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FORMULATION AND SCREENING OF ANTI-RHEUMATIC TRANSDERMAL PAD USING HERBAL EXTRACTS ON NON-IMMUNOLOGICAL ARTHRITIC RATS

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ABSTRACT

In present investigation was intended to formulation and screening of anti-rheumatic activity of herbal extract based transdermal pad using combined petroleum ether extract of *Cardiospermum halicacabum* L. and *Delonix elata* L. leaves (CPCD) on experimental models of arthritis, viz. turpentine oil (acute non-immunological arthritis) and formaldehyde (Chronic non-immunological arthritis) induced arthritis. The extracts obtained from successive extraction were subjected to preliminary phytochemical investigation and antiarthritic activity was evaluated by inducing turpentine oil and formaldehyde. Body weight and histopathological changes were observed. The results indicate that anti-rheumatic transdermal pad (50&100mg of CPCD) and CPCD 400mg/kg protects rats against turpentine oil and formaldehyde induced arthritis. The overall results indicated that oral & topical dosage of CPCD exerts a potent protective effect against turpentine oil and formaldehyde-induced arthritis in rats. These findings demonstrate that the present study validates the ethnomedicinal use of leaves of *Cardiospermum halicacabum* L. and *Delonix elata* L.in the treatment of arthritis conditions.

Key Words:- Anti-rheumatic transdermal pad, *Cardiospermum halicacabum* L. and *Delonix elata* L., turpentine oil and formaldehyde induced arthritis.

INTRODUCTION

Inflammatory diseases including different types of rheumatic diseases are very common throughout the world. Rheumatoid arthritis is an autoimmune disease, which is chronic and one of the oldest known diseases of mankind affecting the majority of population. No substantial progress has been made in achieving a permanent cure of rheumatoid arthritis. Even though various categories like NSAIDs, steroidal anti-inflammatory, DMARDs and immunosuppressant drugs are being used till now, but due to severe side effects of these drugs, the development of new anti-arthritic agents are aimed towards the discovery of safe, potent drugs with minimal side effects (Jadhav *et al*., 2007). Hence, they commonly prefer complementary and alternative medicines (Shankaranarayanan *et al*., 2009).

Cardiospermum halicacabum L. is belongs to Family**:** Sapindaceae. It has been used in Indian traditional medicine for a long time in the treatment of rheumatism, stiffness of the limbs and snakebite. (Sadique *et al*., 1987; Chandra and Sadique, 1989). Experimental pharmacological studies have shown the analgesic, anti-inflammatory, antipyretic, antimalarial, antioxidant

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activity, and anti-ulcer and vasodepressant activities (Gopalakrishnan *et al*., 1976; Sheeba and Asha, 2009; Asha and Pushpangadan, 1999; Waako *et al*., 2005; Sheeba and Asha, 2006).

Delonix elata L. (Family: Fabaceae) is a deciduous tree about 2.5-15 m tall, with a spreading, rather rounded crown, crooked poor stem form and drooping branches. The plant is traditionally used for the treatment of abdominal pains, rheumatism and flatulence. The stem bark of this plant is considered as good febrifuge and is much appreciated as an antiperiodic & anti-inflammatory (Abd EL *et al*., 2011).

There are no reports found for prove synergistic effect of combined extracts of *Cardiospermum halicacabum* L. and *Delonix elata* L. leaves. Therefore the present study was formulation and screening of anti-rheumatic activity of herbal extract based transdermal pad using combined petroleum ether extract of *Cardiospermum halicacabum* L. and *Delonix elata* L. leaves (CPCD) on Non-Immunological Arthritic rats.

MATERIALS AND METHODS

Plant collection

The leaves of *Cardiospermum halicacabum* L. and *Delonix elata* L. used for investigation and it was collected from Tirunelveli District, in the Month of August 2010. The plant was authenticated by Dr.V.Chelladurai, Research Officer Botany. C.C.R.A.S., Govt. of India.

Preparation of extracts

The leaves of plants were dried in shade, separated and made to dry powder. It was then passed through the 40 mesh sieve. A weighed quantity (100gm) of the each powder was subjected to continuous hot extraction in separate Soxhlet apparatus. The extract was evaporated under reduced pressure using rotary evaporator until all the solvent has been removed to give an extract sample. The petroleum ether extract of *Cardiospermum halicacabum* L. and *Delonix elata* L. yielded thick green semi-solid residues. Percentage yield of *Cardiospermum halicacabum* L. and *Delonix elata* L. was found to be 2.5% and 2.3% w/w.

Preliminary phytochemical screening

The phytochemical qualitative chemical composition of petroleum ether extract of *Cardiospermum halicacabum* L. and *Delonix elata* L. using commonly employed precipitation and coloration to identify the major natural chemical groups such as steroids, reducing sugars, alkaloids, phenolic compounds, saponins, tannins, flavonoids, amino acids and glycosides were performed by the standard methods (Harbone, 1973) General reactions in these analysis revealed the presence or absence of these compounds in the crude extracts tested.

