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MEMBRANE STABILIZATION, INHIBITION OF 'HISTAMINE AND PROSTAGLANDIN SYNTHESIS' MEDIATED ANTI-INFLAMMATORY RESPONSE OF SOME INDIGENOUS PLANTS

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ABSTRACT: In the present study the anti-inflammatory, analgesic activity and mechanistic pathway of *Centratherum anthelminticum* (Willd.) Kuntze (CA), *Cissus quadrangularis* Linn. (CQ) and *Kigelia pinnata* DC (KP) was tested in rats using carrageenan induced paw edema method. The central analgesic activity was assessed by radiant heat method, hot plate method, and tail immersion method. The peripheral analgesic action was estimated using acetic acid induced writhing test. To establish the mechanism of action of the hydroalcoholic extract, membrane stabilization, antioxidant, antihistaminic, muscle strength, and coordination activity were performed. In anti-inflammatory activity; CA, CQ, and KP showed maximum inhibition of 77%, 70% and 50% respectively. In analgesic activity, CA and CQ treated animals responded propitiously to both central and peripheral analgesia, but KP treated animals demonstrated significant activity only for peripheral analgesia. This can be attributed to membrane stabilization, anti-oxidant, and antihistaminic potential. All the three test drugs have shown both anti-inflammatory activity and analgesic activity with varying potency and mechanisms of action.

INTRODUCTION: Pain and inflammation are two states associated with numerous diseased conditions. Research strives to search for more potent and efficacious alternatives to manage and overcome such conditions like in hemorrhoid, menstrual disorder, wounds, muscular pains, *etc*. Here we have worked on three indigenous plants well known for their therapeutic potential and tried to establish a possible mechanism of action.

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Cissus quadrangularis Linn. (CQ) (Veldt Grape, Winged Treebine, Bone Setter, Hadjod), a climber belonging to family Vitaceae, is one of the most frequently used medicinal plants and can be found throughout the country. The fresh stem and leaves of *C. quadrangularis* are used for the treatment of hemorrhoid [1], menstrual disorder, scurvy, flatulence, fractures, osteoporosis [2], bacterial infections and it also works as an anti-oxidant [3].

In Ayurveda, it is being used for its medicinal uses in gout, syphilis, venereal disease, piles, leucorrhoea, as an aphrodisiac and the Siddha system of medicine for the treatment of piles, diarrhea, and dysentery and diseases of kapham. The plant is credited with iridoids, tetracyclic

triterpenoids [4], lipids [5], flavonoids, stilbene derivatives, and many others, *e.g.*, resveratrol, piceatannol, pallidal parthenocissus *etc*.

The plant *Centratherum anthelminticum* (Willd.) Kuntze (CA) Family Compositae, commonly known as Somraj and its seeds are known as Kalijiri in Hindi, is distributed throughout in India up to 5500ft and is reported to be a medicinally important plant [6]. This species has a wide variety of applications in traditional medicine, especially for the treatment of fever, cough, diarrhoea, general tonic and possess febrifugal, alterative, anthelminthic [7], antiphlegmatic, cardiac, diuretic [8] and digestive properties. The different extracts of the plant have shown antifertility, antimicrobial, anti-filarial and anti-diabetic activities [9]. The plant is credited with flavonoid [10], saponins, steroids [11], carbohydrate and lipids.

Kigelia pinnata DC. (KP) (Syn. Kigelia Africana Benth) belongs to the family Bignoniaceae is a tree growing in the tropics. In folk medicine, the fruits of the plant are used as dressing for ulcers, purgative and to increase the flow of milk in lactating women. The bark is traditionally used as a remedy for syphilis and gonorrhea [12]. Some interesting, diverse biological studies on *K. pinnata* had been reported such as the anti-implantation, molluscicidal [13] and antimicrobial activities. The extracts of the stem-bark and fruit were screened for their cytotoxic activities and showed promising results against melanoma and renal carcinoma while the root-bark showed activity against KB cells. The plant is credited with monoterpenes, naphthoquinones, coumarins [14], iridoids, flavonoids, lignans [15].

