Protective effects of Phyllanthus amarus against lipopolysaccharide-induced neuroinflammation and cognitive impairment in rats

ABSTRACT

Background: Phyllanthus amarus (PA) is widely studied for its hepatoprotective properties but has recently received increasing attention due to its diverse anti-inflammatory effects. However, the effects of PA in modulating immune responses in the central nervous system leading to protection against functional changes remain unexplored. Therefore, we sought to examine the protective effects of 80% v/v ethanol extract of PA on lipopolysaccharide (LPS)-induced non-spatial memory impairment and neuroinflammation. Methods: Selected major phytoconstituents of PA extract were identified and quantified using high-performance liquid chromatography. Subchronic neurotoxicity was performed in male Wistar rats given daily oral administration of 100, 200, and 400 mg/kg of the PA extract. Their neurobehavioral activities (functional observation battery and locomotor activity) were scored, and the extracted brains were examined for neuropathological changes. Rats were treated orally with vehicle (5% Tween 20), PA extract (100, 200, and 400 mg/kg), or ibuprofen (IBF; 40 mg/kg) for 14 and 28 days before being subjected to novel object discrimination test. All groups were challenged with LPS (1 mg/kg) given intraperitoneally a day prior to the behavioral tests except for the negative control group. At the end of the behavioral tests, the levels of tumor necrosis factor-α (TNF-α), interleukin (IL)-1β, nitric oxide (NO), inducible nitric oxide synthase (iNOS), CD11b/c integrin expression, and synaptophysin immunoreactivity were determined in the brain tissues. Results: Gallic acid, ellagic acid, corilagin, geraniin, niranthin, phyllanthin, hypophyllanthin, phyltetralin, and isonirtetralin were identified in the PA extract. Subchronic administration of PA extract (100, 200, and 400 mg/kg) showed no abnormalities in neurobehavior and brain histology. PA extract administered at 200 and 400 mg/kg for 14 and 28 days effectively protected the rodents from LPS-induced memory impairment. Similar doses significantly ($p < 0.05$) decreased the release of proteins like TNF-α, IL-1β, and iNOS in the brain tissue. NO levels, CD11b/c integrin expression, and synaptophysin immunoreactivity were also reduced as compared with those in the LPS-challenged group. Conclusion: Pre-treatment with PA extract for 14 and 28 days was comparable with pre-treatment with IBF in prevention of memory impairment and alleviation of neuroinflammatory responses induced by LPS. Further studies are essential to identify the bioactive phytochemicals and the precise underlying mechanisms.

Keyword: Phyllanthus amarus; Neuroinflammation; Neuroprotection; Non-spatial memory; Pro-inflammatory markers