Animals used

Wistar strain of albino rats (150-200g) were obtained from the animal house in C.L. Baid Metha College of Pharmacy, Chennai. The animals were maintained in a well-ventilated room with 12:12 hour light/dark cycle in polypropylene cages. The animals were fed with standard pellet feed (Hindustan Lever Limited., Bangalore) and water was given *ad libitum*. Ethical committee clearance was obtained from IAEC (Institutional Animal Ethics Committee) of CPCSEA (Reference No: IAEC/XII/011/CLBMCP/2010-2011.

Drugs and chemicals

Turpentine oil and formaldehyde were purchased from S.D. Fine Chemicals Ltd. (Mumbai, India) and Diclofenac sodium received as gift sample from Dr.Reddy's laboratories Limited (Hyderabad, India).

Preparation of medicated transdermal pad

The equal proportion (1:1) of Rosin (1.5gm) and bees wax (0.5gm) were melted in china dish and Combined petroleum ether extract of *Cardiospermum halicacabum L.* and *Delonix elata L.* leaves (CPCD) (50mg & 100mg), boswellic acid (0.5gm), were added in them followed by menthol (0.5gm), capsicum oleoresin (0.4gm) and 0.1gm of liquid paraffin were added and stirred to get uniform paste. The above paste was speared on special type of crape bandage cloth and dried at room temperature for 10min to obtain anti-rheumatic transdermal pad (Deodhar SD *et al*., 1980; Rajagopal K *et al*., 2005; Lalla JK *et al*., 1988; Khan TA *et al*., 2000; Williams A, 2003). Anti-rheumatic transdermal pad were applied to a small area (approximately $6cm^2$) of skin and subjected to further evaluation.

ACUTE NON-IMMUNOLOGICAL ARTHRITIS

Turpentine oil induced joint odema in rats

Wistar albino rats were fasted for 24hrs before experimentation with free access to water. Acute non-immunological inflammatory joint oedema was induced by injecting 0.02ml of turpentine oil in to the synovial cavity of the knee joint, 30min after the drug administration. Arthritis was induced to all groups of animal except Group I. Diameter of the joint was monitored at 30min, 1, 2, 3, 4, 5^{th} and 6^{th}hr, using micrometer screw gauge (Bhatt *et al*., 1977; Kaithwas G *et al*., 2010).

Experimental design

Group I - Received vehicle (Normal control) 1% w/v SCMC, 1ml/100 g

Group II - Received vehicle (Arthritis control) 1% w/v SCMC, 1ml/100 g

Group III - Received combined petroleum ether extract of *Cardiospermum halicacabum* L. and *Delonix elata* L. (CPCD) (400mg/kg body weight p.o) suspended in 1% w/v SCMC

Group IV – Topically applied anti-rheumatic transdermal pad contain 50mg of combined petroleum ether extract of *Cardiospermum halicacabum* L. and *Delonix elata* L. (CPCD)

Group V – Topically applied anti-rheumatic transdermal pad contain 100mg of combined petroleum ether extract of *Cardiospermum halicacabum* L. and *Delonix elata* L. (CPCD)

Group VI - Received standard drug (Diclofenac sodium, 100mg/kg) p.o, respectively.

CHRONIC NON-IMMUNOLOGICAL ARTHRITIS

Formaldehyde induced arthritis in rats

Group I - Received vehicle (Normal control) 1% w/v SCMC, 1ml/100 g

Group II - Received vehicle (Arthritis control) 1% w/v SCMC, 1ml/100 g

Group III - Received combined petroleum ether extract of *Cardiospermum halicacabum* L. and *Delonix elata* L. (CPCD) (400mg/kg body weight p.o) suspended in 1% w/v SCMC

Group IV - Topically applied anti-rheumatic transdermal pad contain 50mg of combined petroleum ether extract of *Cardiospermum halicacabum* L. and *Delonix elata* L. (CPCD)

Group V – Topically applied anti-rheumatic transdermal pad/day contain 100mg of combined petroleum ether extract of *Cardiospermum halicacabum* L. and *Delonix elata* L. (CPCD)

Group VI - Received standard drug (Diclofenac sodium, 100mg/kg) p.o, for 14 days respectively.

On day 1, 30min after the drug administration chronic non immunological arthritis was induced by sub-plantar injection of 0.1ml of 2% formaldehyde solution and repeated on day 3. Arthritis was induced to all groups of animal except Group I. Arthritis was assessed by measuring the mean increase in paw diameter over a period of 14days using micrometer screw gauge. Body weight changes were observed on day 1 (Initial Body weight) and Day 14 (end of the study) in Formaldehyde induced arthritic rats.

