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AN INVESTIGATION OF PHYTOCHEMICALS, ANTIOXIDANT AND GENOTOXIC POTENTIAL OF *DATURA METEL* LINN.

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ABSTRACT

The use of plants with medicinal properties dates back decades and has been widespread. But regardless of their reported benefits, they are not completely harmless. Datura metel have been used over the years for various medicinal purposes with few reported complaints from its use. There is a need to evaluate the plant's toxicity in a model organism other than man that could translate similar toxicity response. The phytochemicals, antioxidant and genotoxicity of crude aqueous and methanol leaf, seed and root extracts of D. metel was evaluated. The study showed no significant difference in the alkaloids, tanins and saponins in aqueous and methanol extracts. Steroids and terpenoids was not found in all plant parts evaluated regardless of extraction medium. However, flavonoid was higher in leaf and seed methanol extracts than aqueous extracts. Likewise, total flavonoid, total phenol except DPPH in aqueous leaf extract higher than methanol leaf extract. Also, total phenol in root extracts was lower than that observed in root methanol extract. Proliferation in all plant part extracts of aqueous and methanol was significantly lower when compare to the control with leaf extracts having the least mitotic index. The study observed aberrations which include adherent nucleus, c-mitosis, anaphase bridge, binucleate cells and sticky cells. Percentage aberration was highest with leaf methanol extract than other plant part extracts. Both aqueous and methanol extracts of D. metel plant parts showed high proliferation inhibition and increase aberration cells even at 2 mg/ml suggest the need for further safe dose determination of the plant before any medicinal use. Hence, still requires further safety studies to ascertain its dose limits permissive for human usage.

KEY WORDS: antioxidant, *Datura metel*, genotoxicity, phytochemicals, toxicity

INTRODUCTION

Datura metel Lin., is a plant in the family of Solanaceae, indigenous to Mexico, naturalized in many other parts of the world (Satina & Blakeslee, 1941). It is usually found in dump sites in the urban northern part of Nigeria (Mann *et al.,* 2003). Locally, it is known as *zakami* in Hausa, *gegemu* or *apikan* in Yoruba and *Myaramuo* in Igbo with common names such as nightshade plant, Thorn apple Devil's apple, Devil's trumpet etc. (Babalola, 2014). It is a foul-smelling, erect, annual, freely branching herb that forms a bush up to 60 to 150 cm (2-5 ft) tall with long, thick, fibrous, white root; stem is stout, erect, leafy, smooth, and pale yellow-green and leaves are about 8 to 20 cm (3-8 in) long, smooth, toothed, soft, and irregularly

undulated; leaves have a bitter and nauseating taste, which is imparted to extracts of the herb, and remains even after the leaves have been dried. The egg-shaped seed capsule is 3 to 8 cm (1–3 in) in diameter and either covered with spines or bald. At maturity, it splits into four chambers, each with dozens of small, black seeds (Praseetha *et al.,* 2009).

Various parts of the plant are consumed but the seed have been reported to be use as psychoactive substance (Babalola, 2014). Local application includes local application for rheumatic swellings of the joints, lumbago, sciatica, neuralgia, painful tumours, scabies, eczema, allergy and glandular inflammations, pile (Donatus & Ephraim, 2009), swelling gum, breast pain (Rahmatullah *et al.,* 2010), diabetes (Murthy *et al.,* 2004) to mention a few. Scientific studies and the results on antimicrobial, antioxidant and phytochemical screening on ethanol and hydro alcoholic crude extracts of *D. metel* plant have been reported (Okoli *et al.,* 2007).

Despite the widespread use of herbal medicines globally and their reported benefits, they are not completely harmless (Tracy & Kingston, 2007). The presence of cytotoxic and mutagenic substances in their composition or resulting from their metabolism can cause damage to human health (Tedesco & Laughinghouse, 2012). However, the ability for recognition for toxic plants has been by trial and error in recent times. This has made information about their safety and efficacy generally sparse, *D. metel* is no exception. Therefore, there is a need to evaluate the plant's toxicity in a model organism other than man that could translate similar toxicity response.