MATERIALS AND METHODS:

Animals: Both sex Wistar rats weighing 150-200g, as well as Swiss albino mice weighing 25-35g procured from animal house, KIET School of Pharmacy, Ghaziabad, India, were used. All animals were kept in a room maintained under environmentally controlled conditions of 24 ± 1 °C and 12 h light-12 h dark cycle. The animals had free access to water and food. They were acclimatized at least 1 week before starting the experiments. Experimental protocols were approved by our Institute ethical committee, which follows the guidelines of CPCEA (Committee for control and supervision of experiments on animals).

Plant Material and Extraction: Arial parts CQ were collected from the herbal garden of Banasthali Vidyapith-Deemed University, Jaipur. Seeds of CA and fruits of KP were purchased from the local market of Delhi, India. All the three samples were authenticated by Dr. H.B. Singh, Head, Herbarium and Museum Department, NISCAIR, New Delhi, India.

The drugs were dried at 40-50 ºC and tested for their moisture content, foreign matter. The crude drugs were then defatted by Petroleum ether (40-60 ºC) and extracted using triple maceration process with a mixture of distilled water and ethanol (1:1) at constant temperature and pressure. For all the samples 250g drug was extracted and extracts concentrated at reduced pressure to avoid thermal harm to the constituents and finally freeze-dried to obtain yields as 15.1, 17.2 and 7.5 gm for CA, CQ and KP respectively.

Test Drugs, Drug Dosage and Administration: For test extracts 100 and 250 mg/kg body weight dosage were selected concerning the previous literature. The standard drugs used were different for different test models. All test drugs were suspended in 5% tween 80. They were orally administered using Oro-gastric tube in an equivalent volume of 0.5 ml/100 g body weight of the rats and a volume of 0.05 ml/10 g body weight of the mice. Control groups received vehicle only in the same volume and same route of administration.

Anti-inflammatory Activity:

Carrageenan-Induced Paw Oedema: Sprague-Dawley rats of both sex with a body weight between 150 and 200 g were used. The animals were starved overnight. To ensure uniform hydration, the rats received 5 ml of water by stomach tube (controls) and the test drug suspended in the same volume. Thirty minutes later, the rats were challenged by subcutaneous injection of 0.05 ml of 1% solution of carrageenan into the plantar side of the left hind paw. The paw was marked with ink at the level of the lateral malleolus and immersed in mercury up to this mark. The paw volume was measured plethysmographically

immediately after injection, again at 1, 3 and 5 h, after challenge [16].

Analgesic Activity:

Radiant Heat Method: Groups of 6 mice of both sexes with a weight between 25 and 35 g were used for each dose. Before administration of any compound, the normal reaction time was determined. The animal was put into a small cage with an opening for the tail at the rear wall. The tail was held gently. By the opening of a shutter, a light beam exerting radiant heat was directed to the proximal third of the tail. The mouse tries to pull the tail away and turns the head. With a switch, the shutter was closed as soon as this reaction noticed [17].

Hot Plate Method: Groups of 6 rats of either sex with an initial weight of 150 to 200 g were used for each dose. The hot plate, which was commercially available, consists of an electrically heated surface. The temperature was controlled for 55° to 56 °C. This was a copper plate heated surface. The animals were placed on the hot plate and a stop-watch records the time until either licking or jumping occurs. The latency was recorded before and after 1, 2 and 4 h following oral administration of the standard and the test compound [18].

Tail Immersion Method: Young female Wistar rats (150-200 g body weight) were used. They were placed into individual restraining cages leaving the tail hanging out freely. The animals were allowed to adapt to the cages for 30 min before testing. The lower 5 cm portion of the tail was marked and immersed in a cup of freshly filled water of exactly 55 °C. The withdrawal reaction time was recorded in 0.5 s units by a stopwatch. The reaction time was determined before and periodically after either oral administration of the test substance, *i.e.*, after 0.5, 1, 2 and 4 h [19].

