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The protective effect of the aqueous extract of *Sida acuta* BURM.F on lead nitrate-induced genotoxicity

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Abstract

This study investigated the protective effective of *Sida acuta* leaf extracts against the genotoxic effect of lead nitrate, a toxic heavy metal that easily permeate the ecosystem. The genotoxic and anti-genotoxic effects of the aqueous extract of *S. acuta* on onion cells (*Allium cepa* L.) was evaluated using the *Allium cepa* L. assay. Onion bulbs were exposed to 0.25 – 2.5 mg.mL^{-1} concentrations of the plant extract for analyses of induction of cytogenetic damage. There was observed a concentration-dependent decrease in mitotic index of the *A. cepa* roots cells compared to the negative control. Lead nitrate significantly induced chromosomal aberration in *A. cepa* root cells. This effect, however, was significantly ameliorated by the *S. acuta* leaf extract. This effect was demonstrated by the lower frequency of chromosome aberrations in lead nitrate treated root cells after exposure to the extract. Furthermore, the extract restricted the extent of lead-induced cytological aberrations in *A. cepa.* The findings in this study suggested the mitodepressive, antiproliferative and anti-genotoxic potentials of the extract.

Introduction

Plants are source of bioactive compounds with numerous benefits to mankind. Some of them act as antioxidants and anti-mutagens while others act through various mechanisms to prevent or cure diseases and or modulate the harmful effects of xenobiotic effects. This has led to increase in consumption of herbs and herbal supplements worldwide for various reasons. Some people believed it can cure diseases that orthodox medicine are unable to cure (Welz *et al.* 2018) while others believe it is affordable, natural, and thus non-toxic. However there are reports of some medicinal plants being toxic in man or animals (Oyeyemi *et al.* 2015; Ruan *et al.* 2019). Hence the need to establish the safety of medicinal plants. *Sida acuta*, is a common wireweed, a species of the flowering plants of the Mallow family (Malvaceae). It is an herbaceous weed widely distributed in the tropical and subtropical countries (Jindal *et al.* 2012). Renowned for its phytoremediation properties, it acts as a phytoextractor and phytostabilizer of heavy metals (Gupta and Sinha 2007; Putshaka *et al.* 2015; Ameh *et al.* 2019) suitable for decontamination of metals in waste contaminated sites. The different parts of the plants are also used traditionally for medicinal purposes. It is used to treat wound (Adetutu *et al.* 2011), liver disorders (Ekpo and Etim 2009), malaria (Iyamah and Idu 2015), nervous and urinary diseases, blood and bile disorders (Sreedevi *et al.* 2009), headaches, infectious diseases, rheumatism (Enemor *et al.* 2013), asthma, renal inflammation, colds, ulcers and worm infections (Caceres *et al.* 1987; Fokou

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et al. 2015). It has been reported to have antioxidant (Adetutu *et al.* 2011; Nwankpa *et al.* 2015), antineoplastic and antiproliferative (Jang *et al.* 2003; Pieme *et al.* 2010; Mallikarjuna *et al.* 2013), hepatoprotective (Sreedevi *et al.* 2009), neuroprotective (Benjumea *et al.* 2016; Owoeye and Salami 2017; Owoeye *et al.* 2017), antimicrobial (Oboh *et al.* 2007; Adetutu *et al.* 2011; Akinnibosun and Pela 2015), antiplasmodial (Karou *et al.* 2003; Nguyen-Pouplin *et al.* 2007), analgesic (Konaté *et al.* 2012), anti-hyperglycemic and anti-inflammatory activities (Arciniegas *et al.* 2017). Phytochemicals present in the leaves include alkaloids, saponins, tannins, steroids, glycosides and phenolic compounds (Akinnibosun and Pela 2015). Despite its wide usage and potential health benefit, it has been reported to be neurotoxic (Eluwa *et al.* 2013; Enemor *et al.* 2013), although non-toxic to the liver and kidney (Konaté *et al.* 2012). However, little is known about its genotoxic and anti-genotoxicity effects. Studies of genotoxicity and anti-genotoxicity are valuable to establish the safety and efficacy of herbs or natural products (Bast *et al.* 2002).

