



Research Article

EVALUATION OF ACUTE AND CHRONIC ANTI-INFLAMMATORY ACTIVITY IN ETHANOLIC EXTRACT OF AERIAL PARTS OF *CARDIOSPERMUM HALICACABUM* AND *CARDIOSPERMUM CANESCENS* IN ANIMAL MODELSKudaravalli Sreedevi ^{1*}, Jangala Venkateswara Rao ²^{*1} Department of Biotechnology, Sulthan-ul-Uloom College of Pharmacy, Banjara Hills, Hyderabad-500034, Telangana, INDIA.² Department of Pharmaceutical Analysis, Bharath College of Pharmacy, Ibrahimpatnam, Hyderabad-501510, Telangana, INDIA.

Received on: 12-11-2017; Revised and Accepted on: 24-12-2017

ABSTRACT

The present study investigates the acute and chronic anti-inflammatory activity in ethanolic extract of aerial parts of *Cardiospermum halicacabum* and *Cardiospermum canescens* L using carrageenan, Acetic acid, Xylene, PMA induced edema in animals significantly swelling inhibited *** $P < 0.001$ when compared to control group $P < 0.001$ when compared to test ethanolic extract dose 250mg, 500mg $P < 0.001$ when compared to standard drug. And in chronic inflammatory study revealed that treatment of rats with both the extracts of *Cardiospermum halicacabum* and *Cardiospermum canescens* (250 mg/kg and 500 mg/kg) showed significant ($P < 0.001$) reduction in weight of cotton pellet induced granuloma, Formalin induced edema in mice with 500 mg/kg of both extracts significantly ($P < 0.001$) reduced paw thickness whereas 250 mg/kg of both extracts showed lesser effect ($P < 0.01$) in reducing the paw volume.

KEYWORDS: *Cardiospermum halicacabum* and *Cardiospermum canescens* ethanolic extract, Indomethacin, Anti-inflammatory activity, Carrageenan, Indomethacin, Acetic acid, Xylene, PMA, Formalin, Cotton pellets.

INTRODUCTION

Many herbal preparations are being prescribed widely for the treatment of inflammatory conditions [1]. Inflammatory diseases are becoming common in aging society throughout the world. Recent studies indicate that the mediators and cellular effectors of inflammation are important constituents of the local environment of tumors [2]. Various herbal medicines derived from plant extracts are being used in the treatment of a wide variety of clinical diseases, though relatively little knowledge about their mechanisms of action is known [3]. Many factors may be at the origin of the inflammatory process; Infectious agents, ischemia, antigen-antibody interaction, thermal or physical shocks [4]. Steroid drugs, nonsteroidal anti-inflammatory drugs (NSAIDs) and immunosuppressants, usually used for the relief of inflammatory diseases, require long-term treatment and their use is often associated with serious side effects such as bleeding gastrointestinal and peptic ulcers [5]. This has led to the search for alternative treatments. In this regard, secondary metabolites of various medicinal plants have been shown to be effective in the treatment of inflammation and pain [6]. Among these plants, the species of Two species namely *Cardiospermum halicacabum* (family - Sapindaceae) and *Cardiospermum canescens* (Sapindaceae) grow abundantly in waste lands and tropical forests as weed in many parts of the southern India. They are used traditionally for the treatment of inflammation related disorders. So, the present research work has been undertaken with the ethanolic extract of aerial parts of *Cardiospermum halicacabum* and

Cardiospermum canescens were to investigate anti-inflammatory activity.

MATERIALS AND METHODS

Collection and Authentication of plants materials:

The aerial parts of *Cardiospermum halicacabum* and *Cardiospermum canescens* were collected from the foot hills of Tirumala, Chittoor Dist. Andhra Pradesh, India. The plant species were identified and authenticated by the Botanical Survey of India, at Coimbatore, Tamilnadu, India. (Lr.No.BSI/SC/5/23/2006-07/Tech-1465. Dt.11/12/2006) The voucher specimens were deposited in the Department of pharmacognosy, J.S.S.College of pharmacy, Ootacamund. The collected plant material was washed, dried, powdered and stored in labelled airtight containers in a cool and dry place till further use.

Chemicals:

All the chemicals were of analytical grade and were either Sigma or Merk chemicals.

