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Comparative Evaluation of Analgesic and Anti-Inflammatory Activity of *Cissampelos pareira* and *Stephania glabra*

[1]Hem Raj, [1]Avneet Gupta and [2]Neeraj Upmanyu
[1]Department of Pharmacy, CMJ University Shillong, Meghalaya, 793003, India
[2]R.K.D.F. College of Pharmacy, Hoshangabad Road, Bhopal (MP), 462047, India

Corresponding Author: Hem Raj, Department of Pharmacy, CMJ University Shillong, Meghalaya, 793003, India Tel: 9418284867

ABSTRACT

Extracts from *Cissampelos pareira* (CPE) and *Stephania glabra* (SGE) is used to treat pain and swelling in the tribal areas of Himalayan region of India. The anti-inflammatory and analgesic effect of ethanolic extract of the CPE and SGE were studied. The results so obtained were compared with untreated control as well as standard diclofenac and Indomethacin treated groups in a rat model. The tested dose of CPE and SGE were screened for carrageenan induced hind paw edema and by using hot plate method for anti-inflammation and analgesic action. Both CPE and SGE (200 mg kg^{-1} p.o.) significantly ($p<0.001$) reduced the carrageenan induced hind paw edema and analgesia. The comparison of results of other groups with control group were found to be significant ($p<0.001$) except CPE vs SGE after 1 and 3 h. After 5 h CPE vs SGE showed significant ($p<0.05$) results. The analgesic action was tested after 30, 60, 120 and 180 min. CPE and SGE showed significant ($p<0.001$) result with control group after 60, 120 and 180 min. Both CPE and SGE were found to be insignificant with standard group after 60 and 180 min. After 120 min SGE showed significant ($p<0.001$) results with standard group. SGE was found to be insignificant in comparison with CPE. Moreover, CPE and SGE showed the significant ($p<0.001$) anti-inflammatory and analgesic effect as it reduced the elevated paw edema and analgesia. Hence, the efficacy profiles indicate that CPE and SGE are safe alternate for analgesia and inflammation.

Key words: Anti-inflammatory, analgesic, carrageenan

INTRODUCTION

Inflammation is the result of any injury or is a response to an antigen which get entered in the body. Repeated and uncontrolled inflammation may induce to excessive release of chemical mediators of inflammation. This excess release of chemical mediators may lead to different arthritic problems in different ways.

Arthritis is disorder of joints usually associated with pain and stiffness. Arthritis results from infection, trauma degenerative change and autoimmune disease. Arthritis is not a single disease but refers to a group of rheumatic disease and other conditions that can cause pain, stiffness and swelling in the joint (Vashist *et al*., 2012). Mainly arthritis can be divided into three categories viz., rheumatoid, gouty and osteoarthritis (Di Paola and Cuzzocrea, 2008). Osteoarthritis is a wear and

tear type of arthritis with a symptom of pain and degeneration of bones. Because of severe side effects from synthetic medicines to stop inflammation strong intervention of some other system of medicine is needed. For this the drugs from the pant origin could be the best alternate.

Number of plant drugs viz., *Arnica montana*, *Origanum vulgaris*, *Zingiber officinale* (Trease and Evans, 2006) etc., are evaluated for the treatment of inflammation but anti-inflammatory potential of several plants are still unknown. Therefore, for present study three plants viz., *Cissampelos pareira* and *Stephania glabra* are selected for renaissance of their medicinal potential against analgesia and inflammation.

Cissempelos pareira (Menispermaceae) is a climbing shrub, 2-5 m high with a thickened root. Leaves are orbicular in shape with diameter of 7.14 cm. They are veined, glabrous, leathery or membranous. Flowers are green, male ones in spikes, 7-10 cm long, with a little round leaflet at the base of every flower. *Cissempelos pareira* is a perennial climber present tropical and subtropical region of India, ascending up to an altitude of 2000 m. *Cissampelos pareira* is known as Laghupatha in Ayurveda, an Indian traditional system of medicine (Farnsworth, 1966).

Stephania glabra is a climbing shrub having greenish yellowish flowers. Large tubers are present which may be upto 30 kg. *Stephania glabra* grows at subtropical and temperate Himalayas from an altitude of 7000 ft from sea level from Sindh eastward and Khasia hills and Pegu.

MATERIALS AND METHODS

Plant material and chemicals: The plant material (leaves of *Cissampelos pareira* and rhizome of *Stephania glabra*) was collected from 'Gharsi' village hills of Solan District of Himachal Pradesh, India. All plants were authenticated at Department of Forestry, Dr. YS Parmar, University Solan, India. All the plants were linked to UHF-Herbarium with Field book number 12544 and 12546 for *Cissampelos pareira* and *Stephania glabra*, respectively. Powdered material (250 g) of each drug powder was extracted with ethanol after being defatted with petroleum ether using a Soxhlet apparatus and the extracts were filtered, concentrated, independently and dried under reduced pressure to obtain, solid or semisolid extract (Khandelwal *et al*., 1996).

