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Analgesic and anti-inflammatory activity of methanol extract of *Xanthosoma sagittifolium*

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Abstract
Xanthosoma sagittifolium is widely used in the folkloric treatment system of Bangladesh for the treatment of different diseases. The present study was conducted to evaluate the analgesic and anti-inflammatory potentiality of methanol extract of *Xanthosoma sagittifolium* in mice. Analgesic activity was evaluated by tail emersion and acetic acid induced writhing method whereas anti-inflammatory activity was investigated by Carrageenan induced mice paw edema method**.** Our study explored that the analgesic activity followed upward for Diclofenac-Na during the observation within 120 minutes and fall down within 180 minutes range. Likely, the methanolic plant extract at different concentrations showed upward movement and fallen down when it reached at 180 minutes. Comparing to standard drug, the plant extract at 200 mg/kg body weight concentration performed better analgesic activity. The tail emersion method showed that the highest analgesic activity (8.25 ± 0.96) was found after 120 minutes at 200 µg/ml extract. On the other hand, the acetic acid induced writhing method explored that plant extract at a dose of 200 µg/ml produce significant pain inhibition (84.48%). Carrageenan induced mice paw edema method showed that highest % of inhibition (74.77%) was found at a dose of 200µg/ml extract after 120 minutes of time period. Our results show that *X. Sagittifolium* has considerable analgesic and antioxidant activity. So, further research can be performed here to find out the responsible active compounds and to identify the mechanism of actions.

Keywords: Analgesic activity, anti-inflammatory activity, Xanthosoma sagittifolium

1. Introduction
An objectionable sensory and poignant feeling, related with actual or potential damage of tissue is termed as pain [1]. Pain intends to injury and the outcome is the attention in removing pain from the injured part. Stimuli for example mechanical, electrical, thermal, chemical initiates pain sensation by receptors of peripheral region. Brain processes the pain stimuli and transmits the impulses towards the spinal cord and appropriate nerve and commands the biological system to perform required action [2]. Inflammation is a body defense reaction of shortening the expandability of injurious substances. It occurs spontaneously in response to tissue injury for living mammalians. Unusual accumulation of fluids under skin or body cavity, leuko-cyte infiltration, and inflammation caused by histiocytes represent such components of inflammation that can associate the tissue injury [3]. Cyclooxygenase (COX) enzymes specially COX2 helps in the synthesis of prostaglandins (PGs) precisely PGE2 and PGF2a, which is found highly at the inflammation site, thus pain and inflammation can be linked by cyclooxygenase (COX) [4]. According to the study of Enomfon and Umoh (2004) high amount of sodium, potassium, phosphorus was found in *Xanthosoma sagittifolium* corm in raw state. Its beneficial for the patient with high blood pressure to intake this as food supplement, as high potassium -sodium ratio may be an additional benefit in their diet [5]. This plant is used as a food supplement in Africa and South Asia. It's also found that the cooked leaf of the plant *X. sagittifolium* has a good calcium content which helps in preventing osteoporosis [6]. Leaf juice consists of expectorant, astringent, and appetizer property. Extracted juice of leaf-stem attaching parts with salt has showed absorbent property towards inflamed glands and swelled part of lymph nodes. Cooked vegetable contains mucilage and found to be an effective nervine tonic, petiole juice of *X. Sagittifolium* is found stypic, and may be used to arrest arterial hemorrhage. To cure diarrhea decocted peel is given as a folk medicine. In asthmatic patients it prevents excessive secretion of sputum, increases body weight. In alopecia, corm juice is used. It is used in increasing bowel movement, to relieve pain by altering sensitivity of nervous system, lactation, piles, demulcent, and congestion of the portal system. As an antidote to the stings of wasps and other insects, its use is also found.

Few Indian tribe people utilize its corm to treat body pain. In ear discharge due to earache and also as stimulant and expand capillaries to increase blood circulation, internal hemorrhages [7]. Earlier reports showed that it has antioxidant property [8]. However, no report about analgesic activity is available, so the aim of our study was to evaluate the analgesic and anti inflammatory activity of *X. sagittifolium*.

