Analgesic activities of crude ethanolic extract and various fractions of *Adansonia digitata* L. grown at the sindh province of Pakistan

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Abstract: The current study aimed to evaluate the analgesic effects of crude extract and fractions of leaves of *Adansonia digitata* L. (Malvaceae). Fresh leaves were collected, dried under shade and then powdered. Moreover, powder was usedto extract with Ethanol and concentrated under reduced pressure, followed by partitioning with organic solvents i.e. Hexane, Ethylacetate, Butanol and Aqueous. These fractions were analyzed for analgesic effect at dose of 50, 100, 200; mg/kg body weight by acetic acid induced writhing, tail flick and hot plate analgesic models. No acute oral toxicity was observed and extracts considered being saved at a dose of 50-3000 mg/kg body weight. Orally administered extract of *A. digitata* showed analgesic activity described by decrease in writhes counts which was contrast to control. Significant ($P<0.05$-0.001) increased in latency period in hot plate analgesic test when compared Diclofenac sodium (50 mg/kg) which is used as a standard drug. Furthermore, in tail flick test a dose of (50, 100, 200mg/kg body weight) of extracts exhibited significant ($P<0.05$-0.001) analgesia which is dose dependent when compared to control group. These findings of analgesic testing have revealed that leaves extract of this nutritional plants possess remarkable antinociceptive effect.

Keywords: *Adansonia digitata* L., Malvaceae, tail flick test, hot plate test, antinociceptive activity.

INTRODUCTION

Nature has blessed our earth with treasure of medicinal plants since man immemorial they served as a potential source of therapeutic agent for treatment and cure of illness. WHO claimed that over 25% of modern medicine derived from traditional herbal medicine. It is estimated that more than 122 diverse phytoconstituents with biological activity are explored. In the developed countries, 25% of pharmacopoeial drugs are plant based while another 25% are modified pro molecule from plant origin. Hence this is a time to investigate the active novel compounds which can be a potential source of medicine in our health care system. (Sen *et al*., 2010; Dippenaara, 2015).

Pain is a natural defensive stimulus which is always unpleasant both mentally and physically associated with potential tissue damage. Many sources like temperature, chemical and electricity etc. has been contributed in pain sensation triggers by noxious stimuli through peripheral receptors at sufficient threshold. Analgesics are directly acting on central nervous system or peripheral nervous system but they never alters person's alertness. Commonly non-steroidal anti-inflammatory drugs (NSAIDS) and opioids are used in acute as well as chronic painful condition. But due to certain serious side effects caused by these drugs their use have not been long lasting in many cases. The effectiveness of herbal medicine as a powerful analgesic has been accepted globally because they confer economic benefits and have little side effects in contrast to traditional NSAIDS which produces some negative effects on body so there is a constant need to explore plant based analgesic compounds which serve to combat emergency painful situations. (Gomase *et al*., 2011; Kumar *et al*., 2015).

Genus Adansonia has variety of remedial plants including *Adansonia digitata* Linn. (Malvaceae) which is dispersed over tropical, sub-tropical and temperate region including Pakistan, India, Mali, Benin, Sudan etc. (Heywood *et al*., 2007).The common vernicular names of plant are Gorakhimli, baobab, and monkey bread tree. It served as a component of many food and beverage although its use is not limited to medicine. (Wickens, 1982). Traditionally, it is used in prevention and cure of many disease like fever, measles, diarrhea, insect bite, fatigue, asthma (Wood, 1969). Several phytochemicals have been isolated from different plant parts including glycosides, sterols, phenol, carbohydrates, vitamins, minerals, lipids etc. (Chauhan *et al*., 1984). Numerous therapeutic and pharmacological effects have been discovered from different anatomical part of plant which are anti-inflammatory, antioxidant, astringent, hypotensive, antiviral, insecticidal, antipyretic and hepatoprotective. (Shukla *et al*., 2001; Caluwe *et al*., 2010).

The study is designed to determine the analgesic effect of *A. digitata* leaves extract with its different fractions and doses which is not published from the region of Sind, Pakistan.

