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ANTI- INFLAMMATORY STUDY OF PANCHKOLA CHURNA AND IT'S EXTRACT IN WISTAR RAT ANIMAL MODEL

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ABSTRACT

Panchkol churna is a polyherbal traditional preparation in India. The medicinal plants, used in this preparation are *Piper longum* Linn. (Pippali), *Piper chaba* Huntur/*Piper retrofractum*.Vahl. (Chavya), *Plumbago zeylanica* Linn. (Chitraka), *Zingiber officinale* Roscoe (Shunti/Nagara). This formulation is traditionally recommended for various diseases like an abdominal tumor, abdominal pain, loss of appetite, GI disorder, cold, cough, etc. In this study, the polyherbal preparation Panchkola churna and it's extract was prepared and given orally to Wistar albino rats to evaluate anti-inflammatory activity. This study carried out to investigate the anti-inflammatory activity of Panchkola churna at a dose 500mg/kg, 750 mg/kg, 1000mg/kg *p.o* and extract 20 mg/kg, 30 mg/kg and 40 mg/kg b.w. *p.o* in experimental rat models. The study was done in selected two models that are Egg-albumin induced rat paw edema and cotton pellet induced rat paw edema model. Both Panchkola churna and hydroalcoholic extract showed significant activity against inflammation in both models.

Keywords: Churna, Pippali, Edema, Egg Albumin, Granuloma, NSAID

INTRODUCTION

Ayurveda is an oldest healing science of ancient India, which has primarily two objectives protecting the health of healthy individuals and the treatment of diseased ones **[1]**. Ayurvedic medicine is mainly made from herbal plants because plants are easy to collect and available in a vast amount. Plants are used as nutraceuticals, food supplements, pharmaceutics, and preparation of cosmetics like cream, powder, etc. People use traditional medicine for various treatment of disease and used as folk medicine and natural medicine are less costly and have the less adverse effect and the side effect is also rare **[2]**. So herbal medicine is popular day by day and increases in the global market.

Panchkola churna

Churna is applied as a single or mixture of drugs, which is powdered separately and then mixes homogeneously **[3]**. The medicinal plants, used in this preparation are *Piper longum* Linn. (Pippali), *Piper chaba* Huntur/*Piper retrofractum*.Vahl. (Chavya), *Plumbago zeylanica* Linn. (Chitraka), *Zingiber officinale* Roscoe (Shunti/Nagara) **[4] (Table 1)**.

Table 1: Ingredients of Panchkola churna [5, 6]

Sanskrit name	Botanical name	Family	Part used
Pippali and Pippali mula	*Piper longum* Linn.	Piperaceae	Fruit and root
Chavya	*Piper chaba* Hunter/ *Piper retrofractum* Vahl	Piperaceae	Root
Chitrak	*Plumbago zeylanica* Linn.	Plumbaginaceae	Root
Sunthi	*Zingiber officinale* Roscoe	Zingiberaceae	Rhizome

Inflammation

Inflammation is a localized defensive reaction produced by damage or pulverization of tissues, which serve to damage, weaken wall off both the injurious agent and the injured tissue. Inflammation is actuated by chemical mediators that are delivered by host cells in reaction to harmful stimuli **[7]**. When an organism enters an injured tissue, the nearness of the infection is detected by inhabitant cells, basically macrophages. These cells produce cytokines and other mediators that actuate and control the consequent inflammatory reaction. Plasma proteins also produce inflammatory mediators that respond with the organisms or to damaged tissues. A few of these mediators advance the leukocytes to the location where the irritating agent is found. These leukocytes are enacted and they attempt to evacuate the irritating agent by phagocytosis. Enactment of leukocytes is damage to ordinary host tissues. These inflammatory reactions are produced external manifestations that heat (calor), redness (rubor), swelling (tumor), pain (dolor), and loss of function (functio laesa) **[8]**.