2. Materials and Methods

2.1. Preparation of plant materials

The rhizome of *X. sagittifolium* was collected from Bogra city, Bangladesh, in May, 2013, and identified by an expert taxonomist. Rhizome was then washed properly to remove dirty materials and shade dried for several days with occasional sun drying. The fresh sun-dried whole plant material was then dried in an oven at 50 °C and was crushed into coarse powder (500 gm) which was extracted in cold with methanol (1.5 liter) for 7 days. Solvent was evaporated off under reduced pressure in a rotary evaporator to afford a greenish black color mass (8 gm). Powdered plant materials (rhizome) having a weight of about 500 gm were taken in an amber colored reagent bottle and soaked in 1.5 liter of methanol. The bottle with its contents were sealed and kept for a period of about 7 days with occasional shaking and stirring. The whole mixture was then filtered through cotton and then through Whatman No.1 filters paper and was concentrated with a rotary evaporator under reduced pressure at 50 °C temperature to afford crude extract.

2.2. Animals

Fifty Swiss albino mice aged 5-6 weeks, average weight 25-30 gm were used for the experiment. The mice were purchased from the animal laboratory of ICDDR, B. The animals were kept under standard laboratory condition. The temperature was controlled, relative humidity of the room was 70-80%. Care was taken in the food supplements for mice. They were given nutritious foods and for the sake of experiment, the animals were fasted overnight with water provided.

2.3. Study Design

Two types of test were performed: analgesic and anti inflammatory. For analgesic test, mice were assigned into five groups comprising of four mice in each group. Group 1 served as solvent control (1% DMSO) and received the dose of 10 ml/kg body weight, group 2 received Dichlofenac Sodium powder 10 mg/kg body weight and served as a positive control and group 3 to Group 5 received crude methanolic extract, at a dose of 50 mg/kg, 100 mg/kg and 200 mg/kg body weight.

2.4. Analgesic activity

2.4.1. Tail Immersion method

Analgesic activity was evaluated by Chandan Chattopadhyay *et al.* [9] with necessary modification. Group 1 served as solvent control (1% DMSO) and received the dose of 10 ml/kg body weight, group 2 received Dichlofenac Sodium powder 10 mg/kg body weight and served as a positive control group 3 to Group 5 received crud methanolic extract, at a dose of 50 mg/kg, 100 mg/kg and 200 mg/kg body weight respectively by feeding needle. About 5 cm tail of each mouse from the distal end was immersed into the hot water and the reaction time was the time taken by the mice to withdraw its tail from hot water. The observations were made before and after administration of respective drugs at 30 min, 60 min, 90min, and at the end of 120 min.

2.4.2. Writhing method

In this method of Dhirender *et al.* [10], writhing was consistently produced in mice by an intra peritoneal injection of 0.7% aqueous acetic acid. Overnight fasted, healthy adult male albino Swiss mice weighing between 25 to 30 gm in groups of four each were taken for present investigation. Group 1 served as solvent control (1% DMSO) and received the dose of 10 ml/kg body weight; group 2 received Dichlofenac Sodium powder 10 mg/kg body weight and served as a positive control group 3 to Group 5 received crud methanolic extract, at a dose of 50 mg/kg, 100 mg/kg and 200 mg/kg body weight. After of 30 minutes of the administration of the test extracts, all the groups of mice were given the writhing agent, 0.7% aqueous acetic acid, in a dose of 1ml/100gm (b.w) intra-peritonealy. Five minutes after administration of acetic acid the number of writhing produced in these animals were counted for next 10 minutes and the number of writhing produce in the tested groups were compared with those in the control group.

