"AQUEOUS EXTRACT OF *PHYLLANTHUS EMBLICA* AMELIORATES LIPOPOLYSACCHARIDE INDUCED SICKNESS BEHAVIOUR IN MICE"

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Abstract

Sickness behaviour is characterized by anxiety, reduction in body weight, depression, reduced appetite and anhedonia. It can be induced in test animals by bacterial endotoxin,

lipopolysaccharide (LPS). *Phyllanthus emblica* has been reported to possess anti-inflammatory, antioxidant, neuroprotective and anxiolytic activities. The study was undertaken to evaluate the effect of aqueous extract of *Phyllanthus emblica* fruits in LPS induced sickness behaviour and anorexia in mice. Swiss albino mice were pre-treated by *Phyllanthus emblica* (100 and 200 mg/kg, p.o.) or Dexamethasone (1mg/kg, i.p.) for 3 days and then LPS (0.83 mg/kg, i.p.) was administered. At different time intervals of post-LPS challenge, duration of social exploration, anxiety, water and food consumption, and weight loss were assessed to quantify the LPS-induced sickness behavior in mice. Oxidative stress markers levels [reduced glutathione (GSH) and lipid peroxidation (LPO)] in mice brains were also analyzed. Pre-treatment with aqueous extract of *Phyllanthus emblica* (100 and 200 mg/kg) effectively ameliorated LPS-induced sickness behavior by reducing the production of cytokines and suppressing indicators of brain oxidative stress.

Keywords: *Phyllanthus emblica*, lipopolysaccharide, sickness behaviour, anorexia, depression

Introduction

A coordinated series of adaptive behavioural alterations that occur in sick people throughout the course of an infection is known as sickness behaviour. It is characterized by worry,

anhedonia, decreased appetite, and lethargy. Less evident but consistent symptoms of illness include decreased social behavior, diminished pleasure perception, heightened pain sensitivity, and increased timidity.[1] Animal models treated with lipopolysaccharide (LPS) a bacterial endotoxin have been used to study the mechanism of immune system activation-induced sickness behaviour. When LPS is administered to rodents, it produces neuroinflammation, neuronal activation, and sickness behavior in the brain.[2] Reactive oxygen species (ROS) are produced in large quantities by LPS, mainly by neutrophils that infiltrate and macrophages. Because ROS activate transcription factors like nuclear factor kappa B (NFkB) and operate as an intracellular messenger to drive signal transduction, their generation is crucial for host defense and may have an impact on sickness behavior through NFkB-dependent cytokine production.[3] Anxiety, anorexia, depression, loss of interest in routine tasks, and drowsiness are some of its defining characteristics.[4] First-line medications such as non-steroidal anti-inflammatory drugs (NSAID), tricyclic antidepressants (TCA), and selective serotonin reuptake inhibitors (SSRI) are used to treat depression disorders associated with illness; however, these medications have side effects, such as sedation and gastritis, in addition to high resistance, replacement rates, and recurrence of depression.[5] Therefore, it is necessary to find and create medications that are safer and more effective than current treatments, whether they are older or newer and free of these restrictions. To effectively treat depression brought on by illness, natural compounds that demonstrate or maintain brain health are required, such as lutein, zeaxanthin, flavonoids, and amino acids.[6] *Phyllanthus emblica* Linn., also referred to as amla or Indian gooseberry, is a member of the Euphorbiaceae family and has been shown to have a number of biological properties, including anti-inflammatory, anti-oxidant,[8] antiepileptic,[9] antidepressant,[10] and neuroprotective properties, among others. Amla is said to be a rich source of vitamin C[7] among other antioxidants. These factors informed the design of the current investigation, which aims to assess the *Phyllanthus emblica* for LPS-induced sick behaviour in mice.

Materials and methods

Chemicals

Lipopolysaccharide (LPS) (Sigma-Aldrich, St. Louis, USA), Dexamethasone (Cadila Healthcare Ltd, Ahmadabad). All other chemicals and reagents used for the study were of analytical grade procured from approved organizations.

Plant material and preparation of extract [11]

Phyllanthus emblica belonging to family Euphorbiaceae were collected from local region of Tumakuru rural area and authenticated by Professor, S. Chidananda S.S.W.C Tumakuru. Specimen voucher no. P.cog/P.col -03. *Phyllanthus emblica* (80 g) dried fruits were crushed into fine powder and extracted with 1 L boiling water for 30 min. The heated decoction obtained was allowed to cool at room temperature and filtered twice through fine filter paper. The filtrate was then evaporated to dryness on a water bath. The extract was brown in colour. The extract was stored in a desiccator and used for the pharmacological studies by dissolving each time in distilled water.

Experimental animals

For the current investigation, male Swiss albino mice weighing 25–30 g and showing no symptoms of inflammation were employed. The animal house of Sree Siddaganga College of Pharmacy in Tumakuru was the site of experimental investigations. The animals were kept in controlled environments with 12-hour light-dark cycles at a temperature of 23 ± 2 C. The animals were placed in sanitized polypropylene cages with sterile rice husk bedding, and they were randomly assigned to various experimental and control groups. They had unrestricted access to water and regular pellets for their base diet. The Institutional Animal Ethical Committee (IAEC) of Sree Siddaganga College of Pharmacy, Tumakuru, Karnataka, accepted all of the studies that were carried out; approval number: SSCP/IAEC. 237/22-23 Dated 12/08/2023 in accordance with the Committee's recommended criteria for CCSEA, Government of India.