Allium cepa assay is a widely used plant assay for evaluation of genotoxic potential of different compounds/mixtures including medicinal plants (Oyeyemi and Bakare 2013; Sharma *et al.* 2018). It detects genomic mutation (Bonciu *et al.* 2018) with results comparable to those obtained in animal cell lines and is therefore an excellent model to determine the potential genotoxicity of compounds or mixtures.

In view of the widespread use of *S. acuta* in traditional medicine and dearth of information on its anti-genotoxic potentials, this study seeks to investigate the genotoxic and anti-genotoxic effect of the aqueous extract of the leaves of *S. acuta*. Genotoxicity tests can confirm the efficacy of a phytoremediation agent and also give an insight into the safety of medicinal plants for consumption.

Experimental

Collection of plants

Leaves of *S. acuta* were collected within Ondo City and authenticated by a taxonomist at the Department of Forestry, Federal University of Technology, Akure, Nigeria. Voucher specimen was deposited in the Herbarium of the same department (FUTA HERBARIUM: 149). The leaves were air dried and pulverised using electronic blender. The pulverised leaves were extracted by boiling in water at 100 °C as practised by the local people. The extract was filtered and concentrated using rotatory evaporator at 60 °C. The concentrated extract was stored at 4 °C until use.

Allium cepa *assay*

Allium cepa (onion) bulbs of same size were procured from a local market. These were sun dried for two weeks. The dried *A. cepa* bulbs were used for the modified *A. cepa* assay (Fiskesjö 1997; Oyeyemi and Bakare 2013) to evaluate the genotoxic and anti-genotoxic effect of the extract. For the genotoxicity test, onions bulbs were placed on 100 mL beakers filled with tap water for 24 h. After 24 h, three onions per concentration variant were transferred into beakers with four different concentrations (0.25 – 2.5 $mg.mL^{-1}$) of the aqueous extract of *S. acuta* (ESA) for 48 h to permit two complete cell cycles. These concentrations were chosen based on the result of our preliminary range finding test where 0.25 – 20 $mg.mL^{-1}$, were tested. The test sample was changed after the first 24 h. Tap water served as negative control and lead nitrate (10 ppm) served as positive control. After 48 h exposure to ESA, the meristematic cell region of the roots were excised and prepared for microscopic analysis.

Onion bulbs were rooted in tap water for 24 h, transferred into lead nitrate ($PbNO_3$) solution for 24 h and then into the extract for another 24 h. Negative and positive controls are tap water and $PbNO_3$ respectively. As in the genotoxicity study, the meristematic cell regions of the roots were excised after 24 h exposure to the extract and prepared for microscopic analysis. ESA extracts at the above mentioned concentration range (0.25 – 2.5 $mg.mL^{-1}$) were assessed for protective effect against lead, under the same Pb conditions applied.

Slide preparation for both the genotoxicity and anti-genotoxicity studies was carried out as previously described (Oyeyemi and Bakare 2013). Briefly, the root tips (cut at 48 h) were fixed in

Table 1. Summary of the cytological effects of aqueous extracts of *Sida acuta* on *Allium cepa* cells.

Extract concentration [mg.mL^{-1}]	Nº. Dividing cells	Mitotic index [Mean ± SD]	Sticky Chr.	Distur-bed spindle	F	Lag Chr.	A	Scattered / disoriented Ch.	Total aberra-tion	Frequency of aberrant cells [Mean ± SD]
0	221	5.53±2.34	2	7	–	–	6	13	28	0.73±0.36
0.25	237	5.93±2.02	2	–	–	9	5	30	46	1.15±0.17*
0.5	164	4.10±0.64	1	–	1	3	4	25	34	0.85±0.37
1.25	110	2.75±0.96*	–	–	–	4	3	16	23	0.68±0.45
2.5	94	2.35±1.44*	–	–	–	–	6	16	22	0.55±0.33
$PbNO_3$	184	4.60±0.69	14	7	2	1	1	32	57	1.43±0.22*

Extract ***c*** = 0 mg.mL^{-1} = Negative control (Tap water), $PbNO_3$ − *c* = 0.01 mg.mL^{-1}, Chr.− Chromosome, F − Fragment, A − Anaphase bridge, * Significantly different from negative control, ● Significantly different from positive control.

ethanol:glacial acetic acid (3 : 1 v/v), hydrolyzed in 1 N HCl at 60 °C for 5 min and then washed in distilled water. Root tips were squashed on each glass slide and stained with acetocarmine for 10 min. Six slides were prepared per concentration, out of which four were scored.

