EFFECTS OF THE COLD WATER EXTRACT OF THE SEEDS OF 
Datura metel (Solanaceae) ON APOMORHINE AND 
PHENOBARBITONE INDUCED CENTRAL NERVOUS SYSTEM 
ACTIVITIES IN DAY OLD CHICKS

1Simeon Omale*, 2Noel N. Wannang, 1Samuel B. Banwat, 1Dauda A. Dangiwa, 2Felicia 
S. Ohunene, 3Nwamaka C. Anukam and 4Chuks C. Onah

1Department of Clinical Pharmacy and Pharmacy Practice.
2Department of Pharmacology.
3Department of Pharmaceutics and Pharmaceutical Technology, Faculty of Pharmaceutical 
Sciences, University of Jos.
4Department of Veterinary Physiology and Pharmacology, Faculty of Veterinary Medicine, 
University of Nigeria Nsukka.

ABSTRACT
Complimentary medicine has been widely accepted in the management 
of disease and has received a boost by the World Health Organization. 
Datura metel has been employed in the management of psychotic 
disorders by some traditional medicine healers in Nigeria. The Central 
Nervous System (CNS) effects of the cold water extract of the seeds of 
D. metel was investigated on day old chicks. The graded doses (50 
mg/kg, 75 mg/kg and 100 mg/kg) of the extract were administered 
intraperitoneally and compared with the drugs. The LD₅₀ was found to 
be 125 mg/kg and there was a dose dependent reduction of the mean 
pecking value from 8.25 ± 0.57 (50 mg/kg), 6.10 ± 0.57 (75 mg/kg) and 3.00±0.33 (100 
mg/kg) minutes in the test groups. There was a significant decrease (P<0.05) in locomotor 
activities from 46.75 ± 0.57 to 6.00±1.00 and increased sedation from 60.00 ± 1.18 to 360.00 
± 12.76 minutes. There was a decrease in pecking activities from 16.00 ± 1.52 (CPZ alone) to 
1.75 ± 0.44 (CPZ +extract), while sedation increased from 120.00 ± 4.91 to 365.05 ± 9.84. 
There was a significant decrease (P<0.05) in the onset of phenobarbitone induced sleeping 
time and an increase in the duration of sleep. There was a significant decrease (P<0.05) in the

*Corresponding Author
Simeon Omale
Department of Clinical 
Pharmacy and Pharmacy 
Practice.
apomorphine induced stereotyped behavior. The seeds of *D. metel* were found to possess appreciable CNS activities and could be a potential source of anti-psychotic medicines.

**KEYWORDS:** Chlorpromazine, Anti-psychotics, Hallucinogens, Neuroleptics, Stereotyped-behaviour, Locomotor.

**INTRODUCTION**
A wide variety of medicinal plants have been exploited for their depressant action on central nervous system (CNS) functions resulting in a dose dependent calming or sedating effect.[1] Central nervous system depressants such as sedatives and tranquilizers are substances that slow brain activity and as such are used in treating anxiety and sleep disorder.[2]

During the last few decades there has been a resurgence of interest in plants as sources of medicine and novel molecules used in the treatment of various diseases.[3] In this way traditional medicine practitioners have found remedies to a number of diseases. Frequent claims by traditional medicine practitioners of the effectiveness of herbal medicines have stimulated the interest of researchers to evaluate the effectiveness of the commonly used herbs.[3,4]

In Nigeria traditional medicine has been recognized and afforded a formal status in the Nigerian National Health System as indicated by this declaration. “After a prolonged suppression in favour of conventional medicine, the practice and practitioners of traditional medicine hence forth be accorded formal status in the National Health System.”[5]

The plant *Datura metel* (Solanaceae) is a shrub like annual herb with a purple stem, white violet flower and about 1 meter height with alternate simple leaves. The fruits are four-lobed oval thorny, greenish capsules containing several brown kidney shaped seeds when dried. All parts of *D. metel* have been claimed to contain psychotropic properties while the flowers are considered a medicinal herb in Ayurveda.[6] Wannang *et al.*, in (2009) evaluated the analgesic effects of the aqueous seed extract.[7] The family contained alkaloids, tropane, indole, isoquinoline, purine, pyrazole e.t.c. The tropane alkaloids include atropine, hyoscamine, hyoscine or scopolamine and the highest amount of the hyoscine is found in the seeds.[6] The deliriant, hallucinogenic, sedative or depressant effects of *Datura metel* has been reported.[6,8] In Nigeria it has been associated with adolescent rituals and has been abused especially among youth that smoke, chew or prepare water infusion believing it has libido
enhancement properties. D. metel is variously referred to as Zakami (Hausa Fulani), Ejegemi (Ogori) and Jegemi (Idoma) have been abused by many youths of various ethnicities in Nigeria.