Acetic Acid-Induced Writhing: Mice of either sex with a weight between 25 and 35 g were used. The acetic acid in a concentration of 6% was prepared in distilled water and injected intra-peritoneally. Groups of 6 animals are used for controls and treated mice. The mice were placed individually into glass beakers, and five min was allowed to elapse. The mice were then observed for five min and the numbers of writhes were recorded for each animal [20].

Mechanisms of Anti-Inflammatory & Analgesic Activities:

Membrane Stabilization Activity: The experiment was done using heat-induced hemolysis of rat erythrocytes *in-vitro*. Vials containing 20 µl fresh rat blood in 1 ml of phosphate-buffered saline were treated in triplicate with the extract so that the final concentration of the extract in the vials became 0.25, 0.5, 1.0 and 2 mg/ml. 15 µl of saline was used as the control while indomethacin 0.1 mg/ml was used as the positive reference drug. The vials were then incubated for 15 min at 37 °C followed by 54 °C for 25 min, centrifuged and the absorbance of the supernatant was measured at 540 nm spectrophotometrically. The percent inhibition of hemolysis concerning the control was calculated [21].

Antioxidant Activity: The experiment was carried out using thiobarbituric acid reactive substances assay. The vials containing the reagents were treated in triplicate with the extract so that the final concentrations of the extracts in the vials became 1.25, 2.5 and 5 mg/ml. A 100 µg/ml of butylated hydroxytoluene (BHT) was used as the positive reference, and distilled water was used in control. The vials were mixed well and incubated at 95 °C for 60 min, allowed to cool; 5ml of butanol was added, mixed well and centrifuged at 1500 × g. The absorbance of the butanol layer was measured at 532 nm, and the antioxidant index was calculated as follows [22].

$$\text{Antioxidant index} = (1 - T/C) \times 100$$

Where, T is the absorbance of test and C absorbance of control.

Antihistamine Activity: Rats of either sex (n = 6/ group) of which fur on the posterior lateral side have been shaved 24 h earlier were treated with 250 mg/kg of extracts, 0.67 mg/kg of chlor-pheniramine and 5 ml/kg of water, respectively. After 1h, these rats were subcutaneously injected with 0.05 ml of 200 µg/ml histamine dihydro-chloride into the fur removed area of the skin under mild ether anesthesia and the area of the wheel formed after 1.5 min was calculated [18].

Muscle Strength and Co-ordination: Rats of either sex (n = 6/group) were treated either with 100, 250 mg/kg of extracts or water. One hour later, these rats were subjected to bar holding test

(to evaluate muscle strength) and the latency to fall off was determined [18].

Toxicity Studies: Rats were divided into four groups (n = 6) and administered orally with extracts at a dose level of 0.5, 1.5, 3.0 and 5.0 g/kg b.w in a volume of 1 ml/100 g b.w. Animals were watched carefully for 72 h after drug administration and then for the next 7 days. At the end of this experimental period, the rats were observed for signs of toxicity, morphological behavior, and mortality. Distilled water was given to control group with the same volume orally as that used for the extract for comparison.

Analysis of Data: Data are given as means ± S.E.M. Statistical analyses were done by using Student's t-test, one-way ANOVA followed by Dunnett's test. P<0.05 was considered as significant.

RESULTS:

Anti-Inflammatory Activity:

Carrageenan - Induced Paw Edema: On comparison with the control group, all the plants under study have shown anti-inflammatory activity **Table 1**. Test groups have shown dose-dependent response but reduced edema only up to 3 h & no significant suppression at 5 h. The 250 mg/kg dose of CA have shown response equivalent to that of indomethacin 10 mg/kg. The comparative responses of test drugs are in decreasing order of CA, CQ, and KP. The % inhibition was calculated by the formula

$$\% \text{ inhibition} = \{(\text{Control} - \text{Test}) / \text{Control}\} * 100$$

