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Anti-Inflammatory and Analgesic Activity of *Jatropha gossypifolia* in Experimental Animal Models

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Abstract: The present study was done to investigate the anti-inflammatory and analgesic effect of methanolic and petroleum ether extracts of *Jatropha gossypifolia* Linn. We have determined the anti-inflammatory and analgesic activity of methanolic and petroleum ether extracts of dried aerial parts of *Jatropha gossypifolia* by oral administration at doses of 100 and 200 mg/kg/day of body weight to healthy animals. The extracts were studied for their anti-inflammatory activity in carrageenan-induced hind paw edema in rats and the paw volume was measured plethysmometrically at 0 and 3 h after injection. The methanolic and petroleum ether extracts were also evaluated for analgesic activity using Eddy's hot plate method and tail-flick method in albino rats. The methanolic and petroleum ether extracts of *Jatropha gossypifolia*, significantly ($P<0.05$) reduced carrageenan-induced paw edema in rats and analgesic activity evidenced by increase in the reaction time by Eddy's hot plate method and tail-flick method in albino mice. The methanolic and petroleum ether extracts showed a greater anti-inflammatory and analgesic effect comparative to the standard drugs, indomethacin and diclofenac sodium respectively. The present results indicated the methanolic extract of *Jatropha gossypifolia* exhibited more significant activity than petroleum ether extract in the treatment of pain and inflammation.

Key words: Anti-inflammatory activity · Methanolic extract · Eddy's hot plate method · Tail-flick method · Analgesic activity · Inflammation · Carrageenan-induced paw edema

INTRODUCTION

Inflammation or phlogosis is a pathophysiological response of living tissue to injuries that leads to the local accumulation of plasmatic fluid and blood cells. Although it is a defense mechanism, the complex events and mediators involved in the inflammatory reaction can be induced, maintain or aggravate many diseases [1]. However, studies have been continuing on inflammatory diseases and the side effects of the currently available anti-inflammatory drugs pose a major problem during their clinical use [2]. Therefore, development of newer and more powerful anti-inflammatory drugs with lesser side effects is necessary.

The plant *Jatropha gossypifolia* (family: *Euphorbiaceae*) is a bushy gregarious shrub, grows wildly almost throughout India. It possesses significant anticancer, hepatoprotective and pesticidal activity [3-5]. The leaf decoction of *Jatropha gossypifolia* is used for bathing wounds. The stem sap stops bleeding and itching of cuts and scratches [6-8]. The roots are employed against leprosy, as an antidote for snakebite and in urinary complaints. A decoction of the bark is used as an emmenagogue and leaves for stomachache, venereal disease and as blood purifier [9-10]. Two triterpenoids have been isolated from leaves of *Jatropha gossypifolia* Linn. [11]. Three known flavonoids, vitexin, isovitexin and apigenin isolated from leaves of *Jatropha gossypifolia* Linn. [12]. Another flavonoid which produced apigenin with 7% sulphuric acid was not characterised due to poor yield. This is the second instance of occurrence of flavonoid-C-glycoside in *Euphorbiaceae*, the first one being in *Croton zambezicus* [13]. The bark contains the alkaloid "jatrophine" and a lignan "jatrodien" is found in its stems [14-15]. The latex of *Jatropha gossypifolia* yielded two cyclic octapeptides i.e. cyclogossine A and B. The aerial parts contain a new lignan, gossypiline [8, 16-18].

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MATERIALS AND METHODS

Indomethacin, Micro Labs, Bangalore; Carrageenan, Sigma Chemicals; USA and Diclofenac sodium, Apex Labs, Chennai; were used in the experiment. All other chemicals were used of analytical grade.

Plant Materials: Aerial parts of *Jatropha gossypifolia* Linn. were collected in the month of November from Pharmacognosy garden of Department of Pharmaceutical Sciences, Utkal University, Bhubaneswar, Orissa, India. The plant was identified with the help of available literature and authenticated by Regional Research Laboratory, Bhubaneswar. The plants were dried in shade for 15 days and then the aerial parts of the plants were taken for the study.