Experimental design

Swiss Albino mice were randomly divided into five groups (n=6). Group 1: Normal control receives normal saline; Group 2: LPS alone (0.83 mg/kg, i.p.); Group 3: *Phyllanthus emblica* (100 mg/kg p.o.) and LPS (0.83 mg/kg i.p.); Group 4: *Phyllanthus emblica* (200 mg/kg p.o.) and LPS (0. 83 mg/ kg i.p.); Group 5: Dexamethasone (1 mg/kg) and LPS (0.83 mg/ kg i.p.). These therapies were all administered daily for three days. On day three, an hour after the treatments described earlier, LPS was administered. Following the administration of LPS

after two hours, the animals underwent behavioural assessments. Brain was isolated on scarification by overdose of anaesthasia for biochemical measurements like GSH and LPO.

Behavioural tests

Elevated plus-maze [3]

The elevated plus-maze apparatus had an open roof, two arms that were 50 × 10 cm and two that were 50 × 10 × 40 cm closed, and the maze was raised 50 cm from the ground overall. Every mouse was positioned with its head toward the open arm in the center of the raised plus-maze. The number of entries into the open arms of the maze and the amount of time spent there were counted during the five-minute test.

Open field test [12]

Spontaneous locomotor activity was quantified in an open field, a white plastic box (59 x 59 cm) with its floor divided into 16 squares. Line crossings (central and peripheral), rears and climbing were scored for 5 min. A line crossing was counted when all four paws were removed from one square and entered another. Rears were scored when a mouse raised both front paws from the floor and climbs when an animal leaned its front paws against a wall.

Light-dark box method [13]

The light-dark box apparatus consists of an open-top wooden box with two distinct chambers, a dark chamber (25 × 35 × 35 cm), painted black and a bright chamber (30 × 30 × 35 cm), painted white. The two chambers were connected through a small open doorway (7.5 × 5 cm) situated on the floor level at the centre of the partition. The mice were placed in the light compartment and allowed to move freely between the two compartments. Behaviour was observed for a total of 5 min. The number of entries and time spent in the light compartment and the number of transitions between the light and dark compartments was recorded.

Forced swim test [4]

This test was performed according to the method developed by Porsolt et al. (1977) for mice.

Mice were placed in a vertical glass cylinder (26 cm in height, 12 cm in diameter) filled with 25° C water to a depth of 16 cm. the water depth was chosen so that animals swim or float without their hind limbs or tail touching the bottom. For testing, each mouse was placed in the cylinder for 3 min and the duration of floating was scored.

Social behaviour [12]

In this model, a juvenile nonspecific was placed in the home cage of an experimental subject for a brief 5 min test. The social interaction between the subject and juvenile is recorded and the duration engaged in social interaction was determined from the records by a trained observer who was blind to the experimental treatments. Social behaviour was determined as the amount of time that the experimental subject spent investigating (e.g., sniffing, crawling under or climbing over, genital investigation, and following) the juvenile. The Mouse was subjected to the social behaviour test 24 h later, using a novel juvenile.

Feeding behaviour and body weight [4]

Food and water containers were filled daily with a measured amount of standardized pelleted chow and a known amount of water. Food and water intake were measured at 6 and 24 h post LPS treatment and was quantified by subtracting the food and water remaining in the containers and the amount of food and water given in the preceding day. Bodyweight was measured 24th pre, and 24 h post lipopolysaccharide or vehicle challenge.

Sucrose preference test [13]

To assess the sucrose preference mice were provided with two solutions, water and 10 % sucrose solution in bottles with stoppers fitted with ball-type sipper tubes. Before testing conditions, all mice were acclimated to the two-bottle test choice. All mice drink both the water and 10 % sucrose solution but favoured drinking sucrose over water. On the day of testing, fluid and food deprived for 2 h before testing. Each set of mice received the final doses of vehicle, or Dexamethasone 30 min before the LPS shot. Immediately After LPS-injection mice had way into the water and 10 % sucrose solution for the next 24 h. Fluid intake was measured by measuring the water, sucrose bottle at 2 and 24 h.

Biochemical estimations.[13]

The animals were sacrificed under anaesthesia and perfused transcardially with ice-cold saline. The brain was removed, homogenized in cold phosphate-buffered saline (10 % w/v), and the suspension was centrifuged at 12000×g for 15 min at 4° C. The supernatant was used for the following biochemical analysis. The total protein content of the brain homogenate was determined as described by Lowry's method using bovine serum albumin as standard. LPO extent was measured by estimating the amount of malondialdehyde (MDA) formed as described by Gelvan and Saltman (1990), and the results were expressed as nmol MDA/mg protein. The content of GSH was measured according to the method of Ellman (1959), and the values were expressed as nmol/mg protein.

