Evaluation of the Anti-Inflammatory, Anti-Nociceptive and Anti-Pyretic Effect of the Aqueous, Methanolic and N-Hexane Extract of *Datura Metel* seed on Albino Wister Rats

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***Abstract*: This study was designed with the *Aim* of evaluating the potency of n-hexane, methanolic and aqueous seed extract of D.metel as an anti-inflammatory, antipyretic and antinociceptic in animal models. The plant sample was collected at kurgwi in the southern part of plateau state. A total of 63 Albino rats were used in these studies. *Method* the animal models were treated orally with 300mg/kg (n-hexane and methanolic extract) for group 1 and 2 while 300mg/kg 200mg/kg and 100mg/kg (Aqueous extract) for groups 3, 4 and 5 respectively. Antipyretic studies were done using 15% suspension of Brewer's yeast in Albino rats and temperatures were recorded using a digital thermometer. The antinociceptive activity was done using formalin-induced writhing method in mice. The Anti-inflammatory study was done using the Formalin-induced paw oedema the paw size was measured using a vernier caliper. The *results* showed there was a significant decrease in temperature for aqueous extract group 3 with 8.53% compared to the standard drug paracetamol with 8.82% after 120mins. For the antinociceptive activity, there was no analgesia with the Formalin-induced writhing test, In the Formalin –induced paw oedema; the extract test did not have significant effect. In *Conclusion* the aqueous extract of Datura metel seed has better Anti-pyretic activities.**

Keywords: **Anti-Inflammatory, Antipyretic and Antinociceptic**.

I. INTRODUCTION

The use of plants in various parts of the world for both preventive and curative purpose is an age-old tradition and is increasing empirically, with these upsurges, however a thorough scientific investigation is imperative based on the need to provide information on their efficacy and toxicity risks. Many studies have reported successes in validation of medicinal plant species for their antipyretic, anti-inflammatory, and antinociceptive effects respectively (Safari *et al*., 2016,). *Datura metel* is a shrub-like perennial herb commonly known as "Devils trumpet", or "thorn apple", and belongs to the family (Solanacaea), the plant grows in the wild in all the warmer parts of the world (Drake et al 1996); and is cultivated worldwide in all tropical and subtropical region for its ornamental purpose (Glotter *et al* 1973); and is also cultivated for its medicinal properties. *Datura metel* was first described by Linneus in 1753 but no botanical illustration of the plant was given. It is commonly found in the east Asia and India and it is used in traditional Bangladeshi herbal medicine and in traditional Chinese medicine. The flowers of *D.metel* are known as "baimantualo" and used for treatment of skin inflammation and psoriasis (Wang *et al*, 2008); In Nigeria, especially in the northern parts, *Datura metel* is found growing in abundance as weed in farmlands and dumpsites. The leaves and seeds of the plant are used for several purposes and in several ways especially for its psychoactive effect, thus making the plant parts to be abused by the youths who are more prone to dangers of smoking and drug abuse (Kutuma *et al*, 2010).

Synthetic chemicals have for many years been effectively used for the treatment of many illness, traditional plant-derived compounds have been used as medicine since ancient history playing an important role in healthcare especially in the rural areas were access to modern medicine is limited. Plant have been shown to contain photochemical (bioactive compounds), that act as defense systems to combat various diseases. Traditional medicine is therefore defined as the sum total of all the knowledge, skills and practices based on the theories believes and experience indigenous to certain culture, weather applicable or not used in maintenance of health as well as prevention, improvement and treatment of physical and mental illness (WHO 2004).

Datura metel seeds have some medicinal properties which are attributed to the presence and abundance of chemical compounds such as Alkaloid that aid in healing process. Despite the numerous report on the effectiveness of *D.metel* against a vast array of disease, there is need to derive data on specific disease symptoms such as inflammation, pyrexia and nociception. D.*metel* can be explored further as per its diversity of traditional use and wide range of chemical compound reported to be present in the various parts of the plant. In the present investigation, the phytochemistry, pharmacology, traditional uses, of the plant has to be review.

