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Mechanism of Anti-Inflammatory and Anti-Nociceptive Actions of *Acacia modesta* in Animal Models

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Abstract.- Current study was designed to investigate the *in vivo* analgesic and anti-inflammatory potential of extracts of aerial and underground parts of *Acacia modesta* in mice and rat animal models. Formalin-induced inflammation and carrageenan-induced inflammation models were used for the assessment of anti-inflammatory activity. Chemical induced (acetic acid) and thermal induced (hot plate test & tail immersion test) pain models were used for determination of analgesic activity. The leaf extract at 100 mg/kg significantly ($p<0.05$) inhibited (54.69% and 80.58%) licking response in both phases of formalin test. The stem and bark extract dose dependently suppressed both phases and the significant results were obtained at 500 mg/kg. The leaf and bark extracts significantly ($p<0.05$) inhibited the rat paw edema in carrageenan induced inflammation. The leaf, stem and bark extracts showed significant analgesic activity in thermal induced pain models. All the extracts resulted dose dependent analgesic activity for both phases in chemical induced pain models. The current results from our research support the NSAIDs like pharmacodynamic of the plant extract. Flavonoids and terpenoids present in the extracts may be responsible for this promising activity in the experimental models of inflammation and pain.

Key words: *Acacia modesta*, anti-inflammatory, analgesic, formalin, carrageenan, acetic acid.

INTRODUCTION

Inflammation is a complex patho-physiological response of living tissues to harmful stimuli caused by wounds, infections and environmental and cellular changes. It is a protective strategy of human body to counter inflammatory stimuli by initiating healing process. The body counters external harmful stimuli by activating white blood cells, releasing immune system chemicals like cytokines and generation and release of inflammatory mediators and prostaglandins. Nociception like inflammation is also an integral part of human body defense system and is unpleasant feeling in response to minimize the physical harm. Currently anti-inflammatory and anti-nociceptive drugs are synthetic medicines which are not without side effect. Therefore, scientists seek alternative drugs from medicinal plants. These green pharmaceuticals are believed safer (Ahmed *et al*., 2014, 2015; Zia-Ul-Haq *et al*., 2014a,b).

Acacia modesta locally known as *Phulahi* and *palosa* is a medium sized evergreen tree that are found in hilly regions of Pakistan like Punjab (Jhelum, Salt range) and KPK (Dir, Swat). All parts of the plant are used for medicinal purposes. Preparations of parts of the plant are used in the treatment of bacterial dysentery, skin, eyes infection and other sexual diseases caused by bacteria, toothache, wounds healing, as a sexual tonic, pain killer and restorative. The twigs are used for cleansing the teeth as a tooth brush (Chopra *et al*., 1956; Lewis and Elvin-Lewis 1976). Pharmacological investigations have revealed hypoglycemic potential of the seeds (Singh *et al*., 1975) and analgesic and anti-inflammatory potential of the leaf (Bukhari *et al*., 2010) of *A. modesta*. As part of our studies on animal models to assess the anti-inflammatory activities (Khanra *et al*., 2015; Riaz *et al*., 2013; Zia-Ul-Haq *et al*., 2012, 2013), the current study was undertaken to explore the anti-inflammatory and analgesic potential of extracts from different parts of *A. modesta* using common

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in-vivo experimental models.

MATERIALS AND METHODS

Plant materials and extraction

The leaf, stem, bark and root of *A. modesta* were crushed and soaked individually in methanol (90%) for 15 days with occasional shaking. The macerate was filtered, pooled and evaporated by rotary evaporator (BUCHI Switzerland) at 43 °C under reduced pressure. The resulting crude extracts, thick viscous liquids, were labelled as methanolic extracts of leaves (MAL), stem (MASt), bark (MAB), and root (MAR) and stored in a refrigerator until used in various experimental protocols.

Chemicals and animals

The chemicals used in the experiments include: formalin 37% (Fluka Chemie, Switzerland), carrageenan, acetic acid (St. Louis, MO, USA), diclofenac sodium (Bosch Pharma. Ltd. Karachi) and aspirin (Atco Pharma. Pvt. Ltd. Karachi). Swiss albino mice (25-30 g) and spraug dawly rats (200-250 g) both male and female were purchased from the Dow University animal house and were kept in cages with a 12 h light and dark cycle and free access to water and food.