Experimental Animals:

Swiss albino mice (25-30g) and Wistar rats (150-180g) either sex were used in the entire study. They were housed in standard polypropylene cages and kept under controlled room temperature ($24 \pm 2^\circ\text{C}$; relative humidity 60 -70 %) in a 12 h light-dark cycle. The animals were fed with standard laboratory diet and water ad libitum. Food was withdrawing 12h before and during the experimental hours. The experimental protocol was approved by Institutional Animal Ethics Committee No. JSSCP / IACE / PH.D / PH. COLOGY / 02 / 2005-06.Dt.05.09.2005.

Preparation of Herbal Extract:

The powdered drug was repeatedly extracted in a Soxhlet apparatus using ethanol solvents for 48 hours. The extract were collected and concentrated by evaporation and dried in vacuum and used for anti-inflammatory activity.

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Statistical analysis:

Results were analyzed using One way analysis of variance (ANOVA) and expressed as Mean $\pm$ SEM. Data was further subjected to Dunnett's test and differences between means were regarded significant at $P < 0.01$ and $P < 0.05$

Acute Anti-inflammatory studies:**(a) Carrageenan-induced paw oedema in rats:**

Oedema was induced by injecting 0.1ml of carrageenan (1% w/v) in normal saline into the sub planter region of the left hind paw, after 1 hr of extract / standard drug administration orally. The volume of paw was measured with pleythesmometer after 1 hr, 2hr, 3hr, and 5hr of carrageenan injection. Results were determined as the percent inhibition of oedema and were compared with the control [7].

(b) Acetic acid-induced vascular permeability in mice:

The mice were dosed orally with the test substances suspended in 0.3% carboxy methyl cellulose solution (CMC) 30 min before the injection of 0.7% acetic acid-saline solution (i.p., 0.1 ml/10 g b.w). 4% pontamine sky blue (10 ml/kg) was also injected by tail vein after 30 minutes of acetic acid injection. After 20 min, the mice were sacrificed and then the pigment exuded to abdominal cavity was washed with 10 ml of distilled water and centrifuged (3000rpm for 10 min). The absorbance of supernatants was measured at 580 nm using UV-vis spectrophotometer. The vascular permeability effects were expressed in terms of dye amount per 30 g weight of mouse, which leaked into the peritoneal cavity. The results were compared with positive control aspirin.

(c) Xylene induced ear oedema:

Swiss albino mice were selected for the study and divided into groups of six each. One hour after intraperitoneal injection of the extract, 0.03 ml of xylene was applied to the anterior and posterior surfaces of the right ear. The left ear was considered as control. Thirty minutes after xylene application, mice were killed by euthanasia within an atmosphere of ether and both ears were removed. The earlobes were punched and weighed. The increase in weight of the right ear punch over that of left indicated the oedema [8].

(d) PMA induced mouse ear oedema in mice:

Oedema was induced by topical application of 2.5 μ g phorbol-12-myristate-13-acetate (PMA) in 20 μ l acetone to the right ear of mice. The left ear served as control and received only acetone. The hydro alcoholic extract was dissolved in acetone before PMA application. After 4 h, mice were subjected to light anesthesia by ether and then killed by cervical dislocation. The earlobes were punched and weighed. The increase in weight of the right ear punch over that of left indicated the oedema and was measured [9].

Chronic Anti-inflammatory studies:**(a) Cotton pellet-induced granuloma in rats:**

Male Wistar albino rats were used for this study. Granulomatous lesions were induced by surgically implanting two cotton pellets (50 mg) subcutaneously in the dorsal region of the rats, one near each axilla. Plant extract (250 and 500mg/kg body wt.) or vehicle (5 ml/kg body wt.) were given orally once daily for 7 days. On 8th day, the rats were anesthetized under light ether, and the pellets covered by granulomatous tissue were dissected and dried at 60°C to a constant weight. The mean weights for different groups were determined, and compared with the control [10].

(b) Formalin-induced paw oedema:

The animals were pre-treated orally with hydro alcoholic extracts suspended 0.3% CMC (250 and 500 mg/kg body weight). After treatment with plant extracts, the animals were injected with 0.05 ml of 2% formalin (in 0.9% aq. NaCl) into the plantar surface of the left hind paw [11]. The volumes of the paws were measured before the induction and also at various time intervals after the injection. Oedema was expressed as an increase of foot pad thickness in relation to the initial value. Positive control group was treated orally with indomethacin (50 mg/kg).