2.5. Anti-inflammatory

2.5.1. Carrageenan induced mice paw edema

Carrageenan induced paw edema was followed as described by Winter *et al* (1962) [11]. For the study purpose, 0.9 gm/100ml of sodium chloride solution was prepared. At zero hour; sodium chloride (Group 1), Indomethacin (Group 2) and test sample (Group 3, 4, 5) were administered orally by a feeding needle. One hour after administration of these agents, edema was induced by injection of 0.1ml carrageenan (1% w/v in saline) into the sub-plantar region of the left hind paw. Paw thickness was measured using a vernier caliper just before and after the injection of carrageenan at 0, 1, 2, 3 hours.

Measurement of paw volume was done by means of volume displacement technique using. Thin thread immediately after carrageenan injection and after 1, 2, 3 hours. Percentages of inhibition were obtained using the following ratio: [(Vt − Vo) control − (Vt − Vo) treated / (Vt − Vo) control] × 100.

Vt is the average volume for each group after treatment, and Vo is the average volume for each group before any treatment.

3. Results

3.1. Analgesic activity

3.1.1 Tail immersion Test (Thermal stimulus)

The result for analgesic activity for methanolic extract of X. Sagittifolium is shown in the Table 1. No significant difference was found with 1% DMSO (control group) through 180 minutes of observation. The withdrawal of tail from hot water was higher for those groups, treated with methanolic extract & diclofenac-Na, compared to the 1% DMSO group. The highest reaction time was for the extract group at 200mg/kg body weight concentration was 08 seconds at 120 minute while it was 4 seconds for 1% DMSO group and 10seconds for Diclofenac-Na group respectively. The analgesic effects of 1% DMSO, Diclofenac-Na and methanolic extract can be found from the maximum available analgesia (MAA) graph.

Table 1: Evaluation of analgesic activity of methanolic extract of rhizomes of *Xanthosoma sagittifolium* by Tail immersion method.

Groups	Treatment	Dose (mg/kg body wt)	Reaction time (in sec) after administration of drugs at different time(minutes) ± SD			
			30	60	120	180
1.	Control (1% DMSO)	10 ml	3.75 ± 1.26	3.50±1.00	4.00 ± 1.41	3.75 ± 0.96
2.	Diclofenac-Na	10	9.50 ± 1.29	10.25 ± 1.71	10.75 ± 1.26	9.75 ± 1.50
3.	Methanolic Extract	50	6.25 ± 1.89	6.75 ± 1.71	7.00 ± 1.63	6.50 ± 0.58
4.		100	6.75 ± 0.96	7.00 ± 0.82	7.50 ± 0.58	7.00 ± 0.82
5.		200	7.50 ± 0.58	7.75 ± 0.50	8.25 ± 0.96	7.00 ± 0.82

The analgesic effect was of Diclofenac-Na was recorded within the 30, 60, 120, 180 minute interval after oral administration. The MAA remained upward for Diclofenac-Na during the observation within 120 minutes fall down within 180 minutes range. Likely, the MAA of plant extract of different concentrations showed upward movement and fallen down when it reached at 180 minutes. Referring to MAA value, the plant extract at 200mg/kg body weight concentration performed stronger analgesic activity. From our result, it is clear that all the methanolic extract of *X. sagittifolium* shows considerable analgesic activity

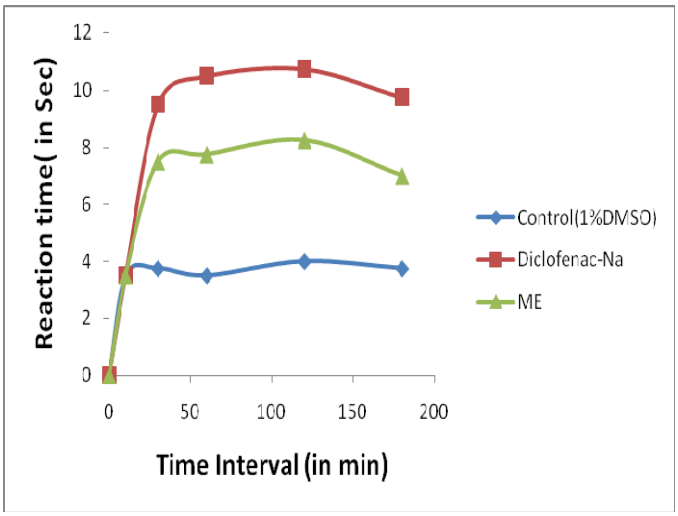

Fig 1: Response time of mice at methanolic extracts of *X. sagittifolium* at different time interval by tell immersion method. Here, ME = Methanolic extract