TABLE 1: EFFECT OF *CENTRATHERUM ANTHELMINTICUM* (CA), *CISSUS QUADRANGULARIS* (CQ) & *KIGELIA PINNATA* (KP) ON CARRAGEENAN (CG) INDUCED PAW OEDEMA OF RATS

Treatment	Oral dose (mg/kg)	Paw volume (ml)			Inhibition (%)		
		1 h	3 h	5 h	1 h	3 h	5 h
CG Control	-	0.54 ± 0.03	0.44 ± 0.02	0.71 ± 0.05	-	-	-
CG + Indomethacin	10	0.11 ± 0.03	0.09 ± 0.02	0.24 ± 0.04	80	78	66
CG + CA	100	0.18 ± 0.07	0.19 ± 0.08	0.35 ± 0.1	65	57	50
CG + CQ	100	0.21± 0.02	0.19 ± 0.08	0.31 ± 0.11	61	55	56
CG + KP	100	0.36 ± 0.05	0.31 ± 0.07	0.48 ± 0.09	33	30	31
CG + CA	250	0.12 ± 0.08	0.12 ± 0.01	0.25 ± 0.03	77	71	65
CG + CQ	250	0.16 ± 0.1	0.14 ± 0.08	0.27 ± 0.01	70	68	61
CG + KP	250	0.28 ± 0.06	0.24 ± 0.06	0.35 ± 0.04	47	44	50

Values are means ± S.E.M. (n=6).
P<0.05 as compared with control are considered significant.

Analgesic Activity:

Radiant Heat Method: In this study, the pentazocine, CA & CQ treated groups have shown a significant and dose-dependent analgesic effect. KP has shown only feeble analgesic activity which was slightly higher with increased dose **Table 2**. Test groups have shown effect only up to 2 h in comparison of standard for up to 4 h.

TABLE 2: EFFECT OF CA, CQ, AND KP ON REACTION TIME AFTER RADIANT HEAT

Treatment	Oral dose (mg/kg)	Time is taken to flick the tail				
		0 hr	30 min	1 h	2 h	4 h
Control	-	3.2 ± 1.2	3.6 ± 1.7	3.7 ± 1.5	4.1 ± 1.1	3.8 ± 1.0
Pentazocine	5	3.5 ± 1.4	9.3 ± 2.1	9.6 ± 2.7	9.7 ± 1.4	8.5 ± 1.1
CA	100	3.3 ± 1.8	6.5 ± 1.3	6.9 ± 1.9	7.0 ± 1.6	5.5 ± 1.8
CQ	100	4.0 ± 2.0	7.1 ± 1.6	7.2 ± 1.0	6.4 ± 1.5	5.1 ± 1.2
KP	100	3.7 ± 1.9	5.5 ± 2.0	5.4 ± 1.4	4.7 ± 1.2	4.5 ± 1.1
CA	250	3.2 ± 1.2	6.9 ± 2.1	7.2 ± 1.9	7.3 ± 1.0	6.0 ± 1.4
CQ	250	3.3 ± 1.0	7.5 ± 2.5	7.9 ± 1.7	6.9 ± 1.2	5.3 ± 1.1
KP	250	3.8 ± 1.1	6.1 ± 1.9	5.9 ± 1.6	5.5 ± 1.8	4.9 ± 1.3

Values are means ± S.E.M. (n=6).
P<0.05 as compared with control are considered significant.

Hot Plate Method: As compared with control, the treatment with indomethacin, CA and CQ produced a significant and dose-dependent increase in reaction time of rats at 1 h after the treatment in hot plate test, showing an analgesic effect **Table 3**. The results produced by KP were comparatively lesser than that of others. However, indomethacin showed an increase in response up to 2 h of treatment.

Tail Immersion Method: As presented in table **Table 4** CA & CQ have shown significant and dose-dependent response to tail immersion test. But like other models, KP did not respond well to the test. The drugs showed a marked increase in reaction time of animals up to 2 h but not much less at 4 h. In comparison, pentazocine showed a potential effect on reaction time.