Phytochemical screening: The plant extracts were dissolved in distilled water and different phytochemical tests were performed for the presence of useful chemical constituents (Khandelwal *et al*., 1996; Wise *et al*., 2008).

Animal housing condition: Animals were housed in a group of four in separate cages under controlled conditions of temperature (22±2°C). All animals were given standard diet (golden feed, New Delhi) and water regularly. Animals were further divided in 6 groups with four animals in each group.

IAEC approval: All animal experiments were approved by Institutional Animal Ethics Committee (IAEC) of Pinnacle Biomedical Research Institute (PBRI) Bhopal (Reg. No. 1283/c/09/CPCSEA). Protocol approval reference No. PBRI/IAEC/12/PN-226.

Analgesic activity: The analgesic activity of the extract was measured by hot-plate method. All drugs were given orally to the respective group rats as a suspension in gum acacia. The rats were

placed on a hot plate maintained at 55±0.5°C. The reaction time was taken as the interval from the instant animal reached the hot plate until the moment animal licked its feet or jumped out. A cut off time of +10 sec was followed to avoid any thermal injury to the paws. The reaction time was recorded before and after +30, +60, +90, +120 and +180 min following administration of test or Diclofenac sodium (9 mg kg^{-1}) drug.

Carrageenan induced paw odem: Edema was induced by giving an intraplantar injection of 0.3% carrageenan (Sigma, St Louis) in a 20 mL volume into the hind left paw using a 26 gauge needle. Paw thickness was measured with electronic digital calipers prior to 1, 3 and 5 h following carrageenan administration. Peak effects occurred by 5 h and carrageenan-induced paw edema returned to almost baseline levels by 24 h, thus only the 5 h data are reported (Bar-Yehuda *et al*., 2009; Shekhar *et al*., 2010; Mukherjee, 2002).

Statistical analysis: Single line ANOVA (Bonferroni t-test) was applied to test the significance of differences between the results of extract-treated and control and standard groups. The results were expressed Mean±SEM value. The difference was considered significant at the conventional level of significance.

RESULTS

Total 8.15% (CPE) and 6.46% (SGE) solidified extract was obtained. For acute toxicity study Swiss albino mice (30±5) of either sex were used. By using 'Organization for Economic Co-operation and Development' (OECD) 423 guidelines LD_{50} was found to be more than 2000 mg kg^{-1} and the effective dose was obtained as 200 mg kg^{-1}.

The response for analgesic activity was recorded after 30, 60,120 and 180 min of treatment. CPE and SGE showed significant ($p<0.001$) results. Both CPE and SGE were insignificant with standard group during study. After 120 min SGE showed significant results but found to be insignificant with comparison to CPE.

Paw thickness was measured with electronic digital calipers on 1, 3 and 5 h after carrageenan administration. Peak effects occurred by 5 h and carrageenan induced paw edema returned to almost baseline levels by 24 h, thus only the 5 h data are reported. Significant ($p<0.001$) decrease in paw volume were obtained for both CPE and SGE. Significant results at $p<0.05$ were obtained after 5 h for CPE vs SGE.

DISCUSSION

The ethanolic extract of leaves of *Cissampelos pareira* and tubers of *Stephania glabra* was examined for toxicity. The OECD guideline 423 was used. Each extract were reported safe at a dose of 200 mg kg^{-1}. The extracts were dissolved in distilled water and then chemical tests for phytochemical screening were performed. Alkaloids, tannins, flavonoids, carbohydrates and phenols were present in CPE whereas, alkaloids, flavonoids, carbohydrates, phenols, saponin were reported to present in SGE.

Analgesic activity: The analgesic activity 50% ethanolic extract of CPE has already been mentioned by providing the rats and mice with 100 mg kg^{-1} of the extract orally (Amresh *et al*., 2007a). The analgesic and antipyretic activity of Gindarudine a morphine like alkaloid compound from *Stephania glabra* has already been mentioned (Semwal *et al*., 2011).

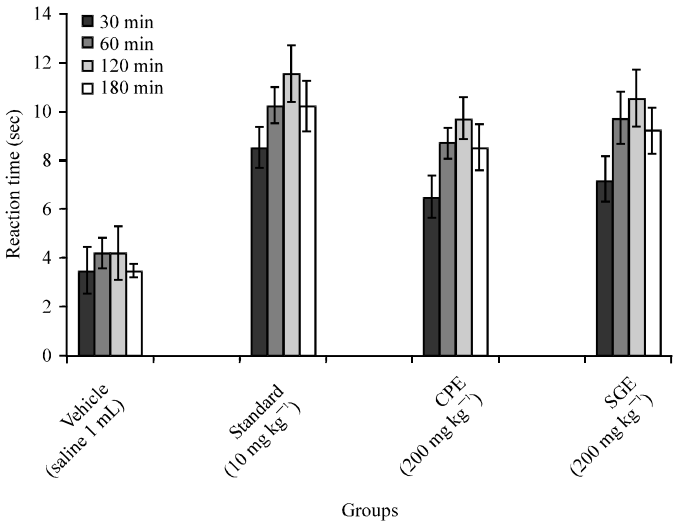

Fig. 1: Analgesic activity of ethanolic extract of CPE and SGE. Each group consist of 6 animals (n = 6); values are Mean±SEM. Signicant ($p<0.001$) result were found between CPE vs vehicle and SGE vs vehicle after 60, 120 and 180 min