NSAIDs are usually indicated for the treatment of acute and chronic conditions

where pain and inflammation present. The production of Prostaglandins (PGs) are activated the inflammation process. In anti inflammatory action, the productions of prostaglandins (PGs) are inhibiting by standard NSAIDs **[9]**. COX-1 and COX-2 are the fatty acid enzymes of Cyclooxygenase (COX). Arachidonic acid forms the PGs and thromboxane under the influence of these enzymes. Most NSAIDs act as non- selective inhibitors of the enzyme COX-1 and COX-2 **[10]**. The most common side effects of NSAIDs are formation of gastric ulcers, prolong the bleeding time and increase blood pressure. These all side effects are due to the inhibition of COX-1 housekeeping role. NSAID corticosteroids and antihistamines are presently used; the potential side effect gives a limitation for their use. There is a need for more naturally available alternatives for the treatment of inflammatory disease **[11]**.

MATERIAL & METHOD

Pharmacological Evaluation

Adult Wistar albino rats of 150 g of either sex were used for the study. Animals were obtained from Central Animal House, Institute of Medical Science, Banaras Hindu University, Varanasi. The animals were housed in large polypropylene cages in a temperature-controlled room (220C). Humidity was maintained properly and a 12 hour light and 12 hr dark cycle were also followed. The animals were provided with standardized pellet feed and clean drinking water. Rats were acclimatized to the standard laboratory condition for 14 days before using the experiment. The body weight of rats measured regularly. The principle of laboratory animal care guidelines was followed. The study has clearance from the Institutional Animal Ethical Committee (IAEC) for the purpose and control and supervision of Experiments on Animals (Dean/2017/CAEC/256).

Preparation of dosage form and Plan of study

The extract (Hydroalcoholic methanol extract) and churna were prepared by the triturating accurately weighed quantity of the extracts against each subject body weight, with a 0.5% solution of Carboxymethylcellulose for oral route administration **(Table 2)**.

Table 2: Plan of study

Group	Test drug	Dose	No. of animal
I. Control	Vehicle	10 ml/kg b.w	6
II. Negative control	Egg albumin /Cotton	0.1 ml/ 10 mg cotton	6
III. Standard (ST)	Albumin+Diclofenac	0.1 ml + 20 mg/kg b.w	6
IV.Churna low (CHL)	EA+Panchkola churna	0.1 ml +500 mg/kg b.w	6
V. Churna mid (CHM)	EA+ Panchkola churna	0.1 ml +750 mg/kg b.w	6
VI. Churna high (CHH)	EA+ Panchkola churna	0.1 ml + 1000 mg/kg b.w	6
VII. Extract low (EXL)	EA +Panchkola extract	0.1 ml + 20 mg/kg b.w	6
VIII. Extract mid (EXM)	EA +Panchkola extract	0.1 ml + 30 mg/kg b.w	6
IX. Extract high (EXH)	EA +Panchkola extract	0.1 ml + 40 mg/kg b.w	6

Pharmacological activities

A. Cotton Pellet induced granuloma method

Adult rats were divided into nine groups of six animals in each group.

- Group 1 [Normal control] - Received vehicle.
- Group 2 [Negative control or Untreated group] - only cotton pellet introduced into sub plantar surface of the right hind paw.
- Group 3 [Standard drug-treated group, Positive control] - Standard drug Diclofenac Sodium injected (20 mg/kg).
- Group 4 [Test group (T1)] - Panchkol churna (500mg/kg.*p.o*. body weight) 1 hour interval after introducing 10 mg cotton pellet.
- Group 5 [Test group (T2)]- Panchkol churna (750mg/kg.*p.o*. body weight)
- Group 6 [Test group (T3)]- Panchkol churna (1000mg/kg.*p.o*. body weight)
- Group 7 [Test group (T3)]- Panchkol churna extract (20mg/kg.*p.o*. body weight)
- Group 8 [Test group (T3)]- Panchkol churna extract (30mg/kg.*p.o*. body weight) □
- Group 9 [Test group (T3)]- Panchkol churna extract (40mg/kg.*p.o*. body weight)