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3.1.2. Writhing Test (Chemical stimulus)

The control group of animals were given only DMSO 1% solution in the dose of 10ml/kg body weight. One group of animal was administered with Diclofenac-Na standard, orally in a dose of 10mg/kg (b.w). After a gap of 30 minutes of the administration of the test extracts, all the groups of mice were given the writhing agent, 0.7% aqueous acetic acid, in a dose of 1ml/100gm (b.w) intraperitoneally. Five minutes after administration of acetic acid, the number of writhing produced in these animals were counted for next 10 minutes and the number of writhing produce in the tested groups were compared with those in the control group and the percentage protection was calculated as show below.

Percentage protection: [(No. of writhes in control - No. of writhes in test) ÷ No. of writhes in control] x 100

Table 2: Evaluation of analgesic activity of methanolic extract of *X. sagittifolium* by Acetic acid induced Writhing method.

Groups	Treatment	Dose	Avg. no. of Writhing ± SD	%
01	Control (1% DMSO)	10 ml/kg	87.00 ± 0.957	-
02	Diclofenac-Na	10 mg/kg	3.75 ± 0.500	95.68
03	Methanolic Extract	50 mg/kg	17.50 ± 0.577	79.88
		100 mg/kg	15.00 ± 1.250	82.75
		200 mg/kg	13.00 ± 0.57	84.48

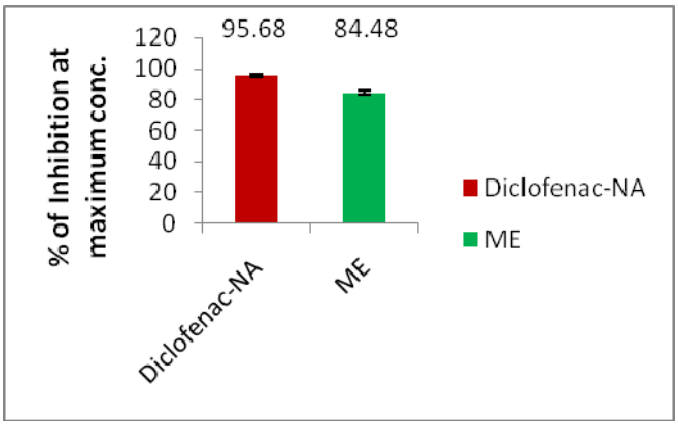

Fig 2: Evalution of analgesic activity of diclofenac-Na and methanolic extract of *X. sagititifolium* by Acetic acid induced Writhing method.

The most potent activity was found in methanolic extract (ME) show % of inhibition (84.84 at 200 µg/ml) after standard (Diclofenac-Na). From our result, it is clear that methanolic extract of *X. sagittifolium* shows considerable analgesic activity.

3.2. Anti-inflammatory Activity

3.2.1 Carrageenan induced mice paw edema

Animals were fasted overnight and were divided into control, standard and different test groups each consisting of four animals. The different test extracts were administrated to the animals in the test groups at the dose of 50,100 and 200 mg/kg by oral route. Animals in the standard group received Indomethacin at the dose of 10 mg/kg, by oral route. Control group animals were received 1% DMSO at the dose of 10ml/kg body weight. Thirty minutes after administration of the respective drugs, all the animals were challenged with 0.1 ml of 1% carrageenan in the sub planter region of left hind paw. Paw volume was measured by using digital plethysmometer before administration of carrageenan and after

30min, 1, 2, and 3 hrs intervals. The efficacy of different drug was tested on its ability to inhibit paw edema as compared to control group.