Preparation of Extracts: Powdered aerial parts (500 g) were packed in soxhlet apparatus. The drug was defatted with petroleum ether (60-80°C) for about 30-35 complete cycles. Defatted material was extracted with two liters of petroleum ether by soxhlet apparatus and then extracted material successively extracted with methanol and finally maceration at room temperature, then these extracts was dried by rotary vaccum dryer. The percent yield of petroleum ether extract and methanolic extract were 4.2% w/w and 5.6% w/w, respectively.

Toxicity Studies: The extracts were given at the dose of 100 and 200 mg/kg/day of body weight per day were selected range from 1/6 to 1/15 of LD_{50} based on the preliminary study conducted at our laboratory and data are not shown in this paper.

Animal: Wister albino rats (120-200 g) and swiss albino mice (20-30 g) of either sex were used. The animals housed under standard laboratory conditions maintained at 25±1°C and under 12 / 12 h light /dark cycle and fed with standard pellet diet (Gold Mohur brand, Lipton India Ltd.) and water *ad libitum*. Animal experiments were approved by the Institutional Animal Ethical Committee for the purpose of Control and Supervision of Experiments on Animals (CPCSEA), constituted under the directives of Ministry of Social Justice and Empowerment, Government of India [Reg. No (678 / 02 / a / CPCSEA)].

Determination of Anti-Inflammatory Activity: The albino rats of either sex were divided into six groups of six animals each. Group I received 0.2 ml of 2% w/v carboxy methyl cellulose suspension orally for 7 days as a control group, Group II received 100 mg/kg body weight of methanolic extract of *Jatropha gossypifolia* (MEJG-I) orally for 7 days, Group III received 200 mg/kg body weight of methanolic extract of *Jatropha gossypifolia* (MEJG-II) orally for 7 days, Group IV received 100 mg/kg body weight of petroleum ether extract of *Jatropha gossypifolia* (PEEJG-I) orally for 7 days, Group V received 200 mg/kg body weight of petroleum ether extract of *Jatropha gossypifolia* (PEEJG-II) orally for 7 days and Group VI received 10 mg/kg of body weight of indomethacin intraperitoneally for 7 days as a standard drug. Acute inflammation was induced in all groups by injecting 0.1 ml of 1% w/v carrageenan into the sub-plantar region of the right hind paw of rats. On 7th day, paw volume was measured 1 h prior to carrageenan injection using plethysmometer and at 0 and 3 h after the carrageenan injection [19]. Mean increase in the paw volume was measured and percent inhibition was calculated (Table 1).

Table 1: Effect of *Jatropha gossypifolia* on Carrageenan-induced Paw Edema

		Mean Paw Volume in ml						
	Dose							Percent
Treatment	(mg/kg)	0 min.	15 min.	30 min.	60 min.	120 min.	180 min	Inhibition
Control	2% CMC	0.79±0.03	1.08±0.11	1.35±0.15	1.72±0.11	1.80±0.11	1.51±0.03	---
MEJG-I	100	0.81±0.10	1.20±0.17	1.44±0.13	1.38±0.17	0.86±0.15	[a]0.74±0.21	50.99
MEJG-II	200	0.76±0.11	0.86±0.14	0.94±0.11	0.85±0.15	0.70±0.14	[a]0.54±0.14	64.24
PEEJG-I	100	0.80±0.12	1.14±0.12	1.32±0.14	1.65±0.14	1.62±0.13	[a]1.44±0.18	04.63
PEEJG-II	200	0.77±0.14	1.18±0.17	1.44±0.17	1.61±0.11	1.49±0.11	[a]1.40±0.11	07.28
Indomethacin	10	0.75±0.09	0.82±0.12	0.88±0.11	0.77±0.15	0.58±0.16	[a]0.31±0.05	79.47

n= 6, Values are expressed as Mean ± SEM, [a]$P < 0.05$ When compared with control group