The use of *Allium cepa* L. (onion) is an excellent model *in vivo* suitable for genotoxic studies and has become well established for the determination of the genotoxic substances in various environments. This is because the root growth dynamics is very sensitive to the pollutants; the mitotic phases are very clear in the onion; it has a stable chromosome number; diversity in the chromosome morphology; stable karyotype; clear and fast response to the genotoxic substances and spontaneous chromosomal damages occur rarely (Firbas & Amon, 2013). Hence the use of *A. cepa* test for such purpose. The aim of the study was therefore to evaluate phytochemical, antioxidant and genotoxicity potential of aqueous and methanol extracts of *D. metel.*

MATERIALS AND METHODS

COLLECTION AND PREPARATION OF PLANT MATERIALS

Fresh leaves, roots and seeds of *D. metel* were collected from Alakia area in Ibadan, Oyo state. The collected plant materials were identified at the herbarium, Lagos State Polytechnic, Ikorodu, Lagos state, Nigeria. The plant materials were washed with distilled water, dried under shade for 30 days and then ground into fine powder using electrical grinder. The powdered materials were stored in airtight containers at 4 ^{o}C until needed.

100 grams each of leaf, root and seed powder of *D. metel* were soaked in 500 ml of distilled water and 350 ml of methanol separately, and kept for 24 hours at room temperature. The mixtures were filtered through a clean muslin cloth and the filtrate again filtered by using Whatmann No.1 filter paper. The above procedure was repeated for another 24 hours before the residuals were discarded. Then, the extracts were concentrated and dried in a rotary evaporator at 37 °C till a sticky mass was obtained. After evaporation, the dried extracts were stored at 4°C until needed.

QUALITATIVE PHYTOCHEMICAL ANALYSIS

Stock solutions were prepared from each of the crude extracts dissolving 100 mg each of the methanol and water extracts in 10 ml of its own mother solvents. The obtained stock solutions were subjected to phytochemical screening using the method of Sangeetha *et al*. (2014). Phytochemicals assayed for include alkaloids, steroids, flavonoids, terpenoids, tannins and saponins.

ANTIOXIDANTS EVALUATION

4 mg of both aqueous and methanol extracts were taken and dissolved in 40 ml of methanol separately. The concentrations of the solution were diluted to 100 µg/ml each. Evaluation of total phenol, total falvonoids and 2,2-diphenyl-1-pycrilhydrazyl (DPPH) was done according to Sangeetha *et al*. (2014).

GENOTOXIC EVALUATION TEST

Solutions from both methanol and aqueous extract were prepared into various concentrations and subjected to cytotoxic evaluation using the *A. cepa* test. Onion bulbs of average size (15-22 mm) in diameter were purchased locally in Mile-12 market, Lagos State Nigeria. They were sun dried and the dried roots present at the base were carefully removed. Bulbs were rooted for 24 hours in distilled water. The rooted bulbs were then transferred into the treatments. Three replicates were set up for each treatment and a control setup, and then left for 48 hours. Root tips of each bulb were harvested, fixed in ethanol/acetic acid (3:1 v/v), fixed on a clean glass slide and stained with Aceto-orcein stain. Prepared slides were then viewed under a microscope.

ANALYSIS OF DATA

Mitotic activity and any aberration kind were recorded for treatments. Mitotic index was estimated according to Sehgal *et al*. (2006)

$$MI = \frac{P + M + A + T}{\text{Total number of cells observed}}$$

where MI, P, M, A, T are mitotic index, prophase, metaphase, anaphase and telophase respectively.

$$PAB = \frac{\text{Total number of aberrant}}{\text{Total number of cells observed}} * 100$$

where PAB is percentage number of aberrant observed

RESULTS AND DISCUSSIONS

Analysis of phytochemicals in leaf, seed and root extracts of *D. metel*

The study evaluated the presence of six phytochemicals in both the aqueous and methanol extract of *D. metel*. The results obtained from phytochemical screening revealed the absence of steroids and terpenoids in all extracts. The level of alkaloids, flavonoids and saponins were higher in both aqueous and methanol extracts of leaf and seeds of the plant than the root. The level of tannins showed no difference in all plants evaluated regardless of the medium of extraction (Table 1). Also more phytochemical concentrations were observed with methanol extracts than water extracts. Generally, some of the secondary metabolites studied in leaf, seed and root parts of *D. metel* were present in higher amount in methanol extracts than the aqueous solvent. This may be as a result of the polarity level of the medium of extraction playing major role in extracting the secondary metabolites as suggested by Ghasemzadeh *et al.*