The test was performed on the rat's animal model using a cotton pellet induced granuloma method. The rats were anesthetized by Diethyl ether anesthesia in the anesthetic chamber, an incision was made on the sub plantar region of the right hind paw of rats by the surgical blade, and 10 mg sterile cotton pellet was introduced or inserted in the subcutaneous tunnel. The cotton pellet sterilized using an autoclave. For the study three groups (4, 5, 6) animals treated with test drug (500, 750, 1000mg/kg.*p.o* respectively), group (7, 8, 9) animals treated with test drug extract (20, 30, 40 mg/kg *p.o* respectively). Group 3 treated with standard drug diclofenac sodium (20mg/kg) administered in *i.p*. route. Group1 treated as a positive control and Group2 treated as a negative control. The doses were given for seven days from the day of cotton pellet insertion. On the 8th day, animals were anesthetized by using diethyl ether and cotton pellets were removed. The moist pellets were weighed and then dry at 60^0C for 24 h after that dry pellets were taken and weighted **[12, 13]**.

%Inhibition =Weight of pellet (control) - Weight of pellet (test) × 100 Weight of pellet (control)

B. Egg albumin induced paw edema

Adult rats were divided into nine groups of six animals in each group.

- Group 1 [Positive control or Normal control] - Received vehicle.
- Group 2 [Negative control or Untreated group] - only cotton pellet introduced into sub plantar surface of the right hind paw.
- Group 3 [Standard drug-treated group]- Standard drug Diclofenac Sodium injected. (20mg/kg), 1-hour interval after introducing 0.1 ml undiluted egg albumin injected in the sub plantar region of the right hind paw.
- Group 4 [Test group (T1)] - *Panchkol churna* (500mg/kg.*p.o.* body weight)1 hour interval after introducing 0.1 ml undiluted egg albumin in sub plantar region
- Group 5 [Test group (T2)] - *Panchkol churna* (750mg/kg.*p.o*. body weight), 1-hour interval after introducing 0.1 ml undiluted egg albumin injected in sub plantar region
- Group 6 [Test group (T3)] - *Panchkol churna* (1000mg/kg.*p.o*. body weight), 1 hour interval after introducing 0.1 ml undiluted egg albumin injected in sub plantar region
- Group 7 [Test group (T3)] - *Panchkol churna* extract (20mg/kg.*p.o*. body weight), 1-hour interval after introducing 0.1 ml undiluted egg albumin injected in sub plantar region
- Group 8 [Test group (T3)] - *Panchkol churna* extract (30mg/kg.*p.o*. body weight), 1-hour interval after introducing 0.1 ml undiluted egg albumin injected in sub plantar region
- Group 9 [Test group (T3)] - *Panchkol churna* extract (40mg/kg.*p.o*. body weight), 1-hour interval after introducing 0.1 ml undiluted egg albumin injected in sub plantar region.

For the study three groups (4, 5, 6) animals treated with test drug (500,750, 1000 mg/kg.*p.o* respectively), group (7, 8, 9) animals treated with test drug extract (20, 30, 40 mg/kg.*p.o* respectively) and Group 3 treated with standard drug diclofenac sodium (20 mg/kg) administered in *i.p.* route. Each rat received 0.1 ml egg albumin after 30 minutes of drug treatment. The paw volume was measured by using a plethysmometer before and 1, 2, 3, 4, 5, and 24 h after induction of edema **[14, 15]**.

Inhibition of edema = 100x (1-a-x)/ b-y

Where a=mean paw volume of treated rats at different times after egg albumin injection. x=mean paw volume of treated rats sometimes after egg albumin injection. b=mean paw volume of control rats at different times after egg albumin injection.

y=mean paw volume of control before egg albumin injection.

