Bulletin of Environment, Pharmacology and Life Sciences
Bull. Env. Pharmacol. Life Sci., Vol 9[10] September 2020 : 49-59

Online ISSN 2277-1808
Journal's URL:http://www.bepls.com
CODEN: BEPLAD
Global Impact Factor 0.876
Universal Impact Factor 0.9804
NAAS Rating 4.95

ORIGINAL ARTICLE **OPEN ACCESS**

Evaluation of antinociceptive and anti-inflammatory activity of crude extracts of *Clerodendrum phlomidis* (L.) leaves in laboratory animals

Ravi V. Patel[1*], Rakeshkumar Jat[1], Jitendra O. Bhangale[2]
[1]Department of Pharmacy, Shri JJT University, Churu-Jhunjhunu road, Jhunjhunu, Rajasthan 333001
[2]Smt. N. M. Padalia Pharmacy College, Navapura, Ahmedabad, 382 210 Gujarat, India
E-mail: rvp251985@gmail.com

ABSTRACT
The petroleum ether, ethyl acetate and alcoholic extract of the leaves of Clerodendrum phlomidis was investigated for its antinociceptive and anti-inflammatory activity in respective animal models. In the present study,leaves were extracted successively and was screened at a dose 100, 200 and 400 mg/kg orally for its antinociceptive activity using writhing, tail immersion and hot plate test while for anti-inflammatory activity, carrageenan, serotonin and histamine induced rat paw edema model used. Oral administration of petroleum ether (200 and 400 mg/kg), ethyl acetate (400 mg/kg) and alcoholic (400 mg/kg) extracts of Clerodendrum phlomidis exhibited significant (p<0.001) antinociceptive activity in writhing, tail immersion and hot plate test. In rat paw edema model by carrageenan, serotonin and histamine, the extract was found to be reduce significantly (p<0.001) the formation of edema with petroleum ether (200 and 400 mg/kg), ethyl acetate (400 mg/kg) and alcoholic (400 mg/kg) extracts of Clerodendrum phlomidis at 1, 2, 3, 4 and 6 h. Clerodendrum phlomidis possesses evident antinociceptive and anti-inflammatory activities. The results signify the traditional uses of Clerodendrum phlomidisfor inflammation and pain.
Keywords: Clerodendrum phlomidis, Anti-inflammatory, Antinociceptive activity

Received 27.06.2020 Revised 30.07.2020 Accepted 04.08.2020

INTRODUCTION

Since ancient times, people believe on medicinal plants as either prophylactic or therapeutically arsenal to maintain healthy life. And also plants are the reservoir of biologically active compounds. Inflammation is physiological protective and defense mechanism that helps body to protect from microbial infection, chemical irritation and wounding. In current scenario, inflammatory diseases are treated with steroidal and non steroidal anti-inflammatory drugs (NSAIDs) that exert their effects by inhibiting the metabolism of arachidonic acid by both cycloxygenase and lipoxygenase enzyme pathways. Chronic usage of NSAIDs has shown several adverse effects like ulceration, bleeding and perforation. To minimize this effect, development of new compound from plant origin is necessary to improve quality, safe and healthy life. Several plants have shown potential for anti-inflammatory activity. Thus, the search for natural products from plant origin having protective properties and possessing minimal side effects.

Clerodendrumphlomidis is commonly known as Ami, belongs to the family Lamiaceae. It is locally called Agnimantha (Sanskrit), Arani (Marathi), Arni (Hindi), Takkari (Tamil), Nelli (Telugu), Munja (Malayalam), Arni (Bengali), Aranimula (Gujarati) and Taggi (Kannada). *Clerodendrumphlomidis*is extensibly used in Ayurveda, Unani and Homeopathic medicine. In traditional systems of medicine, leaves, stem, aerial parts and root of the plant are used in *Shotha*(inflammation), *Prameha*(glycosuria), *Jwara*(coryza), *Upadamsha*(gonorrhea), *Sthaulya*(obesity) etc. The root is used as a bitter tonic and is given in theconvalescence of measles [1]. The plants has been reported to possess Anti-inflammatory activity[2-3], Analgesic activity [4], Antiarthritic activity [5], Antimicrobial activity [6-7], Antiobesity activity [8], Antihepatotoxic activity [9], Antifertility [10], Anti-amnesic activity [11], Anti-asthmatic activity [12], Antioxidant activity[13], Antidiarrhoeal activity [14], Hypoglycemic activity [15] and Immunomodulatory activity [16].

The *Clerodendrum phlomidis* consists ofmany potentially active chemical compounds which acts as drugs for anti-arthritic activity. So this gives strong evidence for the use of plants in different medicines. From the exhaustive literature, no scientific data is available regarding the antinociceptive and anti-inflammatory activities of *Clerodendrum phlomidis* leaves, therefore the present study was carried out to provide pharmacological evidence for the folklore medicinal consideration of *Clerodendrum phlomidis* leaves.

MATERIAL AND METHODS

Collection of plant material

Fresh leaves of *Clerodendrum phlomidis* were collected from local area of Aravalli district, Gujarat, India in the months of September-October. This plant was identified and authenticated to Botanical Survey of India, Pune.

Animals:

Adult male Wistar albino rats, weighing between 180 - 220 g and albino mice (25-30 g) were used and acclimatized to laboratory condition for one week. All animals were housed in well ventilated polypropylene cages at 12 h light/dark schedule with 25±2ºC and 55-65% relative humidity. The rats had fed with commercial pelleted rats chow and water *ad libitum* as a standard diet. Institutional Animal Ethics Committee approved the experimental protocol in accordance with CPCSEA.

Preparation of leaf extract

The leaves were collected and dried in shade and ground. Coarsely powdered leaves were used for the study. Coarsely powdered leaves material (1000 g) was subjected to successive extraction with different solvents (petroleum ether, ethyl acetate and alcohol) (60 – 80ºC) in a soxhlet extractor at a temperature of 45-50ºC to 45 cycles per batch for 2 batches. The extraction was continued until the solvent in the thimble becomes clear indicating the completion of the extraction. After each extraction the solvent was distilled off and concentrated extract was transferred to previously weighed petri dish and evaporated to dryness at room temperature to obtain dried extracts. After completion of drying the petri dish was weighed again. The yield of extract was calculated by subtracting original weight of empty petri dish [17]. The yield of petroleum ether, ethyl acetate and alcohol extract of leaves of *Clerodendrum phlomidis* was9.8, 6.3 and 5.9 g/100 g respectively.