TABLE 3: EFFECT OF CA, CQ AND KP ON REACTION TIME AFTER EXPOSURE TO HOT PLATE METHOD

Treatment	Oral dose (mg/kg)	Time is taken for paw licking			
		0 h	1 h	2 h	4 h
Control	-	10.4 ± 1.2	10.1 ± 0.8	10.7 ± 1.2	11.1 ± 1.0
Indomethacin	10	9.8 ± 0.9	15.2 ± 0.9	16.7 ± 1.1	15.8 ± 1.2
CA	100	11.2 ± 1.2	15.1 ± 0.6	15.2 ± 1.0	13.5 ± 1.1
CQ	100	10.3 ± 0.4	12.8 ± 0.9	12.4 ± 1.7	11.3 ± 1.2
KP	100	10.1 ± 0.8	11.6 ± 0.5	11.0 ± 0.6	10.8 ± 1.2
CA	250	11.4 ± 1.8	16.2 ± 1.0	16.3 ± 1.9	14.8 ± 0.7
CQ	250	11.6 ± 1.1	17.0 ± 1.3	15.6 ± 1.3	13.9 ± 0.8
KP	250	10.3 ± 1.2	12.3 ± 1.8	11.9 ± 0.5	11.0 ± 1.1

Values are means ± S.E.M. (n=6).
P<0.05 as compared with control are considered significant.

TABLE 4: EFFECT OF CA, CQ AND KP ON REACTION TIME AFTER EXPOSURE TO TAIL IMMERSION METHOD

Treatment	Oral dose (mg/kg)	Tail withdrawal time				
		0 hr	30 min	1 h	2 h	4 h
Control	-	2.1 ± 0.2	2.3 ± 0.2	2.1 ± 0.2	1.8 ± 0.1	1.7 ± 0.2
Pentazocine	5	2.3 ± 0.1	4.1 ± 0.2	3.9 ± 0.2	4.0 ± 0.2	3.2 ± 0.3
CA	100	2.2 ± 0.2	2.4 ± 0.2	2.8 ± 0.3	3.0 ± 0.5	2.9 ± 0.2
CQ	100	1.5 ± 0.3	1.8 ± 0.3	2.0 ± 0.1	2.9 ± 0.1	2.7 ± 0.3
KP	100	2.8 ± 0.2	2.9 ± 0.2	3.0 ± 0.2	3.1 ± 0.3	2.8 ± 0.1
CA	250	1.7 ± 0.1	2.0 ± 0.1	2.5 ± 0.3	3.3 ± 0.2	3.1 ± 0.2
CQ	250	2.5 ± 0.2	2.8 ± 0.2	3.0 ± 0.2	3.1 ± 0.2	2.9 ± 0.3
KP	250	2.4 ± 0.1	2.6 ± 0.3	2.8 ± 0.3	2.7 ± 0.4	2.9 ± 0.2

Values are means ± S.E.M. (n=6).
P<0.05 as compared with control are considered significant.

Acetic Acid Induced Writhing: As shown in the **Table 5** all the three test extracts have shown a marked decrease in the number of writhes. The observations were dose dependent but less than standard drug, indomethacin. Unlike other models, KP also responded well to this test.

TABLE 5: EFFECT OF CA, CQ, AND KP ON ACETIC ACID INDUCED WRITHING

Treatment	No. of writhes after 5 min of drug administration	
	Dose 100 mg/kg	Dose 250 mg/kg
Control	39.2 ± 4.3	
Indomethacin	16.6 ± 5.1	
CA	21.4 ± 5.5	18.2 ± 3.9
CQ	22.6 ± 6.0	17.6 ± 4.5
KP	23.4 ± 3.2	19.8 ± 3.7

*Dosage 10 mg/Kg body weight in case of Indomethacin.
Values are means ± S.E.M. (n=6).
P<0.05 as compared with control are considered significant.