(2011). The presence of alkaloids in high quantity did not corroborate with the report of Akharaiyi (2011) who reported a moderate quantity of alkaloids in the leaves of *D. metel*. The absence of terpernoids was also not in corroboration with Akharaiyi (2011) who reported moderate quantity of terpernoids in the seeds and leaves of *D. metel*. More phytochemicals were observed with methanol extracts than the aqueous extracts contrary to the reports of Akharaiyi (2011) who reported more phytochemicals with aqueous extracts than ethanol extracts samples. Methanol extacts showed more flavonoids than the aqueous extracts of both leaf and seeds.

Tannins was found more in the leaves than the roots in the work of Jamdhade *et al*. (2010) which did not agree with this present work which showed similar tannin concentration in this study. Prasanna & Yuwvaranni (2014) reported the absence of alkaloid and the presence of steroids with aqueous extract which did not corroborate with the present study. Sangeetha *et al*. (2014) reported similar result with phytochemicals evaluated in this study. Phytochemical constituents which are present in plant samples are known to be biologically active compounds and they are responsible for different activities such as antimicrobial, antioxidant, antifungal, anticancer and antidiabetic (Hossain & Nagooru, 2011)

Phytochemical constituents which are present in plant samples are known to be biologically active compounds and they are responsible for different activities such as antimicrobial, antioxidant, antifungal, anticancer and antidiabetic (Hassain & Nagooru, 2011). Different phytochemicals have been found to possess a wide variety of pharmacological activities, which may help in protection against chronic diseases (Sangeetha *et al*., 2014). Tannins, glycosides, saponins, flavonoids, and aminoacids have hypoglycemic and anti-inflammatory activities. Terpenoids, and steroids shows analgestic properties and central nervous system (CNS) activities. Saponins are involved in plant defense system because of their antimicrobial activity (Ayoola *et al*., 2008) and also possess hypocholesterolemic and antidiabetic properties. The most effective bio active compounds are alkaloids, aminoacids and saponins these were found in all four types of crude extracts. Flavonoids were found in methanol, chloroform and ethylacetate except hexane extracts. Chloroform and methanol extracts shows the presence of majority phytoconstituents. Many reports are available on flavanoid groups which exhibiting high potential biological activities such as antioxidant, anti-inflammatory, antiallergic reactions (Anyasor *et al*., 2010; Chao *et al*., 2002; Igbinosa *et al*., 2009; Thitilertdecha *et al*., 2008)

TABLE 1: Phytochemical screening for Aqueous and Methanol leaf, seed and root extracts of *D. metel*

Extract	Sample	Alkaloids	Flavonoids	Tannins	Saponins	Steroids	Terpenoids
Aqueous	DLF	++	+	+	++	ND	ND
	DSD	++	+	+	++	ND	ND
	DRT	+	+	+	+	ND	ND
Methanol	DLF	++	++	+	++	ND	ND
	DSD	++	++	+	++	ND	ND
	DRT	+	+	+	+	ND	ND

++: Highly present; +: moderately present; ND: not detected; DLF: sample leaf; DSD: sample seed; DRT: sample root

Antioxidant evaluation

The contents of total flavonoid, total phenol and DPPH were evaluated in plant parts of *D. metel* are shown in Table 2. Sangeetha *et al*. (2014) in their work reported that total phenolic content ranges from 0.53-3.99mg/ml which did not corroborate with this present study which observed total phenol range between 42-116 mg/g. The study showed that antioxidant contents evaluated were highest in the leaf part of *D. metel* for both aqueous and methanol extracts except for DPPH where aqueous seed extract gave the highest value for DPPH than both leaf and root aqueous extracts. Usually in many plants, the leaf shows higher antioxidant activities than other parts (Pyo *et al*., 2004; Wong & Kitts, 2006).