Histological processing and assessment of arthritis damage

On day 14, animals were sacrificed; knee joints were removed and kept in 5% formaldehyde. After decalcification in 5% formic acid, processed for paraffin embedding tissue sections (7 µm thick) were stained with haematoxilin and eosin.

RESULTS

Phytochemical screening

The results of preliminary phytochemical screening of the petroleum ether extract of *Cardiospermum halicacabum* L. revealed that steroids, phenolic compounds, flavonoids, amino acids, glycosides and absence of reducing sugars, saponins, tannins, alkaloids & triterpenoids. The results of preliminary phytochemical screening of the petroleum ether extract of *Delonix elata* L. revealed that presence of alkaloids, steroids, flavonoids, carbohydrates, phenols and absence of glycosides, terpeniods, saponins, tannins.

Effect of oral & topical dosage of CPCD on Turpentine-induced joint oedema in rats

Observations of paw volume were monitored at 30min, 1, 2, 3, 4, 5^{th} and 6^{th}hr post injection of turpentine oil using micrometer screw gauge. The turpentine oil-induced joint oedema control group animals paw volume was increased; it showed signs of arthritis development. The assessment made on the 6^{th}hr showed that the anti-rheumatic transdermal pad (50&100mg/kg b.wt of CPCD) and combined petroleum ether extract of *Cardiospermum halicacabum* L. and *Delonix elata* L. (400mg/kg b.wt of CPCD) treatments significantly reduced ($P < 0.01$) the turpentine oil-induced joint oedema in the respective treatment groups as compared with the arthritis control group (Table 1 & Figure 1).

Oral & topical dosage of CPCD significantly inhibited joint inflammation on turpentine oil-induced joint oedema in rats (77.35, 93.89 & 96.18%) respectively. The positive control Diclofenac sodium (100 mg/kg) also produced significant ($P < 0.01$) inhibition in the turpentine oil-induced joint oedema in rats (95.42%) (Table 2 & Figure 2). Oral & topical dosage of CPCD significantly reduced the paw volume (as compared to control) during the entire 6hrs period of this experiment. The effect of topical transdermal pad (100mg of CPCD) was found to be slightly more than that of standard drug Diclofenac sodium (100 mg/kg) after 6hr of treatment.

Effect of oral & topical dosage of CPCD on Formaldehyde induced arthritis in rats

The effect of standard drug Diclofenac sodium (100mg/kg) and anti-rheumatic transdermal pad (50&100mg/kg b.wt of CPCD), Combined petroleum ether extract of *Cardiospermum halicacabum* L. and *Delonix elata* L. (400mg/kg b.wt of CPCD) has summarized in table 3 & Figure 3. Oral & topical dosage of CPCD significantly ($P < 0.01$) suppressed the inflamed arthritis when compared with control between day 3 and day 14 post injection of formaldehyde administration.

Oral & topical dosage of CPCD significantly suppressed joint inflammation on formaldehyde induced arthritis in rats (76.61, 84.68 & 87.90%) whereas positive control Diclofenac sodium (100 mg/kg) also produced significant ($P < 0.01$) inhibition in the formaldehyde induced arthritis in rats (78.23%) (Table 4 & Figure 4). The effect of topical transdermal pad (50&100mg of CPCD) was found to be slightly more than that of standard drug Diclofenac sodium (100 mg/kg) after 14 days treatment. Oral & topical dosage of CPCD significantly reduced the joint inflammation (as compared to control) during the entire 14days period of this experiment.

Effect of oral & topical dosage of CPCD on Body weight in Formaldehyde induced arthritic rats

The average gain in the body weight on day 14 as compared with the initial body weight in each treatment group has been given in Table 5 & Figure 6. The rats in the arthritis control group lose body weight as compared with oral & topical dosage of CPCD and Diclofenac sodium treated groups.

Effect of oral & topical dosage of CPCD on histopathological changes in Formaldehyde induced arthritic rats

In normal control animals shows no lesions in articular cartilage and vascularity formation into the joint space Arthritis control showed edematous synovium, destructive lesions in articular cartilage and vascularity formation into the joint space in formaldehyde-treated animals. Arthritis rats treated with CPCD (400mg/kg b.w, *p.o*) and anti-rheumatic transdermal pad (50&100mg/kg) observed well protected synovium, articular cartilage into the joint space with normal cellular characteristics like standard drug Diclofenac sodium treated group (Figure 5).