Mechanism of Action:

Membrane Stabilization Activity: As presented in **Table 6**, all three test drugs have shown a marked reduction in hemolysis as compared to control. The reactions were dose dependent up to 2 mg/ml. Interestingly CA at 1 mg/ml shown more response than standard drug, but at 2 mg/ml dose the response was much higher, *i.e.* almost 100% inhibition in hemolysis.

TABLE 6: MEMBRANE STABILIZATION EFFECT OF CA, CQ, AND KP ON HEAT INDUCED HEMOLYSIS

Treatment	Absorbance			
	0.25 mg/ml	0.5 mg/ml	1 mg/ml	2 mg/ml
Control		0.67 ± 0.05		
Indomethacin		0.25 ± 0.02		
CA	0.41 ± 0.01	0.37 ± 0.04	0.21 ± 0.03	0.04 ± 0.02
CQ	0.56 ± 0.07	0.51 ± 0.05	0.42 ± 0.06	0.39 ± 0.05
KP	0.49 ± 0.06	0.41 ± 0.02	0.34 ± 0.03	0.29 ± 0.07

*Dosage 0.1 mg/ml in case of Indomethacin. Values are means ± S.E.M. (n=3).
P<0.05 as compared with control are considered significant.

Anti-Oxidant Activity: The antioxidant effect of KP was higher than that of CA & CQ. All three extracts at various dose showed a clear dose-dependent and significant response **Table 7**. The response of KP at a dose of 1 mg/ml was slightly less than standard drug BHT at 100 µg/ml. The percentage inhibition was calculated using the formula given below.

[1-(Test/Control)] × 100

TABLE 7: ANTI-OXIDANT ACTIVITY OF CA, CQ, AND KP

Treatment	Absorbance		
	0.25 mg/ml	0.5 mg/ml	1 mg/ml
Control		0.68	
BHT		0.31 (53.7%)	
CA	0.56 (16%)	0.53 (20%)	0.47 (29%)
CQ	0.58 (13%)	0.55 (17%)	0.52 (21%)
KP	0.51 (23%)	0.47 (29%)	0.42 (36%)

*Dosage 100 µg/ml in case of BHT. Values are means ± S.E.M. (n=3).
P<0.05 as compared with control are considered significant.

Anti-Histamine Activity: As compared with control, treatment with CA & KP significantly reduced the area of wheel formed on rat skin. But CQ did not respond well to antihistaminic activity **Table 8**. Standard drug chlorpheniramine also significantly reduced the area of wheel.

TABLE 8: ANTIHISTAMINIC ACTIVITY OF CA, CQ AND KP AS INDICATE BY THE AREA OF THE WHEAL

Treatment	Oral dose (mg/kg)	The diameter of wheal after 1.5 min (in mm)
Control	-	12.2 ± 0.9
Chlorpheniramine	0.67	7.5 ± 1.6
CA	250	8.6 ± 1.2
CQ	250	10.7 ± 0.5
KP	250	9.3 ± 0.8

Values are means ± S.E.M. (n=6).
P<0.05 as compared with control are considered significant.

Muscle Strength and Co-ordination: When compared with control, the treatment with CA & KP failed to significantly alter the latency to fall in the bar holding test. Although, CQ showed slight response, it was not much significant as compared with control.

DISCUSSION: Studies suggests that the three test plant extracts, *i.e.* CA, CQ, and KP have dose-dependent activity against inflammation as revealed in the carrageenan-induced paw edema model. In comparison to standard drug indomethacin (78%), CA has shown almost similar

the effect at a dose of 250 mg/kg (71%), while CQ and KP have less effect, *i.e.* 68% and 44% respectively.

Carrageenan-induced edema has been commonly used as an experimental animal model for acute inflammation and is believed to be biphasic. The early phase (1-2 h) of carrageenan model is mainly mediated by histamine, serotonin & increased synthesis of prostaglandins in damaged tissue surroundings. The late phase is sustained by prostaglandin release and mediated by bradykinin, leukotriene, polymorphonuclear cells and prostaglandins produced by tissue macrophages. So the inhibition in 1-2 h by all extracts suggests the involvement of suppression in histamine and inhibition of synthesis of prostaglandins. Flavonoids are already reported in these plants, which are known to inhibit the enzyme prostaglandin synthesis, more significantly the endoperoxide and reported to produce anti-inflammatory response [18, 23].