Apomorphine induced stereotyped behavior has been utilized in investigating the CNS activities of many substances. Apomorphine is a dopamine agonist with high affinity for D₄ receptors and moderate affinity for D₂, D₃, D₅ and α adrenergic receptors thus acting on the CNS to produce a stereotyped behavior.

Phenobarbitone a barbiturate derivative used in the management of epilepsy and acts by enhancing the synaptic inhibition of Gama Amino Butyric Acid sub type A (GABAa) receptors. Chlorpromazine is a Phenothiazine derivative used as an anti-psychotic agent mainly as a result of its D₂ blocking activities. It reduces spontaneous and locomotor activities and potentially causes neuroleptic induced extrapyramidal side effects.

This study is aimed at testing for the CNS activities of the cold water extract of the seeds of D. metel in day-old chicks using phenobarbitone induced sleeping time and Apomorphine induced stereotyped behavior.

MATERIALS AND METHODS
The ripped fruits of D. metel were obtained in Jos, Plateau State Nigeria and authenticated by Mr I.A. Kareem a taxonomist in the Federal College of Forestry Jos. The seeds were removed from the fruits and air-dried for seven days. The dried seeds were crushed into fine particles using a motorized blender. Ethical clearance was obtained from the Ethical committee on the use of laboratory animals Department of Pharmacology, Faculty of Pharmaceutical Sciences, University of Jos.

A 70 g quantity of the powdered seeds were weighed into a beaker containing 300 ML of distilled water and shake intermittently for 72 hours after which the extract was evaporated to dryness at a controlled temperature of about 45 ºC. The LD₅₀ of the extract was determined in the day-old cockerels using the Lorke methods.

Effects of cold water extract of the seeds of D. metel on the behavioral activities of the day old cockerels was determined by dividing the animals into four groups of four chicks each. A pilot study was conducted using 50 mg/kg, 75 mg/kg and 100 mg/kg of the seed extract of D. metel. Groups one, two and three were administered 50 mg/kg, 75mg/kg and 100 mg/kg of
the extract intraperitoneally respectively. Two chicks were observed at a time for pecking, abnormal movement, aggression, sedation, staggering, bizarre posture and scratching of body parts. The fourth group that served as control was given equivalent volume of distilled water used for dilution of the extract for each bird (Table 1).

Two ampoules of chlorpromazine (CPZ) hydrochloride (25 mg/ml) were dissolved in 20 ml of distilled water to produce 2.5 mg/ml stock solution. After a pilot study a dose of 60 mg/kg of chlorpromazine was chosen as the optimum dose that produced the desired effect. Another group of a day old chicks were divided into four groups of four chicks each. Group 1 was administered 60 mg/kg of CPZ while groups 2, 3 and 4 were pretreated with 60 mg/kg of CPZ and immediately administered 50 mg/kg, 75 mg/kg and 100 mg/kg respectively of the extract. All administrations were done through intra peritoneal route and the animals were observed for CNS activities (Table 2).

Two ampoules of phenobarbital sodium (200 mg/ml) were obtained and dissolved in 20 ml of distilled water to produce a stock solution of 10 mg/ml. Effects of the extract on phenobarbitone induced sleeping time was investigated in the chicks by dividing the chicks into four groups of four chicks each. Group 1 which served as the control was administered 55 mg/kg of phenobarbitone, while groups 2, 3, and 4 were pre treated with 50 mg/kg, 75 mg/kg and 100 mg/kg of the extract and after 30 minutes, 55 mg/kg of the Phenobarbitone sodium was administered to each group. The onset and duration of phenobarbitone induced sleeping time was observed and recorded (Table 3).