Chemicals and drugs

Suspension of petroleum ether, ethyl acetate and alcohol extract of leaves of *Clerodendrumphlomidis* was prepared in sodium carboxy methyl cellulose (CMC, 0.3 %) using distilled water. All the extracts was accomplished via oral gavage.

Test Animals

Wistar rats (180-220 g) and Male Swiss albino mice (25-30 g) were divided into eleven groups containing six animals each as follows Group I: Vehicle control rats received distilled water (10 ml/kg, p.o.), Group II: Standard (10 mg/kg, p.o.), Group III: PECP (100 mg/kg, p.o.), Group IV: PECP (200 mg/kg, p.o.), Group V: PECP (400 mg/kg, p.o.), Group VI: EACP (100 mg/kg, p.o.), Group VII: EACP (200 mg/kg, p.o.), Group VIII: EACP (400 mg/kg, p.o. Group IX: ACP (100 mg/kg, p.o.), Group X: ACP (200 mg/kg, p.o.), Group XI: ACP (400 mg/kg, p.o.).

PRELIMINARY PHYTOCHEMICAL STUDIES

Preliminary qualitative phytochemical screening for the identification of the phytoconstituents of the petroleum ether, ethyl acetate and alcohol extract of leaves of *Clerodendrumphlomidis*has been carried out [18].

ACUTE ORAL TOXICITY OF THE EXTRACT

Adult Albino mice (25-30 g) were divided into five groups containing ten mice each. The mice were fasted for 6 h and access only water *ad libitum* before experimental study. Differentgroup of animals received with different doses of petroleum ether, ethyl acetate and alcohol extract of leaves of *Clerodendrumphlomidis* i.e. 1000, 2000, 3000 and 4000 mg/kg respectively. All the doses and vehicle were administered orally. The animals were observed for 72 h for mortality [19-20].

ANTINOCICEPTIVE ACTIVITY

Writhing test

All the drug treatments were given 1 hour before i.p. injection of 0.6 % (v/v) acetic acid, at a dose of 10 ml/kg [21]. Writhing is a syndrome characterized by a wave of contraction of the abdominal musculature followed by a wave of contraction of hind limbs. The hind limbs contractions that occurred over a period of 10 min were counted. A reduction in time of writhing initiation and number of writhing as compared to the vehicle treated group was considered as evidence for the analgesia.

Tail immersion test

The lower 5 cm portion of the tail was immersed in a beaker containing water and temperature maintained at 55 ± 0.5ºC [22]. The time in seconds for tail withdrawal from the water was taken as the reaction time, with a cut-off time of immersion set at 10s. The reaction time was measured 1 h before and 0.5, 1, 2, 3, 4 and 6 h after oral administration of drugs [23-24].

Hot Plate Method

Mice were placed on a hotplate maintained at a temperature of 55 ± 1ºC for a maximum time of 15 s. The time between placement of animal on the hot plate and occurrence of licking of the fore or hind paws, shaking or jumping off from the surface was recorded as response latency. Mice with basal latencies of more than 10 s were eliminated from the study. The testing of response latencies was measured before distraction (basal) and 30, 60 and 90 min. after treatment. The cut off time for hotplate latencies was set at 15 s [24-25].

ANTI -INFLAMMATORY ACTIVITY

Carrageenan induced rat paw Oedema

Oedema was induced by 0.1 ml of 1% carrageenan solution into the left hind paw. The pretreatment time was 1 h before carrageenan injection. The paw volume was recorded immediately and at 1 h, 2 h, 3 h, 4 h and 6 h by using plethysmometer (UGO Basile 7140). Mean increase in the volume of oedema was measured [26-27].

Serotonin and Histamine induced rat paw Oedema

The animal were treated in a manner similar to that of carrageenan induced rat paw edema protocol, different only in the administration of the inflammatory stimulus which was induced by sub-planter injection of serotonin (0.05 ml of 1 %) and histamine (0.05 ml of 1 %), respectively. The paw volume was measured as mentioned earlier [28-29].

Statistical analysis

All the values were expressed as mean ± SEM. Statistical evaluation of the data was done by two-way ANOVA followed by Bonferroni's multiple comparison test, with the level of significance chosen at P <0.001 using Graph-Pad Prism 5, San Diego, CA software.

RESULTS AND DISCUSSION

Pain, a sign of inflammation, is a complex process which involves enzyme activation, mediator release, cell migration, extravasation of fluid, tissue breakdown, as well as tissue proliferation. The present study establishes the antinociceptive and anti-inflammatory activity of the petroleum ether, ethyl acetate and alcoholic extracts of the leaves of *Clerodendrum phlomidis* using different animal models.

*Clerodendrum phlomidis (*L.) is the reservoir for many potentially active chemical compounds which acts as drugs against various diseases and disorders. The petroleum ether extract of *Clerodendrum phlomidis* (L.) showed the presence of alkaloids, terpenoids, and flavonoids; ethyl acetate extract of *Clerodendrum phlomidis* (L.) showed the presence of tannins, alkaloids, terpenoids, saponins and glycosides; and alcoholic extract of *Clerodendrum phlomidis* (L.) showed the presence of sterols and flavonoids.While administering of all extracts orally, there was no mortality found up to the dose of 4000 mg/kg and to be safe at all doses used. By the results, we have taken 400 mg/kg as the therapeutic dose and made variations by taking 100 mg/kg as lower dose and 400 mg/kg as higher dose.

Many studies reported that inflammation and pain are associated with disease of various clinical conditions like arthritis, vascular and cancer diseases. Moreover, many traditional, medicinal and folklore plants have been found to alleviate inflammation and pain in vitro and in vivo system. *Clerodendrum phlomidis* is a medicinal plant commonly used traditionally for pain relief and other medicinal use.