Inflammation: The term refers to a generalized non-specific beneficial response of tissue to injury. It involves a complex cascade of events both local and systemic. The local events

involve phagocytic cells recruitment, removal of both endogenous and exogenous debris, while systemic responses involve haemostatic changes. Cellular mechanisms of inflammation involve relaxation of vascular smooth muscle cells causing vasodilation, alteration of vascular permeability due to contraction of cytoskeleton in epithelial cells, migration of phagocytes to inflamed area and phagocytosis (Allen *et al*., 1988). Inflammatory process is involved in pathogenesis of various diseases and has both acute and chronic phase.The acute phase is characterized by fever, pain and edema while in chronic phase there is cellular proliferation, activation of complement, fibrinolytic system and hyaluronidase activity. The acute inflammatory model can be induced by carrageenan (Christopher *et al.,* 2003), formalin, serotonin, histamine, bradykinnin and prostaglandins.

Pain: Pain is an unpleasant sensory and emotional experience associated with actual or potential tissue damage. In muscles, visceral, and cutaneous tissues, transduction of high threshold input involving chemical, thermal and mechanical stimuli to electrophysiological activity occurs at the specialized free nerve endings of nociceptive primary afferent. The transductive mechanism involves activation of cationic channels on free nerve endings directly by biophysical properties of the high threshold noxious stimuli, and directly by changing the composition of micro- and macro-environments produced by such stimuli or trauma. Thermal nociceptive transduction is mediated via vanilloid type receptor cation channels (TRPV). TRPV1 responds to noxious heat greater than 45 degrees centigrade and are capsaicin 3sensitive. TRPV2 is not capsaicin sensitive and has a thermal threshold of 52 degrees centigrade. Cold and menthol - receptor CNR - 1/T8 responds to noxious cold i.e. 8- ?$°C and menthol. Both cold and hot responsive channels respond to thermal changes by increasing Na^+, K^+ or Ca^{++} ion channels flux causing membrane depolarization and transduction. High threshold mechanical stimuli affect non-specific channels by distorting collagenous bridging elements between membranes of free nerve endings and surrounding tissue matrix. This causes changes in channel configuration producing inward Na^+, K^+ or Ca^{++} currents. (Giordano *et al*., 2005)

Antinociceptive Systems: Pain can be modulated at different levels including the spinal cord. Inhibitory interneuron's from laminae I and V receives collaterals from A-delta and C-fibers. These interneuron's synapse on primary afferent and secondary order neurons within the horizontal spinal cord segment. The transmitter substances released by these neurons include GABA, glycine, dynorphin and endogenous cannabinoids. Other sites where pain modulation takes place are dorsal column by activation of A-delta mechano-stimulation, brain. Stem level and mid brain by the sensory cortex (Giordano *et al.,* 2005).Several hormones that have been shown to modulate pain include corticotrophin releasing hormone and sex hormones (Craft *et al*., 2004). Several methods are used in management of both acute and chronic pain. They include use non-steroid anti-inflammatory drugs (NSAIDs), opioids, vacupuncture, nerve blockade etc. The NSAIDs are widely used and are available over the counter. Examples include acetylsalicylic acid, paracetamol diclofenac etc. These groups of drugs have antipyretic and analgesic as well as anti-inflammatory effects. Most NSAIDs act peripherally by inhibiting cyclo-oxygenase mediated synthesis of prostaglandins (Vane *et al*., 1971). Prostaglandins sensitize peripheral nerve endings hence facilitating pain behavior (Lim *et al*., 1970). It has been showed that the central analgesic effect of NSAIDs is due to the inhibition of spinal cyclo-oxygenase activity. Opioid Analgesics are very potent examples include Morphine, Pethidine, Codeine, Heroin etc. The analgesic effect of opiods is mediated via mu delta or kappa opioid receptors. They cause analgesia in the central nervous system by reducing neuronal excitability (Diaz *et al.*, 2000).