Figure 1. Effect of oral & topical dosage of CPCD on Turpentine oil induced joint inflammation in rats

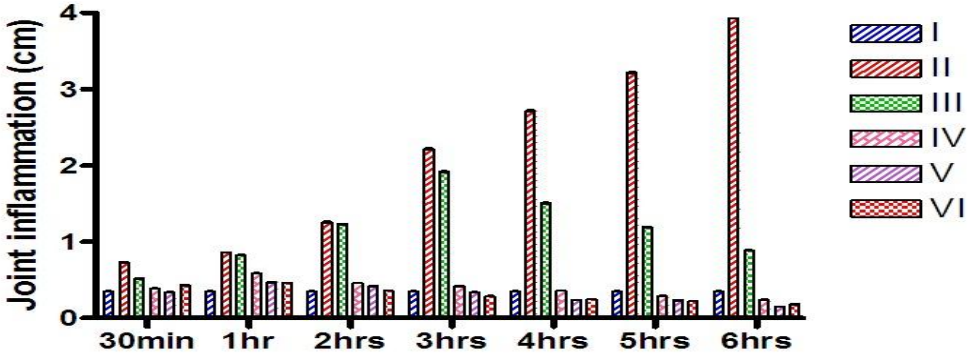


Figure 2. Percentage inhibition of oral & topical dosage of CPCD on Turpentine oil induced joint inflammation in rats

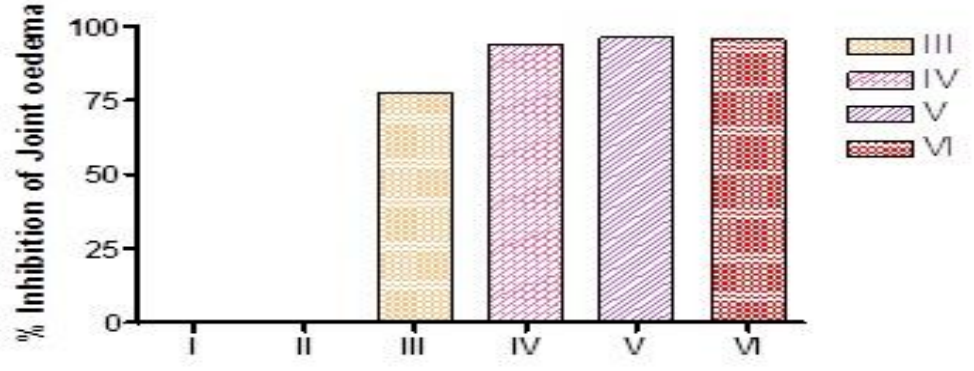


Figure 3. Effect of oral & topical dosage of CPCD on Formaldehyde induced arthritis in rats

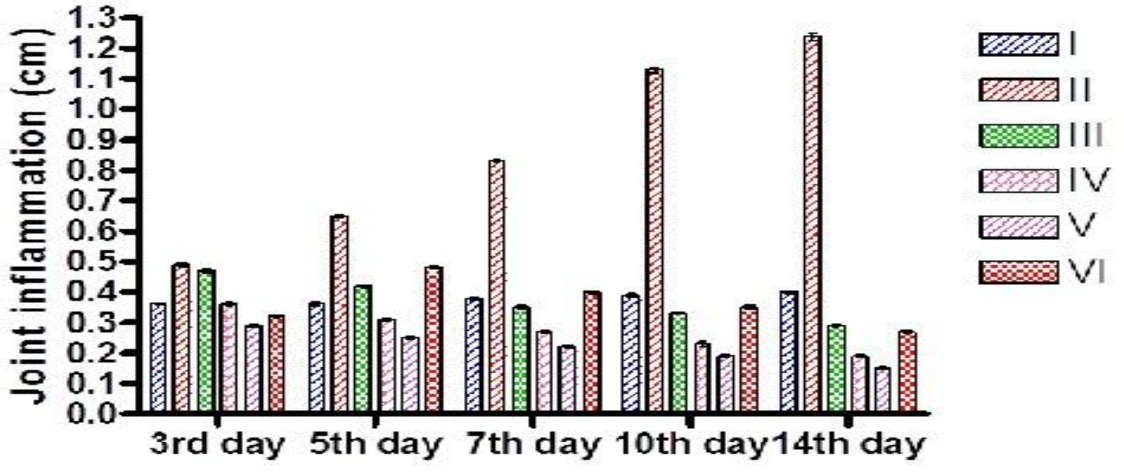


Figure 4. Percentage inhibition of oral & topical dosage of CPCD on Formaldehyde induced arthritis in rats