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MATERIAL AND METHODS

Collection of plant material

A.digitata fresh leaves were collected in the month of September from University of Karachi, in 2015.The plant was deposited at herbarium (Voucher specimen no 103) of Department of Pharmocognosy, Faculty of Pharmacy, University of Karachi where the plant sample was identified by Prof. Dr. Ghazala H. Rizwani.

Chemicals

All chemicals were obtained from Merck, Germany. i.e. Absolute Ethanol (EtOH), n-Hexane (n Hex), Ethylacetate (EtoAC), n-Butanol (n-BuOH), Dimethyl sulfoxide, acetic acid. While diclofenac sodium (voren) was purchased from local market.

Preparation of plant extracts

The aerial part of the plant were cleaned with distilled water, dried under shade for 5 days. 10kg of leaves were soaked in EtOH (90%) at room temperature for 8-12 days. The percolate was filtered through Whatmann no.1 filter paper. Then remaining solvent was evaporated by rotary evaporator (Eyela, Japan) at 40^{o}C under reduce pressure. This process was repeated thrice and then combine all three filtrates to obtain crude EtOH extract (550g). The gummy crude extract was first partitioned in equal volume of distilled water and n-Hex by the ratio of 1:1 to get organic n-Hx and Aqueous (Aq) layer followed by EtoAC and n-BuOH. All these organic solvents were evaporated by using rotary evaporator to obtain semi solid masses of n-Hex (30g), EtoAC (45g), n-BuOH (80g) and Aq (90g).A portion of EtOH extract and its fraction were used for acute toxicity and pharmacological activities.

Experimental animals

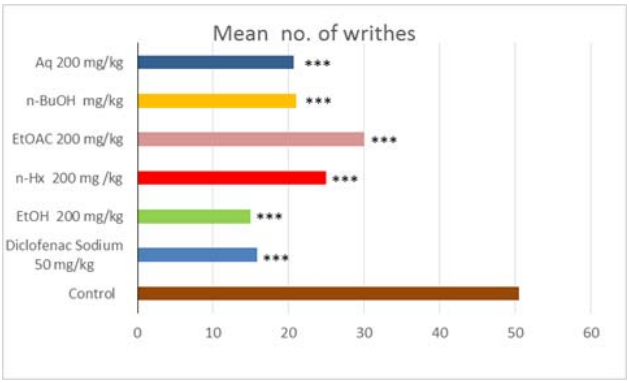
Adult Wistar Albino mice (20-25g) of either sex were bought from animal house of ICCBS, University of Karachi. In the animal house of Department of Pharmacology, University of Karachi animals were retained in well aerated laboratory cages at a temperature of 27±2^{o}C, standard laboratory diet and water were given to the mice and they were kept on dark and light cycles of 12h. These animal studies were conducted according to guide lines of Department of Pharmacology, University of Karachi.

Acute toxicity

Acute toxicity of the crude EtOH extract of leaves were analyzed by divided the twelve animals into control and treated groups. The Normal saline was given to control group while treated group were received different doses of Crude EtOH extract (50, 100, 500, 1000, 2500, 3000 mg/kg body weight p.o). With a gap of 15 min changes in autonomic and behavioral responses were noted up to 4h while sign of mortality and toxicity were assessed up to 7 days. (Zaoui *et al*., 2002).

Acetic acid induced mouse writhing test

For assessment of analgesia acetic acid 0.6% induced intraperitoneally in mice before the administration of extracts .Group I (control group) received saline solution, group II used 50mg/kg diclofenac sodium as positive control while the groups III, IV and V were given with 50, 100 and 200mg/kg of the crude extract (EtOH) respectively. The remaining groups i.e. VI, VII, VIII and IX received 200mg/kg dose of n-Hx, EtoAC, n-BuOH, Aq extract. All the drugs were given orally. The abdominal constrictions examined after 5min of acetic acid injection and observed for the interval of 10 to 15 min. (Koster *et al*., 1959)



Values are expressed as mean ± S.E (n=6). Statistical significance were calculated by ANOVA followed by post hoc test when compare to the control group *P<0.05, ** P<0.01, ***p<0.001.