Pharmacological activity describes the beneficial or adverse effect of a drug on living matter. When a drug is a complex chemical mixture, the activity is exerted by the substance active ingredient or the phamarcophore but can be modified by the other constituent. *D.metel* on the other hand possess many pharmacological activities which are reviewed as follows. The anti-hyperglycemic and hypoglycemic effect of *D.metel* seed in normal Wister albino diabetic rats and diabetic rats was investigated by

(Monira and Munani, 2012); for its potential activity and explain that *D.metel* seed powder was suspended in 1% sodium (Mc in form of mucilage), and given to normal diabetic rats, with blood glucose level above 300mg/dl orally at a dose rate of 25, 50 and 70mg/kg body weight, blood sampling at different time from within 24hrs and dose dependent anti-hyperglycemic activity was also observed with *D.metel* in alloxan induced hyperglycemic rats. This study gave a conclusion that the usage of *D.metel* seed for controlling diabetics may be validated by this study and the seed offer a promise for the development of potent phytomedicine for diabetes (Murthy *et al.,* 2004);

Akharaiyi, 2011; Investigate the antioxidant activity of the aqueous extract of *D.metel* leaf, stem bark and roots and bring result that the aqueous extract of *D.metel* leaf, stembark and roots show phytochemical and antioxidant activity between 49.30-23,82% and concluded that the plant can be considered as a natural source of antioxidant. Wannang *et al.,2009*; gave evaluations on the analgesic property of aqueous extract of D.metel seed, From the result obtained, the aqueous extract (100,200 and 300mg/kg) showed no significant analgesic in both radiant heat tail flick model and the acetic acid induced writhing model for nociception.

II. MATERIALS AND METHOD

Collection of plant materials

Seeds of D.*metel* were collected from bushes and also residence of Kurgwi in the southern part of Plateau State, Nigeria in 2016. This plant is believed by the locals to have

medicinal value against wounds and other disease conditions. Aqueous infusion of *D. metel* is traditionally used by locals to control New Castle Disease in poultry. The plant material was identified at the federal college of forestry Jos, plateau state, Nigeria.

Animal models

Albino Wistar rats of about 92-250g body weight were used in this study. These animals were maintained in the experimental room at the Animal House, NVRI Vom. The room was set at controlled conditions of 25 ± 2°C temperature, 55% humidity to acclimatize the animals. The rats were kept in a cage and fed with standard chow and water *ad libitum*.

Drugs and Chemicals

The drugs and chemicals used in this experiment are Formalin, NaCl (normal saline), brewer's yeast, which were prepared in the laboratory and paracetamol, diclofenac were purchased from a registered pharmacy. All drugs and chemical are of analytical grade.

Equipments

vernier calliper, digital thermometer, cotton wool, beaker, rotary evaporator, water bath, conical flask, freeze dryer, measuring cylinder, mortar and pestle, hand gloves.

Administration

All drugs and extracts were administered orally whereas formalin and brewer's yeast were administered intraperitonealy and subcutaneously according to body weight.

Preparation and Extraction of plant material

Aqueous extraction

The aqueous extraction was carried out based on method described by Harborne et.,al 1984 with slight modification**.**

Methanolic extraction

The methanolic extraction was carried out based on method described by Rauf and Udin et al., 2012 with slight modification

N-hexane extraction

The methanolic extraction was carried out based on method described by Rauf and Udin et al., 2012 with slight modification