A total of 1,000 cells per slide and 4,000 cells per concentration were scored for both the genotoxicity and anti-genotoxicity studies. The mitotic index (MI) and frequency of aberrant cells were calculated as follows:

$$\text{MI [\%]} = (\text{number of dividing cells/total number of cells})\ x\ 100$$

$$\text{Frequency of aberrant cells [\%]} = \frac{\text{Number of aberrant cells}}{\text{Number of cells scored (1,000)}}\ x\ 100$$

Statistical analysis

Statistical analysis was performed using IBM-SPSS 23.0 software. Data were presented as mean ± standard deviation. Analysis involving comparison of means was carried out using one-way analysis of variance (ANOVA) followed by Duncan posthoc test where necessary. *P*-value of < 0.05 was considered significant.

Results

Genotoxicity study

This study investigated the potential genotoxic effect of the aqueous extract of the leaves of *S. acuta* using the *A. cepa* assay. The ESA extract caused a reduction in MI of onion cells after 48 h exposure compared with the negative control. The reduction in MI was significant ($P > 0.05$) at 1.25 and 2.5 mg.mL^{-1} (Table 1). The tested doses of *S. acuta* did not significantly induced chromosomal aberrations except at the lowest concentration (0.25 mg.mL^{-1}). The frequency of aberration decreased with increasing concentration (Table 1). The frequency of aberration at 1.25 and 2.5 mg.mL^{-1} is lesser than the background frequency observed in the control. There were normal chromosomes (Fig. 1) while various types of aberrations which include spindle aberration (Fig. 2a), vagrant chromosome (Fig. 2b-d), C-mitosis (Fig. 2e), disturbed spindle (Fig. 2f), anaphase bridge (Fig. 2f-2g), sticky chromosome (Fig. 2h-2i) polar deviation at telophase (Fig. 2j).

Anti-genotoxicity study

In the anti-genotoxicity study, the ability of the ESA extract to mitigate lead nitrate induced genotoxicity in *A. cepa* cells was investigated. The extract significantly ($P < 0.05$) reduced MI across the tested ESA concentrations compared to both the negative and positive controls. Lead nitrate significantly ($P < 0.05$) increased the frequency of chromosome aberrations compared to that of the negative control. This frequency was restored to level comparable to that of the negative control by the extract (Table 2).

Discussion

Humans are constantly exposed to genotoxins in the environment. Some of these only cause alteration in the somatic cells, which although may not be passed onto the next generation, may have serious health implications. Herbs have been consumed over the ages for the prevention

Table 2. Summary of the cytological effects of the aqueous extracts of *Sida acuta* on *A. cepa* cells pre-treated with lead nitrate.

Extract concentration [mg.mL^{-1}]	Nº. Dividing cells	Mitotic index [Mean ± SD]	Sticky Chr.	Disturbed spindle	F	Lag Chr.	A	Scattered / disoriented Ch.	Total aberration	Frequency of aberrant cells [Mean ± SD]
0	221	5.53± 2.34	2	7	–	–	6	13	28	0.70±0.36●
0.25	65	1.63±1.48*●	1	6	–	–	–	7	14	0.35±0.37●
0.5	61	1.53±0.32*●	1	–	–	–	1	6	8	0.20±0.28●
1.25	51	1.28±0.30*●	–	–	–	–	–	–	0	0.00±0.00●
2.5	32	1.05±0.13*●	–	–	–	–	–	2	2	0.05±0.10●
$PbNO_3$	195	4.89±0.62*	36	20	3	8	6	23	96	2.40±0.61*

Extract ***c*** = 0 mg.mL^{-1} = Negative control (Tap water), $PbNO_3$ − *c* = 0.01 mg.mL$^{-1,}$ Chr.− Chromosome, F − Fragment, A − Anaphase bridge, * Significantly different from negative control, ● Significantly different from positive control.

and treatment of several ailments with the presumption that they are safe (Elgorashi *et al.* 2002). However, concern has been raised over the safety of these herbs as some herbs with therapeutic effects have also been reported to be toxic (Oyeyemi *et al.* 2015; Amadi *et al.* 2018; Ruan *et al.* 2019). This study investigated the genotoxicity and anti-genotoxicity of the aqueous extract of *Sida acuta*, a widely used medicinal plants.