Aqueous root extract showed the least DPPH while methanol root extract showed least for both total flavonoids and DPPH. Aqueous seed extract gave the least total flavonoids while methanol seed extract gave the least total phenol among evaluated sample parts. This is similar to Akharaiyi (2011) who also reported higher antioxidant activity in the leaves of *D. metel*. More antioxidant activities were observed with aqueous extracts than ethanol extracts of the plant. More phytochemicals were also reported for aqueous extracts than ethanol extract (Akharaiyi, 2011).

TABLE 2: Antioxidant screening for aqueous and methanol leaf, seed and root extracts of *D. metel*

Extract	Plant Part	Total Flavonoid (mg of QE/g)	Total Phenol (mg of QE/g)	DPPH (IC_{50})
Aqueous	DLF	7.64	116.75	49.85
	DSD	1.19	78.63	65.99
	DRT	2.00	42.00	3.45
Methanol	DLF	4.07	106.80	81.01
	DSD	3.64	46.95	56.34
	DRT	3.36	64.70	12.06

DLF: sample leaf; DSD: sample seed; DRT: sample root; IC_{50}: Inhibition concentration at 50%; DPPH: 2,2-diphenyl-1-pycrilhydrazyl

Genotoxic evaluation of *D. metel* extracts

Genotoxicity and cytotoxicity tests using *A. cepa* test *in vivo* have been validated by several researchers, who jointly performed animal testing *in vitro* and the results obtained are similar providing valuable information for human health (Vicentini *et al*., 2001; Teixeira *et al*., 2003). Cell proliferation evaluation of water and methanol extracts treatments is presented in Table 4. There was a significant difference between the varied aqueous extract concentrations and the control. Although, the different stages of mitosis observed among the various plant parts varied, there was significant difference between the evaluated plant parts regardless of concentration. Methanol extracts were observed to be significantly reduced when compare to both the control and aqueous extracts evaluated in the study although similar result was observed in terms of plant part comparison and concentration differences (Table 3). In this study, all concentrations evaluated showed reduction in mitotic index when compared to control for both aqueous and methanol extracts in all plant parts used. Mitotic index in the methanol extract was significantly lower than that observe with aqueous plant part extracts. The leaf extracts in both medium of extraction was observed to have lower proliferation index when compared to the other plant parts.

TABLE 3: Proliferation evaluation of aqueous and methanol extracts of *D. metel* plant parts

Sample	Conc. (mg/ml)	Total cells	P	M	A	T	DC	MI
Aqueous Extract								
CTRL	0	1000	339	5	35	160	539	0.54[a]
DLF	2	1001	66	22	8	18	114	0.19[b]
	4	1006	61	19	12	13	105	0.15[b]
	6	980	50	18	17	15	100	0.10[b]
	8	1000	52	21	13	7	93	0.09[bc]
DRT	2	1000	78	23	21	10	132	0.23[b]
	4	1001	54	20	21	11	106	0.21[b]
	6	1006	60	25	19	9	113	0.21[b]
	8	995	72	15	10	12	109	0.20[b]
DSD	2	992	79	25	11	13	128	0.20[b]
	4	997	78	8	14	9	109	0.18[b]
	6	991	60	13	17	10	100	0.15[b]
	8	1002	59	15	10	13	97	0.12[b]
Methanol Extract								
DLF	2	1000	23	17	22	10	72	0.03[c]
	4	988	24	14	21	12	71	0.03[c]
	6	890	21	16	20	8	65	0.02[c]
	8	1032	20	12	19	21	72	0.02[c]
DRT	2	987	23	12	12	12	59	0.10[c]
	4	993	22	20	10	11	63	0.08[c]
	6	978	21	18	15	8	62	0.08[c]
	8	987	22	11	16	10	59	0.07[c]
DSD	2	996	19	17	16	19	71	0.07[c]
	4	1055	27	12	20	13	72	0.07[c]
	6	1018	21	11	18	15	65	0.06[c]
	8	1014	21	17	16	8	60	0.05[c]

DLF: sample leaf; DSD: sample seed; DRT: sample root; P: prophase, M: metaphase, A: anaphase, T: telophase, MI: mitotic index, DC: dividing cells, MI: mitotic index.