Fig. 1: Analgesic effect of Leaves extracts by Acetic acid induced abdominal constriction in mice

Tail flick test in mice

Mice were randomly allotted to nine groups of six animal in each. Two third of the tail was dipped on a water bath sustained at 50±2^{o}C.Normal saline (0.9%10ml p.o) was given to a control group while reference group received diclofenac sodium (50mg/kg body weight p.o).The doses of crude ethanolic extract (50, 100 and 200mg/kg body weight p.o) were given to group III, IV and V. n-Hx, EtOAC, n-BuOH and Aq (200mg/kg body weight p.o) were given to groups VI, VII, VIII and IX. When the animal withdraw its tail from hot water taken as reaction time .while 10 sec was measured as cut off time .The reaction time was noted at an intervals of 0, 30, 60, 90, 120, 150, 180 min. (Owoyele *et al*., 2004). Tail flick antinociceptive index (TFAI) was determined through the expression.

TFAI = reaction time-baseline/cut-off time x 100

Hot plate test

When placed on hot plate, mice of both sexes has been screened on the basis of their response. Control group, reference group and treatment groups were given their respective treatments at particular doses with oral route same as described as earlier. Hot plate was used to check

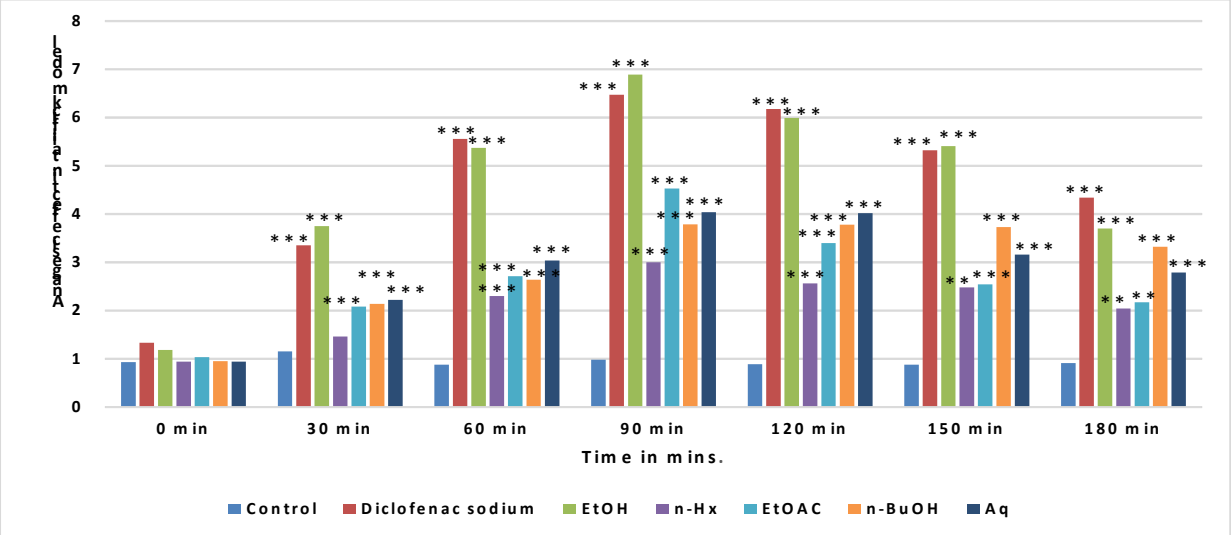
Table 1: Acute toxicity of Ethanolic leaves extract of *A. digitata* L.

Treatments	Dose (mg/kg)	Gross behavior effect	No. of animal died (n=6)
Control (Normal saline)	-	No change	0
ADLE	50	No change	0
	100	No change	0
	500	No change	0
	1000	No change	0
	2500	No change	0
	3000	No change	0

(ADLE: *Adansonia digitata* leaves extract)

Table 2: Effects of various leaves extract of *A.digitata* by acetic acid induced writhing test

Treatments	Given Dose mg/kg	Mean no. of writhes ± S.E.M	%inhibition
Control	-	50.5±2.34	-
Diclofenac Sodium	50	15.83±0.75***	68.65
EtOH	50	32.83±2.48***	34.99
	100	25.00±1.67***	50.49
	200	15.00±1.54***	70.29
n-Hx	200	37.66±1.36***	25.42
EtOAC	200	30.00±1.37***	40.59
n-BuOH	200	21.00±2.52***	58.4
Aq	200	20.66±2.65***	59



Animal were pretreated by oral administration of extract and fractions i.e. EtOH, n-Hx, EtOAC, n-BuOH and Aq (200 mg/kg body weight),), Diclofenac sodium (50 mg/kg, bodyweight) and normal saline. Values were expressed as mean ± S.E (n=6). Statistical significance were calculated by ANOVA followed by post hoc test when compare to the control * $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$.