Anti-inflammatory activity

Formalin test

Mice were divided into six groups (n=5). 20 µl of a 2% formalin solution in saline (0.9%) was injected into the dorsal hind paw of each individual and immediately placed in the observation box. After the formalin injection, two different phases, neurogenic phase (0-15 min) and inflammatory phase (15-30 min) of rigorous licking/biting of the hind paw were observed. The two phases were recorded separately to examine the drug effect. Mice were provided with different doses of the extracts (100, 300 and 500 mg/kg oral administration), aspirin (300 mg/kg oral administration) or diclofenac sodium (20 mg/kg intraperitonial administration) 30 min prior to formalin administration. Controlled mice were provided vehicle (saline 10 ml/kg). The mean number of licks and bites on the injected paw of each animal was recorded and considered as indicative of nociception (Hunskaar and Hole, 1987). The results of the treated animals were compared with control group and the percent inhibition was calculated.

Rat paw edema assay (Carrageenan test)

Six groups (n=5) of rats were randomly made. The control received vehicle only, 2nd, 3rd and 4th groups were served with crude extracts (100, 300 and 500 mg/kg orally). The fifth and sixth groups were treated with aspirin (300 mg/kg p.o.) and diclofenac sodium (20 mg/kg i.p.) respectively. Freshly prepared suspension (0.05 ml) of 1% (w/v) carrageenan was injected into the sub-plantar area of the right hind paws of the rats. The paw size of the rats was measured hourly by wrapping a cotton thread around the paw and measuring the length of the thread (Hess and Miloning, 1972; Owoyele *et al*., 2004). The percent inhibition of edema was calculated.

Analgesic activity

Acetic acid induced writhing method

Six groups (n=5) of mice were made, control (group 1) extract treated (group 2, 3, and 4) standard drug aspirin (group 5) and diclofenac sodium (group 6). Acetic acid (1%) solution 0.1 ml/10g body weight (b.w.) was administered intraperitoneally (*i.p.*). Writhing movements (consisting of contraction of the abdominal muscles, stretching of hind limbs and periodic arching of the body) were counted for 30 min using a hand tally counter after acetic acid administration (Koster *et al*., 1959). The results were compared with the control and the percent inhibition was calculated.

Hot plate method

Mice were divided into six groups as above and hot plate analgesiometer was used for this test. The extracts and the standard drug were dissolved/suspended in distilled water and orally administered. The control group received saline only (Eddy and Laimbach, 1953; Dharmasiri *et al*., 2003). The latency time (sec) measured for the animal to respond either in the form of jumping or paw licking was noted at time points 0, 30, 60, 120 and 180 min for each group. After observations, animals were returned to their home cages.

Tail immersion or tail flick test

Five groups of mice were randomly made (n=5). The extracts and the standard drug aspirin were administered orally. Hot water (51± 1°C) in a digital water bath was used for this experiment. The time taken by the animals to remove their tails out of the water was recorded in the period 30 min after drug administration.

Statistical analysis

The results expressed as mean±SEM. Student's *t* Test was used for comparison between the experimental and control groups. Multiple groups were analyzed by one way ANOVA followed by Dunnett's T test. $P<0.05$ was considered statistically significant.

RESULTS

Effects on formalin induced inflammation

In the formalin induced inflammation the leaf, stem, bark and root extract of *A. modesta* (100, 300 and 500 mg/kg p.o.) reduced licking response (both phases) in mice (Table I). Leaf at dose 100 mg significantly inhibited (54.69% and 80.58%) licking response in both phases respectively. With increase in dose the anti-inflammatory action of the leaf decreased. Stem and bark extracts showed dose dependent suppression in paw-licking response. Stem extract significantly suppressed both phases at 500 mg/kg while the bark gave significant results for second phase of inflammation. The root extract of the plant although suppressed both phases of inflammation but the prominent inhibition were observed at 300 mg/kg for the second phase and at 500 mg/kg for first phase (neurogenic phase).

Effects on carrageen an induced paw edema

The carrageen an induced inflammatory response (illustrated by increase in paw volume) lasted three hours. The inhibitory action of *A. modesta* leaf, bark, roots and stem extracts against paw edema is described in Table II. The results were measured in mm and the percent inhibition of edema (inflammation) for all extracts (leaf, stem, bark and root) at doses 100, 300 and 500 mg/kg were calculated for 1, 2 and 3 hr time points. The extracts showed dose dependent inhibition of edema. The leaf and bark extract of the plant gave the most significant results. The standard drugs aspirin (300 mg/kg) and diclofenac sodium (20 mg/kg) markedly reduced the edema (26.28%, 38.20%, 62.84%) and (24.57%, 37.26%, 61.26%), respectively.