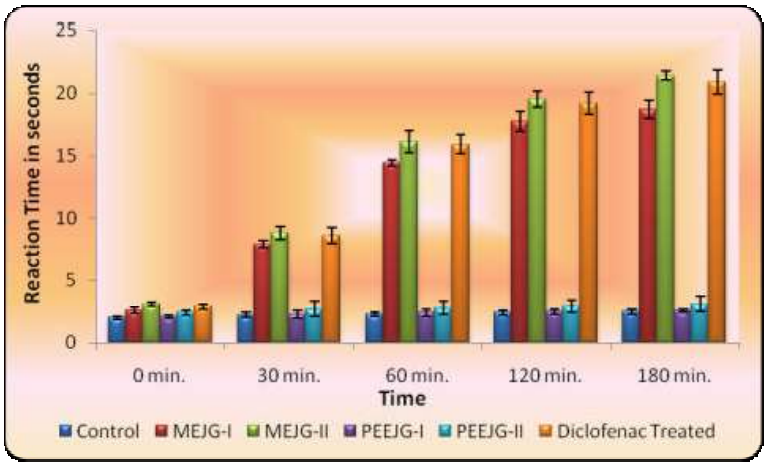

Fig. 1: Analgesic activity of *Jatropha gossypifolia* by tail-flick method. n= 6, Values are expressed as Mean ± SEM, $P < 0.05$ When compared with control group

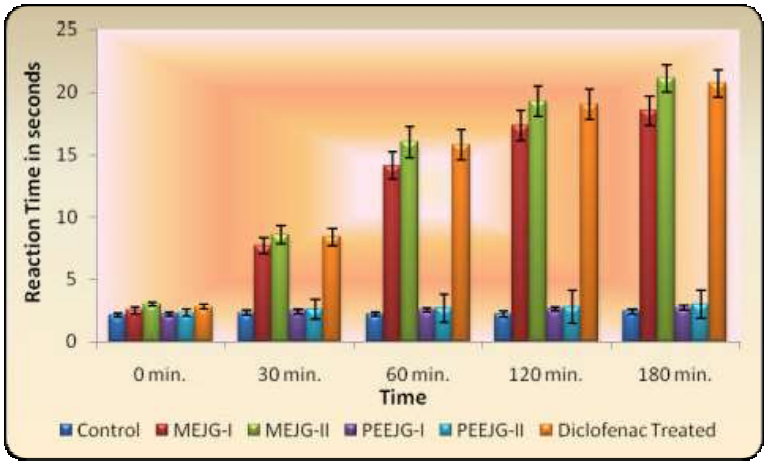

Fig. 2: Analgesic activity of *Jatropha gossypifolia* by Eddy's hot plate method. n= 6, Values are expressed as Mean ± SEM, $P < 0.05$ When compared with control group

Percentage of inhibition = 100 (1-Vt / Vc)

Where,
Vc= Edema volume in control
Vt= Edema volume in test / standard compound.

Determination of Analgesic Activity: *Analgesic activity by tail flick method:* The albino mice were divided into six groups of six animals each. Group I received 0.2 ml of 2% w/v carboxy methyl cellulose suspension orally for 7 days as a control group, Group II received 100 mg/kg body weight of methanolic extract of *Jatropha gossypifolia* orally for 7 days, Group III received 200 mg/kg body weight of methanolic extract of *Jatropha gossypifolia* orally for 7 days, Group IV received 100 mg/kg body weight of petroleum ether extract of *Jatropha gossypifolia* orally for 7 days, Group V received 200 mg/kg body weight of petroleum ether extract of *Jatropha gossypifolia* orally for 7 days and Group VI received 1 mg/kg of body weight of diclofenac sodium intraperitoneally for 7 days as a standard drug. The reaction time was recorded using tail flick analgesiometer at 0, 30, 60, 120 and 180 minutes time interval after the drug administration [20]. The temperature was maintained at 50-55°C and data are represented in Fig. 1.