Statistical Analysis

The data were expressed as mean ± SEM. The statistical analysis of data was done by using One-way analysis of variance (ANOVA), followed by Kruskal-Wallis non-parametric test for grading for aggression and other data Tukey 's multiple comparison test by using Graph Pad Prism 5.0 (USA).

Results

Behavioural tests

Assessment of plus maze response

In elevated plus maze (EPM) test, peripheral LPS administration induced a panicogenic symptoms in mice decreased both the number of open arm entries, the time spent in open arm and a significant increase in the number of entries in closed arm and the time spent in closed arms when compared with the normal control group. Pretreatment with aqueous extract of *Phyllanthus emblica* (100 and 200 mg/kg, p.o) and Dexamethasone (1 mg/kg, i.p.) attenuated the LPS mediated effects and increased both the number of open arm entries and time spent in open arm also significant decrease in the time spent in the closed arm compared with LPS challenge group.

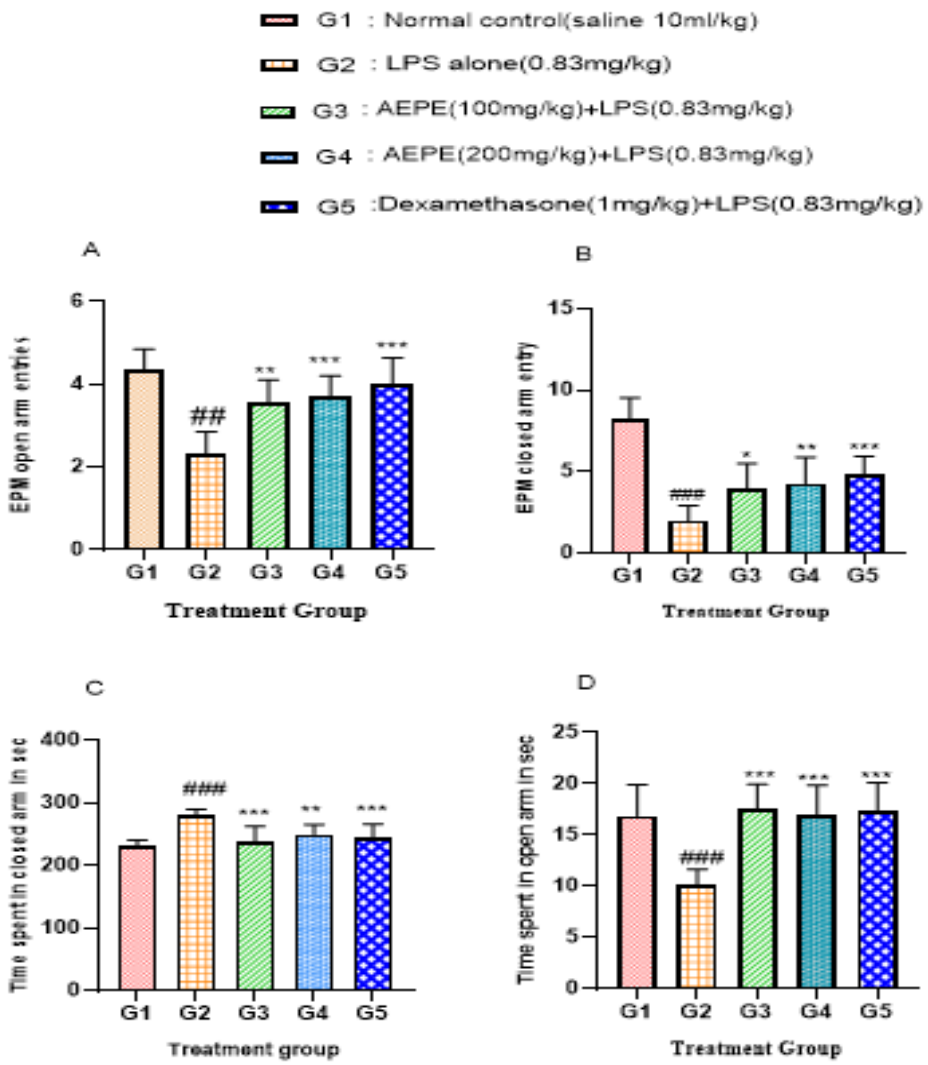

Figure no:01 Effect of pre-treatment of aqueous extract of *Phyllanthus emblica* on LPS treated mice in the elevated plus maze (EPM)

(A) Open arm entry (B) Closed arm entry (C) Time spent in closed arm and (D) Time spent in open arm. Results are shown as mean ± SEM. $^{\#}p<0.05$, $^{\#\#}p<0.01$ and $^{\#\#\#}p<0.001$ v/s Normal control; $^{*}p<0.05$, $^{**}p<0.01$ and $^{***}p<0.001$, when compared with the LPS alone group.

Light-dark box

After LPS injection to mice, it resulted in decreased number of entries, time spent and transition in light compartment compared to normal control respectively. Treatment with aqueous extract of *Phyllanthus emblica* (100 and 200 mg/kg) and Dexamethasone (1 mg/kg) prior to LPS shot significantly increased the time spent in light compartment and the number of transitions in comparison with the LPS treated group.