Our data showed a decline in the MI in both the genotoxicity and anti-genotoxicity studies. This is in line with previous reports on several medicinal plants and/or natural products (Shetty *et al.* 2017; Sharma *et al.* 2018). Suppression of MI correlates with cytotoxicity in plant cells (Shetty *et al.* 2017) and is thus an indication that *S. acuta* extracts at given concentrations are cytotoxic in this study. This suggested that the extract interfered with the cell cycle (Oyeyemi and Bakare 2013), inhibited DNA synthesis and cell cycle progression, which resulted into decreased cellular proliferation (Qin *et al.* 2015). This could probably be the basis of the antiproliferative effect of *S. acuta* reported in various cancer cell lines (Pieme *et al.* 2010; Thondawada *et al.* 2016).

The chromosome aberration induced by the extract in this study was, however, very low and comparable with that observed in the negative control. The extract at the high concentrations reduced the background frequency of chromosome aberration. This implies it is not genotoxic and can even prevent occurrence of spontaneous damage to the genetic material. The chromosome aberrations observed were physiological aberrations due to spindle inhibition (spindle aberration at anaphase (Fig. 2a), vagrant chromosomes (Fig. 2b-2d), C-mitosis (Fig. 2e) disturbed spindles (Fig. 2f) and disoriented chromosomes (Fig. 2j) or chromatin dysfunction such as stickiness (Fig. 2h). This shows that the extract probably contains spindle inhibitor(s). Inhibition of mitotic spindle is an important strategy in the development of anticancer drugs, as it inhibits the cell cycle progression (Zhu *et al.* 2016). The observed genotoxicity could due to the presence of alkaloids and tannins in this plant

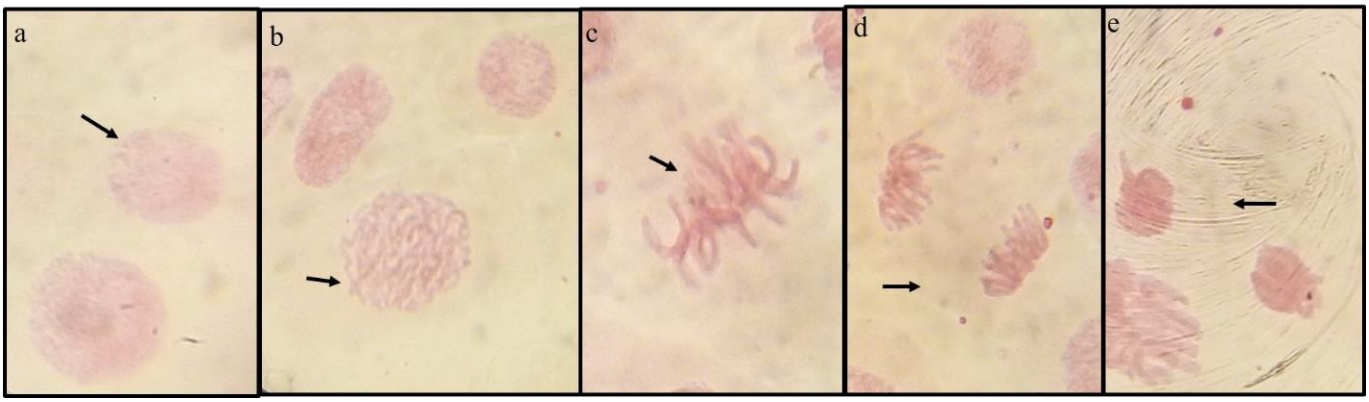

Fig. 1. Normal chromosomes observed in *Allium cepa* cells exposed to aqueous extract of *Sida acuta:* (**a**) interphase; (**b**) prophase; (**c**) metaphase; (**d**) anaphase; (**e**) telophase.