CA and CQ also responded hot plate method for analgesia very well suggesting suppression of acute pain. However, KP failed to produce a significant effect in this model. CA and CQ have shown a significant and dose-dependent response to the models of both centrally acting analgesics (Tail flick method, tail immersion method and hot plate method) and peripherally acting analgesics (Acetic acid induced writhing). But KP failed to respond to one model of central analgesic. Furthermore, a dose-dependent and significant response to membrane stabilization, antihistaminic and anti-oxidant activity were observed.

The lack of anti-inflammatory activity at the second phase may indicate the short duration of action and increase of leukotriene at second phase caused by the inhibition of prostaglandin synthesis diverts the reaction towards an increase in leukotriene synthesis [24]. This suggests that the response may be due to prostaglandin synthesis inhibition, membrane stabilization, and antioxidant activity. Interestingly, although all extract showed membrane stabilization activity, 2 mg/ml of CA was very promising. A possible explanation for the stabilizing activity could be an increase in the surface area/volume ratio of the cells which could be brought about by an expansion of membrane or shrinkage of the cell and an interaction with a membrane protein. Moreover, it has also been shown that the deformability and the cell volume of erythrocyte are closely related to the intracellular content of calcium. Hence, it may be speculated that the cytoprotective effect in erythrocyte membrane may be due to the ability to extract to alter the influx of calcium into the erythrocyte [21].

The anti-inflammatory response can include influencing the known arachidonate metabolism, inhibiting either certain transcription factors or the production and scavenging of the free radicals produced during the process, and by acting on the cells implicated in the process, such as macrophages and lymphocytes. For this reason, the study of the antioxidant capacity of plant extracts and their potential effects on pro-inflammatory cells has been studied. And test extracts showed a good response to the antioxidant activity. The strong antihistaminic activity supports the use of CA in skin problems for itching. It also has a proven antimicrobial action which further supports its action.

CONCLUSION: With these observations, it is concluded that CA, CQ, and KP have appreciable anti-inflammatory and analgesic activity, which is dose-dependent. CA and CQ have shown analgesic activity in the models of both the central analgesic system and peripheral analgesic system. But KP acts mainly on the peripheral analgesic system. Since all plants have flavonoids in their credit, so antioxidant and membrane stabilization activity plays a vital role for anti-inflammatory and analgesic activity.

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REFERENCES:

1. Bah S, Paulsen BS, Diallo D and Johansen HT: Characterization of cysteine proteases in Malian medicinal plants. Journal of Ethnopharmacology 2006; 107: 189-198.
2. Shirwaikar A, Khan S and Malini S: Antiosteoporotic effect of ethanol extracts of Cissus quadrangularis Linn. on ovariectomized rat. Journal of Ethnopharmacology 2003; 89: 245-250.
3. Luseba D, Elgorashi EE, Ntloedibe DT and Staden JV: Antibacterial, anti-inflammatory and mutagenic effects of some medicinal plants used in South Africa for the treatment of wounds and retained placenta in livestock. South African Journal of Botany 2007; 73: 378-383.