Fig. 2: Antinociceptive Index of extracts by tail flick test

the pain sensation in animals by subjecting the animals in hot plate maintained at 53±2.°C. If the animal licked and raised their paws considered as respond to pain. To avoid paw damage a cut off time was recorded as 30 sec (Dharmasiri *et al*., 2003). Percent analgesia was calculated using the following formula:

% Analgesia = (Test latency–control latency) / (Cut-off time-control latency) x 100

STATISTICAL ANALYSIS

The experimental data were expressed as mean ± SEM of six mice. For statistical evaluation one way ANOVA was

Table 3: Analgesic effects of various extracts by tail flick test

Treatments	Dose (mg/kg)	0 min	30 min	60min	90min	120 min	150min	180 min
Control	–	0.93 ±0.09	1.15 ±0.15	0.88 ±0.05	0.98 ±0.12	0.89 ±0.08	0.88 ±0.12	0.91 ±.039
Diclofenac Sodium	50	1.33 ±0.02	3.35*** ±0.09	5.56 *** ±0.08	6.47 *** ±0.14	6.18 *** ±0.16	5.32*** ±0.24	4.34*** ±0.38
EtOH	50	0.95 ±0.06	3.79 *** ±0.71	4.96 *** ±1.03	5.44 *** ±1.02	4.87 *** ±0.92	4.89 *** ±0.91	2.34** ±0.56
	100	0.95 ±0.06	2.74 *** ±0.28	3.58 *** ±0.45	4.05 *** ±0.87	3.37 *** ±0.42	3.19 *** ±0.36	2.40 *** ±0.66
	200	1.18 ±0.44	3.75 *** ±0.22	5.37 *** ±0.31	6.89 *** ±0.15	5.99 *** ±1.00	5.41 *** ±0.83	3.70 *** ±0.62
n-Hx	200	0.94 ±0.1	1.46 ±0.68	2.30 *** ±0.67	3.00 *** ±0.81	2.56 *** ±0.92	2.48 ** ±0.50	2.04 ** ±0.53
EtOAC	200	1.03 ±0.65	2.08 *** ±0.84	2.71 *** ±0.72	4.53 *** ±0.66	3.40 *** ±0.84	2.54 *** ±0.72	2.17** ±0.66
n-BuOH	200	0.95 ±0.06	2.14 *** ±0.21	2.64 *** ±0.34	3.79 *** ±0.89	3.78 *** ±0.67	3.73 *** ±0.52	3.32 *** ±0.51
Aq	200	0.94 ±0.05	2.22 *** ±0.29	3.04 *** ±0.04	4.04 *** ±0.51	4.02 *** ±0.79	3.16 *** ±0.19	2.79 *** ±0.33

Table 4: Analgesic effects of leaves extract on hot plate Analgesiometer in mice

Treatments	Dose (mg/kg)	0 min	30 min	60min	90min	120 min	150min	180 min
Control		6.00 ±0.63	6.67±0.51	6.00±0.89	6.00±0.89	6.00±0.89	6.00±0.89	6.00±0. 89
Diclofenac sodium	50	6.50± ±0.83	12.50 ±0.54***	17.17± 1.4***	15.50± 1.5***	11.17± 1.2***	10.84± 1.7***	10.5± 1.2***
EtOH	50	7.00± 0.89	9.65± 1.03***	12.33± 1.50***	14.67± 1.86***	14.33± 2.25***	11.25± 0.75***	10.25± 0.98***
	100	6.33± 0.51	9.66± 0.81***	12.66± 1.75***	14.66± 1.75***	11.66± 0.81***	10.33± 0.54***	9.33± 0.81***
	200	6.66± 0.51	11.33± 0.81***	12.66± 0.51***	17.33± 1.63***	16.00± 2.96***	13.16± 1.60***	11.33± 1.21***
n-Hx	200	6.17± 0.75	7.67± 1.50	7.33± 1.50	8.17± 0.75	7.5± 1.37	6.5± 0.83	6.00± 0.89
EtoAC	200	6.67± 1.03	7.33 ±1.36	7.67± 1.03	7.33± 1.03	6.67± 1.21	6.67± 1.36	6.67± 1.03
n-BuOH	200	6.50± 0.54	12.33 ±1.86***	15.34± 2.65***	13.33± 1.50***	10.33± 0.51**	7.50± 0.54	6.67± 0.51
Aq	200	6.67± 0.51	13.17 ±0.75***	14.84± 2.48***	11.33± 2.58***	10.50± 2.25***	9.50± 1.78***	7.84± 2.13