The analgesic activity for CPE and SGE was examined by using hot plate method. The results so obtained after 30, 60, 120 and 180 min (Fig. 1) were compared. CPE and SGE showed significant ($p<0.001$) result with control group after 60, 120 and 180 min. Both CPE and SGE were found to be insignificant with standard group after 60 and 180 min. After 120 min SGE showed significant result with standard group but CPE did not. SGE was found to be insignificant with CPE.

Anti-inflammatory activity: However, the anti-inflammatory activity for CPE extracts has already been mentioned by several researchers (Kumar *et al.*, 2010; Amresh *et al.*, 2007a, b; Gopalakrishna *et al.*, 2010; Bansod *et al.*, 2010). The 50% ethanolic extract has been reported to be 59.55-64.04% effective for the treatment of acute inflammation on carageenan induced inflammation (Kumar *et al.*, 2010). Bansod *et al.* (2010) has reported the anti-inflammatory activity on rats by treating them with 400 mg kg^{-1} ethanolic extract of CPE on carrageenan induced rat paw edema. In folklore medicine system decoction of *Stephania glabra* has been used for the treatment of rheumatic bodyache and fever (Maity *et al.*, 2004).

In the present study, for anti-inflammatory activity, all the groups were first injected with 0.3% carrageenan in a 20 mL volume into the hind left paw using a 26 gauge needle. For group 1, 1 mL saline solution was injected with and labeled as control group. Indomethacin 5 mg was given to group 2 orally and labeled as standard group. Group 3, 4 were administered with 200 mg kg^{-1} of extract CPE and SGE, respectively. The paw volume was measured with digital caliper on day 1st, 3rd and 5th h; the percentage inhibition was also calculated (Fig. 2). Results so obtained were compared among each other. The comparison of results of other groups with control group were found to be significant ($p<0.001$) except CPE vs SGE after 1 and 3 h. After 5 h CPE vs SGE showed significant result at $p<0.05$. Comparison of standard group with other groups showed significant ($p<0.001$) results except with group 4 (Fig. 2).

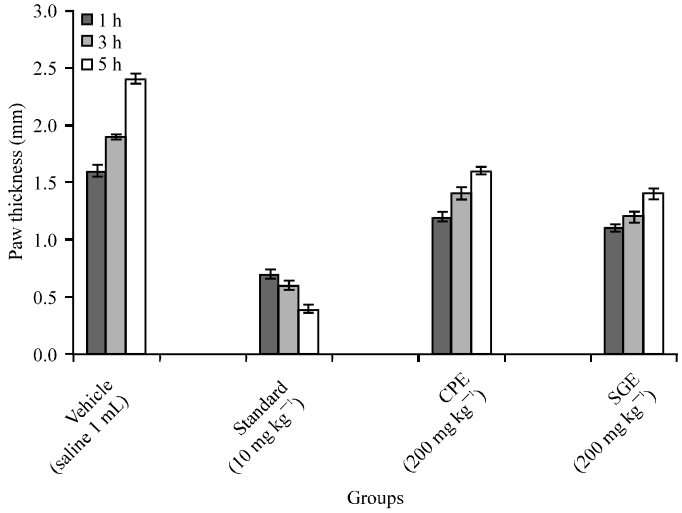

Fig. 2: Anti-inflammatory activity of ethanolic extract of CPE and SGE. Each group consist of 6 animals (n = 6); values are Mean±SEM. Significant ($p<0.001$) results except CPE vs SGE after 1 and 3 h. After 5 h CPE vs SGE showed significant result at $p<0.05$

Anti-inflammatory and analgesic effects were significantly reported for all extracts, as these extracts inhibited the carrageenan induced paw edema and increase in response time. These results support the use of leaves *Cissampelos pareira* and tubers of *Stephania glabra* as herbal medicine for the treatment of analgesia and inflammation.

CONCLUSION

It is concluded that ethanolic extract of stem of leaves of *Cissampelos pareira* and tubers of *Stephania glabra* possess significant ($p<0.001$) anti-inflammatory and analgesic activity against experimentally induced paw edema. This may be due to the presence of active Phytoconstituents and their influence on the prostaglandins pathway. Further research, to isolate anti-inflammatory principle and exact mechanism involved, is needed.

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