Volume of edema = Final Paw Volume - Initial Paw Volume

Percentage inhibition of paw edema was calculated by the formula as below.

The% of Inhibition of Paw edema = $[(V_C - V_T)/ V_C] \times 100$

Where, V_C= Paw edema of control group and V_T = Paw edema of treated group.

Table 3: Detarmination of paw volume of Mice at different time for *X. sagittifolum* methanolic extract.

Groups	Treatment	Dose (mg/kg body wt)	Initial paw volume	Paw volume at different time interval (in mm)			
				30 min	60 min	120 min	180 min
1.	Control (1% DMSO)	10	0.90±0.01	1.45±0.01	1.75±0.02	2.01±0.01	1.79±0.11
2.	Indomethacin	10	1.18±0.014	1.27±0.026	1.37±0.035	1.46±1.033	1.34±0.021
3.	Methanolic Extract	50	0.94±0.112	1.24±0.079	1.40±0.008	1.58±0.034	1.48±0.021
4.		100	1.15±0.121	1.43±0.088	1.52±0.094	1.59±0.097	1.51±0.091
5.		200	1.12±0.021	1.30±0.063	1.31±0.059	1.32±0.008	1.36±0.054

From the table we find that, comparing with the indomethacin group (standard) and the groups of plant extract, paw volume rate was notable at 100 mg/kg body weight concentration rather than the other groups.

Table 4: Determination of volume of edema of mice at different time for methanolic extract

Groups	Treatment	Dose (mg/kg body wt)	Volume of edema at different time interval (in mm).			
			30 min	60 min	120 min	180 min
1	Control (1% DMSO)	10 ml/kg	0.55	0.85	1.11	0.89
2	Indomethacin	10	0.09	0.19	0.28	0.16
3	Methanolic Extract	50	0.30	0.46	0.64	0.54
4		100	0.28	0.37	0.44	0.36
5		200	0.18	0.19	0.25	0.24

The table shows volume of edema for indomethacin (control group) and methanolic extracts of different concentrations. Edema volume found decreased in rate for the methanolic extracts rather than the indomethacin, also from the graph we find that the fall of edema volume occurs after 120 minute, when it is 180 minutes, the graph is fallen apart.

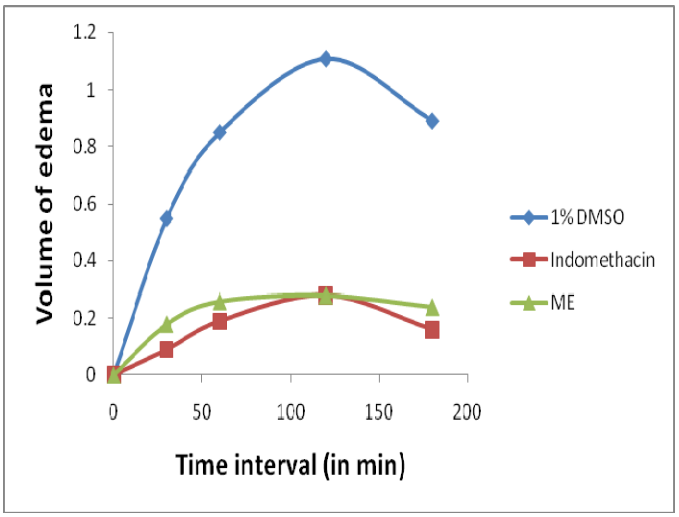

Fig 3: Volume of edema of mice at time interval with 1% DMSO, indomethacin and methanolic extract.