followed by post hoc Tukey's tests. Effects were showed to be significant at P≤0.05 level. SPSS software version 20 was used to process the data.

RESULTS

Acute toxicity

No toxicity has been experienced in various leaves extracts to the dose of (50, 100, 500, 1000, 2500 and 3000) mg/kg body weight and showed no lethal signs and mortality of tested animals. table 1.

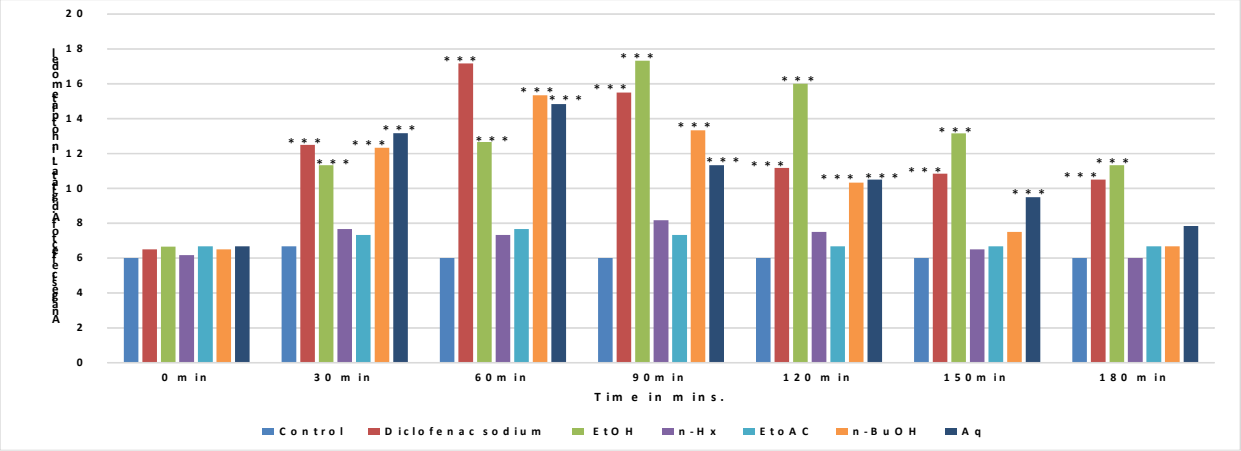
Analgesic activity of extracts

Acetic acid induced writhing test

Peripheral analgesic activity of leaves extract of *A. digitata* was analyzed by acetic acid abdominal constriction test. Crude EtOH extract at a dosage of 200 mg/kg showed prominent activity i.e. 70.29%. Nevertheless, diclofenac sodium showed 68.65% reduction at 50mg/kg p.o. respectively table 2

Tail flick test

In tail flick test all the tested extracts of leaves were significant (P<0.01) and dose dependent. The most



Animal were pretreated by oral administration of extracts and fractions i.e.EtOH, n-Hx, EtOAC, n-BuOH and Aq (200 mg/kg, body weight), Diclofenac sodium (50 mg/kg, body weight) and normal saline (NS). Values were expressed as mean ± S.E (n=6). Statistical significance were calculated by ANOVA followed by post hoc test when compare to the control *p<0.05; **p<0.01; ***p<0.001.

prominent decrease in painful sensation was seen in case of EtOH 200mg /kg body weight i.e. 6.89 sec at 90min of drug administration while diclofenac sodium 50mg/kg body weight delays latency time at 6.47 sec after 90min of dose administration table 3.