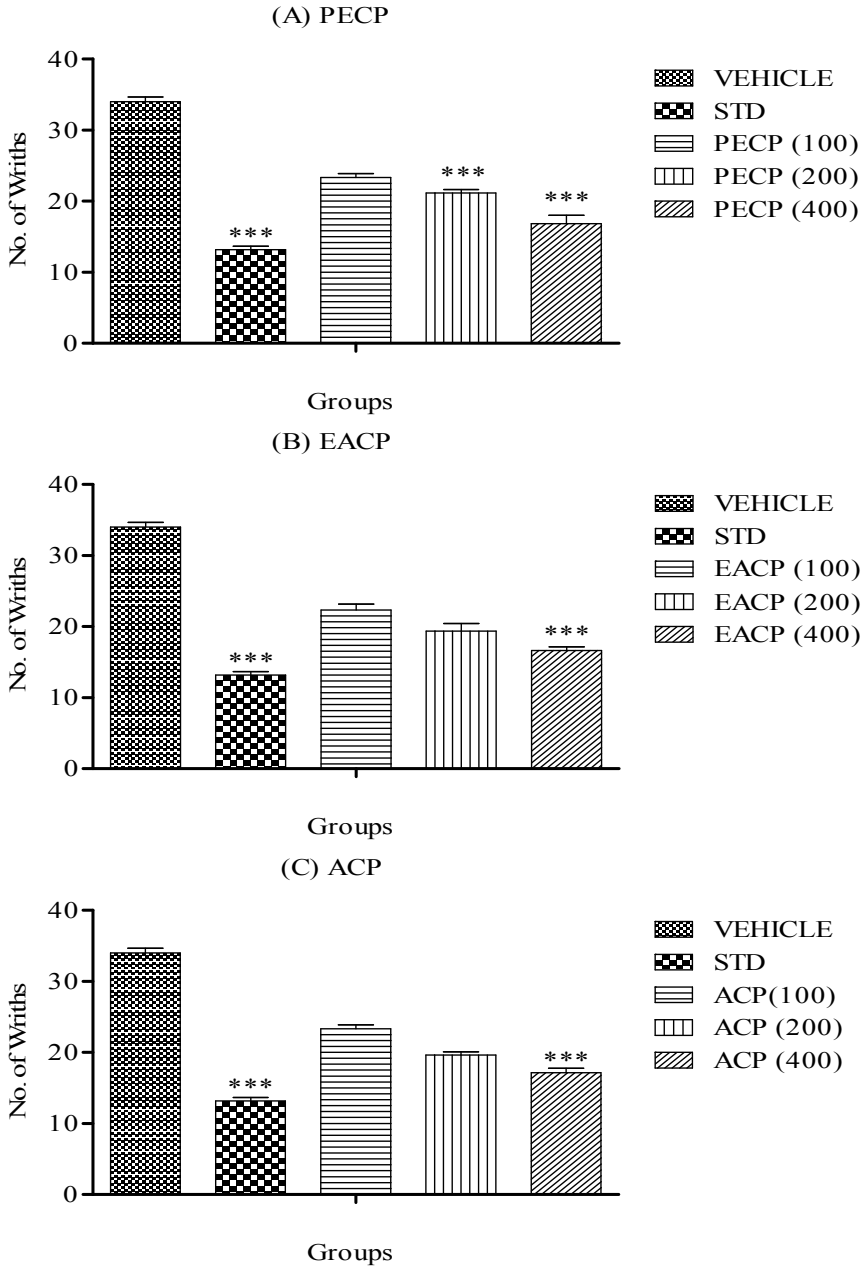
Antinociceptive activity was performed using writhing, hot plate and tail immersion test. All the extractsat higher doses exhibited antinociceptive activity. In the writhing test, peritoneal receptors are postulated to be partly involved in the abdominal writhing response seems to be exposed to the prostanoid system by nociceptive stimulus [30]. Acetic acid induced abdominal constriction is a very sensitive procedure for peripheral analgesic agents, and has also been associated with prostanoid [31-32] as well as lipoxygenase products [33].

Higher doses petroleum ether(200 and 400 mg/kg),ethyl acetate(400 mg/kg) and alcoholic(400 mg/kg) extracts of *Clerodendrum phlomidis* significantly ($p<0.001$) reduced nociceptice stimuli i.e. writhing and stretching's induced by acetic acid (Figure 1). While lower doses (100 and 200 mg/kg, p.o.) did not show significant effect compared to vehicle treated animals.

The first phase of tail immersion and hotplate test results showed central protective effect of all extract. The tail immersion test indicated that the pharmacological actions were mediated by mu (μ) opioid receptors rather than kappa (k) and delta receptors [34-35]. The reaction time of animal showed a significant increase ($p<0.001$) with increasing latency (time).

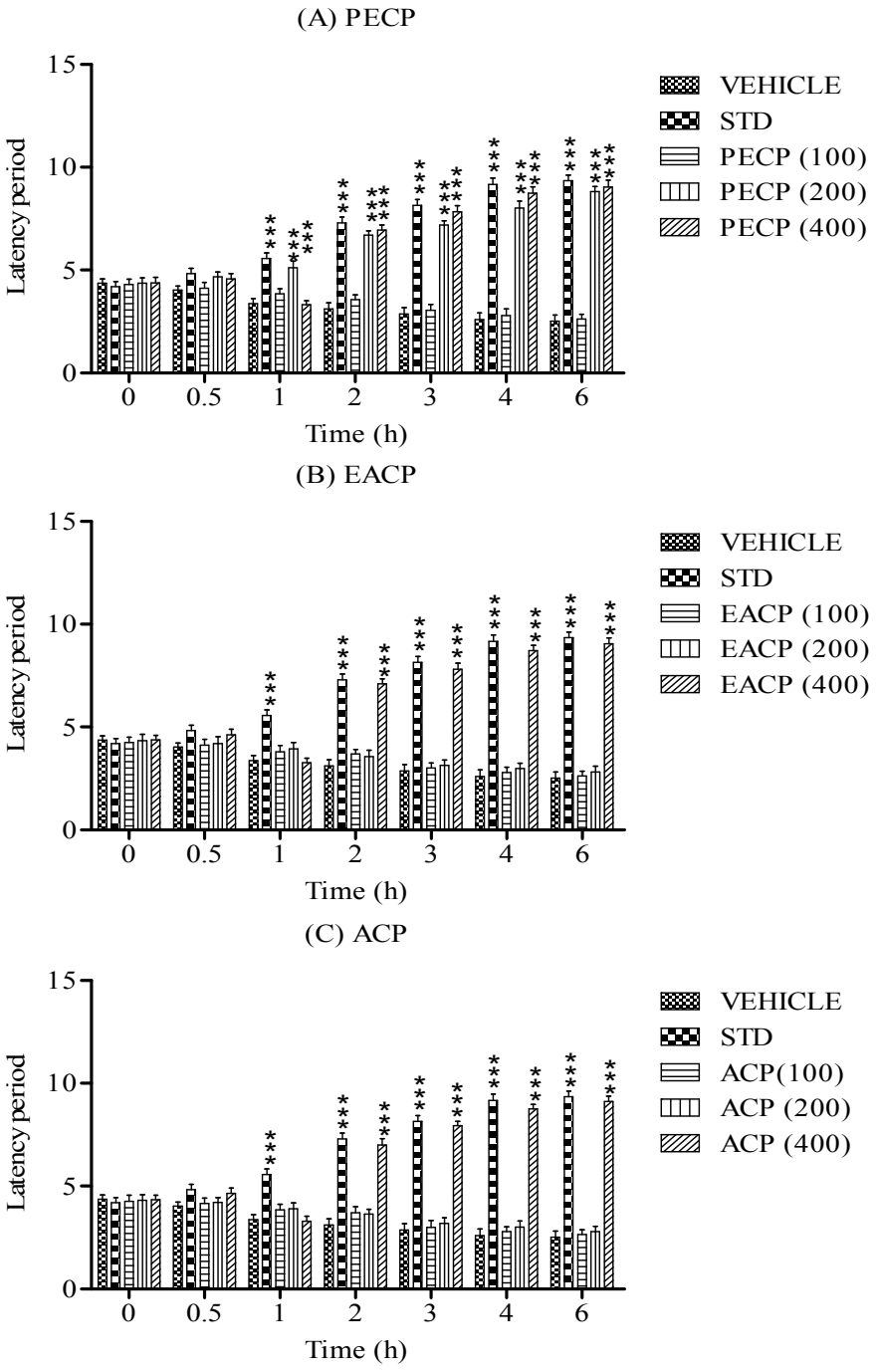
Oral administration of PECP(200 and 400 mg/kg); EACP and ACP (400 mg/kg) exhibited significant ($p<0.001$) increased pain latencies at 1, 2, 3, 4 and 6 h as compared to vehicle treated animal in tail immersion test (Figure 2). Treatment with PECP(100 mg/kg); EACP and ACP (100 and 200 mg/kg, p.o.) did not show significant activity. The latency response was found to be significantly ($p<0.001$)increased with the pretreatment of PECP(200 and 400 mg/kg); EACP and ACP (400 mg/kg, p.o.) at 20, 60 and 90 min in hot plate test (Figure 3).