RESULT

Statistical analysis

All results are expressed as Mean ± S.E.M (n=6 in each group). Statistical comparison was determined by one-way ANOVA followed by Tukey's multiple comparison tests using graph pad prism (**Table 3**).

Effect of Panchkol churna at CHL (500mg/kg, *p.o*), CHM (750mg/kg, *p.o*), CHH (1000mg/kg, *p.o*) and extract of Panchkola EXL (20mg/kg, *p.o*), EXM (30mg/kg, *p.o*), EXH (40mg/kg, *p.o*) on Cotton pellet induced paw edema model in rats. Values were expressed as Mean± S.E.M (n=6). Statistical comparison was analyzed by one way ANOVA followed by Tukey's multiple comparison tests **(Figure 1)**.

Effect of Panchkola churna at CHL(500mg/kg, p.o),CHM(750mg/kg, p.o),CHH(1000mg/kg, p.o) and extract of Panchkola EXL(20mg/kg, p.o), EXM (30mg/kg, p.o), EXH (40mg/kg, p.o) on Egg white induced inflammation model in rats. Values are expressed as Mean± S.E.M (n=6). Statistical comparison was analyzed by one way ANOVA followed by Tukey's multiple comparison tests **(Table 4, Figure 3)**.

Effect of Panchkola churna at CHL (500mg/kg, *p.o*), CHM(750mg/kg, *p.o*),CHH(1000mg/kg, *p.o*) and extract of Panchkola EXL(20mg/kg, *p.o*), EXM (30mg/kg, *p.o*), EXH (40mg/kg, *p.o*) on Egg white induced inflammation model in rats. Values are expressed as Mean± S.E.M (n=6). Statistical comparison was analyzed by one-way ANOVA followed by Tukey's multiple comparison tests **(Figure 4)**.

Table 3: Anti-inflammatory activity of Panchkol churna and extract on Cotton pellet induced paw edema in Wistar rats

Group	Dose	The dry weight of granuloma	Inhibition (%)
NC	Un treated	31.2334±2.031	_
ST	Diclofenac sodium	5.2667±0.5643	83.13%
CHL	500mg/kg	21.8±0.8614	30.20%
CHM	750mg/kg	9.7667±0.5340	68.72%
CHH	1000mg/kg	7.95±0.9326	74.54%
EXL	20mg/kg	20.334±0.8872	34.89%
EXM	30mg/kg	9.2±1.868	70.54%
EXH	40mg/kg	4.81667±1.239	84.57%

All the values were expressed as mean±S.E.M (n=6), P<0.0001.so there is a significant difference between P-value.