Hot plate test

Leaves extract of *A.digitata* produced analgesia by hot plate method at 50±2°C are shown in fig. 1. Crude EtOH (50, 100, 200) while n-BuoH and Aq extract 200mg/kg body weight showed that reaction time was significant. The most significant (P<0.001) increase in latency time noticed against 200mg/kg body weight of EtOH extract was 17.33±1.63 after 90 min of administration whereas standard drug (50mg/kg p.o.) shows latency time at 17.17±1.4sec and both remained significant up to 180min table 4.

DISCUSSION

Pharmacological screening provides a foresight about curative potential of herbs and believes to be unavoidable (Azam *et al*., 2016). Natural products could be the finest possible choice for successful management of painful conditions. (Marmitt *et al*., 2016).

The analgesic effect of various leaves extract of different doses of *A. digitata* using *in vivo* nociception models were examined by three different methods i.e. acetic acid abdominal constriction assay, tail flick and hot plate tests. Both of thermal tests (hot plate and tail flick) have been documented to analyze central analgesic activity while acetic acid induced writhing assay examine for peripheral analgesic activity. On the basis of data obtained by assays, it was noted that analgesia produced by standard drug and *A. digitata* leaves extract are parallel and dose dependent (for ethanol extract only) and this action might observed due to antagonizing the cyclooxygenase enzyme which ultimately inhibits the formation of prostaglandins (Das *et al*., 2010). In hot plate test *A. digitata* lengthened the thermal reaction time same as that of NSAIDS which produce analgesia generally by desensitized the afferent neurons of brain by blocking the formation and secretion of endogenous prostaglandins, bradykinin and other pain causing noxious stimuli (Prempeh *et al*., 2008). The tail flick reaction is measured to be a spinally mediated reflex which is generated by inhibitions of spinal channels. (Trongsakul *et al*., 2003; Vogel, 2002). Writhing test induced by acetic acid showed abdominal constrictions in animals which depends on the secretion of proinflammatory cytokines i.e. tumor necrosis factor-α,interleukin-1β and IL-8, from macrophages and mast cells and their concentration is increased in peritoneal fluid, it is believed that prostaglandins provoked the writhing response (Ribeiro *et al*., 2000; Bartolini *et al*., 1987). In the current study, writhing response was significantly decreases peripherally in mice by tested extracts might be due to inhibition of arachidonic acid metabolites synthesis.

Literatures reveals that plant possess the several bioactive phytoconstituents i.e. flavonoids, saponins, steroids, Protein, tannins (Doriane *et al*. 2013; Ouafae *et al*., 2017). Particularly flavonoids acts as an antioxidant and reduces oxidative stress by decreasing phospholipase A2 which stops the conversion of phosphatidic acid to arachidonic acid (Bahmani *et al*., 2014). Proteins, steroids, saponins, and tannins are found rich in plants could also contribute to antinociceptive action of leaves extracts. (Mondal *et al*., 2014; Adeyemi *et al*., 2011; Leal *et al*., 2016).

A study conducted in Bangladesh has shown that methanolic extract of leaves (200mg/kg) possessed dose dependent analgesic effect (4.13 s) that was comparable to that of standard drug morphine (5.0 s) which perform its analgesic action by supraspinal (μ, K, δ, σ) and spinal (μ,

K, δ) receptors. Similarly 200mg/kg oral dose of methanolic leaves extract reduced writhes remarkably 21.1% in formalin induced model. (Tahia *et al*., 2015; Bhattacharya *et al*., 2014). In contrast, in our study we used diclofenac sodium as positive control which exerts its action through inhibition of arachidonic acid metabolites path ways and results are highly significant at 200 mg/kg that is 70.29% inhibition which is also confirm by the previous reported data of methanolic leaves extract. It also indicates that our results are remarkably significant i.e. 49% than the previous published work. Same in case of tail flick test ethanolic extract at 200 mg/kg delays painful sensations in 6.89 sec at 90min while in previous data methanolic extract of leaves inhibits painful stimulus in 4.13 sec at 90min and it is slightly modified which may be due to the solvent polarity. In best of our knowledge no work has been previously done by hot plate test in leaves extracts.