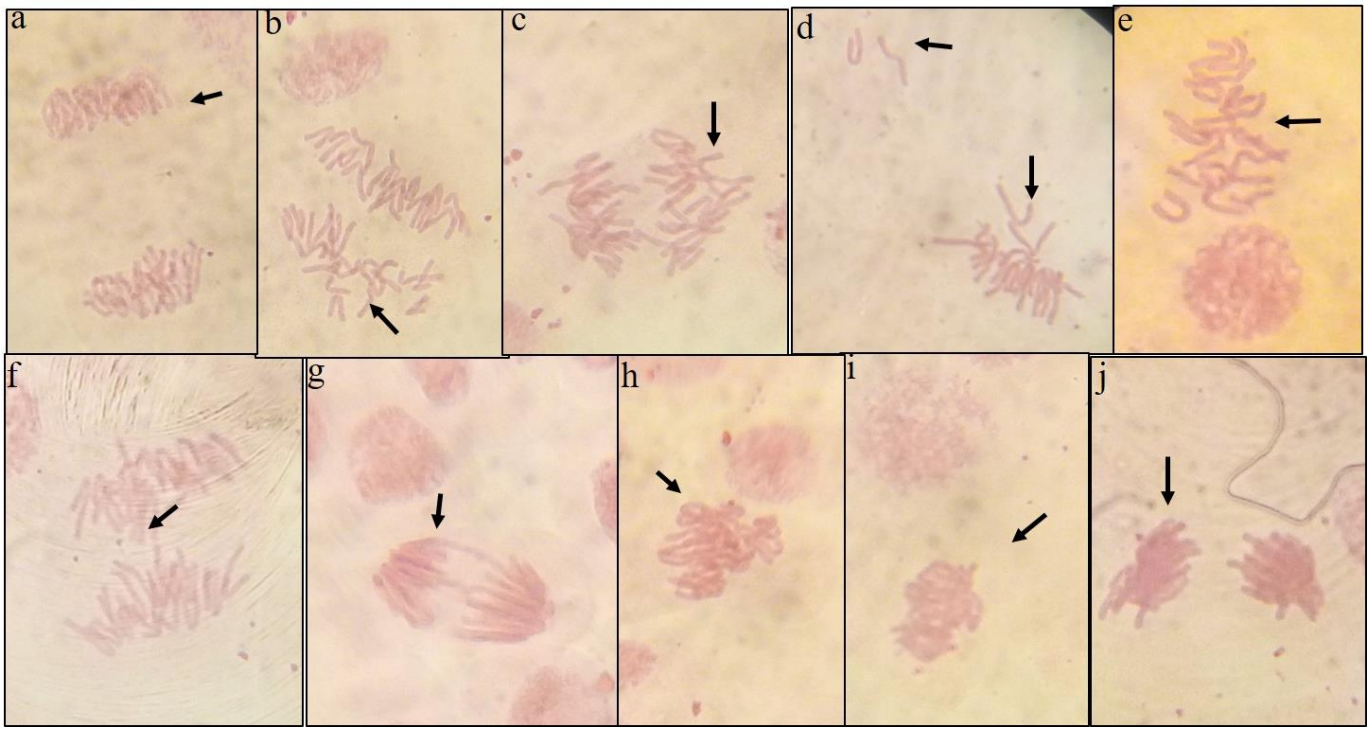

Fig. 2. Chromosomal aberrations induced in *Allium cepa* root cells by the aqueous extract of *Sida acuta*.: (**a**) spindle aberration at anaphase; (**b**, **c**) vagrant chromosome at anaphase; (**d**) vagrant chromosome at metaphase; (**e**) C-mitosis; (**f**) disturbed spindle with anaphase bridge; (**g**) anaphase bridge; (**h**, **i**) sticky chromosome; (**j**) polar deviation at telophase.

