701 (3)	157 (5)
O3—H3A···O4	0.8200	1.8800	2.607 (3)	147.00
O2W—H4OW···O6^{iii}	0.70 (7)	2.19 (7)	2.819 (5)	151 (7)
O2W—H4OW···O7^{iii}	0.70 (7)	2.58 (7)	3.160 (5)	142 (7)
O10—H10A···O11^{iv}	0.8200	1.9100	2.717 (4)	166.00
O11—H11O···O10^{v}	0.50 (5)	2.26 (5)	2.717 (4)	152 (6)
O2W—H23W···O3^{i}	0.74 (7)	2.27 (7)	2.972 (5)	159 (6)
C11—H11A···O12	0.9300	2.5000	3.259 (3)	139.00
Symmetry codes: (i) −*x*+1, *y*, −*z*+1; (ii) *x*, *y*−1, *z*; (iii) −*x*+1/2, *y*+1/2, −*z*; (iv) −*x*+1/2, *y*+1/2, −*z*+1; (v) −*x*+1/2, *y*−1/2, −*z*+1.				

Table S4. Redocking energy and interaction of ligands (1YL, E8Z, and 1D1) with target proteins (4M0E, 6FVZ, and 4I5P), respectively.

Compound	Target (PDB code)	Ligand	Receptor	Interaction	Distance	E (kcal/mol)	Docking score (kcal/mol)
1YL (PDB code)	AChE (4M0E)	C18 1	5-ring TRP286 (A)	H-pi	3.31	–0.3	–6.4471
		6-ring	6-ring TRP286 (A)	pi-pi	3.86	–0.1	
		6-ring	6-ring TRP286 (A)	pi-pi	3.62	–0.1	
E8Z (PDB code)	MAO-B (6FVZ)	CAK 14	SG CYS172 (A)	H-donor	3.22	–0.6	–7.5971
		6-ring	CA CYS172 (A)	pi-H	3.49	–1.1	
		6-ring	CB ILE199 (A)	pi-H	2.70	–0.6	
1D1 (PDB code)	PLK-2 (4I5P)	C8 9	O GLU160 (A)	H-donor	3.16	–1	–8.5290
		O23 1	O HOH519 (A)	H-acceptor	2.84	–2.4	
		O23 1	O HOH617 (A)	H-acceptor	3.07	-0.9	
		N7 11	N CYS162 (A)	H-acceptor	2.89	–5.3	
		5-ring	CD1 LEU88 (A)	pi-H	4.16	–0.7	

IR3G: Isorhamnetin-3-O-β-D-glucoside; AChE: Acetylcholine esterase; MAO-B: Monoamine oxidase type B; PLK-2: Polo-like kinase-2; 1YL: Dihydrotanshinone I; E8Z: N-(3,4-dimethylphenyl)-4-oxidanylidene-chromene-3-carboxamide; 1D1: (7R)-8-cyclopentyl-7-ethyl-5-methyl-2-(1H-pyrrol-2-yl)-7,8-dihydropteridin-6(5H)-one.

References:

1. Sheldrick, G. M., A short history of SHELX. *Acta Crystallogr. A* **2008,** 64, (Pt 1), 112-122.
2. Sheldrick, G. M., SHELXTL-PC (Version 5.1), Siemens analytical. instruments, Inc., Madison, WI, 1997.
3. Allen, F. H.; Kennard, O.; Watson, D. G.; Brammer, L ;·Orpen, A. G.; Taylor, R., Tables of Bond Lengths determined by X-Ray and Neutron Diffraction. Part. 1. Bond Lengths in Organic Compounds. *J. Chem. Soc., Chem. Soc. Perkins Trans. 2* **1987**, S1–S19·