Effects on acetic acid induced writhes

The peripheral analgesic activities of the leaf, stem, bark and root methanol extracts of *A. modesta* were assessed by acetic acid induced writhing method. The extracts exhibited dose-dependent reduction in the number of writhing movements of the experimental animal, expressed as a percentage. The leaf extract showed significant results (75.3%, 74.28%), (78.76%, 80%) and (80.12%, 85.71%) for both phases at 100, 300 and 500 mg/kg respectively. The stem and root extracts of the plant showed moderate to significant inhibition of nociception at 300 and 500 mg/kg. The bark extract showed significant reduction in writhing movements (55.92%, 61.71%), (63.95%, 75.14%), (73.70%, 77.28%) at 100, 300 and 500 mg/kg doses respectively. Acetyl salicylic acid (standard drug) gave 61.72% and 75.14% inhibition of writhing movements while diclofenac sodium (standard drug) gave 56.66% and 72.42% inhibition for the first and second phases respectively. All the measurements were found to be significant in comparison with control (Table III).

Hot plate test

The analgesic effects of the four plant extracts were evaluated by thermal induced pain model (hot plate test) at three different doses (100, 300 and 500 mg/kg). The dose dependant increase in the latency time observed is presented in Table 5. The leaf and bark extracts produced highly significant results at 300 and 500 mg/kg doses while the stem extract produced significant results at a dosage of 300 mg/kg. The root extract of *A. modesta* gave moderate results at all administered doses. The measurements were found to be significant ($P<0.05$) in comparison with control (Table IV).

Tail flick test

The anti-nociceptive effects of the leaf, stem, bark and root extracts of *A. modesta* was also evaluated by tail immersion test using digital water-bath. White albino mice were orally treated with

Table I.- Assessment of anti-inflammatory activity of *Acacia modesta* on formalin induced inflammation in mice.

Treatment	Dose (Oral)	Mean No. of Licking and biting ±S.E.M		Inhibition (%)	
		1st phase	2nd phase	1st phase	2nd phase
Control (Saline)	10 mL/kg	119.2± 2.88	110.2± 2.58	-	-
MAL	100 mg/kg	54± 1.52*	21.4± 1.29**	54.69*	80.58**
	300 mg/kg	65.8± 1.69	48.2±1.24	44.79	56.26
	500 mg/kg	87.2± 2.70	59.2±1.99	26.84	46.27
MASt	100 mg/kg	93.8± 3.26	102.2± 1.83	21.30	7.44
	300 mg/kg	58.6± 2.02	39.2± 3.62*	51.34	64.42*
	500 mg/kg	41.4± 2.14**	32± 2.03**	65.26**	70.96**
MAB	100 mg/kg	105.2± 1.99	80.6± 2.12	11.74	26.86
	300 mg/kg	97± 1.79	74.6± 1.73	18.62	32.30
	500 mg/kg	72.8± 1.24	35± 1.93**	38.92	68.18**
MAR	100 mg/kg	93± 2.46	70± 1.82	21.97	36.47
	300 mg/kg	61± 1.59	25.4± 1.60**	48.82	76.95**
	500 mg/kg	53.8± 2.38*	59± 3.31	54.86*	46.46
Aspirin	300 mg/kg	45± 1.35	49.2± 0.45	62.24	55.35
Diclofenac sodium	20 mg/kg	65.8± 1.69	41.2± 1.24	44.79	62.61

Mean ± SEM; N = 5; Significance with respect to control: *, Significant results; **, highly significant results.

Table II.- Assessment of anti-inflammatory activity of *Acacia modesta* on carrageenan induced inflammation in rats.