Percentage aberration (PAB) was higher with methanol extract than aqueous extracts of *D. metel* evaluated in the study. PAB was not significantly different between the plant parts so also between concentrations (Table 4). The cytotoxic effect of *D. metel* extract treatments was evident as observed by a significant decrease in the mitotic index. Our observations support the antiproliferative effects of *D. metel* extracts similar to that reported by Danhof and McAnally (1983). The production of chromosome abnormalities in all the plant parts' extracts can be regarded as a reliable evidence of the genotoxicity of the plant's part. The results indicated that all the treatments induced different types of chromosomal abnormalities in non-dividing cells as well as different mitotic stages. These abnormalities were observed to affect almost all the stages of mitosis. Plants and toxins such as *Calotropis procera* and podophylatoxins have been described to impact negatively on these processes to cause cell proliferation inhibition or arrest (Sehgal *et al.*, 2006).

TABLE 4: Proliferation evaluation of aqueous and methanol extracts of *D. metel* plant parts

Sample	Conc. (mg/mL)	Total cells	AN	CMIT	BRG	BNC	STK	PAB
Aqueous Extract								
CTRL	Neg.	1000	0	0	0	0	0	0
DLF	2	1001	37	16	1	2	0	5.59
	4	1006	38	15	5	1	2	6.06
	6	980	42	12	3	3	5	6.63
	8	1000	33	19	9	5	2	6.80
DRT	2	1000	15	15	3	1	1	3.50
	4	1001	21	12	3	0	0	3.60
	6	1006	20	10	4	3	2	3.88
	8	995	19	18	4	2	1	4.42
DSD	2	992	16	20	1	1	0	3.83
	4	997	27	18	2	1	1	4.91
	6	991	26	17	8	3	1	5.55
	8	1002	29	22	2	7	0	5.99
Methanol Extract								
DLF	2	1000	41	18	7	3	6	7.50
	4	988	51	20	6	5	8	9.10
	6	890	55	21	11	6	2	10.67
	8	1032	53	36	13	8	3	10.94
DRT	2	987	25	10	11	8	5	5.98
	4	993	24	16	5	12	3	6.06
	6	978	36	18	4	3	3	6.54
	8	987	30	30	2	2	2	6.69
DSD	2	996	39	13	9	5	0	6.62
	4	1005	38	25	3	7	1	7.36
	6	1018	35	27	10	2	2	7.47
	8	1014	45	18	5	9	3	7.89

DLF: sample leaf; DSD: sample seed; DRT: sample root; TOT: total cells counted; AN: adherent nucleus; CMT: c-mitosis; BRG: bridge; BNC: bi-nucleate; STK: sticky cells; PAB: percentage aberration (%)

Aberrations observed in the study include adherent nucleus, c-mitosis, anaphase bridge, binucleate cells and sticky cells. Adherent nucleus was observed to be the highest aberration among both the aqueous and methanol extracts while the least aberration was sticky cells (Table 4; Figure 1). In aetiology terms, c-mitosis has been explained to occur due to inhibition of microtubule formation during mitosis and this may lead to aneuploidy and cell death, while stickiness is due to interchromosomal linkages of sub-chromatid strands coupled with excessive formation of nucleoproteins and inappropriate protein-protein interaction (Chattopadhyay *et al.*, 2004; Turkoglu, 2007). The latter is also believed to have resulted from altered physico-chemical properties of DNA due to interactions with other chemicals viz-aviz: mutagens, carcinogens and clastogenic agents (Badr & Ibrahim, 1987). Adherent nucleus was observed as the highest aberration in all test plant part extracts regardless of extraction medium. This is followed by C-mitosis. This indicates a relatively as suggested in the works of Badr &

Ibrahim (1987). The observation of binucleated cells formation signifies inhibition of cytokinesis following telophase (Majewska *et al.*, 2003). In *A. cepa*, such inhibition arrest cell plate formation and this has been attributed to phlamogram inhibition at the early stage of telophase (Badr & Ibrahim, 1987; Majewska *et al.*, 2003). Generally, these aberrations were observed to be mostly caused by root extract of *D. metel* concentrations, suggesting their greater genotoxic effects on *A. cepa* when compared with extracts from other plant parts regardless of the concentrations of the extract. Furthermore, some of the chromosomal aberrations educe by *D. metel* were also comparable to effects due to NaN_3, a known mutagenic and clastogenic agent (Iwalokun *et al*., 2011).