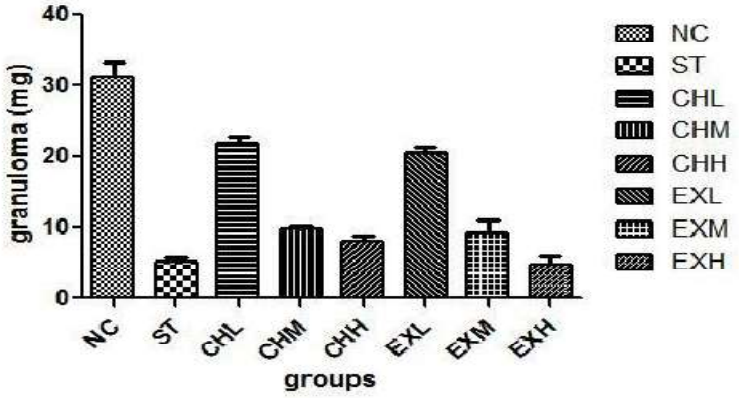

Figure 1: Cotton pellet induced paw edema

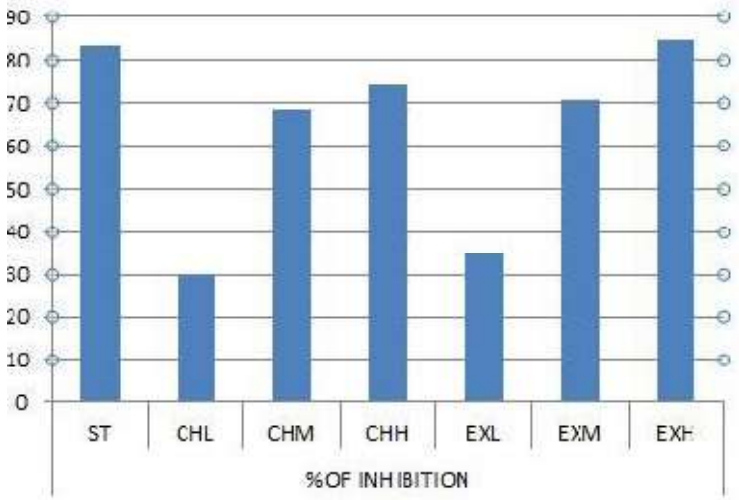

Figure 2: Graph for the percentage of inhibition

Table 4: Anti-inflammatory activity of Panchkol churna and extract on egg white induced paw edema in Wistar rats

Exp Groups	1 hour	2 hour	3 hour	4 hour	5 hour
NC	0.23±0.009661	0.21±0.009661	0.17±0.009661	0.102±0.002633	0.025±0.002236
Standard	0.092667±0.004055	0.084±0.003864	0.068±0.003864	0.042667±0.0008433	0.0115±0.001360
CHL 500mg/kg	0.1858334±0.001900	0.1575±0.007246	0.1275±0.007246	0.082334±0.002946	0.02±0.001962
CHM 750mg/kg	0.1248334±0.004693	0.1155±0.005314	0.1005116667±0.001276	0.0131667±0.001321	0.007525±0.001755
CHH 1000mg/kg	0.1122334±0.004196	0.084315±0.003879	0.068255±0.003879	0.007525±0.001755	0.0131667±0.001321
EXL 20mg/kg	0.1608334±0.006730	0.147±0.006763	0.119±0.006763	0.018±0.001342	0.018±0.001342
EXM 30mg/kg	0.1341667±0.008207	0.105±0.004830	0.085±0.004830	0.0115±0.001118	0.0115±0.001118
EXH 40mg/kg	0.09478334±0.003363	0.07758334±0.001343	0.0426828334±0.0006464	0.0015±0.0003416	0.0015±0.0003416

All values are expressed as Mean±S.E.M (n=6). Statistical comparison was analyzed by one-way ANOVA followed by Turkey's multiple comparison test.

