

**Supplementary Data 1. Histopathological evaluation scoring of brain tissue of various groups**

**Score description**

Score	Description	Percentage tissue occupied
0	Within normal limits	0
1	Very minimal	0-10
2	Mild	11-20
3	Moderate	21-40
4	Sever	41-100

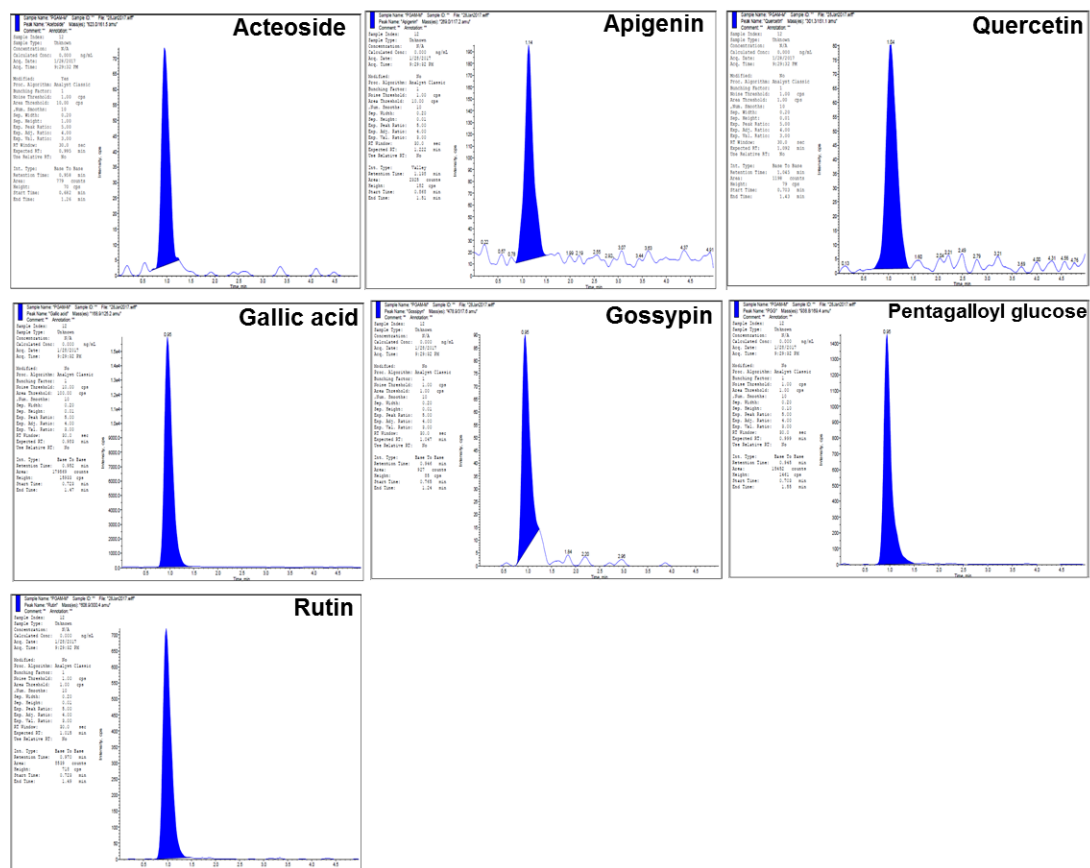
**Groupwise histopathology scoring and statistical analysis results**

Parameter	Groupwise scoring (Mean± SEM)				
	Control	I/R Control	Quercetin 20 mg	MePG 200 mg	MePG 400 mg
Cerebral edema	0.15 ± 0.20	3.57 ± 0.20 <sup>***</sup>	0.42 ± 0.20 <sup>**</sup>	1.00 ± 0.32 <sup>ns</sup>	0.71 ± 0.14 <sup>*</sup>
Leukocyte infiltration	0.15 ± 0.14	3.85 ± 0.14 <sup>***</sup>	0.57 ± 0.24 <sup>*</sup>	1.14 ± 0.26 <sup>*</sup>	0.70 ± 0.16 <sup>*</sup>
Vascular congestion	0.28 ± 0.12	3.57 ± 0.20 <sup>***</sup>	0.58 ± 0.13 <sup>**</sup>	1.00 ± 0.30 <sup>ns</sup>	0.42 ± 0.24 <sup>**</sup>
Necrosis	0.14 ± 0.14	3.71 ± 0.14 <sup>***</sup>	0.62 ± 0.20 <sup>**</sup>	1.00 ± 0.30 <sup>*</sup>	0.57 ± 0.20 <sup>**</sup>

**Note:** I/R, Ischemia-reperfusion, MePG- Methanolic leaf extract of *Punica granatum*

The scoring ranks of the various groups were statistically compared by (non-parametric test) Kruskal-Wallis test followed by Dunn's Multiple Comparison Test using Graph Pad version 5.01. The brain tissue of various groups were evaluated for above listed 4 parameters, in the observations the I/R control animals showed significant histopathological lesions compared to sham control (P < 0.01). The MePG (400 mg/kg) and Quercetin (20 mg/kg) treatment showed significantly less histoarchitectural lesions of brain tissue compared to I/R control group (P < 0.01), and but MeCO (200 mg/kg) group showed characteristic features of cerebral damage compared to I.R control, and hence showed very mild protection (P<0.05).

## Supplementary Data 2. Compounds detected in LC-MS/MS analysis of Methanolic leaf extract of *P. granatum*



Compounds namely Acteoside, Apigenin, Quercetin, Gallic acid, Gossypin, Pentagalloyl glucose and Rutin were identified from methanolic leaf extract of *P. granatum* (MePG) by LC-MS/MS analysis.

**Supplementary Data 3. LC-MS/MS Quantification of phytoconstituents in methanolic leaf extract of *P. granatum***

<b>Compound</b>	<b>Peak retention time (min)</b>	<b>DP (V)</b>	<b>FP (V)</b>	<b>CE (V)</b>	<b>CXP (V)</b>	<b>Precursor ion (m/z)</b>	<b>Product ion (m/z)</b>	<b>Peak area (counts)</b>	<b>Reference compound peak area (counts)</b>	<b>Concentration of compound in extract (ng/mg)*</b>
Acteoside	0.958	-66	-320	-52	-7.0	623.01	161.5	779	97836	7.96
Apigenin	1.138	-66	-340	-42	-5	268.97	117.20	2325	5028	462.41
Gallic acid	0.952	-60	-200	-30	-5.9	168.95	125.20	123052	179569	685.26
Gossypin	0.946	-66	-290	-32	-1.0	478.9	317.6	927	43866	21.13
PGG	0.945	-101	-350	-78	-7	938.84	169.40	15452	1326	11653.09
Quercetin	1.045	-60	-200	-30	-5.9	301.3	151.1	1198	31504	38.03
Rutin	0.970	-66	-340	-52	-3	608.93	300.40	8539	29022	294.23

**Note:** PGG; Pentagalloyl glucose, DP, Declustering potential; FP, Focusing potential; CE, Collision energy; CXP, Collision cell exit potential. \*Concentration of reference compounds is 1000 ng/mL.