III. BIOCHEMICAL ANALYSIS/EXPERIMENTAL DESIGN

Determination of antinociceptive activity

To determine the antinociceptive activity of the plant extract, a formalin−induced writhing test was carried out using a method described by Wheeler-Aceto *et al.,* 1990. Groups of 3 mice each were used as test and control specimen, animals in group VII were given normal saline (negative control) and group VI were given diclofenac, group III, IV, and V were orally administered with 300, 200 and 100 mg/kg of the aqueous extract respectively, likewise group I, and II were given orally the n-Hexane and methanolic extract of *D.metel* at the highest dose of 300mg/kg respectively. 30 minutes after the treatment, 0.05mls of 2.5% formalin was injected intraperitonealy into the sub planar surface of the left hind paw. The animals were subsequently kept in a chamber and were observed for 60mins. The behavior observed after formalin administration includes licking, biting, elevation or shaking the injected paw. Time spent in these behavioral states was noted as the latency of nociception. Two phases of nociception were observed which represent acute and chronic pain. The two phases are thought to involve two distinctly different stimuli. The early phase was observed between 0-5 minutes and is thought to be due to direct stimulation of nociceptors by the chemical (Dubuisson *et al.,* 2000).The late phases start 15-30 minutes after formalin injection and it is due to inflammatory pain process (Toilsen *et al.,* 1992). Percentage protections against writhing movement (% inhibition of writhing) were taken as an index of analgesia and it was calculated as follows:

% Inhibition=Wr (Control) – Wr (test group) / Wr (Control) X 100

Where Wr = Mean number of writhing.

Determination of anti-inflammatory activity

To determine the anti-inflammatory effect of the extract in mice, a formalin induced inflammation was carried out as described by Hosseinzadeh and Younesi (2002). Inflammation was induced by intraperitoneal injection of 0.0.5ml of 2.5% formalin into the left hind paw of each mouse. Hourly changes in paw sizes and reduction of edema around the paw was determined using a venier caliper for four hours, inflammation was induced 30min after extract and drug administration. Inhibition in paw size was determine using the formula

$$\% \text{ inhibition of inflammation} = \left(\frac{C-T}{C}\right) x\ 100$$

Were C is control paw edema and T is treated paw edema

Determination of antipyretic activity

The antipyretic activity of the plant extract was evaluated using Brewer's yeast induced pyrexia as described by Loux *etal*., (1972). According to the protocol, 15% aqueous suspension of Brewer's yeast was first prepared using normal saline. A suspension of the Brewer's yeast was used for induction of fever, a digital thermometer was inserted into the rectum and the initial temperature was recorded. Any animal with a temperature above 37.2°C was excluded and fever was induced by injection of 10ml/kg body weight of 15% Brewer's yeast suspension subcutaneously in the back below the nape of the neck, food was withdrawn but they give access to water till after the experiment. They were kept for 18 hours, temperature was taken again and only animals with body temperature of at least 38°C and those that had a minimum of

1°C rise in temperature were used for the test. Aqueous extract of 300, 200 and 100mg/kg were administered orally according to body weight to group III, IV and V respectively, and also the methanolic and n-hexane extract were administered orally to group I and II at the highest dose of 300mg/kg respectively, while Paracetamol tablet (Emzor brand) was crushed and diluted with normal saline and administered orally to group VI at a dose of 150mg/kg body weight (positive control) normal saline was administered orally to group VII (negative control) at a dose of 1.0ml/body weight. The rectal temperatures were recorded at 30mins time intervals of 0, 30, 60, 90, and 120. Minutes after administration of test extract.

IV. RESULT OF THE STUDY

The result of this investigation on the antinociceptive, anti-inflammatotory and antipyretic effect of aqueous, methanolic and n-hexane seed extract of D.metel is as follows

4.1: Anti-inflamatory effect of D.metel seed. The anti-inflammatory analysis of the n-hexane, methanolic and aqueous extract of *D.metel* seed was evaluated and the result obtain is shown in the table below.