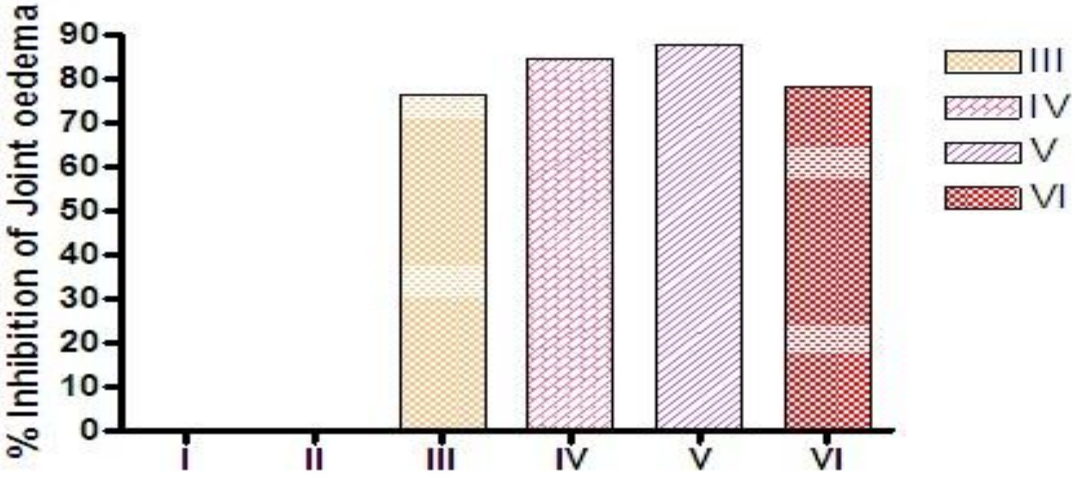
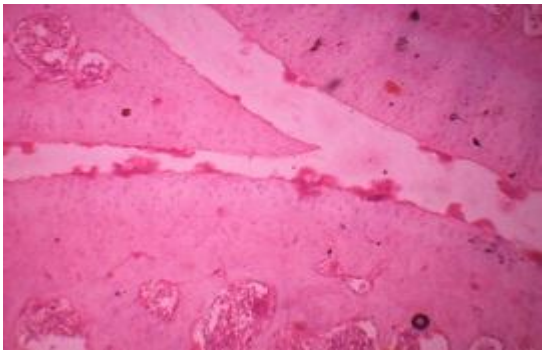
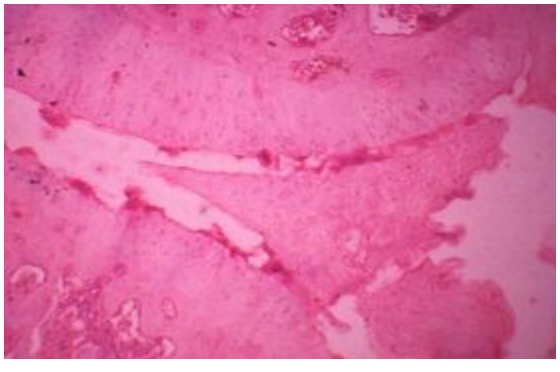


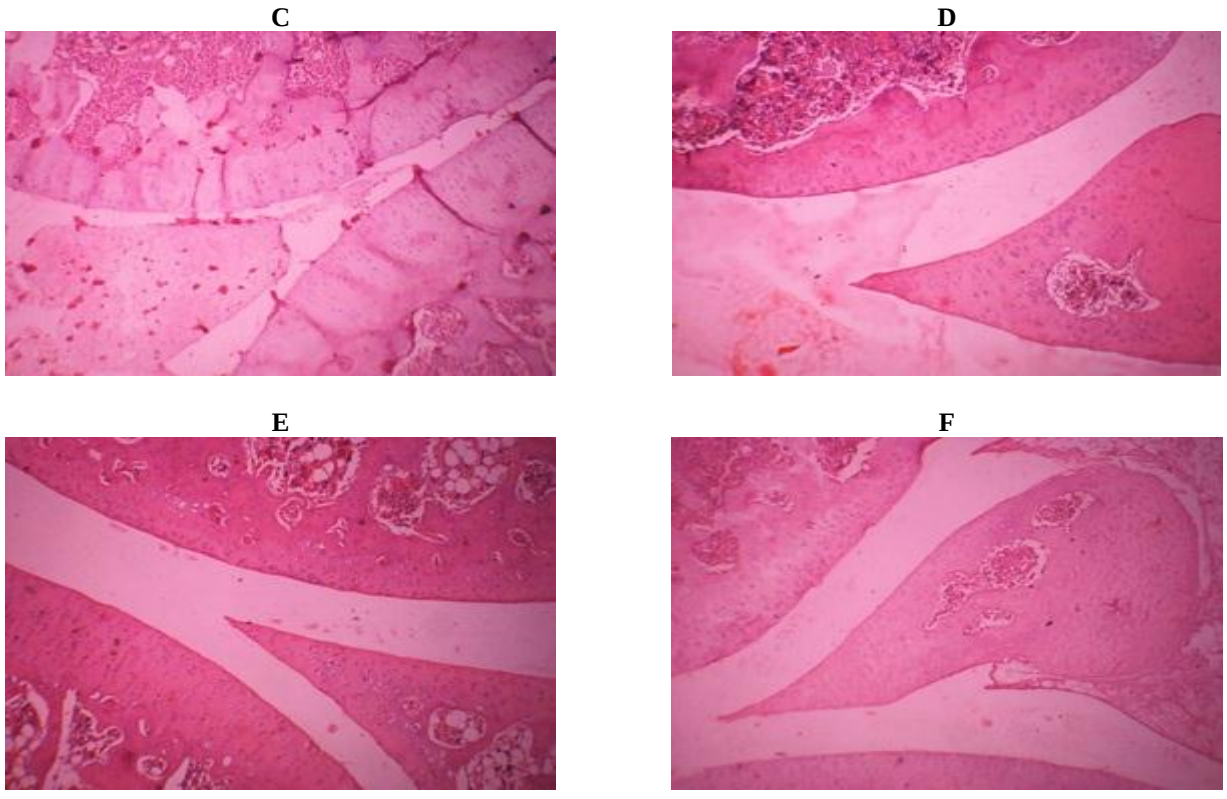
Figure 5. Effect of oral & topical dosage of CPCD on histopathological analysis in Formaldehyde induced arthritis in rats