4. Gupta MM and Verma RK: Unsymmetric tetracyclic triterpenoid from *Cissus quadrangularis*. Phytochemistry 1990; 29(1): 336-337.
5. Gupta MM and Verma RK: Lipid constituents of *Cissus quadrangularis*. Phytochemistry 1991; 30(3): 875-878.
6. Bhatia D, Gupta MK, Bharadwaj A, Pathak M, Kathi G and Singh M: Anti-diabetic activity of *Centratherum anthelminticum* kuntze on alloxan induced diabetic rats. Pharmacologyonline 2008; 3: 1-5.
7. H¨ordegen P, Cabaret J, Hertzberg H, Langhans W and Maurer V: *In-vitro* screening of six anthelmintic plant products against larval *Haemonchus contortus* with a modified methyl-thiazolyl-tetrazolium reduction assay. Journal of Ethnopharmacology 2006; 108: 85-89.
8. Koti BC and Purnima A: Diuretic activity of *Centratherum anthelminticum*. International Journal of Green Pharmacy 2008; 2(4): 228-231.
9. Bhatia D, Gupta MK, Gupta A, Singh M and Kaithwas G: Pharmacognostical studies on seeds of *Centratherum anthelminticum* Kuntze. Natural Product Radiance 2008; 7(4): 326-329.
10. Tian G, Zhang U, Zhang T, Yang F and Ito Y: Separation of flavonoids from the seeds of *Vernonia anthelmintica* Willd by high-speed counter-current chromatography. Journal of Chromatography A 2006; 1049: 219-222.
11. Mandal S and Mukhopadhyay B: Concise synthesis of two trisaccharides related to the saponin isolated from *Centratherum anthelmintic*. Tetrahedron 2007; 63: 11363-11370.
12. Saini S, Kaur H, Verma B, Ripudaman and Singh SK: *Kigelia africana* (Lam.) Benth. - An overview. Natural Product Radiance 2009; 8(2): 190-197.
13. Weiss CR, Moideen SVK, Croft SL and Houghton PJ: Activity of extracts and isolated naphthoquinones from *Kigelia pinnata* against *Plasmodium falciparum*. Journal of Natural Products 2000; 63(9): 1306-1309.
14. Govindachari TR, Patankar SJ and Viswanathan N: Isolation of structure of two new dihydroisocoumarins from *Kigelia pinnata*. Phytochemistry 1971; 10: 1603-1606.
15. Inoue K, Inouye H and Chen CC: A naphthoquinone and a lignan from the wood of Kigelia pinnata. Phytochem 1981; 20(9):2271-2276.
16. Amira S, Dade M, Schinella G and Rios JL: Anti-inflammatory, antioxidant, and apoptotic activities of four plant species used in folk medicines in the Mediterranean basin. Pakistan Journal of Pharmaceutical Science 2012; 25(1): 65-72.
17. Vogel HG: Drug discovery and evaluation. Spriger: Berlin, Edition 2nd, 2002.
18. Dharmasiri MG, Jayakody JRAC, Galhena G, Liyanage SSP and Ratnasooriya WD: Anti-inflammatory and analgesic activities of mature fresh leaves of *Vitex negundo*. Journal of Ethnopharmacology 2003; 87: 199-206.
19. Ahmad F, Khan RA and Rasheed S: Study of analgesic and anti-inflammatory activity from plant extracts of *Lactuca scariola* and *Artemisia absinthium*. Journal of Islamic Academic Science 1992; 5(2): 111-114.
20. Chakraborty A, Devi RKB, Rita S, Sharat Chandra K and Singh TI: Preliminary studies on anti-inflammatory and analgesic activities of *Spilanthes acmella* in experimental animal models. Indian Journal of Pharmacology 2004; 36(3): 148-150.
21. Shinde UA, Phadke AS, Nair AM, Mungantiwar AA, Dikshit VJ and Saraf MN: Membrane stabilizing activity - a possible mechanism of action for the anti-inflammatory activity of *Cedrus deodara* wood oil. Fitoterapia 1999; 70: 251-257.
22. Verma N, Khosa RL and Pathak AK: Antioxidant and free radical scavenging activity of fruits of *Ficus bengalensis* Linn. Pharmacologyonline 2008; 3: 206-215.
23. Das S, Haldar PK, Pramanik G and Suresh RB: Evaluation of anti-inflammatory activity of *Clerodendron infortunatum* Linn. extract in rats. Global Journal of Pharmacology 2010; 4(1): 48-50.
24. Shewale VD, Deshmukh TA, Patil LS and Patil VR: Anti-inflammatory activity of *Delonix regia* (Boj. Ex. Hook). Advances in Pharmacological Sciences 2012; 789713: 1-4.

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