Table 1: Anti-inflammatory effect of n-hexane, methanolic and aqueous extract of *D.metel* seed on percentage change in paw diamenter after 0hr, 1hr, 2hrs, 3hrs and 4hrs

GROUPS	TREATMENT	Percentage change in paw diameter(mm) after Drug administration				
		0hr	1hr	2hrs	3hrs	4hrs
I	N-hexane extract 300mg/kg	0.54 ± 0.01^{a} (19.4)	0.68 ± 0.03^{a} (23.9)	0.71 ± 0.01^{a} (22.8)	0.75 ± 0.03^{a} (21.0)	0.78 ± 0.03^{a} (20.4)
II	Methanolic extract 300mg/kg	0.53 ± 0.02^{a} (20.9)	0.72 ± 0.07^{b} (10.0)	0.69 ± 0.04^{a} (25.0)	0.69 ± 0.02^{a} (27.4)	0.77 ± 0.01^{a} (21.4)
III	Aqueous extract 300mg/kg	0.48 ± 0.05^{a} (28.4)	0.65 ± 0.05^{a} (27.8)	0.64 ± 0.0^{b} (30.4)	0.66 ± 0.07^{b} (30.5)	0.77 ± 0.1^{b} (21.0)
VI	Aqueous extract 200mg/kg	0.57 ± 0.01^{a} (15.0)	0.75 ± 0.06^{b} (16.7)	0.77 ± 0.0^{b} (16.3)	0.80 ± 0.05^{a} (15.8)	0.87 ± 0.0^{b} (11.2)
V	Aqueous extract 100mg/kg	0.55 ± 0.01^{a} (17.9)	0.66 ± 0.06^{b} (26.7)	0.76 ± 0.04^{a} (17.4)	0.77 ± 0.09^{b} (18.9)	0.8 ± 0.03^{a} (18.4)
VI	Diclofenac sodium standard drug 75mg/kg	0.53 ± 0.02^{a} (20.9)	0.34 ± 0.01^{a} (62.2)	0.33 ± 0.01^{a} (64.1)	0.39 ± 0.01^{a} (58.9)	0.29 ± 0.03^{a} (70.4)
VII	Normal saline negative control	0.67 ± 0.02^{a} (-)	0.90 ± 0.01^{a} (-)	0.92 ± 0.01^{a} (-)	0.95 ± 0.01^{a} (-)	0.98 ± 0.01^{a} ^{ss}(-)

Mg/kg = dosage administered (mg) according to body weight (kg).
Hr = change in paw diameter (mm) after Drug administration

Data are expressed as Mean values ± SD with the same small letter" a" across the rows are statistically significant from one another by ANOVA followed by Turkey Krammers multiple comparison test ($p<0.05$)

Same small letters "b" across the rows are significantly different from the foriegn by ANOVA followed by Turkey Krammers multiple comparison test ($p<0.05$)

Percentage inhibitions of inflammation are in brackets. ( ), (-) means no inhibition

Anti-nociceptive effect of D.metel seed. The anti-nociceptive analysis of the n-hexane, methanolic and aqueous extract of *D.metel* seed was evaluated and the result obtain is shown in the table below

Table; 2

Group	Treatment	Mean paw licking time (secs)	Percentage inhibition of paw licking
1	n-hexane extract 300mg/kg	26.0±1.28b	(26.9)
2	Methanolic extract 300mg/kg	24.63±1.94b	(30.0)
3	Aqeous extract 300mg/kg	34.0±0.71b	(4.49)
4	Aqeous extract 100mg/kg	29.4±0.51b	(17.4)
5	Aqeous extract 200mg/kg	28.2±0.78b	(20.7)
6	Diclofenac standard drug 100mg/kg	8.80±0.374b	(75.2)
7	Normal saline	35.6±249b	----

.Mg/kg = dosage administered (mg) according to body weight (kg).

Secs = Mean Writhing time.

Percentage inhibitions of writhing are express in bracket ( )

Data are expressed as Mean values ± SD with the same small letter" b" across the rows are significantly different from one another by ANOVA followed by Turkey Krammers multiple comparison test ($p<0.05$).

Antipyretic Effect of D.metel seed: The anti-pyretic analysis of the n-hexane, methanolic and aqueous extract of *D.metel* seed was evaluated and the result obtain is shown in the table below.