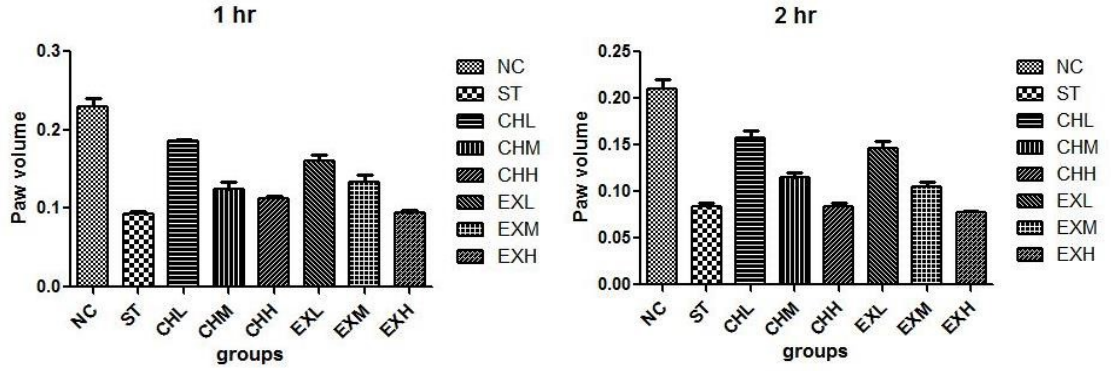

Figure 3: Egg white- induced rat Paw edema

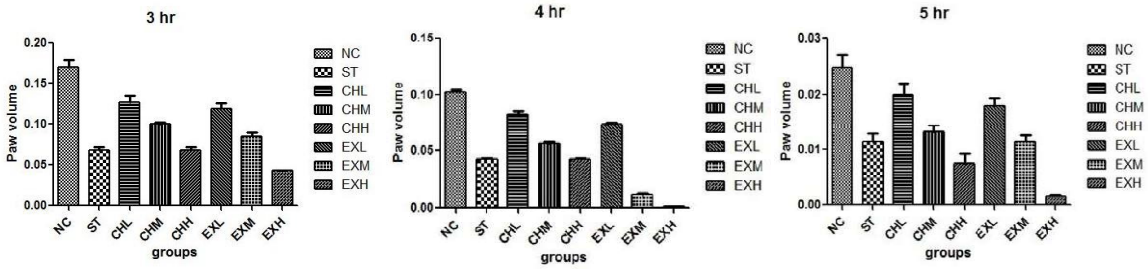

Figure 4: Egg white- induced rat Paw edema

DISCUSSION

Indian system of medicines, polyherbal formulations are more preferable over organometallic formulations for the treatment of various diseases. Polyhedral formulations are used not only for the treatment of diseases but also for the maintenance of good health. These formulations act through a holistic approach with fewer side effects. Recently growth of polyherbal formulations increases exponentially, to maintain this trend proper quality control with new approaches of treatment is necessary for the classical formulation **[16]**. In this study, a similar approach was made to explore the new biological activity of a classical ayurvedic formulation i.e. Panchkol churna. It is an ayurvedic classical formulation consists of Pippali fruit (*Piper longum* Linn.), Pippali mula (*Piper longum* Linn.), Chavya (*Piper chaba* Hunter/ *Piper retrofractrum* Vahl.), Chitrak (*Plumbago zeylanica* Linn.) and Sunthi (*Zingiber officinalis* Roscoe*)*. This formulation traditionally recommended for various diseases like an abdominal tumor, abdominal pain, loss of appetite, GI disorder act as an anti-inflammatory agent, and also use in cold, cough, etc **[17]**.

In this study, the polyherbal preparation Panchkola churna and it's extract was prepared and given orally to Wistar albino rats to evaluate anti-inflammatory activity. This study carried out to investigate the anti-inflammatory activity of Panchkola churna at a dose 500mg/kg, 750 mg/kg, 1000mg/kg *p.o* and extract 20 mg/kg, 30 mg/kg and 40 mg/kg b.w. *p.o* in experimental rat models. The study was

done in selected two models that are Egg-albumin induced rat paw edema and cotton pellet induced rat paw edema model.

Both Panchkol churna and hydroalcoholic extract showed significant activity against inflammation in both models. The extract and churna reduced inflammation in Wistar albino rats induced by egg albumin and cotton pellet in a dose-dependent manner. The extract in high dose (40mg/kg) showed a significant effect against inflammation, whereas a high dose of churna showed comparatively less effect than extract.

In egg white induced paw edema, paw edema causes by inducing phlogistic agent egg albumin. Several inflammatory mediators like histamine, kinins, and prostaglandin play an important role in the mechanism of inflammation. Cotton pellet-induced granuloma formation is a characteristic aspect of a well-known chronic and sub-chronic inflammatory test model **[18]**.

The paw volume of egg white induced model of standard, CHL, CHM, CHH, EXL, EXM, EXH at 1 hour was found to be 0.092667±0.004055, 0.1858334±0.001900, 0.1248334±0.004693, 0.1122334±0.004196, 0.1608334±0.006730, 0.1341667±0.008207, 0.09478334±0.003363 and in 5 hour inflammation was very less amount, 0.0115±0.001360, 0.02±0.001962, 0.007525±0.001755, 0.0131667±0.001321, 0.018±0.001342, 0.0115±0.001118, 0.0015±0.0003416. So the extract of high dose showed most significant effect in inflammation.