However the findings of this research work produced significant effects on all analgesic models which could be due to genetic diversity, environmental conditions under which the plant has grown as well as season of collection of plant part changes the quality and quantity of phytochemicals found in plants.

CONCLUSION

In the light of our observations, it would be concluded that leaves extract contain both peripheral and central significant analgesic activities. Among all extracts crude ethanolic extract showed prominent results when compared with standard diclofenac Sodium which confirm its usage in traditional system of medicine as a pain killer agent but more research is necessary to access mode of action and discovery of new phytopharmaceuticals of clinical utility.

REFERENCES

Adeyemi OO, Adeneye AA and Alibi ET (2011). Analgesic activity of aqueous seed extract of *Hunteria umbellate* (K.schum) HallierF in rodents. *Indian J. Exp. Boil.*, **49**: 698-703.

Azam S, Saqib MS, Zar F, Ahmad B, Khan I, Zeb Z and Khan I (2016). Antibacterial, antifungal, phytotoxic, Antioxidant and haemagglutination activities of organic fractions of *Arisaematurtuosum*. *Pak. J. Pharm. Sci*., **29**(3): 991-997.

Bartolini A, Galli A, Ghelardini C, Giotti A, Malcangio M, Malmberg Aiello P and Zucchi PL (1987). Antinociception induced by systemic administration of local anaesthetics depends on a central cholinergic mechanism. *Br. J. Pharmacol*., **92**(4): 711-721.

Bhattacharya A, Agrawal D, Sahu KP, Kumar S, Mishra SS and Patnaik S (2014). Analgesic effect of ethanolic leaf extract of *Moringaoleifera* on albino mice. *Indian J Pain.,* **28**(2): 89-94.

Bahmani M, Shirzad H, Majlesi M, Shahinfard N and Rafieian-Kopaei M (2014). A review study on analgesic applications of Iranian medicinal plants. *Asian Pac. J. Trop. Med*., 7(1):43-53.

Chauhan JS, Cahturvedi R and Kumar S (1984). A new flavonol glycoside from the root of *A. digitata*. *Planta Medica*., **50**: 113.

Caluwé DE, Halamová K and Damme VP (2010). *Adansoniadigitata* L. A review of traditional uses, phytochemistry and pharmacology. *Africa Focus*., **23**(1): 11-51.

Doriane ED jeussi, Jaures AK Noumedem, Jackson A Seukep, Aime G Fankam, Igor KVoukeng, Simplice B Tankeo, Antoine HLN kuete and victor kuete (2013). Antibacterial activities of selected edible plants extracts against multi drug resistant gram negative bacteria. *BMC Complementary and alternative Medicine*., **13**: 64.

Dharmasiri MG, Jayakody JR, Galhena G, Liyanage SS and Ratnasooriya WD (2003). Anti-inflammatory and Analgesic activities of mature fresh leaves of *Vitexnegundo. J. Ethnopharmacol*., **87**(2-3): 199-206.

Das BN, Biswas BK and Moghal M (2010). Study of analgesic activity of bark of *Xeromphis spinose*. *Pharmacie. Globale.*, **2**(1): 1-3.

Dippenaara JM (2015). Herbal and alternative medicine: The impact on anesthesia. *South. Afr. J. Anaesth. Analg*., **21**(1): 15-20.

Gilman AG, Rall TW, Neis AS and Taylor P (1991). Lipid derived autacoids: Eicosanoids and platelet activating factor *In*: Goodman and Gilman's. The pharmacological basis of therapeutics. 8th ed. Pergamon Press. New York, pp. 607-08.

Gomase VP, Shire SP, Nazim S and Choudhari BA (2011). Development and evaluation of analgesic polyherbal formulation containing some indigenous medicinalplants. *Int. J. Pharm. Bio. Sci*., **2**(3): 119-127.

Hirose K, Jyoyama H, Kojima Y, Eigyo M, Hatakeyama H (1984). Pharmacological properties of 2- [44-#(2-# triazolyloxy)-phenyl [propionic acid (480156-5)], a new nonsteroidal anti-inflammatory agent. *Arzeim For sch/Drug Res*., **34**: 280-86.

Heywood HV, Bummitt KR, Culham A and Seberg O (2007). Flowering plant families of the world. Rev ed., Firefly Books LtdRichmond Hill, Canada.