Treatment	Dose (Oral)	Mean diameter of rat paw in mm ± S.E.M			% inhibition		
		1h	2h	3h	1h	2h	3h
Control (Saline)	10mL/kg	17.5±2.67	21.2±3.37	25.3±2.97	-	-	-
MAL	100mg/kg	13.3±1.42	13.5±2.24	12.3±1.24	24.00**	36.32**	51.38*
	300mg/kg	13.0±1.39	12.4±1.23	9.7 ±2.13	25.71**	41.50**	61.66**
	500mg/kg	12.7±1.34	11.1±0.91	9.2 ±2.99	27.42**	47.64**	63.63**
MASt	100mg/kg	15.2±1.32	15.3±1.21	17.1±1.21	13.14	27.83	32.41
	300mg/kg	14.8±1.99	13.9±1.58	16.1±2.99	15.42	34.43*	36.36
	500mg/kg	14.2±2.99	13.3±1.47	13.0±1.09	22.75*	37.26**	48.61
MAB	100mg/kg	13.4±1.99	14.2±1.11	14.1±1.21	23.42*	33.01	44.26
	300mg/kg	13.7±1.12	13.7±1.82	12.0±1.42	21.71	35.37*	52.83*
	500mg/kg	12.8±0.63	11.5±1.32	9.6±1.32	26.9**	45.23**	62.05**
MAR	100mg/kg	15.2±1.13	14.3±1.73	15.0±0.73	13.14	32.54	40.71
	300mg/kg	14.8±1.81	13.8±1.72	14.1±0.73	15.42	34.28	44.26
	500mg/kg	13.6±1.32	14.8±1.18	15.2±1.32	22.28*	29.52	39.92
Aspirin	300mg/kg	12.9±1.35	13.1±0.45	9.4± 0.45	26.28	38.20	62.84
Diclofenac sodium	20mg/kg	13.2±1.31	13.3±1.27	9.8±0.75	24.57	37.26	61.26

Mean ± S.E.M; N = 5; Significance with respect to control: *, Significant results; **, highly significant results.

Table III.- Assessment of analgesic activity of *Acacia modesta* on acetic acid induced writhing in mice.

Treatment	Dose (Oral)	Mean No. of Writhes ± S.E.M		Inhibition (%)	
		1st phase	2nd phase	1st phase	2nd phase
Control (Saline)	10 ml/kg	81± 4.47	70 ± 3.87	-	-
MAL	100 mg/kg	20±1.32**	18±1.24**	75.30**	74.28**
	300 mg/kg	17.2 ±1.39**	14± 0.43**	78.76**	80.00**
	500 mg/kg	16.1 ±1.34**	10 ± 0.89**	80.12**	85.71**
MASt	100 mg/kg	43±1.21	31±1.49	46.91	55.71
	300 mg/kg	36.2±0.48*	23.6±0.79*	55.30*	66.28*
	500 mg/kg	32.3±0.77*	25.9±0.69*	60.12*	63.0*
MAB	100 mg/kg	35.7±0.90**	26.8±2.21	55.92**	61.71
	300 mg/kg	29.2±1.22**	17.4±0.92	63.95**	75.14**
	500 mg/kg	21.3±1.72**	15.9±0.73**	73.70**	77.28**
MAR	100 mg/kg	49.0±1.23	36.3±0.93	39.50	48.14
	300 mg/kg	45.6±1.71**	28.5±1.62	43.70	59.28
	500 mg/kg	40.1±1.38	20.2±1.52*	50.49	71.14**
Aspirin	300 mg/kg	31.6± 1.35	17.2±0.45	61.72	75.14
Diclofenac sodium	20 mg/kg	35.1±2.31	19.3±3.13	56.66	72.42

Mean ± S.E.M; N = 5; Significance with respect to control: *, Significant results; **, highly significant results.

Table IV.- Assessment of analgesic activity of *Acacia modesta* on hot plate model in mice.

Variation flicking time with ± SEM (Time in sec at 55 ± 1ºC)						
Treatment	Dose (Oral)	Latency time (s)				
		0 h	0.5 h	1st h	2nd h	3rd h
Control (Saline)	10ml/kg	6.3± 0.12	6.8±0.13	7.0±0.09	7.1±0.12	6.7±0.14
MAL	100 mg/kg	8.5±0.12	12.1±0.12*	14.2±0.11	18.1±0.13**	16.0±0.12*
	300 mg/kg	8.4±0.10	12.0±0.07*	15.0±0.13*	17.8±0.10**	15.9±0.11*
	500 mg/kg	8.6±0.12	11.0±0.11	15.3±0.14*	18.3±0.11**	16.5±0.10**
MASt	100 mg/kg	7.8±0.11	9.7±0.12	13.6±0.12	16.9±0.12	15.6±0.13
	300 mg/kg	8.0±0.13	10.0±0.10	15.1±0.09*	17.3±0.12*	16.3±0.12*
	500 mg/kg	7.9±0.11	9.9±0.13	14.0±0.12	17.6±0.11*	15.2±0.10
MAB	100 mg/kg	8.7±0.10	11.0±0.13	15.3±0.11*	17.8±0.13**	17.0±0.12**
	300 mg/kg	8.3±0.13	13.0±0.11**	16.2±0.13**	18.7±0.12**	16.8±0.12**
	500 mg/kg	8.9±0.09	12.0±0.12*	15.8±0.13**	18.3±0.10*	16.9±0.11**
MAR	100 mg/kg	8.1±0.12	10.3±0.09	12.6±0.14	15.1±0.14	14.6±0.09
	300 mg/kg	8.5±0.13	11.0±0.13	13.0±0.12	15.6±0.13	15.0±0.12
	500 mg/kg	8.3±0.08	9.9±0.11	11.9±0.11	14.8±0.12	14.2±0.13
Aspirin	300 mg/kg	8.3±0.12	13.0±0.11	16.1±0.14	19.1±0.15	17.0±0.14