Table 5: Determination of % of inhibition of paw edema of mice at different time for methanolic extract

Groups	Treatment	Dose (mg/kg body wt)	% inhibition of paw edema (mm)			
			30 min	60 min	120 min	180min
1	Indomethacin	10	83.63	77.64	74.77	82.02
2	Methanolic Extract	50	45.45	45.88	42.34	39.32
3		100	49.09	56.47	60.36	59.55
4		200	67.27	69.41	74.77	73.03

The most potent activity was found in methanolic extract (ME). It showed highest % of inhibition (74.77 at 200µg/ml) after standard (Indomethacin) at 120 minutes of time period. From our result, it is clear that methanolic extract of *X. Sagittifolium* shows considerable anti-inflammatory activity.

4. Discussion

In the tail immersion model, methanolic extract of *X. sagittifolium* provided good analgesic activity by increasing the reaction time of mice in comparison with control group. Along with tail immersion, hot plate method is also used in many cases to study centrally acting analgesics [12]. In these models, the nociceptors are sensitized by sensory nerves and the involvement of endogenous substances like prostaglandins are minimized [13]. In high temperature and pressure pain sensation of animals can be increased by analgesic drugs that are centrally acting [14]. Higher concentration gave better effect. Diclofenac sodium was used as reference drug. Comparing with control, diclofenac sodium produced massive analgesic effect under all observation times. High dose of methanolic extract gave similar effect of Diclofenac sodium. The steps involved in the tail immersion test, is based on the follow-up of morphine-like drugs which specifically extends the reaction time of typical tail withdrawal behavior in mice [15].

Acetic acid-induced writhing method induces sensation of pain by initiating inflammatory response and such kind of pain stimulus tends to release arachidonic acid from tissue [16]. Acetic acid induced writhing method is highly useful model for screening analgesic drugs [17]. 0.7% glacial acetic acid intraperitoneal injection produced abdominal writhing. Chemo sensitive nociceptors are activated in animals by acetic acid, which develops writhing effect [18]. It was also found that the level of analgesia produced by acetic acid-induced method is indicated by the decrease of abdominal constriction's percentage number [19]. Acute inflammation is biphasic. First phase starts with the release of few neurotransmitters, and kinins after giving the phlogistic agent injection in the first few hours [20]. Second phase relates to the prostaglandins like substances release within 2-3 hours. Second phase is sensitive to both the clinically useful steroidal and nonsteroidal anti-inflammatory agent [21]. Carrageenan-induced paw edema model has commonly been used to assess the anti edematous effect of the drug. Carrageenan releases inflammatory and pro inflammatory mediators like histamine, bradykinin, prostaglandins, leukotrienes, etc.) [22]. Here, high concentration of methanolic extract provided significant percentage of paw edema inhibition.

5. Conclusion

According to the results of the present study, it can be concluded that the plant extract of *Xanthosoma sagittifolium* possesses potential analgesic anti-inflammatory activity. This finding justifies the use of *Xanthosoma sagittifolium* in folk medicine to treat in pain. However, further chemical studies are required to isolate the bioactive compounds and elucidate the precise molecular mechanisms responsible for the pharmacological activities of the plant.