Table 3: Anti-pyretic effect of n-hexane, methanolic and aqueous extract of *D.metel* seed

GROUP	TREATMENT	Mean change in rectal temperature (^{O}C) after drug administration				
		0min	30min	60min	90min	120min
I	n-hexane extract 300mg/kg	37.6±0.69 %i.f 1.05	37.6±0.20 %i.f 2.08	38.3±0.80 %i.f 2.30	37.9±1.13 %i.f 3.81	38.2±1.80 %i.f 3.81
II	Methanolic extract 300mg/kg	35.8±0.45 %i.f 7.73	37.8±0.31 %i.f 1.56	37.9±0.40 %i.f 3.31	38.1±0.44 %i.f 3.30	37.9±0.44 %i.f 4.53
III	Aqueous extract 300mg/kg	36.6±0.10 %i.f 5.67	37.1±1.30 %i.f 3.50	37.4±1.10 %i.f 4.60	37.1±0.98 %i.f 5.84	36.3±0.70 %i.f 8.56
IV	Aqueous extract 200mg/kg	37.4±0.30 %i.f 3.61	36.4±0.60 %i.f 5.21	37.5±1.03 %i.f 4.34	37.8±0.75 %i.f 4.06	37.5±0.13 %i.f 5.54
V	Aqueous extract 100mg/kg	37.6±0.92 %i.f 3.09	36.8±0.39 %i.f 4.17	37.7±0.75 %i.f 3.83	37.1±0.20 %i.f 5.84	36.8±0.79 %i.f 7.30
VI	Paracetamol (EMZOR) drug 150mg/kg	37.3±0.93%i.f 3.87	36.5±0.65%i.f 4.9	36.1±1.08%i.f 7.91	36.0±0.93%i.f 8.63	36.2±0.75 %i.f 8.82
VII	Normal saline (control)	38.8±0.10 %i.f-	38.4±0.53 %i.f-	39.2±0.27 %i.f-	39.4±3.71 %i.f-	39.7±0.11 %i.f-

Mg/kg = dosage administered (mg) according to body weight (kg).
Min = change in rectal temperature (^{O}C) after drug administration.

Data are expressed as Mean values ± SD with the same small letter" a"across the rows are statistically significant from one another by ANOVA followed by Turkey Krammers multiple comparison test ($p<0.05$)

Same small letters "b" across the rows are significantly different from the foreign by ANOVA followed by Turkey Krammers multiple comparison test ($p<0.05$)