A



B





(**A**) Normal control: No lesions in articular cartilage and vascularity formation into the joint space; (**B**) Arthritis control: edematous synovium, destructive lesions in articular cartilage and vascularity formation into the joint space in formaldehyde-treated animals; (**C**) Arthritis rats treated with CPCD (400mg/kg b.w, *p.o*): moderate edematous synovium, slight destructive lesions in articular cartilage; (**D**) Arthritis rats treated with Topically applied anti-rheumatic transdermal pad (50mg/kg): mild edematous synovium, slight destructive lesions in articular cartilage; (**E**) Arthritis rats treated with topically applied anti-rheumatic transdermal pad (100mg/kg): observed well protected synovium, articular cartilage into the joint space with normal cellular characteristics;(**F**) Arthritis rats treated with Diclofenac sodium 100mg/kg b.w, *p.o*: observed well protected synovium, articular cartilage into the joint space with normal cellular characteristics.

Figure 6. Effect of oral & topical dosage of CPCD on Body weight in body weight in Formaldehyde induced arthritis in rats

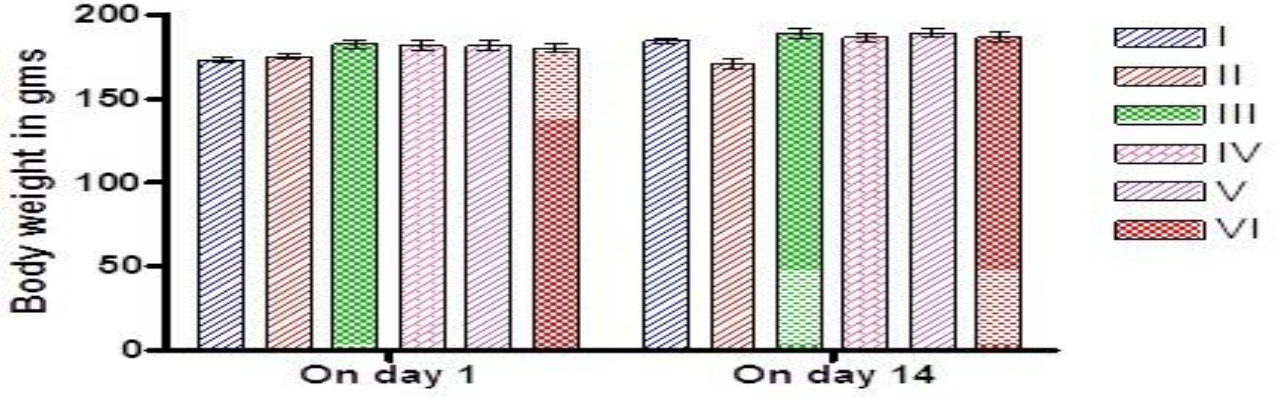


Table 1. Effect of oral & topical dosage of CPCD on Turpentine oil induced joint inflammation in rats