Table No: 01 Effects of pre-treatment of aqueous extract of *Phyllanthus emblica* on LPS-induced sickness behaviourof mice tested in the light-dark box.

Groups	Treatments	Number of entries to light compartment	Time spent in light compartment (in sec)	Number of transitions
1	Normal control (saline 10 ml/kg)	4.33±0.21	41.75±1.25	4.66±0.21***
2	LPS alone (0.83 mg/kg, i.p.)	2.33±0.21$^{\#\#}$	18.25±0.79$^{\#\#}$	1.62±0.26$^{\#\#}$
3	AEPE (100 mg/kg, p.o.) + LPS (0.83 mg/kg, i.p.)	3.40±0.24*	40.38±3.76***	2.83±0.30**
4	AEPE (200 mg/kg, p.o.) + LPS (0.83 mg/kg, i.p.)	3.57±0.20**	48.13±1.04***	3.40±0.24***
5	Dexamethasone (1 mg/kg, i.p.) + LPS (0.83 mg/kg, i.p.)	3.40±0.24*	43.75±0.55***	3.33±0.21***

Values are given as mean ± SEM. for group of eight animals each. The intergroup variation was measured by One-way Analysis of Variance (ANOVA) followed by Tukey's post hoc test. The symbols denote the significance levels: $^{\#\#}p<0.01$ and $^{\#\#\#}p<0.001$ v/s Normal control; $^{*}p<0.05$ and $^{**}p<0.01$ when compared with LPS alone group

Open field test

a. Effect on line crossings

The open field test was performed two hours after the injection of LPS. Pre-treatment with aqueous extract of *Phyllanthus emblica* (100 and 200 mg/kg) and Dexamethasone (1 mg/kg) significantly attenuated LPS induced changes and increased the peripheral number of line crossings when compared to the LPS alone treated group.

b. Effect on rearing and climbing behaviour

LPS alone also significantly decreased the number of climbs and rears. The number of climbs when compared to LPS challenged group were significantly increased by aqueous extract of

Phyllanthus emblica (100 and 200 mg/kg) and Dexamethasone (1 mg/kg) pre-treatment respectively.