Effects of apomorphine induced stereotyped behaviour was investigated by dissolving 200 mg of apomorphine hydrochloride and sodium metabisulphate (an antioxidant) to improve the stability of apomorphine) in 1.0 L of warm distilled water to produce 0.2 mg/ml. The chicks were divided into four groups of four chicks each. Group 1 were administered with the pre determined dose (0.2 mg/kg of apomorphine) subcutaneously while groups 2, 3 and 4 were pretreated with 50 mg/kg, 75 mg/kg and 100 mg/kg respectively of D. metel and after 30 minutes administered apomorphine 0.2 mg/kg and observed for stereotyped behaviour (Table 4).

The data collected were entered into Statistical Package for Social Science (SPSS 16.0) and analyzed using analysis of variance (ANOVA).
RESULTS
The \(LD_{50}\) was obtained to be about 125 mg/kg. There was a dose dependent reduction of the mean pecking value 8.25 ± 0.57 (50 mg/kg), 6.10 ± 0.57 (75 mg/kg) and 3.00 ± 0.33 (100 mg/kg) of the test group compared with the control 19.75 ± 1.17 (Table 1). There was a dose dependent decrease in movement of the chicks from 46.75 ± 0.57 (control) to 12.00 ± 0.15 (50 mg/kg), 10.25 ± 0.10 (75 mg/kg) and 6.00 ± 1.00 (100 mg/kg) respectively (Table 1). Sedation was increased from 60.00 ± 1.18 (control) to 360.00 ± 12.76 minutes (100 mg/kg).

When the chicks were pre-treated with chlorpromazine (CPZ) 60 mg/kg and later administered graded doses of the extract the following results were obtained for locomotor activities. 120.00 ± 0.91 (CPZ 60 mg/kg), extract 172.65 ± 6.41 (50 mg/kg), 241.15 ± 12.94 (75 mg/kg) and 365.05 ± 12.94 (100 mg/kg) (Table 2). Likewise pecking activities were reduced as follows, 16.00 ± 1.52 (CPZ 60 mg/kg), extract 5.25 ± 1.52 (50 mg/kg), 4.25 ± 1.52 (75 mg/kg) and 1.75 ± 0.44 (100 mg/kg) and aggression was totally abolished (Table 2). Movement was reduced from 16.75 ± 1.72 (CPZ 60 mg/kg) to 4.50 ± 0.41 (100 mg/kg) (Table 2). There was a dose dependent decrease on the onset of phenobarbitone induced sleeping time from 2.50 ± 0.57 at 50 mg/kg to 1.25 ± 0.33 at 100 mg/kg of the extract (Table 3). The results of apomorphine induced stereotyped behavior when co-administered with the extract was as follows, pecking activities 22.00 ± 0.81, 2.78 ± 0.89 and 12.75 for 50 mg/kg, 75 mg/kg and 100 mg/kg of the extract respectively (Table 3). Movement activities decreased from 116.50 ± 1.24 apomorphine alone to 15.32 ± 0.41 for apomorphine and 100 mg/kg extract (Table 3). There was a dose dependent decrease in aggression from 16.75 ± 0.71 to 5.60 ± 0.54 (Table 3). Fighting episode decreased from 15.75 ± 10.80 to 2.71 ± 0.54 (Table 3).

### Table 1: EFFECTS OF COLD WATER EXTRACT OF THE SEEDS OF *Datura metel* ON THE BEHAVIOURAL ACTIVITIES IN A 2-3 DAY OLD CHICKS

<table>
<thead>
<tr>
<th>Dose of extract (mg/kg)</th>
<th>Pecking</th>
<th>Movement</th>
<th>Staggering</th>
<th>Aggression</th>
<th>Sedation</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>food</td>
<td>non food</td>
<td>self</td>
<td></td>
<td></td>
</tr>
<tr>
<td>50</td>
<td>8.25±0.57*</td>
<td>5.25±0.57*</td>
<td>3.75±1.15</td>
<td>12.00±0.15**</td>
<td>8.75±0.75 *</td>
</tr>
<tr>
<td>75</td>
<td>6.10±0.57*</td>
<td>2.50±0.57**</td>
<td>2.50±0.57</td>
<td>10.25±0.10 **</td>
<td>6.00±1.00 *</td>
</tr>
<tr>
<td>100</td>
<td>3.00±0.33**</td>
<td>1.75±0.57**</td>
<td>0.00**</td>
<td>6.00±1.00 **</td>
<td>3.25±0.57</td>
</tr>
<tr>
<td>Control</td>
<td>19.75±1.7</td>
<td>12.25±0.27</td>
<td>3.75±0.57</td>
<td>46.75±0.57</td>
<td>0.00</td>
</tr>
</tbody>
</table>

n= 4, \(P<0.05\).