RESULTS AND DISCUSSION**Acute Anti-inflammatory studies:****(a) Effect of *Cardiospermum halicacabum* and *Cardiospermum canescens* on Carrageenan induced paw edema in rats:**

The effects of 50% ethanolic extract of *Cardiospermum halicacabum* and *Cardiospermum canescens* at two dose levels (250 mg/kg and 500 mg/kg) in carrageenan induced rat paw edema was studied. The results revealed that all extracts tested at two dose levels (250 mg/kg and 500 mg/kg) showed significant protection in the acute inflammation induced by carrageenan. In particular, at 500 mg/kg both the extracts were capable of producing 83-88% protection. The onset of action in all the extracts tested was observed more than 50% at the end of 2hrs itself.

Further, the results when compared with 0 Hr reading of same group at specific dose levels tested (250 mg/kg and 500 mg/kg), it was observed that ethanolic extract of *Cardiospermum halicacabum* started showing the protection after 2 hrs at 250 mg/kg whereas 500 mg/kg showed at the end of 1 hr itself and continued till the end of 5 hrs and quite comparable with that of Ibuprofen. The onset of action of 500 mg/kg of *Cardiospermum canescens* started from 3rd hr and lasted up to 5th hr whereas the 250 mg/kg has shown its effect only at 5th hour. The onset of action and percentage inhibition of paw edema of both extracts CC 500 and CH 250 were identical showing that both are equitant. The results were tabulated in table no. 1.

Table No. 1: Effect of *Cardiospermum halicacabum* and *Cardiospermum canescens* on Carrageenan induced paw edema in rats

Treatment	Paw Volume (ml) and % inhibition of paw edema							
	0 Hr	1 Hr	2 Hr	3 Hr	5 Hr			
Control (CMC)	0.11 $\pm$ 0.008	0.66 $\pm$ 0.03***	0.95 $\pm$ 0.04***	1.18 $\pm$ 0.02***	1.51 $\pm$ 0.07***	-	-	-
Ibuprofen (25 mg/kg)	0.11 $\pm$ 0.010	0.22 $\pm$ 0.02	0.18 $\pm$ 0.005	0.16 $\pm$ 0.008	0.12 $\pm$ 0.01	92		
CH ethanol extract (250 mg/kg)	0.12 $\pm$ 0.019	0.41 $\pm$ 0.03#	0.37 $\pm$ 0.03#	0.31 $\pm$ 0.04	0.225 $\pm$ 0.04	85		
CH ethanol extract (500 mg/kg)	0.13 $\pm$ 0.007	0.36 $\pm$ 0.04#	0.32 $\pm$ 0.03	0.27 $\pm$ 0.02	0.18 $\pm$ 0.02	88		
CC ethanol extract (250 mg/kg)	0.19 $\pm$ 0.007	0.53 $\pm$ 0.04##	0.47 $\pm$ 0.03##	0.4 $\pm$ 0.03#	0.31 $\pm$ 0.03	80		
CC ethanol extract (500 mg/kg)	0.13 $\pm$ 0.01	0.47 $\pm$ 0.03##	0.41 $\pm$ 0.03#	0.34 $\pm$ 0.02	0.25 $\pm$ 0.02	83		

Values are expressed as mean $\pm$ S.D; n=6; * $P < 0.05$, ** $P < 0.01$, *** $P < 0.001$ when compared to 0 Hr reading; One way ANOVA was applied followed by Dunnet's test

(b) Effect of *Cardiospermum halicacabum* and *Cardiospermum canescens* on acetic acid induced vascular permeability in mice:

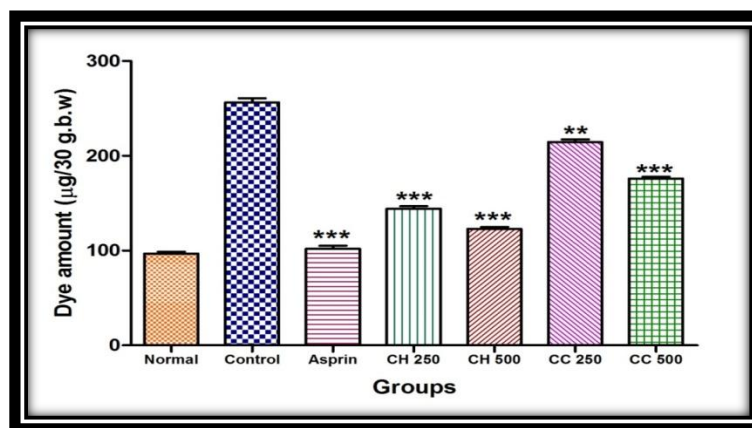
The intraperitoneal injection of acetic acid caused squirming and increased the capillary permeability that was measured by direct estimation of plasma-bound dye (Pontamine Sky Blue) which has leaked into the peritoneal cavity. The study revealed that both extracts of