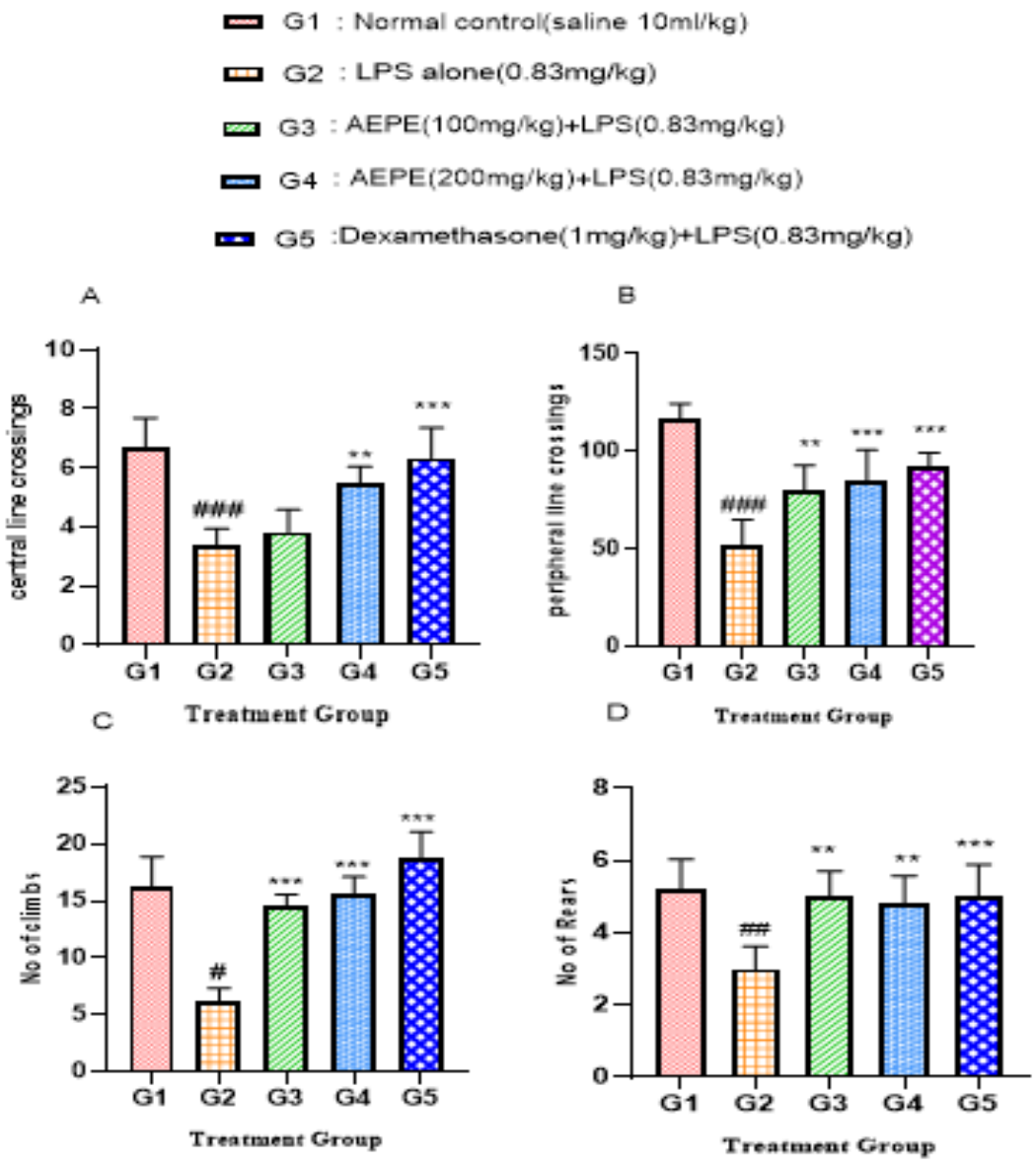

Figure no: 02 Effects of pre-treatment of aqueous extract of *Phyllanthus emblica* on LPS induced sickness behaviour in the open field test (OFT).

(A)Central line crossing (B) Peripheral line crossings (C) Number of Climbs and (D) Number of rears. Results are shown as mean ± SEM. $^{\#}p<0.05$, $^{\#\#}p<0.01$ and $^{\#\#\#}p<0.001$ v/s Normal control; $^{*}p<0.05$, $^{**}p<0.01$ and $^{***}p<0.001$, when compared with the LPS alone group.

Forced swim test

The forced swim test was performed to check immobility in LPS-induced mice. Pre-treatment with aqueous extract of *Phyllanthus emblica* (100 and 200 mg/kg) and Dexamethasone (1 mg/kg) once daily for three consecutive days prior to LPS shot significantly decreased the floating time when compared to the LPS alone administered group

Social behaviour

Pre-treatment with aqueous extract of *Phyllanthus emblica* (100 and 200 mg/kg) and Dexamethasone (1 mg/kg) showed significantly increased and social interaction time respectively when compared to LPS alone group aqueous extract of *Phyllanthus emblica* at high dose showed better recovery than the low dose.

Table no: 02 Effects of pre-treatment of aqueous extract of *Phyllanthus emblica* on LPS-induced sickness behaviour of mice in the forced swim test and social interaction test.

Groups	Treatments	Interaction time(sec)	Floating time(sec)
1	Normal control (saline 10 ml/kg)	99.75±1.63	51.43±5.25
2	LPS alone (0.83 mg/kg, i.p.)	19.86±0.96$^{\#\#}$	109.2±6.0$^{\#\#}$
3	AEPE (100 mg/kg, p.o.) + LPS (0.83 mg/kg, i.p.)	77.38±3.3**	72.80±4.60**
4	AEPE (200 mg/kg, p.o.) + LPS (0.83 mg/kg, i.p.)	101.5±2.42***	82.17±6.85*
5	Dexamethasone (1 mg/kg, i.p.) + LPS (0.83 mg/kg, i.p.)	97.38±1.22***	68.43±5.41***

Values are given as mean ± SEM. for group of eight animals each. The intergroup variation was measured by One-way Analysis of Variance (ANOVA) followed by Tukey's post hoc test. The symbols denote the significance levels: $^{\#\#}p<0.01$ and $^{\#\#\#}p<0.001$ v/s Normal control; $^{***}p<0.001$ when compared with LPS alone group.

Feeding behaviour

Assessment of food and water consumption

LPS challenge led to a marked decrease in food and water consumption in mice. This decrease was significantly prevented by *Phyllanthus emblica* (100 and 200mg/kg)