Control = distilled water only.
Table 2: EFFECTS OF CO-ADMINISTRATION OF CHLORPROMAZINE (CPZ) AND THE SEED EXTRACT OF *D. metel* ON BEHAVIOURAL ACTIVITIES OF A 2-3 DAY OLD CHICKS

<table>
<thead>
<tr>
<th>Treatments (mg/kg)</th>
<th>Pecking</th>
<th>Movement</th>
<th>Staggering</th>
<th>Aggression</th>
<th>Sedation</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>food</td>
<td>non-food</td>
<td>self</td>
<td></td>
<td></td>
</tr>
<tr>
<td>A</td>
<td>16.00±1.58</td>
<td>6.75±0.33</td>
<td>1.25±0.41</td>
<td>16.00±1.72</td>
<td>0.00</td>
</tr>
<tr>
<td>B</td>
<td>5.25±1.52*</td>
<td>0.00**</td>
<td>0.00</td>
<td>6.21±1.57*</td>
<td>0.00</td>
</tr>
<tr>
<td>C</td>
<td>4.25±1.52*</td>
<td>1.75±0.57</td>
<td>0.00</td>
<td>5.75±0.52*</td>
<td>0.00</td>
</tr>
<tr>
<td>D</td>
<td>1.75±0.44**</td>
<td>0.00</td>
<td>0.00</td>
<td>4.50±0.41*</td>
<td>0.00</td>
</tr>
</tbody>
</table>

n = 4, P<0.05

A = CPZ 60 mg/kg (control)
B = CPZ 60 mg/kg + Extract 50 mg/kg
C = CPZ 60 mg/kg + Extract 75 mg/kg
D = CPZ 60 mg/kg + Extract 100 mg/kg

Table 3: EFFECTS OF THE SEED EXTRACT OF *D. metel* ON PHENOBARBITONE INDUCED SLEEPING TIME IN A 2-3 DAY OLD CHICKS

<table>
<thead>
<tr>
<th>Treatments</th>
<th>Onset of sleep</th>
<th>Duration of sleep</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>2.50±0.57</td>
<td>130.25±3.50</td>
</tr>
<tr>
<td>B</td>
<td>2.00±0.00</td>
<td>362.75±4.97**</td>
</tr>
<tr>
<td>C</td>
<td>2.00±0.00</td>
<td>530.00±14.61**</td>
</tr>
<tr>
<td>D</td>
<td>1.25±0.33*</td>
<td>1440±4.81***</td>
</tr>
</tbody>
</table>

n = 4, P<0.05

A = Phenobarbitone 55 mg/kg
B = Phenobarbitone 55 mg/kg + Extract 50 mg/kg
C = Phenobarbitone 55 mg/kg + Extract 75 mg/kg
D = Phenobarbitone 55 mg/kg + Extract 100 mg/kg
Table 4: EFFECTS OF THE EXTRACT OF THE SEED OF *D. metel* ON APOMORPHINE INDUCED STEREOTYPED BEHAVIOUR IN A 2-3 DAY OLD CHICKS

<table>
<thead>
<tr>
<th>Treatments (mg/kg)</th>
<th>Pecking</th>
<th>Movement</th>
<th>Aggression</th>
<th>Fighting episode</th>
<th>Sedation</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>food</td>
<td>non-food</td>
<td>self</td>
<td></td>
<td></td>
</tr>
<tr>
<td>A</td>
<td>42.50±3.17</td>
<td>60.00±0.37</td>
<td>30.50±2.27</td>
<td>116.50±1.24</td>
<td>16.75±0.71</td>
</tr>
<tr>
<td>B</td>
<td>22.00±0.81*</td>
<td>36.50±3.50</td>
<td>17.25±0.34</td>
<td>48.00±0.41*</td>
<td>12.00±0.00</td>
</tr>
<tr>
<td>C</td>
<td>2.78±0.89**</td>
<td>26.27±0.44*</td>
<td>4.75±0.70</td>
<td>30.10±0.83</td>
<td>10.50±0.70</td>
</tr>
<tr>
<td>D</td>
<td>12.75±0.83*</td>
<td>4.51±0.44**</td>
<td>5.50±0.44*</td>
<td>15.32±0.41**</td>
<td>5.60±0.54*</td>
</tr>
<tr>
<td>E</td>
<td>29.75±1.71</td>
<td>12.75±1.27</td>
<td>4.20±0.75</td>
<td>46.50±0.70</td>
<td>0.00</td>
</tr>
</tbody>
</table>

n = 4, *P<0.05*

A = Apomorphine 0.2 mg/kg
B = Apomorphine 0.2 mg/kg + Extract 50 mg/kg
C = Apomorphine 0.2 mg/kg + Extract 75 mg/kg
D = Apomorphine 0.2 mg/kg + Extract 100 mg/kg
E = Distilled water