Figure 1 : Effect of (A) Petroleum ether, (B) Ethyl acetate, (C) Alcohol extract of *Clerodendrum phlomidis*on Acetic acid induced writhing test



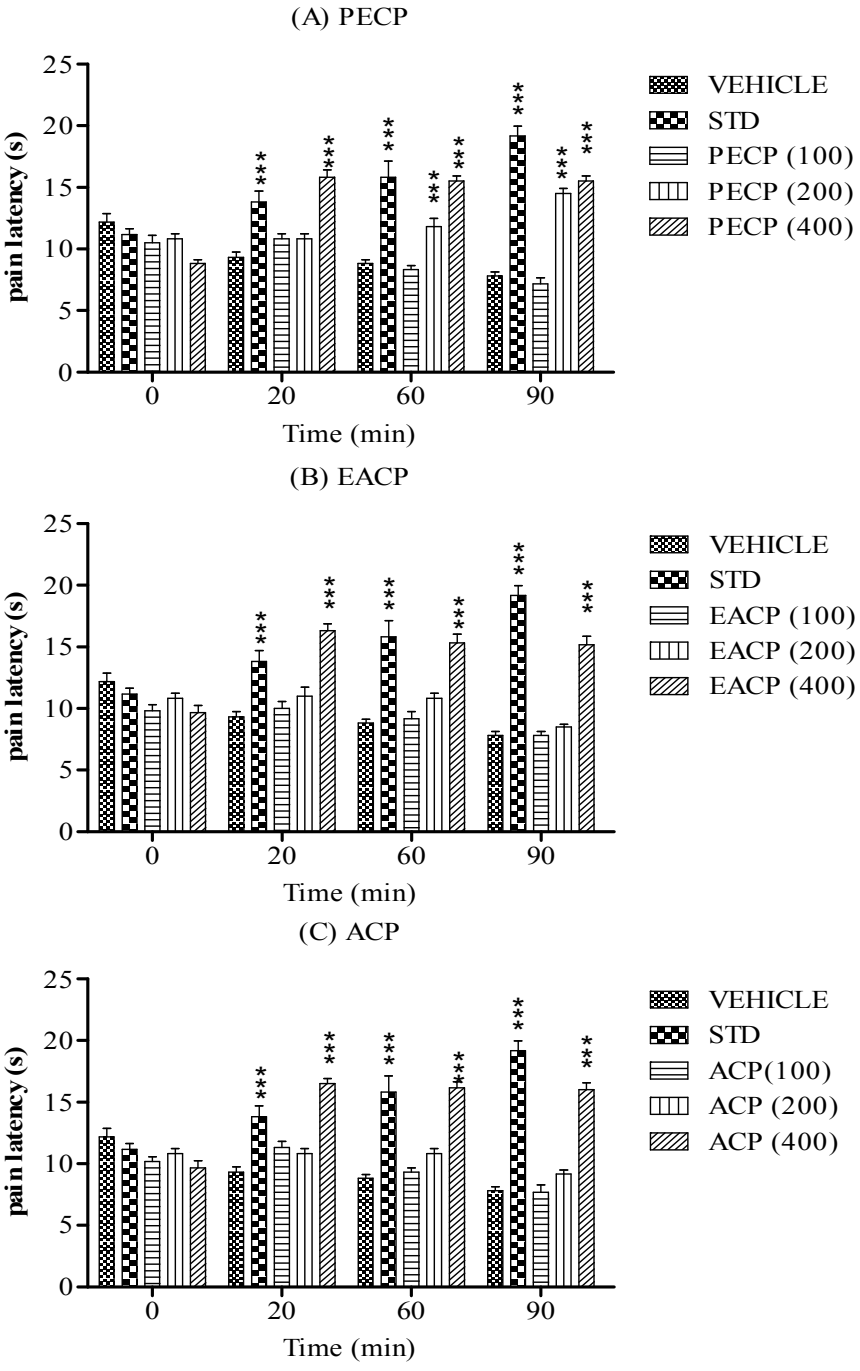
Values are Mean±S.E.M. from 6 animals in each group and statistical analysis was carried out by two way ANOVA followed by Bonferroni test. ***P < 0.001 compared to vehicle treated animals.