Mean ± S.E.M; N = 5; Significance with respect to control: *, Significant results; **, highly significant results.

Table V.- Assessment of analgesic activity by tail flick model in mice.

Treatment	Dose (Oral)	Variation flicking time with ± SEM (Time in sec at 51 ± 1ºC)						
		0h	0.5h	1.0h	1.5h	2.0h	2.5h	3.0h
Control (Saline)	10 ml/kg	1.70 ±0.19	1.90 ±0.17	1.70±0.08	1.07 ±0.17	1.63 ±0.11	1.30 ±0.11	1.20 ±0.16
MAL	100 mg/kg	1.01 ±0.11	3.80 ±0.17	4.30±0.23**	3.40±0.15*	4.84±0.13*	4.70±0.21*	3.02 ±0.17
	300 mg/kg	1.00 ±0.23	3.70 ±0.13	3.82±0.17**	4.00±0.12**	3.21±0.23	4.40 ±0.31	3.20 ±0.22
	500 mg/kg	1.17 ±0.12	4.21±0.33*	4.71±0.22**	5.20±0.23**	6.20±0.19**	6.42±0.20**	5.11±0.11**
MASt	100 mg/kg	1.04 ±0.15	3.61 ±0.14	3.21 ±0.16	3.42 ±0.15*	3.45 ±0.23	3.83 ±0.12	2.85 ±0.10
	300 mg/kg	1.07 ±0.13	2.99 ±0.18	3.45±0.26*	2.70 ±0.20	4.07±0.10*	3.99 ±0.26	3.38 ±0.21
	500 mg/kg	1.05 ±0.12	3.80 ±0.14	3.11 ±0.17	3.46 ±0.14*	4.19±0.19*	3.99 ±0.21	2.89 ±0.20
MAB	100 mg/kg	1.05 ±0.11	3.30 ±0.22	3.99±0.19**	3.27 ±0.24	3.49±0.25	4.14±0.15*	3.78±0.18*
	300 mg/kg	1.12 ±0.20	4.28±0.27*	3.81±0.33**	4.12±0.35**	4.71±0.15*	5.20±0.33**	4.03±0.11**
	500 mg/kg	1.24 ±0.17	4.21±0.28*	4.08±0.22**	5.16±0.11**	5.22±0.19*	6.18±0.13**	5.30±0.23**
MAR	100 mg/kg	1.2 ±0.33	2.25 ±0.10	2.97±0.12	3.18 ±0.21	3.77±0.20	3.98±0.19	3.70±0.13*
	300 mg/kg	1.37 ±0.19	2.42 ±0.25	2.74±0.20	3.90±0.31**	3.82 ±0.32	3.95±0.23	3.34 ±0.24
	500 mg/kg	1.13 ±0.26	3.21 ±0.21	3.39±0.20*	3.76±0.31**	4.25±0.39*	4.62±0.15*	3.30 ±0.24
Aspirin	300 mg/kg	1.00 ±0.05	4.81±0.24*	3.85±0.24*	3.67±0.13*	5.62±0.35*	5.40±0.13**	3.84±0.24*

Mean ± S.E.M; N = 5; Significance with respect to control: *, Significant results; **, highly significant result.

crude extracts 30 min prior to the experiment. Experimental animals displayed a dose dependent latency response in the tail immersion test. The leaf and bark extracts showed highly significant results, while the stem and root extracts exhibited moderate results. Aspirin (standard drug) was used in this protocol (Table V).