Cardiospermum halicacabum and *Cardiospermum canescens* (250 mg/kg and 500 mg/kg) significantly decreased the vascular permeability. Moreover, CC500 significantly ($P < 0.001$) decreased the vascular permeability when compared to CC 250. The results were tabulated in table 2 and shown in Fig. 1.

Table No. 2: Effect of *Cardiospermum halicacabum* and *Cardiospermum canescens* on acetic acid induced vascular permeability in mice

S.no	Group	Amount of P.S.B (µg/30g b.wt)
1	Normal	96.98 ± 4.83
2	Control	256.22 ± 13.13
3	Asprin (100 mg/kg)	102.07 ± 5.53***
4	<i>Cardiospermum halicacabum</i> (CH) (250 mg/kg)	144.23 ± 8.01***
5	<i>Cardiospermum halicacabum</i> (CH) (500 mg/kg)	122.95 ± 5.76*** ^{€€€}
6	<i>Cardiospermum canescens</i> (CC) (250 mg/kg)	214.43 ± 8.21**
7	<i>Cardiospermum canescens</i> (CC) (500 mg/kg)	176.15 ± 5.68*** ^{†††}

Values are expressed as mean ± S.D; n=6; ***P<0.001 when compared to control group; ^{€€€}P<0.001 when compared to CH 250; ^{†††}P<0.001 when compared to CC 250; One way ANOVA was applied followed by Turkey's multiple comparison test.

Fig. 1: Effect of *Cardiospermum halicacabum* and *Cardiospermum canescens* on acetic acid induced vascular permeability in mice

(c) Effect of *Cardiospermum halicacabum* and *Cardiospermum canescens* on xylene-induced ear edema swelling in mice:

The circular sections of mice ears were cut and measured. The results showed that both extracts of *Cardiospermum halicacabum* and *Cardiospermum canescens* (250 mg/kg and 500 mg/kg) significantly (P<0.001) inhibited the ear swelling. Further, the CC 500 showed the equipotent activity as that of CH 250. Moreover, CC 500 was significantly (P<0.001) inhibited the ear swelling when compared to CC 250 showing the dose dependent activity. The results were tabulated in table 3.

(d) Effect of *Cardiospermum halicacabum* and *Cardiospermum canescens* on PMA induced ear edema in mice:

The punched ear lobes were weighed after PMA application. The results showed that both extracts of *Cardiospermum halicacabum* and *Cardiospermum canescens* (250 mg/kg and 500 mg/kg) significantly inhibited the ear swelling and shown dose dependent activity. Further, the CC 500 showed the equipotent activity as that of CH 500. The results were tabulated in table 4.

Table No. 3: Effect of *Cardiospermum halicacabum* and *Cardiospermum canescens* on xylene-induced earedema swelling in mice.

S.No	Treatment	Ear Swelling (mg)	Inhibition (%)
1	Control (CMC)	30.38 ± 2.34	-
2	Ibuprofen (25 mg/kg)	11.85 ± 1.56***	61
3	<i>Cardiospermum halicacabum</i> (CH 250 mg/kg)	17.75 ± 1.91***	42
4	<i>Cardiospermum halicacabum</i> CH 500 mg/kg)	14.05 ± 1.05*** [€]	54
5	<i>Cardiospermum canescens</i> (CC 250 mg/kg)	24.75 ± 2.26***	18
6	<i>Cardiospermum canescens</i> (CC 500 mg/kg)	18.38 ± 1.47*** ^{†††}	39

Values are expressed as mean ± S.D, n=6; ***P<0.001 when compared to control group; [€]P<0.05 when compared to CH 250; ^{†††}P<0.001 when compared to CC 250; One way ANOVA was applied followed by Turkey's multiple comparison test.