Groups	Design of treatment	Joint inflammation (cm)						
		30min	1hr	2hrs	3hrs	4hrs	5hrs	6hrs
I	Normal Control (1%w/v SCMC, 1ml/100g)	0.35±0.0047**[a]	0.35±0.0047**[a]	0.35±0.0047**[a]	0.35±0.0047**[a]	0.35±0.0047**[a]	0.35±0.0047**[a]	0.35±0.0047**[a]
II	Arthritis Control (1%w/v SCMC, 1ml/100g)	0.73±0.0042	0.86±0.0036	1.26±0.0080	2.22±0.0079	2.72±0.0076	3.22±0.0076	3.93±0.0062
III	CPCD (400mg/kg b.w, *p.o*)	0.52±0.0057**[b]	0.83±0.0090**[b]	1.23±0.0073**[b]	1.92±0.0094**[b]	1.51±0.0097**[b]	1.19±0.0072**[b]	0.89±0.0097**[b]
IV	Topical Transdermal pad (50mg of CPCD)	0.39±0.0055**[b]	0.59±0.0062**[b]	0.46±0.0043**[b]	0.42±0.0058**[b]	0.36±0.0043**[b]	0.29±0.0043**[b]	0.24±0.0043**[b]
V	Topical Transdermal pad (100mg of CPCD)	0.34±0.0042**[b]	0.47±0.0043**[b]	0.42±0.0042**[b]	0.34±0.0042**[b]	0.24±0.0031**[b]	0.23±0.0049**[b]	0.15±0.0031**[b]
VI	Diclofenac sodium (100mg/kg b.w, *p.o)*	0.43±0.0040**[b]	0.46±0.0043**[b]	0.36±0.0049**[b]	0.29±0.0043**[b]	0.25±0.0042**[b]	0.22±0.0026**[b]	0.18±0.0021**[b]

Values are expressed as mean ± S.E.M. (N=6). * P<0.05, ** P<0.01;

a - Group I compared with Group II;

b – Group III - VI compared with Group II. (ANOVA followed by Dunnett's test).

Table 2. Percentage inhibition of oral & topical dosage of CPCD on Turpentine oil induced joint inflammation in rats

Groups	Design of treatment	% Inhibition
I	Normal Control (1%w/v SCMC, 1ml/100g)	-
II	Arthritis Control (1%w/v SCMC, 1ml/100g)	-
III	CPCD (400mg/kg b.w, *p.o*)	77.35
IV	Topical Transdermal pad (50mg of CPCD)	93.89
V	Topical Transdermal pad (100mg of CPCD)	96.18
VI	Diclofenac sodium (100mg/kg b.w, *p.o)*	95.42

Table 3. Effect of oral & topical dosage of CPCD on Formaldehyde induced arthritis in rats

Groups	Design of treatment	Joint diameter (cm)				
		3rd day	5th day	7th day	10th day	14th day
I	Normal Control (1%w/v SCMC, 1ml/100g)	0.36±0.0033**[a]	0.36±0.0050**[a]	0.38±0.0042**[a]	0.39±0.0047**[a]	0.40±0.0047**[a]
II	Arthritis Control (1%w/v SCMC, 1ml/100g)	0.49±0.0070	0.65±0.0048	0.83±0.0048	1.13±0.0079	1.24±0.0117
III	CPCD (400mg/kg b.w, *p.o*)	0.47±0.0042**[b]	0.42±0.0054**[b]	0.35±0.0054**[b]	0.33±0.0034**[b]	0.29±0.0026**[b]
IV	Topical Transdermal pad (50mg of CPCD)	0.36±0.0043**[b]	0.31±0.0036**[b]	0.27±0.0042**[b]	0.23±0.0070**[b]	0.19±0.0033**[b]
V	Topical Transdermal pad (100mg of CPCD)	0.29±0.0043**[b]	0.25±0.0031**[b]	0.22±0.0056**[b]	0.19±0.0025**[b]	0.15±0.0042**[b]
VI	Diclofenac sodium (100mg/kg b.w, *p.o)*	0.32±0.0048**[b]	0.48±0.0060**[b]	0.40±0.0042**[b]	0.35±0.0058**[b]	0.27±0.0048**[b]

Values are expressed as mean±S.E.M. (N=6). * P<0.05, ** P<0.01; a - Group I compared with Group II;
b – Group III - VI compared with Group II. (ANOVA followed by Dunnett's test).

Table 4. Percentage inhibition of oral & topical dosage of CPCD on Formaldehyde induced arthritis in rats

Groups	Design of treatment	% Inhibition of Joint oedema
I	Normal Control (1%w/v SCMC, 1ml/100g)	-
II	Arthritis Control (1%w/v SCMC, 1ml/100g)	-
III	CPCD (400mg/kg b.w, *p.o*)	76.61
IV	Topical Transdermal pad (50mg of CPCD)	84.68
V	Topical Transdermal pad (100mg of CPCD)	87.90
VI	Diclofenac sodium (100mg/kg b.w, *p.o)*	78.23

Table 5. Effect of oral & topical dosage of CPCD on Body weight in body weight in Formaldehyde induced arthritis in rats