6. References

1. Fan S, Ali NA, Basri DF. Evaluation of analgesic activity of the methanol extract from the galls of Quercus infectoria (Olivier) in rats. Evidence-Based Complementary and Alternative Medicine 2014; 2014:976764.
2. David Arome, Akpabio Inimfon Sunday, Edith Ijeoma Onalike, Agbafor Amarachi. Pain and inflammation: Management by conventional and herbal therapy. Indian J Pain. 2014; 28(1):5-12.
3. Amdekar S, Roy P, Singh V, Kumar A, Singh R, Sharma P. Anti-Inflammatory Activity of Lactobacillus on Carrageenan-Induced Paw Edema in Male Wistar Rats. International Journal of Inflammation 2012; 2012:752015.
4. Bhowmick R, Sarwar MS, Dewan SM, Das A, Das B, Uddin MM *et al.* In vivo analgesic, antipyretic, and anti-inflammatory potential in Swiss albino mice and in vitro thrombolytic activity of hydroalcoholic extract from Litsea glutinosa leaves. Biol Res 2014; 29:47-56.
5. Njoku PC, Ohia CC. Spectrophometric Estimation Studies of Mineral Nutrient in Three Cocoyam Cultivars. Pakistan Journal of Nutrition. 2007; 6 (6):616-619.
6. de Oliveira GL, Holanda Cavalcanti Andrade Ld, Morais de Oliveira AF. Xanthosoma sagittifolium and Laportea aestuans: species used to prevent osteoporosis in Brazilian traditional medicine. Pharm Biol 2012; 50(7):930-2.
7. Prajapati R, Kalariya M, Umbarkar R, Parmar S, Sheth N. *Colocasia esculenta*: A potent indigenous plant. Int J Nutr Pharmacol Neurol. Dis 2011; 1:90-6
8. Shajeela PS, Kalpanadevi V, Mohan VR. Potential antidiabetic, hypolipidaemic and antioxidant effects of Xanthosoma sagittifolium extract in alloxan induced diabetic rats. Int J Pharm Pharm Sci 2013; 5(1):27-31
9. Chattopadhyay C, Chakrabarti N, Chatterjee M, Chatterjee S, Bhattacharyay D, Ghosh D. Evaluation of acute anti-inflammatory and analgesic activities of green tea decoction on experimental animal models. Int J Nutr Pharmacol Neurol Dis. 2012; 2:20-5.
10. Kaushik D, Kumar A, Kaushik P, Rana AC. Analgesic and anti-inflammatory activity of Pinus roxburghii Sarg. Advances in Pharmacological Sciences 2012; 2012:245431.
11. Winter CA, Risley EA, Nuss GW. Carrageenan-induced oedema in the hind paw of rat as an assay for anti-inflammatory activity. ProcSoc. Exp Biol Ther 1962; 111:544-547.
12. Woolfe G, MacDonald AD. The evaluation of analgesic action pethidine hydrochloride. J Pharmacol Exp Ther 1994; 80:300
13. Bachlav RS, Gulecha VS, Upasani CD. Analgesic and Anti-inflammatory Activity of *Argyreia Speciosa* roots. Indian J Pharmacol 2009; 41(4):158-161.
14. Esam QNAIS. The analgesic effect of the ethanolic extract of Matricaria aurea. Turk J Biol. 2011; 35:347-352
15. Toma WO, Graciosa JS, Hiruma CA, Andrade FDP, Vilegas W, Souza-Brita ARM. Evaluation of the analgesic and anti-edamatogenic activities of *Quassia mara* barks extract. J Ethnopharmacol. 2003; 85:19-23.
16. Lorke D. A new approach to practical acute toxicity. Archives of Toxicology 1983; 53:275-289.
17. Raquibul SM, Hossain, MM, Aktar R, Jamila M, Mazumder MEH, Alam MA, *et al.* Analgesic Activity of the Different Fractions of the Aerial Parts of *Commenila Benghalensis* Linn. International Journal of Pharmacology 2010; 6(1):63-67.
18. Onasanwo SA, Elegbe RA. Antinociceptive and Anti-inflammatory Properties of the leaf Extract of *Hedranthera barteri* in Rats and Mice. African J Biomedical Research. 2006; 2:109-118.
19. Machioro M, Blank MFA, Moura RHV, Antioniolli AR. Antinociceptive Activity of the Aqueous Extract of *Erythrina velutina* leaves. Fitoterapia 2005; 76:637-642.
20. Bhukya B, Anreddy RNR, William CM, Gottumukkala KM. Analgesic and anti-inflammatory activities of leaf extract of Kydia calycina Roxb. Bangladesh Journal of Pharmacology. 2009; 4(2):101-104.
21. Brooks PM, Day RO. Non-steroidal anti-inflammatory drugs differecnce and similarities. New England Journal of Medicine. 1991; 324:1716-1725.
22. Amdekar S, Roy P, Singh V, Kumar A, Singh R, Sharma P. Anti-Inflammatory activity of Lactobacillus on carrageenan-induced paw edema in male Wister rats. International Journal of Inflammation 2012; 2012:752015.