Table No. 4: Effect of *Cardiospermum halicacabum* and *Cardiospermum canescens* on PMA induced ear oedema in mice

S.No	Treatment	% Inhibition
1	Indomethacin	81.26
2	<i>Cardiospermum halicacabum</i> (CH250 mg/kg)	43.34
3	<i>Cardiospermum halicacabum</i> (CH500 mg/kg)	68.43
4	<i>Cardiospermum canescens</i> (CC250 mg/kg)	38.16
5	<i>Cardiospermum canescens</i> (CC500 mg/kg)	62.41

Values are expressed as mean ± S.D; n = 6

Chronic Anti-inflammatory studies:

(a) Effect of *Cardiospermum halicacabum* and *Cardiospermum canescens* on Cotton pellet induced granuloma in rats:

The effect of ethanolic extracts of *Cardiospermum halicacabum* and *Cardiospermum canescens* (250 mg/kg and 500

mg/kg) in cotton pellet induced granuloma formation in rats was studied and the percentage inhibition of granuloma was calculated. The study revealed that treatment of rats with both the extracts of *Cardiospermum halicacabum* and *Cardiospermum canescens* (250 mg/kg and 500 mg/kg) showed significant (P<0.001) reduction in weight of cotton pellet

induced granuloma. Moreover, *Cardiospermum halicacabum* and *Cardiospermum canescens* extracts showed the anti-inflammatory effects dose dependently. Although, the groups treated with *Cardiospermum halicacabum* has less efficacy when compared to the *Cardiospermum halicacabum* treated groups, the activity of CC 500 is equipotent to CH 250. The results were provided in table 5 and Fig. 2.

(b) Effect of *Cardiospermum halicacabum* and *Cardiospermum canescens* on paw edema induced by formalin in mice:

The effect of ethanolic extracts of *Cardiospermum halicacabum* and *Cardiospermum canescens* (250 mg/kg and 500 mg/kg)

in formalin induced paw edema in mice was studied and the paw thickness was measured. The study revealed that treatment of mice with both the extracts of *Cardiospermum halicacabum* and *Cardiospermum canescens* (250 mg/kg and 500 mg/kg) showed significant ($P < 0.001$) reduction of paw thickness. Further, the extracts showed dose dependent activity in reducing the paw edema. Moreover, the activity of CC 500 is equipotent to CH 250. The results were detailed in table 6 & Fig. 3.

Table No. 5: Effect of *Cardiospermum halicacabum* and *Cardiospermum canescens* on Cotton pellet induced granuloma in rats

S.No	Treatment	Increase in weight of pellet (mg)	% inhibition
1	Control (CMC)	122.65 $\pm$ 5.75	0
2	Ibuprofen (25 mg/kg)	40.97 $\pm$ 5.00***	66.66
3	<i>Cardiospermum halicacabum</i> (CH250 mg/kg)	87.67 $\pm$ 4.19***	28.40
4	<i>Cardiospermum halicacabum</i> (CH500 mg/kg)	47.33 $\pm$ 5.22***	61.29
5	<i>Cardiospermum canescens</i> (CC250 mg/kg)	95.1 $\pm$ 9.16***	22.31
6	<i>Cardiospermum canescens</i> (CC500 mg/kg)	75.42 $\pm$ 4.45***	38.34

Values are expressed as mean $\pm$ S.D; n=6; *** $P < 0.001$ when compared to control group; One way ANOVA was applied followed by Turkey's multiple comparison test.

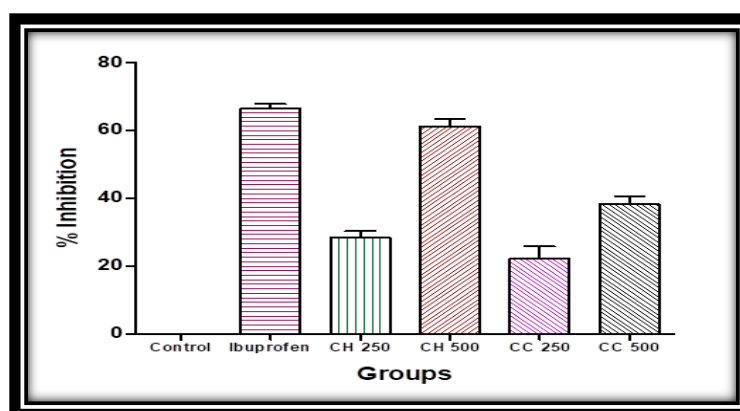


Fig. 2: Effect of *Cardiospermum halicacabum* and *Cardiospermum canescens* on Cotton pellet induced granuloma in rats