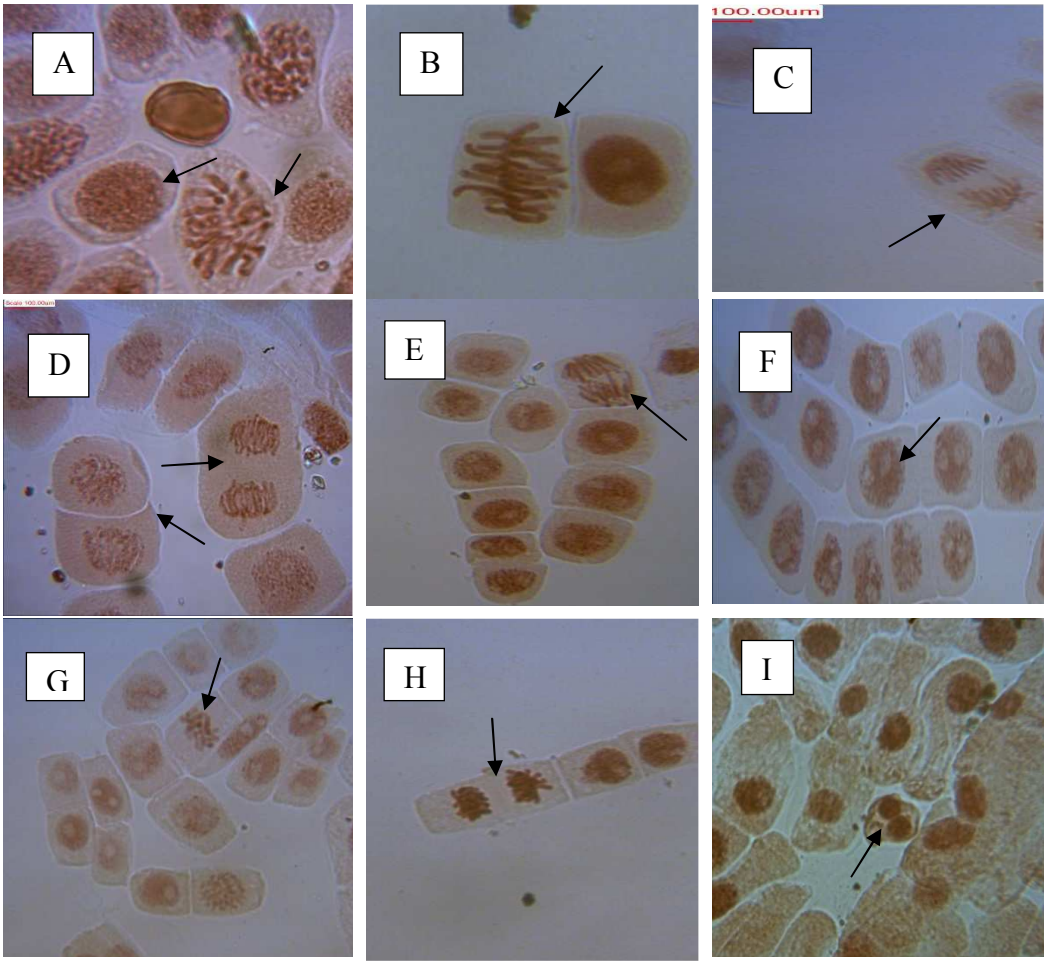

FIG. 1. Cell aberrations observed during the study (A) Prophase (B) Metaphase (C) Anaphase (D) Telophase (E) Anaphase bridge (F) Adherent nucleus (G) C-mitosis (H) Sticky cell (I) Bi-nucleate cell

Studies using bioindicators of toxicity and mutagenicity, such as the *in vivo* test of *A. cepa* are necessary for contributing to their safe and efficient use (Ianovici *et al,* 2009; Tedesco & Laughinghouse, 2012).

CONCLUSIONS

Extracts of *D. metel* plant parts elucidates that methanol root extract was the most toxic from this study with aqueous leaf extract being the least toxic in the *A. cepa* test. This suggest the need for safe dose determination of the plat before any medicinal use. Hence, still requires further safety studies to ascertain its dose limits permissive for human usage.

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