Figure 2 : Effect of (A) Petroleum ether, (B) Ethyl acetate, (C) Alcohol extract of *Clerodendrum phlomidis* on Tail immersion test



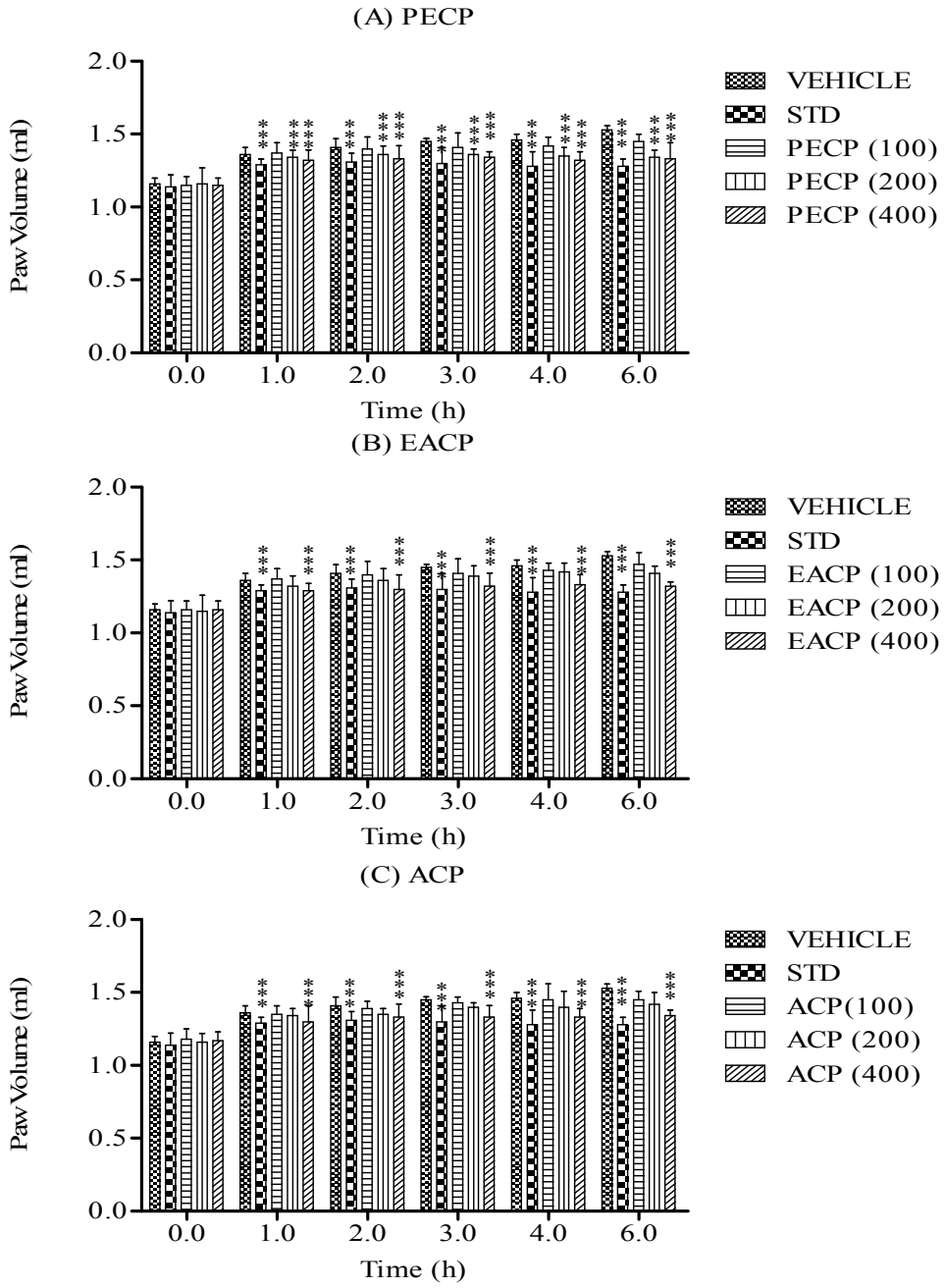
Values are Mean±S.E.M. from 6 animals in each group and statistical analysis was carried out by two way ANOVA followed by Bonferroni test. ***P < 0.001 compared to vehicle treated animals.

Figure 3: Effect of (A) Petroleum ether, (B) Ethyl acetate, (C) Alcohol extract of *Clerodendrum phlomidis* on Hot plate test



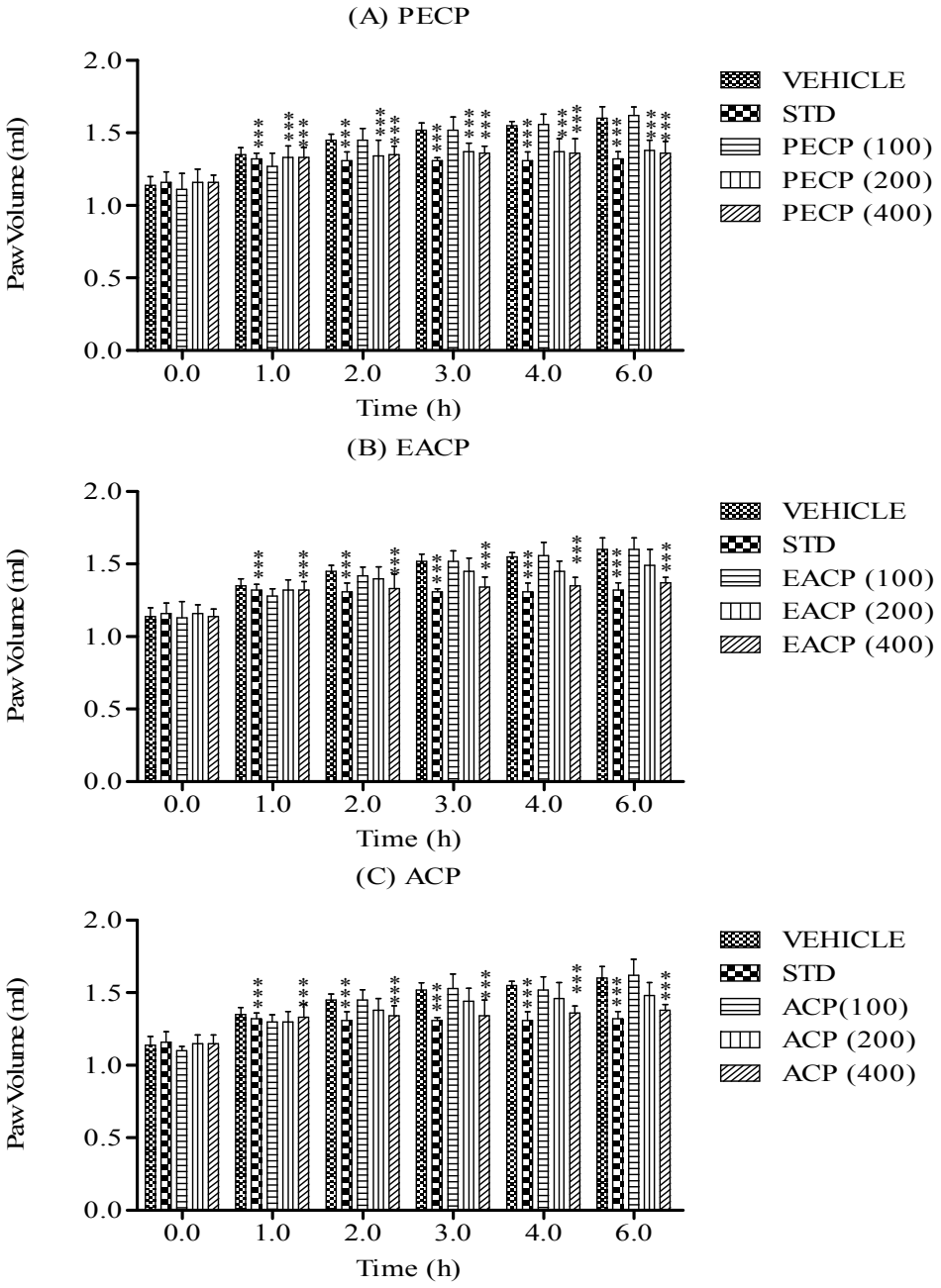
Values are means ± S.E.M from 6 animals in each group and statistical analysis was carried out by two way ANOVA followed by Bonferroni test. ***p<0.01 compared to vehicle treated animals.