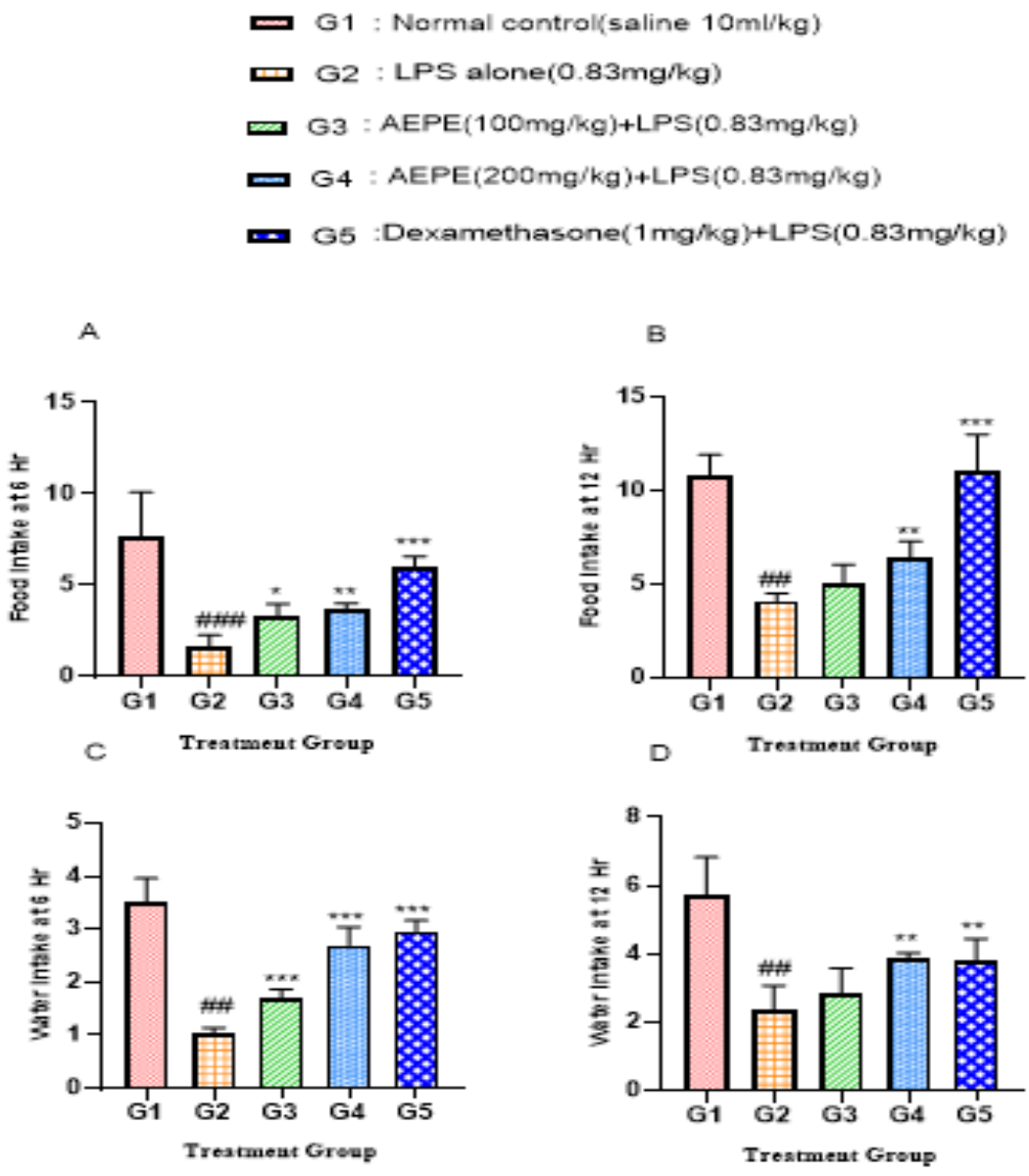

Figure no: 03 Effects of pre-treatment of aqueous extract of *Phyllanthus emblica* on food intake and water intake in LPS treated mice.

Food intake 6 h (A) and 24 h (B), water intake 6 h (C) and 24 h (D). Results are shown as mean ± SEM. $^{\#}p<0.05$, $^{\#\#}p<0.01$ and $^{\#\#\#}p<0.001$ v/s Normal control; $^{*}p<0.05$, $^{**}p<0.01$ and $^{***}p<0.001$, when compared with the LPS alone group.

Body weight

There was a significant decreased % of body weight in mice treated with LPS when compared to control mice. Pre-treatment with aqueous extract of *Phyllanthus emblica* (100 and 200 mg/kg) and Dexamethasone (1 mg/kg) showed increased % of body weight when compared to LPS treated mice.

Body temperature

LPS treated mice showed significantly increased % of rectal temperature recorded on digital thermometer when compared to normal control mice. Pre-treatment with aqueous extract of *Phyllanthus emblica* (100 and 200 mg/kg) and Dexamethasone (1 mg/kg) showed significant drop off in body temperature when compared to LPS treated group high dose of aqueous extract of *Phyllanthus emblica* showed good results.

Table no: 03 Effects of pre-treatment of aqueous extract of *Phyllanthus emblica* on body weight and bodytemperature in LPS-treated mice.

Groups	Treatments	% Decrease in body weight	% Increase in body temperature
1	Normal control (saline 10 ml/kg)	-6.01±0.44	0.29±0.02
2	LPS alone (0.83 mg/kg, i.p.)	-10.50±0.37$^{###}$	4.04±0.21$^{##}$
3	AEPE (100 mg/kg, p.o.) + LPS (0.83 mg/kg, i.p.)	-8.44±0.39*	3.28±0.19*
4	AEPE (200 mg/kg, p.o.) + LPS (0.83 mg/kg, i.p.)	-7.65±0.58***	2.85±0.24**
5	Dexamethasone (1 mg/kg, i.p.) + LPS (0.83 mg/kg, i.p.)	-7.24±0.39***	2.68±0.25***

Values are given as mean ± SEM. for group of eight animals each. The intergroup variation was measured by One-way Analysis of Variance (ANOVA) followed by Tukey's post hoc test. The symbols denote the significance levels: $^{###}p<0.001$ v/s Normal control; $^{*}p<0.05$ and $^{***}p<0.001$ v/s LPS alone group.