Groups	Design of treatment	Body weight in gms (±SEM)		
		On Day 1	On Day 14	Change in body weight
I	Normal Control (1%w/v SCMC, 1ml/100g)	173±1.633[a]	184.5±1.708[a]	11.5±0.4282[a]
II	Arthritis Control (1%w/v SCMC, 1ml/100g)	175.33±1.994	170.83±2.613	-4.17±0.98.04
III	CPCD (400mg/kg b.w, *p.o*)	182.5±2.473[b]	188.83±2.798**[b]	6.17±1.014**[b]
IV	Topical Transdermal pad (50mg of CPCD)	181.5±2.918[b]	186.50±2.895**[b]	5±0.4472**[b]
V	Topical Transdermal pad (100mg of CPCD)	181.83±2.535[b]	189.33±2.539**[b]	7.50±0.6191**[b]
VI	Diclofenac sodium (100mg/kg b.w, *p.o)*	180.33±2.704[b]	186.67±2.848**[b]	6.33±1.333**[b]

Values are expressed as mean ± S.E.M. (N=6). * P<0.05, ** P<0.01;
a - Group I compared with Group II;
b – Group III - VI compared with Group II. (ANOVA followed by Dunnett's test).

DISCUSSION AND CONCLUSION

In the present study we have evaluated the antiarthritic activity of oral & topical dosage of CPCD by using two experimental models of arthritis, viz. turpentine oil (acute non-immunological arthritis) and formaldehyde (Chronic non-immunological arthritis) induced arthritis.

A large number of studies have indicated that anti-inflammatory and anti-arthritic activities of plants may be attributed to their natural phenolic components, flavanoids and steroids (Han T *et al*., 2007). In fact, Zhu *et al*. (2011) found that the anti-inflammatory activity of *Desmodium podocarpum* ethanol extract was related to the presence of five major families of compounds in this shrub: phenols, phytosterols, arylpropionic acids, saponins, and enols. In addition, Mothana *et al*. (2012) concluded that the anti-inflammatory effect of the *Loranthus regularis Steud ex Sprague* methanol extract was associated with its flavonoid content. Along the same line, Loganayaki *et al*. (2012) reported that flavonoids, streoids and phenolic constituents of *Ammannia baccifera L.*

Above researchers has confirmed the effect of oral & topical dosage of CPCD, because the phytochemical screening of petroleum ether extract of *Cardiospermum halicacabum* L. and *Delonix elata* L. leaves confirmed the presence of steroids, phenolic compounds, amino acids, glycosides and flavonoids. The petroleum ether extract of *Cardiospermum halicacabum* L. containing betasitosterol was found to have high anti-inflammatory and anti-arthritic effects. Betasitosterol is considered to be the most important anti-inflammatory compound obtained from CPCD and its anti-arthritic activity is attributed to the inhibition of microtubules in proinflammatory cells including macrophages.

Effect of oral (400mg/kg) & topical dosage of CPCD (50&100mg) against turpentine oil-induced joint edema in rats showed that it inhibited joint edema gradually at 1, 2, 3 4, 5 & 6hr after treatment compared to control. The acute inflammatory response in the knee joint of rat induced by turpentine oil was significantly reduced by oral (400mg/kg) & topical dosage of CPCD (50&100mg).

As there are some sequential release of the inflammatory mediator's histamine and serotonin in early phase; kinin like substances in intermediate phase; prostaglandins in late phase; reported in turpentine oil-induced joint. The possible inhibitory effect of oral & topical dosage of CPCD in turpentine oil-induced joint edema on different phases of inflammation, which in turn could inhibited either lipoxygenase and/or cyclooxygenase as reported previously (Riaz N *et al*., 2007; Gautam R *et al*., 2011).

Inflammation induced by formaldehyde is biphasic, an early neurogenic component is mediated by substance P and bradykinin followed by a tissue mediated response where histamine, 5-HT, prostaglandins and bradykinin are known to be involved (Wheeler-Aceto and Cowan, 1991). In the formaldehyde-induced inflammation, the oral & topical dosage of CPCD demonstrated significant anti-inflammatory activity that lasted up to 14 days, suggesting its long duration of action.

In the oral & topical dosage of CPCD treated groups except arthritis control group, there was restoration of the body weights of the rats. A report by (Patil and Suryavanshi, 2007) suggests that the decrease in the body weight during inflammation is due to deficient absorption of nutrients through the intestine and that treatment with anti-inflammatory drugs normalizes the process of absorption. The evident restoration of the body weight of rats in the oral & topical dosage of CPCD treated groups may involve improvement of intestinal absorption of the nutrients and a reduction in the distress caused by the severity of the arthritis.

From the results obtained in the present study, it may be concluded that the oral & topical dosage of CPCD possesses potent anti-inflammatory and anti-arthritic activity against both the exudative and proliferative phases of inflammation. The present observations suggested that oral & topical dosage of CPCD has a positive influence on different phases of chronic inflammatory states. Further studies concerning the mechanism of the anti-arthritic action as well as isolation of the active principles responsible for such activity should be conducted in future.

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