Figure4: Effect of (A) Petroleum ether, (B) Ethyl acetate, (C) Alcohol extract of *Clerodendrumphlomidis*on Carrageenan induced rat paw oedema



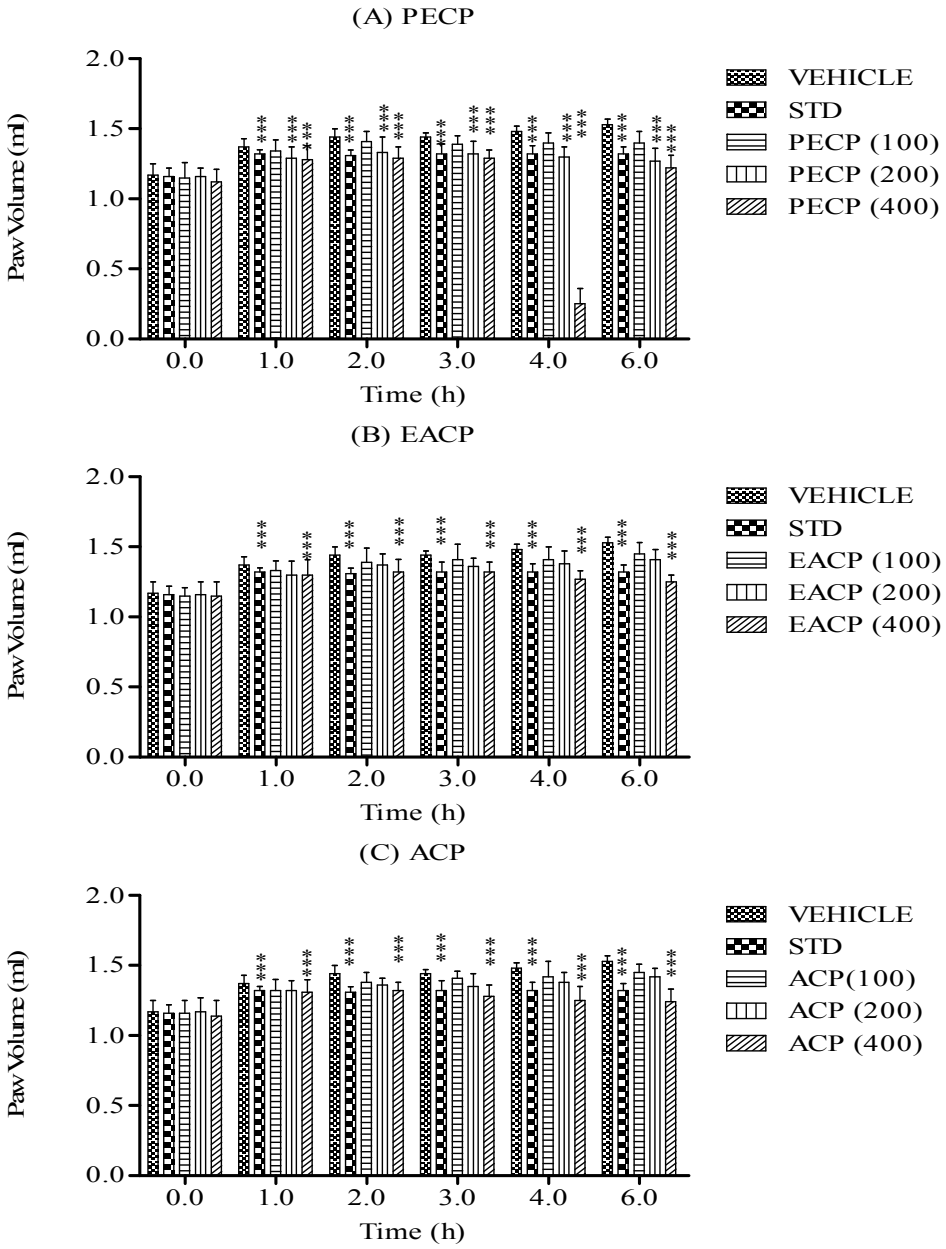
Values are Mean±S.E.M. from 6 animals in each group and statistical analysis was carried out by two way ANOVA followed by Bonferroni test. ***P < 0.001 compared to vehicle treated animals.

Figure 5 : Effect of (A) Petroleum ether, (B) Ethyl acetate, (C) Alcohol extract of *Clerodendrumphlomidis* on Serotonin induced rat paw oedema



Values are Mean±S.E.M. from 6 animals in each group and statistical analysis was carried out by two way ANOVA followed by Bonferroni test. ***P < 0.001 compared to vehicle treated animals.

Figure 6 : Effect of (A) Petroleum ether, (B) Ethyl acetate, (C) Alcohol extract of *Clerodendrum phlomidis* on histamine induced rat paw oedema



Values are means ± S.E.M from 6 animals in each group and statistical analysis was carried out by two way ANOVA followed by Bonferroni test. ***p<0.01 compared to vehicle treated animals.