Sucrose preference test

Pre-treatment with aqueous extract of *Phyllanthus emblica* (200 mg/kg) significantly re-established the preference for sucrose solution at 2 and 24 h when compared with the LPS treated group. Dexamethasone (1 mg/kg) in fact prevented this LPS induced fall in sucrose preference and re-established the same. Animals pre-treated with aqueous extract of *Phyllanthus emblica* (100 mg/kg) not showed significant differences in sucrose preference at both 2 and24 h post LPS

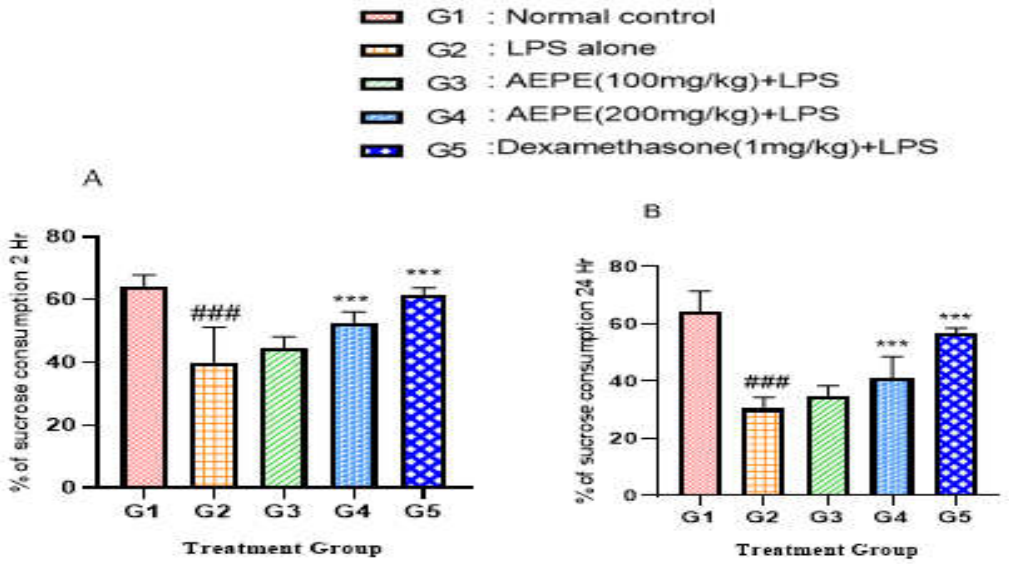

Figure no: 04 Effects of pre-treatment of aqueous extract of *Phyllanthus emblica* on preference for 10% sucrose solution in LPS treated mice.

2h (A) and 24 h (B) time interval for preference of 10% sucrose. Results are shown as mean ± SEM. $^{\#}p<0.05$, $^{\#\#}p<0.01$ and $^{\#\#\#}p<0.001$ v/s Normal control; $^{*}p<0.05$, $^{**}p<0.01$ and $^{***}p<0.001$, when compared with the LPS alone group. $^{*}p<0.05$, $^{**}p<0.01$ and $^{***}p<0.001$ when compared with the LPS alone group.

Biochemical estimations

Reduced glutathione (GSH)

A significant diminution in GSH levels was observed in the brain homogenates of LPS treated mice when compared to the control group. Pre-treatment with Dexamethasone (1 mg/kg) showed significantly elevated GSH levels. Aqueous extract of *Phyllanthus emblica* (100 and 200 mg/kg) also significantly enhanced the GSH levels.

Lipid peroxidation (LPO)

The level of MDA in LPS alone treated mice was significantly increased when compared with the normal control treated group. Prior treatment with aqueous extract of *Phyllanthus emblica* (100 and 200 mg/kg) and Dexamethasone (1 mg/kg) significantly attenuated LPS mediated effects and decreased the levels of MDA. Lower dose of aqueous extract of *Phyllanthus emblica* showed better results than the higher dose.

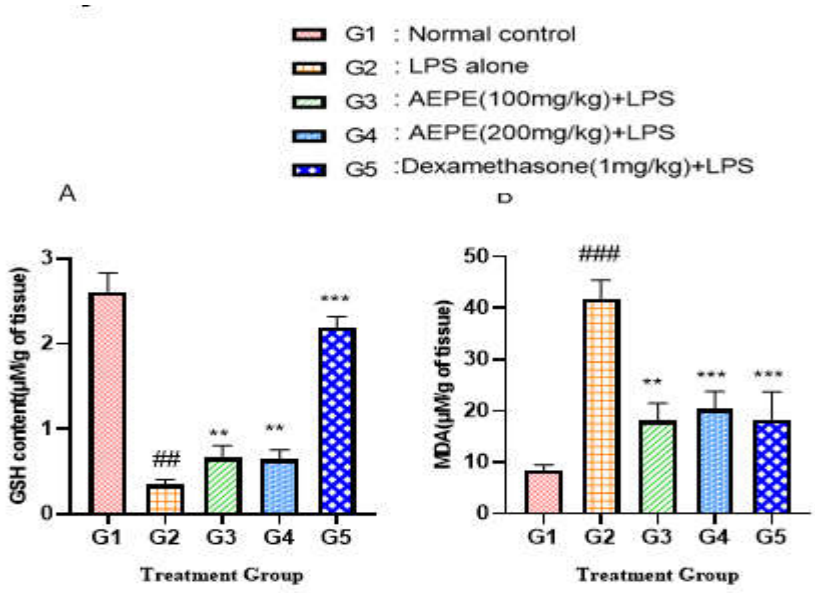

Figure no: 05 Effects of pre-treatment of aqueous extract of *Phyllanthus emblica* on (LPS) on brain oxidativestress parameters in mice.