DISCUSSION

In formalin-induced inflammation two different phases are involved: neurogenic phase (first phase), in which formalin stimulate the nerve fibers and produce pain and inflammatory phase (second phase), in which inflammatory mediators (histamine, serotonin, prostaglandin and bradykinin) causes pain, are involved (Hunskaar and Hole, 1987; Murray *et al*., 1988). The leaf extract exhibited a striking reduction in both phases and was even superior to the standard drug during the second phase. The stem and bark extracts of *A. modesta* caused dose-dependent reductions in both phases and significant reduction was observed at higher dose. The root extracts of *A. modesta* also showed dose-dependent anti-inflammatory action in both phases of formalin induced inflammation, with the most promising results at 300 and 500 mg/kg doses (Table I). The literature indicates that centrally acting analgesics (opoids) inhibit both phases of inflammation evenly, while NSAIDs inhibit, formalin-induced nociception in the late phase (Shibata *et al*., 1989; Santos *et al*., 1994). The plant extracts exhibited inhibition during both phases indicates the involvement of a central mechanism. Some other species of *Acacia* (*ferruginea* and *nilotica)*, have already been reported to have central mechanism of action (Almeida *et al*., 2001; Dhar *et al*., 1968). The anti-inflammatory effect of *A. modesta* (all extracts) was, however, predominantly observed in the late phase of the test suggesting potent peripheral action.

Based on the traditional application of *Acacia* preparations in the management of inflammatory conditions, the anti-inflammatory potential of the leaf, stem, bark and root extracts of *A. modesta* was also appraised through rat paw edema (carrageenan-induced edema) model (Table II). The leaf and bark extracts showed a marked reduction in paw edema of the experimental model, similar to that observed with the reference drugs. The carrageenan-induced edema is supposed to be bi-phasic, the first phase (early phase) which is mediated by serotonin and histamine (edema production) and the secondary (late phase) in which bradykinin and prostaglandins maintain the vascular permeability (Burch and DeHaas, 1990; Di Rosa *et al*., 1971). In this study,

the late phase of paw edema was predominantly inhibited by all extracts of *A. modesta* demonstrating that the anti-inflammatory action is because of the suppression/inhibition of prostaglandin's activity. It is known that NSAIDs have a clear mechanism whereby the synthesis of prostaglandin is inhibited, thus reducing inflammation and swelling (Skoutakis *et al*., 1988). Compounds that inhibit carrageenan-induced edema also can inhibit the cyclooxygenase enzyme (Selvam and Jachak, 2004). With regards to these reports, we infer that the anti-inflammatory action of *Acacia* extracts on (carrageenan-induced) inflammation during the late phase may be possibly mediated via these mechanisms.

To evaluate analgesic activity, the widely used chemical (acetic acid) and thermal-induced pain models (hot plate and tail flick/immersion test) were employed. Acetic acid is commonly used to evaluate peripheral analgesics because it increases the level of mediators (histamine, serotonin and prostaglandins) in peritoneal fluids that produces nociception (Collier *et al*., 1968; Deraedt *et al*., 1980). In the current research, the leaf, stem, bark and root extracts inhibited acetic acid induced writhes in both phases of experimental mice, similar to the activity of standard drugs signifying that the anti-nociceptive action of the extracts might be due to reticence of the prostaglandin role (Ferreira, 1972). The significant pain reduction due to administration of extracts might be related to the interaction of extract constituents with enzymes acting in the prostaglandin pathways. Peripherally acting drugs are assumed to alleviate pain by inhibiting cyclo-oxygenase in the arachidonic acid pathway (Levine and Taiwo, 1994). The experiential analgesic effect of the extracts in the chemical (acetic acid) induced pain model suggests that constituents have NSAID like activity. Some species of genus *Acacia* like *A. nilotica* and *A. ferruginea* are reported to, have central pain inhibition activity (Almeida *et al*., 2001; Dhar *et al*., 1968). The central analgesic activity of *A. modesta* was evaluated through the hot plate and tail immersion assays because these tests are considered to be selective for centrally acting drugs. All extracts of *A. modesta* significantly increased the latency time and promising results were observed with the leaf and bark extracts. It is known that any agent that causes prolongation of latency must be acting centrally (Gul *et al*., 2014). Therefore the methanol extracts (*i.e*., individual constituents of these) must also have central activity. The leaf, bark, stem and root extracts of *A. modesta* exhibited both types of pain inhibition. The analgesic effect of the extracts in both chemical (peripheral) and thermal induced (central) pain models suggest that components of these extracts act via central and peripheral mechanisms.

CONCLUSION

The methanol extracts of the leaf, stem, bark and roots of *A. modesta* possess anti-inflammatory and analgesic properties. The current investigations from our research support the NSAIDs like effects of the plant. The present study on *A. modesta* indicates a new natural source to be explored for the development of novel anti-inflammatory and analgesic drugs. Furthermore, the findings also rationalize folkloric use of *A. modesta* in the management of inflammation and pain.

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