For screening of anti-inflammatory activity, carrageenan induced paw edema, is the most widely used primary model. Carrageenan induced oedema is a multimediated phenomenon that liberates proinflammatory mediators like histamine, 5-HT, kinins and prostaglandins at different time intervals. It is believed to be biphasic the first phase (60 min) involves the release of serotonin and histamine while the second phase (over 60 min) is mediated by prostaglandins, the cyclooxygenase products, and the continuing between the two phase is provided by kinins [36-37]. Development of oedema induced by carrageenan is commonly correlated with early exudative stage of inflammation [38]. Oral administration of PECP(200 and 400 mg/kg); EACP and ACP (400 mg/kg) showed significant (p<0.001) reduction in paw edema at 1, 2, 3, 4 and 6 h compared to vehicle treated animals in carrageenan induced rat paw edema (Figure 4).

The histamine is a basic amine related with inflammatory and allergic process causing both vasodilation and increase of vascular permeability [39]. Administration of PECP(200 and 400 mg/kg); EACP and ACP (400 mg/kg, p.o.) showed significant ($p<0.001$) reduction in paw volume at 1, 2, 3, 4 and 6 h compared to vehicle treated animals in serotonin (Figure 5) and histamine (Figure 6) induced rat paw edema.

The phytochemical analysis of this extract revealed that it contains alkaloids, saponins, flavonoids, terpenoids and glycosides. On these, flavonoids and saponins are well known for their ability pain perception. Flavonoids also have anti-inflammatory properties due to their inhibitory effects on enzymes involved in the production of the chemical mediator of inflammation[40].

In view of the results, *Clerodendrum phlomidis* can be effective in acute inflammatory disorders. Considering that there are only a few preliminary data reported in the literature regarding the antinociceptive and anti-inflammatory propertiesof *Clerodendrum phlomidis*, and that it has been largely used in folk medicine to treat inflammatory disorders mainly rheumatism.

So we can conclude that the present study has shown that the petroleum ether, ethyl acetate and alcohol extracts of *Clerodendrum phlomidis* leaves possess antinociceptive and anti-inflammatory activities that may be mediated through inhibition of inflammatory mediators such as bradykinin and prostaglandins. More detailed phytochemical studies are, however, necessary to identify the active principle(s) and exact mechanism(s) of action.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interests regarding the publication of this paper.

REFERENCES

1. Sharma, P.C., Yelne, M.B. & Dennis, T.J. (2001). Database on medicinal plants used in Ayurveda. Vol II: Central Council for Resaerch in Ayurveda and Siddha Publication, New Delhi, 1-7.
2. Vijayamirtharaj, R., Vincent, S. &Senthilkumar**,** N. (2011). Anti-inflammatory activity of chloroform extract of aerial part of *Clerodendrum phlomidis* Linn. *Res. J. Pharm. Bio. Chem. Sci***.,** 2(1): 390-395.
3. Reshma, R., Parekar, K.K., Dash, P.A., Marathe, A.A., Apte, M. &Nirmala, N.R. (2012). Evaluation of anti-inflammatory activity of root bark of *clerodendrum phlomidis*in experimental models of inflammation. Int. J. Appl. Pharm., 3(3):54-60.
4. Vijayamirtharaj, R., Vincent, S. &Nachimuthu, S. (2011). Analgesic activity of *Clerodendrum phlomidis* linn. (Aerial parts). Int. J. Pharm., 2(1):120- 123.
5. Kilimozhi, D., Parthasarathy, V. &Amuthavalli., N. (2009). Effect of *Clerodendrumphlomidis*on adjuvant induced arthritis in rats - A radiographic densitometric analysis. Int. J. Pharm. Tech. Res., 1(4):1434-1441.
6. ***Sathish, M.***, Priyadarsini, R., Sunitha, P.G. &Saraswathy, T. (2013). Antimicrobial activity of the extracts and isolated compounds of *clerodendrumphlomidis*. *Int. J. Pharm* **&** *Pharm.* Sci., 5(4):362-366.
7. Vincent, S., Vijayamirtharaj, R. & Ramesh, R. (2011). Anthelmintic potential of aerial part of *Clerodendrumphlomidis*. Res. J. Pharm. Bio. Chem. Sci., 2(2): 329-333.
8. Vijay, R., Chidrawar, K., Patel, N., Havagiray, R., Chitme, S. &Shiromwar, S. (2012). Pre-clinical evolutionary study of *Clerodendrumphlomidis*as an anti- obesity agent against high fat diet induced C57BL/6J mice. Asian Pac. J. Trop. Biomed., S1509-S1519.
9. Amita, V. &Bahar, A. (2009). Anti-hepatotoxic activity of *Clerodendrumphlomidis*. Int. J. Pharm.Tech Res., 1(4):1028-1031.
10. Kumar, D., Kumar, A. &Prakash, O. (2010). Post-coital antifertility activity of *Clerodendrum phlomidis* Linn. Dichloromethane root extract. Pharmacologyonline., 3: 479-485.
11. Joshi, Anumanthachar & Krupa, M. (2008). Antiamnesic evaluation of *C. phlomidis*Linn. bark extract in mice. Braz. J. Pharm.Sci., 44(4):717-724.
12. Vincent, S., Vijay, A.R., Jeevanantham, P. &Saravanan, R. (2014). In-vitro and in-vivo anti asthmatic activity of *Clerodendrum phlomidis* Linn. in Guinea Pigs. Int. J. Res. Rev. Pharm. App. Sci., 2(1), 15-28: 2249-1236.
13. Sathish, M.,Tharani, C.B. &Niraimathi, V. (2011). Free Radical Scavenging Activity of Various Extracts from Root of *Clerodendrumphlomidis*(Linn.) evaluated by three in vitro methods. Res. J. Pharm. Bio. Chem. Sci., 2(3),755-761.
14. Rani, S., Ahamed, N., Rajaram, S., Saluja, R., Thenmozhi, S. &Murugesan, T. (1999). Anti-diarrhoeal evaluation of *Clerodendrum phlomidis* Linn. leaf extract in rats. J Ethnopharmacol, 68(1-3): 315-319.
15. Sneha, J.A. & Sanjay, S. (2011). Alpha amylase inhibitory and hypoglycemic activity of *Clerodendrum multiflorum*Linn. Stems. Asian J. Pharm. Clin. Res., 4(2): 99-102.
16. Gokani, R., Lahiri, S.K., Santani**,** D.D. & Shah, M.B**. (**2007). Evaluation of Immunomodulatory Activity of *Clerodendrum phlomidis* and *Premnaintegrifolia* Root Int. J. Pharmacol., 3(4):352-356.
17. Bhangale, J., Acharya, S. &Deshmukh, T. (2013). Antihyperglycaemic activity of ethanolic extract of *Grewia asiatica* (l.) Leaves in alloxan induced diabetic mice. World J. Pharm. Res., 2(5):1486-1500.
18. Harborne JB. (1998). Phytochemical methods, 3rdedn, Chapman and hall, London.
19. Ravichandran, V., Suresh, B., Sathishkumar, M.N., Elango, K. &Srinivasan, R. (2007). Antifertility activity of hydroalcoholic extract of *Ailanthus excels* (Roxb): An ehanomedicines used by tribals of Nilfiris region in Tamilnadu. J. Ethanopharmacol., 112: 189-191.