(Oboh and Onwukaeme 2007). These phytochemicals have been associated with chromosomal damage (Oyeyemi and Bakare 2013). Heavy metals are big menace in the environment. They threaten human health as they easily enter human body through the food chain. Lead (Pb^{2+}) is one of the most toxic heavy metals (Abdullah *et al.* 2014). Lead moves into and throughout ecosystems and contaminate the vegetation, air, water and soil (Samal *et al.* 2017). The toxicity of lead nitrate in several systems has been reported. Its genotoxicity in *A. cepa* has been established (Oyeyemi and Bakare 2013; Atoyebi *et al.* 2015). ESA significantly mitigated the genotoxicity induced by $PbNO_3$ in this study as the frequency of chromosome aberration was reduced below that observed in the negative control. This buttressed the phytoremediation ability of *Sida acuta*, as phytoremediation agents are known to deplete the genotoxicity of effluents or any other environmental contaminants (Di Gregorio *et al.* 2015; Basílico *et al.* 2017). The observed chromosomal aberration are also structural and not numerical. Structural chromosomal alterations occur as a result of DNA breaks, inhibition of DNA synthesis or replication of altered DNA. Chromosomal aberrations such as chromosome bridges and breaks, are indicators of a clastogenic action while abnormal segregation of chromosomes (lag chromosome, scattered/disoriented chromosome and C-metaphases) occur either spontaneously or by the action of aneugenic agents (Nefic *et al.* 2013). $PbNO_3$ induced disoriented chromosomes predominantly, showing that it is an aneugenic agent. However ESA, mitigated this aneugenic effect demonstrating its antigenotoxic effect. One of the mechanisms of lead induced genotoxicity is oxidative stress (Dai *et al.* 2012; Taie *et al.* 2019). ESA having antioxidant property (Subramanya *et al.* 2015) possibly inhibited bioaccumulation of Pb^{2+} in *A. cepa* cells. *S. acuta* is phytostabilizer of several heavy metals (Ameh *et al.* 2019) with the ability to inhibit the mobility/bioavailibity of Pb^{2+}, thus preventing $PbNO_3$ induced oxidative stress and ultimately DNA damage and or genotoxicity.

Noteworthy, the observed anti-genotoxic effect was accompanied by severe cytotoxicity as indicated by very low MI. In oocytes, when there is DNA damage, the spindle assembly checkpoint induces mitotic index arrest to inhibit the progression of cells harbouring the DNA damage (Marangos

et al. 2015). This pathway is not naturally activated in somatic cells (Collins *et al.* 2015). *S. acuta* being a natural spindle inhibitor probably activates this pathway in cells harbouring DNA/chromosomal damage resulting in the arrest of the cell cycle progression in those cells. Prolonged mitotic inhibition leads to inhibition of further cell proliferation or induction of apoptosis (Hain *et al.* 2016). Hence the complete inhibition of proliferation observed at the high concentration. Alkaloid isolated from *S. acuta* triggered apoptosis in human gastric adenocarcinoma cells (Ahmed *et al.* 2011). The low MI observed in the anti-genotoxic study may corroborate the apoptosis inducing effect of the plant.

In this study, the aqueous extract of *S. acuta* showed antiproliferative, mitodepressive and anti-genotoxic effects. Its ability to modulate the mitotic spindle is probably one of its key mechanisms of action. However, caution should be taken against indiscriminate consumption of the extract as it has the potential to be cytotoxic.

Conclusion

This study shows the potential of *S. acuta* to inhibit lead induced genotoxicity. *S. acuta* is a spindle inhibitor with the potential to interfere with cell cycle and inhibit mitosis. This buttresses its potential as an anticancer agent. There is a need to further explore the effect of *S. acuta* on cell cycle and proliferation so as to gain further insight into its molecular mechanism of action.

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Conflict of Interest

The authors declare that they have no conflict of interest.

References

Abdullah M, Rahman F, Gnanasegaran N, Govindasamy V, Kasim NH, Musa S (2014) Diverse effects of lead nitrate on the proliferation, differentiation, and gene expression of stem cells isolated from a dental origin. Sci. World J. 2014: 235941.

Adetutu A, Morgan WA, Corcoran O (2011) Ethnopharmacological survey and in vitro evaluation of wound-healing plants used in South-western Nigeria. J. Ethnopharmacol. 137: 50-56.

Ahmed F, Toume K, Ohtsuki T, Rahman M, Sadhu KS, Ishibashi M (2011) Cryptolepine, isolated from *Sida acuta*, sensitizes human gastric adenocarcinoma cells to TRAIL-induced apoptosis. Phytother. Res. 25: 147-150.

Akinnibosun FI, Pela B (2015) Evaluation of the phytochemicals and the antibacterial properties of *Sida acuta* leaf extract and their effects on wound bacterial isolates. ChemSearch J. 6: 70-77.

Amadi PU, Agomuo EN, Agada AI, Njoku UC, Ifeanacho MO, Okereke JC (2018) Toxicities of selected medicinal plants and floras of lower phyla. Alexandria J. Med. 54: 587-596.

Ameh EG, Omatola OD, Akinde SB (2019) Phytoremediation of toxic metal polluted soil: screening for new indigenous accumulator and translocator plant species, northern Anambra Basin, Nigeria. Environ. Earth Sci. 78: 345.