The value of the inhibitory action Panchkol churna and its hydroalcoholic extract against granuloma formation in rats induced by cotton implantation are shown in table no 4. The churna and extract were found to significantly reduce the granuloma formation. In the cotton pellet granuloma model, which is widely used to assess its efficacy against the proliferative phase of inflammation in which tissue degeneration and fibrosis occur, inflammation and granuloma develop during several days. This model is an indication of the proliferative phase of inflammation. Inflammation involves the proliferation of macrophages, neutrophils, and fibroblasts, which are basic sources of granuloma formation. The result showed an inhibitory action in a dose-dependent manner **[19]**.

The paw volume of cotton pellet induced model of standard, CHL, CHM, CHH, EXL, EXM, EXH was found to be 5.2667±0.5643, 21.8±0.5643, 8.88334±1.107, 7.95±0.9326, 20.334±0.8872, 9.2±1.868, 4.81667±1.239. Therefore, extract a high dose showed a significant effect on standard drug Diclofenac sodium. The % of inhibition was found to be 83.13%, 30.20%, 68.72%, &4.54%, 34.89%, 70.54%, 84.57% in ST, CHL, CHM, CHH, EXL, EXM, EXH. The present study

indicates that the hydroalcoholic extract of panchkola having excellent anti-inflammatory activity.

Egg albumin induced granuloma in Wistar rat animal modal study confirms that significant anti-inflammatory activity of Panchkol churna at a dose at 500mg, 750mg, and 1000 mg/kg body weight in a dose-dependent manner. Panchkol extract showed anti-inflammatory activity at a dose at 20mg, 30mg, and 40 mg/kg body weight in a dose-dependent manner. All doses on behalf of statistical findings showed anti-inflammatory activity in dose-dependently at 1st, 2nd, 3rd, 4th, and 5th hour but at sixth-hour inflammation of all groups reduces and showed paw volume same as before treatment. Animals treated with Extract showed a better effect than churna, ultimately we can say on behalf of statistical findings that Panchkol churna showed anti-inflammatory activity in dose-dependently.

Cotton pellet induced paw edema in the Wistar rat animal model showed that the Negative control group, only sterilized by autoclave cotton pellet inserted in the sub plantar region of right hind paw under anesthetic condition (diethyl ether) by surgical procedure and there was no drug administered. Therefore, the percentage of inhibition of paw edema found 0% in the negative control-treated group. The standard drug-treated group, which treated with Diclofenac sodium at 20 mg/kg b.w. showed 83.13% inhibition of paw edema. Panchkola churna low dose treated group at 500 mg/kg reduces 30.20% inhibition of paw edema was found. Panchkola churna middle dose treated group at 750 mg/kg b.w. reduces 68.72% inhibition of paw edema was found. Panchkola churna high dose treated group at 1000 mg/kg b.w. reduces 74.54% inhibition of paw edema was found. Panchkola churna extract low dose treated group at 20 mg/kg reduces 34.89% inhibition of paw edema was found. Panchkola churna extract middle dose treated group at 30 mg/kg reduces 70.54% inhibition of paw edema was found. Panchkola churna extract high dose treated group at 40 mg/kg reduces 84.57% inhibition of paw edema was found which was greater than standard.

CONCLUSION

In this study, Panchkola churna was prepared by the classical method, and further, the anti-inflammatory activity study of both Panchkol churna and extract revealed significant activity against inflammation in both models. The extract and churna reduced inflammation in Wistar albino rats induced by egg albumin and cotton pellet in a dose-dependent manner, which can be used as a potential anti-inflammatory agent in the future. Further

study is necessary for the betterment of the formulation.

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Conflicts of interest-NIL

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