Table No. 6: Effect of *Cardiospermum halicacabum* and *Cardiospermum canescens* on paw edema induced by formalin in mice

S.No	Treatment	Edema (mm X 10 ⁻²)
1	Control (CMC)	38.16 $\pm$ 3.71
2	Indomethacin (50 mg/kg)	22.50 $\pm$ 2.50***
3	<i>Cardiospermum halicacabum</i> (CH250 mg/kg)	27.00 $\pm$ 1.78***
4	<i>Cardiospermum halicacabum</i> (CH500 mg/kg)	21.33 $\pm$ 2.80***
5	<i>Cardiospermum canescens</i> (CC250 mg/kg)	31.66 $\pm$ 2.94**
6	<i>Cardiospermum canescens</i> (CC500 mg/kg)	25.5 $\pm$ 1.87***

Values are expressed as mean $\pm$ S.D; n=6; *** $P < 0.001$ when compared to control group; One way ANOVA was applied followed by Dunnet's test.

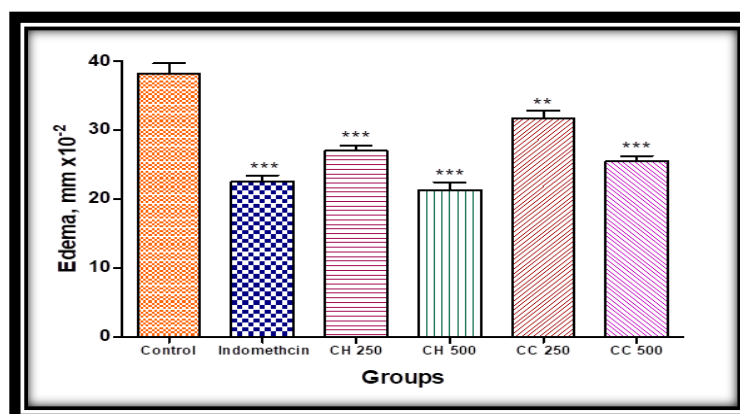


Fig. 3: Effect of *Cardiospermum halicacabum* and *Cardiospermum canescens* on paw edema induced by formalin in mice

DISCUSSION

The investigation on plant based medicine will be a useful strategy in the discovery of new lead molecules eliciting both anti-inflammatory and anti-ulcer activity, which can be used in long term treatment of chronic inflammatory diseases like rheumatoid arthritis with peptic ulcer, as the conventional treatment with synthetic anti-inflammatory drugs (NSIDS) induces gastric ulcers if they are used for chronic inflammatory conditions.

In the search for new anti-inflammatory drugs Carrageenan-induced rat paw edema is the widely used model and in which agents have a significant predictive value by inhibiting the mediators of acute inflammation. After subplantar injection of Carrageenan, in the first 3hr of inflammation shows a biphasic response [12]. A rapid rise in foot volume occurs immediately and followed by a diminution of foot volume occurs at the end of one hour, which has been attributed to the release of prostaglandins and changes in the vascular permeability. The inflammation volume reaches its maximum level in the late phase (approximately by 3 hrs) then it begins to decline.

In the present study, carrageenan induced paw edema treatment with ethanolic extract of *Cardiospermum halicacabum* and *Cardiospermum canescens* at both doses (250 mg/kg and 500 mg/kg) reduced the first phase of edema up to 46% followed by exertion of their maximum anti-inflammatory effect in the late phase. The late phase action of CC 500 extract was evidenced by the marked reduction (72%) in the paw volume by the end of 2nd hour after induction and the effect was continued by the end of the study (5 hrs) up to 83% inhibition of paw volume.

It has been established that the late phase of carrageenan induced paw edema was due to the release of Platelet activating factor, histamine, serotonin, bradykinin, and even over production of prostaglandins [13]. This is also confirmed later by in the experiment that one or more mediators are released by carrageenan-induced paw edema in second phase. This indicates that the possible mechanism of action of the ethanolic extract of *Cardiospermum canescens* as anti-inflammatory agent by acting on late phase mainly by inhibiting the mediators of inflammation, most probably by inhibiting the PAF, which are present in the pro-inflammatory cells like neutrophils and mast cells.