Koster R, Anderson Mand DeBear EJ (1959). Acetic acid for analgesic screening. *Fed. Proceed*, **18**: 412-416.

Kumar CU, Pokuriand VK and Pingali U (2015). Evaluation of the Analgesic Activity of Standardized Aqueous Extract of *Terminalia chebula* in Healthy Human Participants Using Hot Air Pain Model. *J. Clin. Diagn. Res*., **9**(5): 01-04.

Leal LSS, Silva RO, Araujo TSL, Silva VG, Barbosa ALR, Medeiros JVR, Oliveira JS and Ventura CA (2016). The anti-inflammatory and antinociceptive

effects of proteins extracted from *Acacia farnesiana* seed. *Rev. Bras. Pl. Med. Campinas.,* **18**(1): 38-47.

Mondal H, Salna S, Awing K, Hossain H, Ablat WA, Islam KM, Jahan AI, Sadhu KS, Hussain GM, Shilpi AJ and Juddin S (2014). Central stimulating and analgesic activity of the ethanolic extract of Alternantherasessilis in mice. *BMC. Complement. Altern. Med*., **14**: 398.

Marmitt JD, Bitencourt S, Silva ECDA, Goettert IM and Rempell C (2016). Medicinal plants of Renisus with analgesic activity. *J. Crit. Rev*., **3**(3): 1-4.

Owoyele BV, Olaleye SB, Oke JM and Elegbe RA (2004). Anti-inflammatory and analgesic activities of *Nothospondiasstaudtii. Nigerian J. Physiol. Sci.,* **19**(1-2): 102-105.

Ouafae El Yahyaoui, Nabil AIT Ouaaziz, Ilias Guinda, Amal Sammama, Saloua Kerrouri, Bahia Bouabid, Mohamed El Bakkall, Ali Quyou, L Aicha Lrhorfi and Rachid Bengueddour (2017). Phytochemical screening and thin layer chromatography of two medicinal plants *Adansoniadigitata* (Bombacaceae) and *Acacia raddiana* (Fabaceae). *JPP*, **6**(1): 10-15.

Prempeh ABA and Mensah#Attipoem J (2008). Analgesic activity of crude aqueous extract of the root bark of *Zanthoxylumxanthoxyloides. Ghana Med. J*., **42**(2): 79-84.

Ribeiro RA, Vale ML, Thomazzi SM, Paschoalato AB, Poole S, Ferreira SH and Cunha FQ (2000). Involvement of resident macrophages and mast cells in the writhing nociceptive response induced by Zymosan and acetic acid in mice. *Eur. J. Pharmacol*., **387**(1): 111-118.

Shukla YN, Dubey S, Jain SP and Kumar S (2001). Chemistry, biology and uses of *Adansoniadigitata*: a review. *J. Medi. Aroma. Plant Sci*., **23**: 429-434.

Sen S, Chakraborty R, Biplab D, Ganesh T, Raghavendra HG and Debnath S (2010). Analgesic and anti-inflammatory herbs: A potential source of modern medicine. *IJPSR*, **1**(11): 32-44.

Trongsakul S, Panthong A, Kanjanapothi D and Taesotiku T (2003). The analgesic, antipyretic and anti-inflammatory activity of *Diospyrosvariegatakuruz*. *J. Ethanopharmacol*., **85**(2-3): 221-25.

Tahia F, Majumder P, Sikder AAM and Rashid MA (2015). Studies of bioactivities of *Adansoniadigitata* (L.). *Dhaka Univ. J. Pharm. Sci.* **14** (2): 157-162.

Wood RBC (1969). Baobab - African tree of legend myth and mystry'. Sunday news magazine, Tanzania. pp.7-8.

Wickens GE (1982). The baobab, Africa's upside-down tree. Kew Bulletin, **37**: 171-202.

Vogel HG (2002). Drug Discovery and Evaluation Pharmacological Assays. 2nd Ed., Springer, New York. pp.716-17.

Zaoui A, Cherrah Y, Mahassini N, Alaoui K, Amarouch H and Hasser M (2002). Acute and chronic toxicity of *Nigella sativa* fixed oil. *Phytomedicine.*, **9**(1): 69-74.