DISCUSSION

The LD_{50} (125 mg/kg) of the seed extract of *D. metel* implies that the extract was slightly toxic and should be used with caution based on the safety profile proposed by Lorke (1983), that classified substances according to their LD_{50} as follows: Very toxic (LD_{50} < 1.0 mg/kg), toxic (LD_{50} 1 mg/kg to 10mg/kg), less toxic (LD_{50} 11mg/kg to 100 mg/kg), slightly toxic (LD_{50} 101mg/kg to 1000mg/kg), non toxic LD_{50} 1001 to 5000mg/kg) and practically safe (LD_{50} > 5000mg/kg).

There was a significant reduction (*P<0.05*) in the movement and pecking activities of the test groups (Table 1). The dose dependent sedation started as early as 5 minutes and lasted for about 3 to 6 hours in the test groups as compared with the control which lasted for about an hour. Sedation observed with the control group could be attributed to fluid over-load and handling during administration. Feeding was totally abolished in the test groups while the control groups exhibited normal feeding and pecking activities (Table1). There was a dose dependent decrease and intermittent staggering combined with aggression (pushing one another) and abnormal movement (bizarre posture, hiding behind each other) in the test groups.

Pre-treatment with CPZ (60 mg/kg) and then graded doses of the extract produced a dose dependent increase in sedation and a significant decrease (*P<0.05*) in pecking activities.
(Table 2). The sedative effects of the cold water extract of the seed of *D. metel* augments that of CPZ and could be said to act through the same pathway as CPZ. Chlorpromazine is a dopamine receptor antagonist and therefore depresses the medullarly system.

There was a graded dose decrease ($P<0.05$) in the onset of phenobarbitone induced sleeping time and a significant increase ($P>0.05$) in the duration of sleep compared with the control (Table 3). The extract exhibited drowsiness and eventual sleep in the chicks similar to phenobarbitone and this lasted for twenty four hours post administration.

Effects of apomorphine induced stereotyped behaviour was investigated as seen by the initial increase in locomotor activities of the chicks before the administration of the extract (Table 4). The extract decreased the locomotor activities of the chicks from 116.50± 1.24 (0.2 mg/kg apomorphine) to 15.32± 0.41 (apomorphine 0.2 mg/kg + extract 100 mg/kg). There was also a corresponding decrease ($P<0.05$) in both the aggression and fighting episode when compared with the control.

The active constituents of *D. metel* such as hyoscine, hyoscamine and dutametine might be responsible for these Central Nervous System (CNS) effects. The alkaloids of *D. metel* are known antagonists of muscarinic cholinoreceptors in the CNS as well peripheral system, producing long lasting sedation, calmness and drowsiness.[14]

The interaction of the extract with apomorphine resulted in a partial abolition of the apomorphine induced stereotyped behavior. Apomorphine a dopaminergic agonist acted on the dopamine receptors to bring about stereotyped behavior observed in the chicks. Chlorpromazine a known dopaminergic receptor antagonist produced a degree of calmness in the chicks comparable with that of the extract.[12] The decreased stereotyped behavior observed therefore may be due in parts to blockade of the dopamine receptors by the extract, thereby reducing the action of apomorphine or possibly due to depressant effects at the medullarly centre of the brain.

**CONCLUSION**

The cold water extract of the seed of *D. metel* exhibited central nervous system effects comparable to phenobarbitone, chlorpromazine and decreases the stereotyped behavior induced by apomorphine thereby authenticating the use by traditional medicine healers in the treatment of psychotic disorders.
ACKNOWLEDGEMENT

We are grateful to Africa Centre of Excellence for Phytomedicine Research and Development (ACEPRD) for providing the publication fee for this article.

REFERENCES