The acetic acid induced writhing assay and increased vascular permeability is a useful model in mouse to evaluate mild analgesic anti-inflammatory drugs. Acetic acid causes algesia and increases the vascular permeability by liberating endogenous substances including serotonin, histamine, PGs, bradykinin and substance P which stimulate pain nerve endings (Collier et al., 1968) [14]. Non-narcotic analgesics could inhibit writhing by interfering with the local reaction to peritoneal irritation and so *Cardiospermum* reduce the intensity of afferent nervous stimulation. In the present study, the intra peritoneal injection of acetic acid caused writhing and an increased in capillary permeability that was measured by direct estimation of Pontamine Sky Blue dye. Treatment with 500 mg/kg of both *Cardiospermum halicacabum* and *Cardiospermum canescens* extracts significantly ($P < 0.001$) reduced leakage of Protamine Sky Blue dye into the peritoneal cavity.

Xylene is a local irritant which induces the neurogenic inflammation by releasing number of potential substances from capsaicin-sensitive sensory neurones such as neuropeptides, substance P to initiate the inflammation PMA (phorbol 12-myristate 13-acetate) is a potent tumour promoter and local irritant. Local application of PMA produces a longer-lasting edema associated with marked influx of neutrophils and mononuclear cells as well as predominant formation of leukotriene B₄ (LTB₄). The release of mediators resulted in the formation of edema and increased vascular permeability [15]. Treatment with hydro alcoholic extracts of *Cardiospermum halicacabum* and *Cardiospermum canescens* at both doses levels (250 mg/kg and 500 mg/kg) significantly ($P < 0.001$) reduced Xylene and PMA induced ear edema in mice. The extracts may be showed anti-inflammatory activity by inhibition of neuropeptides, substance P, and leukotriene B₄ rather than by inhibiting prostaglandins [16]. The extracts were further evaluated by cotton pellet induced granuloma formation to understand their potential use in the chronic inflammatory phase. The cotton pellet-induced granuloma is widely used to assess the transudative and proliferative components of chronic inflammation [17]. Cotton pellet granuloma is the index of proliferative phase of inflammation. Chronic inflammation and proliferation occurs because of cotton pellet (a foreign body) activates the macrophages and neutrophils, which are

modulators of granuloma formation. Therefore, decrease in granuloma weight indicates the suppression of proliferative phase [18]. The results of the present study indicates that 500 mg/kg of both *Cardiospermum halicacabum* and *Cardiospermum canescens* extracts significantly ($P < 0.001$) suppressed granuloma formation induced by cotton pellets. Formalin induced edema in mice is one of the most suitable test procedures to screen Chronic anti-inflammatory agents, as it closely resembles human arthritis (Joseph et al., 2005). Formalin induced edema has been shown to be biphasic and to originate mainly from a neurogenic inflammation followed by participation of kinins and leukocytes with their proinflammatory factors, including prostaglandins to induce the chronic inflammation [19]. Treatment with 500 mg/kg of both *Cardiospermum halicacabum* and *Cardiospermum canescens* extracts significantly ($P < 0.001$) reduced paw thickness whereas 250 mg/kg of both extracts showed lesser effect ($P < 0.01$) in reducing the paw volume. These results suggest that the extracts CHE and CCE inhibited the acute and chronic phase of inflammation in a dose dependent manner.

CONCLUSION

Our study identified the extract exhibited a strong anti-inflammatory activity which was expressed 3 and 6h after the induction of the edema by injection of various induced agents. These results allow us to conclude that 500 mg/kg of both *Cardiospermum halicacabum* and *Cardiospermum canescens* arial parts have potential for the development of new treatment against inflammatory conditions.

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How to cite this article:

K. Sreedevi, J. Venkateswara Rao. EVALUATION OF ACUTE AND CHRONIC ANTI-INFLAMMATORY ACTIVITY IN ETHANOLIC EXTRACT OF AERIAL PARTS OF *CARDIOSPERMUM HALICACABUM* AND *CARDIOSPERMUM CANESCENS* IN ANIMAL MODELS. J Sci Res Pharm 2017;6(12):179-184.

Conflict of interest: The authors have declared that no conflict of interest exists.

Source of support: Nil