(A) Reduced glutathione and (B) Lipid peroxidation. Results are shown as mean ± SEM. $^{\#}p<0.05$, $^{\#\#}p<0.01$ and $^{\#\#\#}p<0.001$ v/s Normal control; $^{*}p<0.05$, $^{**}p<0.01$ and $^{***}p<0.001$, when compared with the LPS alone group.

Discussion

Sickness behaviour is a synchronized set of adaptive immune, physiological and behavioural changes that build up during the way of an infection to combat it and promote survival. As described earlier, sickness behaviour in animals can be reliably induced by the administration cytokine cytokine-inducing agents like LPS. LPS binds to immune cells and initiates signalling cascades that activate the transcription factor, NFkB to upregulate expression of among other genes, the inflammatory cytokines IL-1β, IL-6 and TNF-α. These released cytokines then in turn relay signals to the CNS macrophages and microglia to produce the same cytokines, targeting neuronal substrates and eliciting sickness behaviour.[13]

Dexamethasone, a potent synthetic glucocorticoid, has anti-inflammatory and immunosuppressant effects by interfering with inflammatory cytokines and TNF-α. Hence, Dexamethasone was used as a standard reference.[14] Intra-peritoneal injection of LPS (0.83 mg/kg) produces a depressive-like behaviour, anorexia, adipsia, anhedonia and a reduction in exploratory behaviour in the tested animal models.[15]

Previous studies postulate that LPS administration in mice induces an anxiety-like behaviour on EPM. In the present study, LPS administration induced panicogenic symptoms in mice decreased the number of entries in the open and closed arm, decreased the duration of time spent in the open arm and increased in the closed arm. Pre-treatment with aqueous extract of *Phyllanthus emblica* significantly attenuated the effects of LPS indicating its anxiolytic activity.[16] An open field test was used to study the effect of aqueous extract of *Phyllanthus emblica* on LPS-induced hypoactivity and exploratory behaviour in mice.[17] Pre-treatment with aqueous extract of *Phyllanthus emblica* and Dexamethasone to LPS-treated animals resulted in increased peripheral, central and total number of line crossings and number of climbs and rears when compared with LPS-alone, treated animals.

Sickness behaviour shares many overlapping features with symptoms of depression. The behavioural despair induced by LPS was assessed by measuring the immobility time in FST[18]. Pre-treatment with both doses of aqueous extract of *Phyllanthus emblica* significantly attenuates LPS-induced depression. Pre-treatment with Dexamethasone also produced a significant antidepressant effect in LPS-treated animals.

The social interaction test is another indication of an anxiolytic effect and it was designed to assess the subject's motivation to engage in social interaction with juvenile nonspecific at different time intervals in LPS-injected animals.[12] The outcome of the test reveals that LPS-treated mice were associated with a reduction in social interaction time, and it was attenuated by pre-treatment with *Phyllanthus emblica.* Administration of LPS to animals exhibited a

marked reduction in food and water intake, which might be due to the augmentation of IL-1, IL-6 and TNF-α that affect the hypothalamic region.[13] Pre-treatment with *Phyllanthus emblica* and Dexamethasone significantly attenuated LPS-mediated anorexia and showed an increase in food and water intake when compared with LPS-alone-treated animals, which might be due to reduced cytokines levels. LPS-treated mice decreased body weight may be due to the action of the increased cytokine. Our results suggested the aqueous extract of *Phyllanthus emblica* treated group showed increased body weight. Therefore, the pre-treatment of aqueous extract of *Phyllanthus emblica* significantly inverted the action of LPS.

Anhedonic behaviour is a basic characteristic feature of depression and depression-like behaviour; hence the anhedonic behaviour was assessed by measuring the consumption of sucrose solution.[13] Outcome of the sucrose preference test indicates the anti-anhedonia effect of aqueous extract of *Phyllanthus emblica* against LPS-challenge and was confirmed by increased sucrose preference in aqueous extract of *Phyllanthus emblica* pre-treated animals when compared with LPS alone group. Compared with the aqueous extract of *Phyllanthus emblica*, the anti-anhedonia effect of Dexamethasone was more prominent.

An experimental study illustrates the role of oxidative stress and neuroinflammation in the pathogenesis of sickness behaviour. Pro-inflammatory cytokines and activated microglia induced by LPS cause a drastic increase in the production of ROS and peroxides, which may further lead to inflammation, lower antioxidant status and consequently cause neurobehavioral alterations.[19] In our study, pre-administration of aqueous extract of *Phyllanthus emblica* to LPS-injected animals significantly attenuated LPS-induced increase in LPO levels and depletion of GSH content in the brain thereby showing good antioxidative action against LPS-induced oxidative stress in mice brains.

Conclusion

The results obtained by the present study imply the amelorative effect of aqueous extract of *Phyllanthus emblica* against LPS-induced sickness behaviour and anorexia in mice. This effect may be attributed to its anti-inflammatory and antioxidant effect. However, to elucidate its mechanism of action at molecular level further studies are required.

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Conflicts of interest

The authors declare no conflict of interest.

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