20. Bhangale, J. &Acharya, S. (2014).Antiarthritic activity of *Cynodondactylon* (L.) Pers. Indian. J. Exp. Biol., 52: 215-222.
21. Zakaria, M.N., Islam, M.W. &Radhakrishnan, R. (2001). Anti-nociceptive and anti-inflammatory properties of *Carallumaarabica*. J. Ethnopharmacol., 76: 155-158.
22. Janssen, P.A.J., Niemegeers, C.J.E. &Dony, J.G.H. (1963). The inhibitory effect of fentanyl and other morphine-like analgesics on the warm water induced tail withdrawal reflex in rats. Arzneimittel-Forsch., 6: 502–507.
23. Vogel, G.H. & Vogel, W.H. (1997). Drug Discovery and Evaluation. Pharmacological Assays. Springer., 360–418.
24. Bhangale, J., Patel, R., Acharya, S. &Chaudhari, K. (2012). Preliminary studies on anti-inflammatory and analgesic activities of *JasminumSambac*(L.) Aiton in experimental animal models. Am. J. Pharm. Tech. Res., 2(4): 1-10
25. Eddy, N.B. &Leimback, D. (1953). Synthetic analgesics. II. Dithienylbutenyl and dithienylbutylamines. J. Pharmacol. Exp. Ther., 107: 385–393.
26. Winter, C.A., Risley, E.A. &Nuss, G.W. (1962). Carrageenan-induced edema in hind paw of the rat as an assay for anti-inflammatory drugs. P. Soc. Exp. Biol. Med., 111: 544–547.
27. Young, H., Luo, Y., Cheng, H., Hsieh, W., Liao, J. &Peng, W. (2005). Analgesic and anti-inflammatory activities of [6]-gingerol. J. Ethnopharmacol., 96: 207–210.
28. Maity, T.K., Mandal, S.C., Mukharjee, P.K., Saha, K., Das, J., Pal, M. &Saha, B.P. (1998). Studies on anti-inflammatory effect of *Cassia tora* leaf extract (FamLeguminosae). PTR. Phytother. Res., 12: 221-223.
29. Mandal, S.C., Maity, T.K., Das, J., Saba, B.P. & Pal, M. (2000). Antiinflammatory evaluation of *Ficusracemosa* Linn. Leaf extract. J. Ethnopharmacol., 72: 87-92.
30. Ngumfo, E., Dimo, T. &Azebaze, A. (2007). Ant-inflammatory and anti-nociceptive activities of the stem bark extracts from *Allanblackia monticola* STANER L.C. (Guttiferae). J. Ethanopharmacol., 114: 417-424.
31. Ronaldo, A.R., Mariana, L.V., Sara, M.T., Adriana, B.P.P., Steve, P., Ferreira, S.H. & Fernando Q.C. (2000). Involvement of resident macrophages and mast cells in the writhing nociceptive response induced by zymosan and acetic acid in mice. Eur. J.Pharmacol., 387: 111-118.
32. Deraedt, R., Jouquey, S., Delevallee, F. &Flahaut, M. (1980). Release of prostaglandins E and F in an algogenic reaction and its inhibition. Eur. J. Pharmacol., 61(1):17-24.
33. Dhara, A.K., Suba, V., Sen, T., Pal, S. & Chaudhari, A.K.N. (2000). Preliminary studies on the anti-inflammatory and analgesic activity of methanolic fraction of the root extract of *Tragia involucrate* Linn. J. Ethanopharmacol., 72: 265-268.
34. Schmauss, C. &Yaksh, T.L. (1984). In vivo studies on spinal opiate receptor systems mediating antinociception. II. Pharmacological profiles suggesting a differential association of mu, delta and kappa receptor with visceral chemical and cutaneous thermal stimuli in the rat. J. Pharmacol. Exp. Ther., 228: 1–12.
35. Aydin, S., Demir, T., Ozturk, Y. & Baser, K.H.C. (1999). Analgesic activity of NepetaitalicaL. Phytother. Res., 13: 20–23.
36. Perianayagam, J.B, Sharma, S.K. &Pillai, K.K. (2006). Anti-inflammatory activity of *Trichodesma indicum* root extract in experimental animals. J. Ethanopharmacol., 104: 410-414.
37. Brito, A.R.M.S. & Antonio, M.A. (1998). Oral anti-inflammatory and antiulcerogenic activities of a hydroalcoholic extract and partitioned fractions of *Turneraulmifolia* (Turneraceae). J. Ethanopharmacol., 61: 215-228.
38. Adedapa, A., Sofidiya, M. O., Inaphosa, V., Inaya, B., Masika, P. J. &Afolayan, A. J. (2008). Antiinflammatory and analgesic activities of the aqueous extract of *CussoniaPaniculata*stem bark, Rec Nat Prod; 2(2): 46-53.
39. Rang, H.P., Dale, M. M. & Ritter, J. M. (2001). Pharmacology, 4thedn, Guanabara Koogan, Rio De Janeiro: 174-188, 691.
40. Owoyele, V. B., Oloriegbe, Y. Y., Balogun. E. A. &Soladoye, A. O. (2005). Analgesic and anti-inflammatory properties of *Nelsoniacanescens* leaf extracts. J Ethanopharmacol; 99: 153-156.

CITATION OF THIS ARTICLE

Ravi V. Patel, Rakeshkumar Jat, Jitendra O. Bhangale. Evaluation of antinociceptive and anti-inflammatory activity of crude extracts of *Clerodendrum phlomidis* (L.) leaves in laboratory animals. Bull. Env. Pharmacol. Life Sci., Vol 9[10] September 2020 : 49-59