Analgesic Activity by Eddy's Hot Plate Method: The method as described by Turner, 1965 was adopted [20]. Mice were divided into six groups of six animals each and drug treatments were given as per tail-flick method. Animals were placed on the Eddy's hot plate maintained at 55±1°C. The reaction time in control and treated animals

was recorded at 0, 30, 60, 120 and 180 minutes after the treatment and data are represented in Fig. 2.

Statistical Analysis: Results were expressed as Mean±SEM, statistical significance was calculated by applying *t- test*. P<0.05 was considered as significant.

RESULTS

In the present study, carrageenan-induced Paw edema method shows the result given in Table 1. Methanolic extract of *Jatropha gossypifolia* at 100 mg/kg body weight per day (MEJG-I) when given orally as a suspension the paw volume were reduced by 50.99% whereas in case of methanolic extract of *Jatropha gossypifolia* at 200 mg/kg body weight per day (MEJG-II) shows 64.24% inhibition after 3 h which indicate that effect of methanolic extract of *Jatropha gossypifolia* is reflect in dose dependent manner. Both MEJG-I and MEJG-II showed inhibitory effect on carrageenan-induced paw edema thus, exhibiting anti-inflammatory effect against acute inflammation.

In case of petroleum ether extract of *Jatropha gossypifolia* at 100 mg/kg body weight per day (PEEJG-I) reduced the paw volume 04.63% and petroleum ether extract of *Jatropha gossypifolia* at 200 mg/kg body weight per day (PEEJG-II) exhibited 07.28% reduction in paw volume after 3 hr so petroleum ether extract of *Jatropha gossypifolia* don't possess significant anti-inflammatory activity when compared with control and Indomethacin treated animals (Table 1). It may be due to absence of flavonoid in the petroleum ether extract.

For the determination of analgesic activity, we used two methods i.e. tail-flick method and Eddy's hot plate method. Figure 1 and 2 shows; the analgesic activity profile of MEJG-I and MEJG-II showed significant (P<0.05) analgesic activity when compared with control as well as standard drug but in case of PEEJG-I and PEEJG-II don't exhibit significant analgesic activity when compared with control and Diclofenac treated animals. Thus MEJG-I and MEJG-II extracts exhibited marked central analgesic effect as evidenced by significant increase in reaction time when compared to the control.

DISCUSSION

Inflammation has different phases the first phase is caused by an increase in vascular permeability, the second one by infiltrate of leucocytes and the third one by granuloma formation. We determined anti-inflammatory activity by using inhibition of carrageenan-induced inflammation which is one of the most feasible methods to screen anti-inflammatory agents. The development of carrageenan-induced edema is bi-phasic; the first phase is attributed to the release of histamine, serotonin and kinins and the second phase is related to the release of prostaglandins and bradykinins [21-25]. We observed that MEJG-I and MEJG-II showed significant inhibition against carrageenan-induced paw edema in the dose dependent manner but in case of PEEJG-I and PEEJG-II failed to possess anti-inflammatory effect may be due to absence of flavonoid in the petroleum ether extract. This response tendency of the extract in carrageenan-induced paw edema revealed good peripheral anti-inflammatory properties of the methanolic extract. This anti-inflammatory effect of MEJG-I and MEJG-II may be due to the presence of flavonoids. It has been reported that a number of flavonoids possess anti-inflammatory [26] and analgesic [27] activities. Flavonoids are known to inhibit the enzyme prostaglandin synthetase, more specifically the endoperoxidase and reported to produce anti-inflammatory effects [28]. Since, prostaglandins are also involved in the pain perception; inhibition of their synthesis might be the possible reason for the analgesic activity of the methanolic extract. The presence of flavonoid identified might be responsible for the analgesic and anti-inflammatory activities in methanolic extract.

Thus, it is concluded that the methanolic extract of aerial parts of *Jatropha gossypifolia* produces significant analgesic and anti-inflammatory activities in dose dependent manner.

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