% i.f this represents the percentage inhibition of fever

V. DISCUSION, CONCLUTION AND RECOMENDATION

Discussion

The search for bioactive components which can be used as non-conventional analgesics, and antipyretics has received considerable attention in recent times because of the increasing worldwide development of lasting solutions to pain, inflammation and fever which are safe to human and with no side effects as seen with modern medicine. This study was oriented to evaluate the curative ability of n-hexane, methanolic and aqueous seed extract of D.metel against pain, inflammation and fever. These evaluations of antinociceptive, anti-inflammatory and antipyretic effect of the n-hexane, methanolic and aqueous seed extract was done by formalin induced pain and inflammation and also brewer's yeast induced pyrexia in albino rats. intraperitonealy injection of a dilute aqueous formalin (formaldehyde) solution into the dorsal surface of the rat or mouse hind paw elicits two distinct quantifiable nociceptive behaviors, i.e. flinching/shaking and licking/biting of the injected paw [Dubuisson *et al.*, 1977 and Tjolson *et al.*, 1992]. This formalin-induced nociceptive behavior shows an early and a late phase. The early phase, which starts immediately following injection of formalin, only lasts approximately 5 min and is probably due to direct chemical stimulation of nociceptors (acute pain). The second phase, which lasts 20 to 40 min, starts approximately 15 to 30 min following formalin injection and experimental data suggest that peripheral, inflammatory processes are involved [Haley et al., 1989]. In this study, n-hexane, methanolic and aqueous seed extracts of *Datura metel* showed no significant antinociceptive effect by increasing the formalin-induced paw licking time in both phases. These results is similar to other previous studies on evaluation of antinociceptive activities of plant extracts, that the n-hexane, methanolic and aqueous extracts of *D.metel* demonstrated an increase in the formalin-induced paw licking time is consistent with [Wannang *et al.*, 2009]. The antinociceptive activity of *D.metel* seed extract was found not to be significant on formalin induced model ($P<0.05$). In conclusion, it may also be said from the study that traditional uses of aqueous extract of *D.metel* seed for the treatment of various types of pain conditions has got no definite basis, as revealed from the experimental results. In the formalin test, the Albino rats used were treated with several treatments (300, 200, and 100mg/kg) for aqueous extract while n-hexane and methanolic at 300mg/kg seed extract of *D.metel* to reduce inflammation. Formalin test is a biphasic response where first phase is the direct effect of formalin which involves neurogenic pain, the pain is usually initiated when harmful mechanical, thermal or chemical stimuli agitate the peripheral terminals of particular main afferent neuron named nociceptors [Tominaga *et al* 2004]. In this study, it was noticed that exposure of formalin induced inflammation to various treatments resulted in no significant inhibition of inflammation in 1-4hrs compared to the standard drug diclofenac, which shows the highest percentage inhibition of 70.4% in the 4hr at a dose of 75mg/kg at $p< 0.05$. The aqueous n-hexane and methanolic extracts of *D.metel* was found not to significantly suppress the inflammation when treated at different concentrations. Brewer's yeast was used to induce fever in albino mice. Fever was recorded 18 hrs after yeast injection since yeast takes a total of about 19 hours to cause the elevation of body temperature [Turner 1965]. Subcutaneous injection of Brewer's yeast induces pyrexia by increasing the synthesis of prostaglandin. It is considered as a useful test for the screening of plants materials as well as synthetic drugs for their antipyretic effect [Khan *et al*., 2009, Devi *et al*., 2003].

Yeast induced pyrexia is called pathogenic fever and its etiology could be the production of prostaglandins [Molts 1993]. The inhibition of prostaglandin synthesis could be the possible mechanism of antipyretic action as that of paracetamol and the inhibition of prostaglandin can be achieved by blocking the cyclo-oxygenase enzyme activity. There are several mediators for pyrexia and the inhibitions of these mediators are responsible for the antipyretic effect [Rawlins *et al*., 1973]The oral administration of n-hexane and methanolic seed extract of *D.metel* at a dose of 300mg/kg and aqueous extract 300, 200 and 100mg/kg respectively does not significantly attenuated rectal temperature of yeast induced pyrexia albino mice compared to standard antipyretic drug (Paracetamol) which has %8.82 inhibition at 120mins at a dose of 150mg/kg. The Aqueous extract at a dose of 300mg/kg show a significant inhibition of pyrexia by %8.56 at 120min. Thus it can be postulated that aqueous extract of *D.Metel* Contained A Significantly Pharmacologically Active Principle(S) That Interfere With The Release Of Prostaglandins.

Conclusion

The significant reduction in pyrexia in Albino rats when treated with standard drugs (Paracetamol) as well as different doses of *D.metel* extracts, reflect that aqueous seed extract of *D.metel* is endowed with potent antipyretic properties. It can be said that aqueous extract of *D.metel* seed has minimal antipyretic activity in the tested models. However, the extracts possess no anti-inflammatory and antinociceptive effect on the tested rats.

Recommendation

Analytical methods such as HPLC, Spectrophotometric method for the analysis of plant materials should be developed. These methods should be validated for use in further analysis of plants to allow the control use of these plant materials for treatment of many disease conditions and as traditional medicine

CONFLICT OF INTEREST

No conflict of interest among researchers

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