Arciniegas A, Pérez-Castorena AL, Nieto-Camacho A, Kita Y, De Vivar AR (2017) Anti-hyperglycemic, antioxidant, and anti-inflammatory activities of extracts and metabolites from *Sida acuta* and *Sida rhombifolia*. Quim. Nova 40: 176-181.

Atoyebi SM, Oyeyemi IT, Dauda BA, Bakare AA (2015) Genotoxicity and anti-genotoxicity of aqueous extracts of herbal recipes containing *Luffa cylindrica* (L), *Nymphaea lotus* (L) and *Spondias mombin* (L) using the *Allium cepa* (L) assay. Afr. J. Pharm. Pharmacol. 9: 492-499.

Basílico G, Magdaleno A, Paz M, Moretton J, Faggi A, de Cabo L (2017) Agro-industrial effluent phytoremediation with *Lemna gibba* and *Hydrocotyle ranunculoides* in water recirculating mesocosms. Clean Soil Air Water 45: 1600386.

Bast A, Chandler RF, Choy PC, Delmulle LM, Gruenwald J, Halkes SB, Keller K, Koeman JH, Peters P, Przyrembel H, de Ree EM, Renwick AG, Vermeer IT (2002) Botanical health products, positioning and requirements for effective and safe use. Environ. Toxicol. Pharmacol. 12: 195-211.

Benjumea DM, Gómez-Betancur IC, Vásquez J, Alzate F, García-Silva A, Fontenla JA (2016) Neuropharmacological effects of the ethanolic extract of *Sida acuta*. Rev. Bras. Farmacogn. 26: 209-215.

Bonciu E, Firbas P, Fontanetti CS, Wusheng J, Karaismailoğl MC, Liu D, Menicucci F, Pesnya DS, Popescu A, Romanovsky AV, Schiff S, Ślusarczyk J, De Souza CP, Srivastava A, Sutan A, Papini A (2018) An evaluation for the standardization of the *Allium cepa* test as cytotoxicity and genotoxicity assay. Caryologia 71: 191-209.

Caceres A, Giron LM, Martinez AM (1987) Diuretic activity of plants used for the treatment of urinary ailments in Guatemala. J. Ethnopharmacol. 19: 233-245.

Collins JK, Lane SI, Merriman JA, Jones KT (2015) DNA damage induces a meiotic arrest in mouse oocytes mediated by the spindle assembly checkpoint. Nat. Commun. 6: 8553.

Dai W, Liu S, Fu L, Du S, Xu Z (2012) Lead (Pb) accumulation, oxidative stress and DNA damage induced by dietary Pb in tilapia (*Oreochromis niloticus*) Aquac. Res. 43: 208-214.

Di Gregorio S, Giorgetti L, Ruffini Castiglione M, Mariotti L, Lorenzi R. (2015) Phytoremediation for improving the quality of effluents from a conventional tannery wastewater treatment plant. Int. J. Environ. Sci. Technol. 12: 1387-1400.

Ekpo M, Etim PC (2009) Antimicrobial activity of ethanolic and aqueous extracts of *Sida acuta* on microorganisms from skin infection. J. Med. Plants Res. 3: 621-624.

Elgorashi EE, Taylor JL, Maes A, De Kimpe N, Van Staden J, Verschaeve L (2002) The use of plants in traditional medicine: potential genotoxic risks. S. Afri. J. Bot. 68: 408-410.

Eluwa MA, Ubah CO, Akpantah AO, Asuquo OR, Ekanem TB, Akpan EP, Isamoh TE (2013) Neurohistological study of the effect of ethanolic leaf extract of *Sida acuta* on the cerebral astrocytes of adult wistar rats. Int. J. Pharm. Sci. Invent. 2: 7-10.

Enemor VH, Okoye VN, Awoke UL (2013) Effects of ethanol extract of *Sida acuta* leaves on some organ function parameters and physiologically important electrolytes in normal wistar albino rats. Am. J. Drug Discov. Dev. 3: 194-199.

Fiskesjö G (1997) *Allium* test for screening chemicals; evaluation of cytologic parameters. *In* Wang W, Gorsuch JW, Hughes JS (Eds.), Plants for Environmental Studies, CRC Lewis Publishers, Boca Raton, New York, pp. 308-333.

Fokou PV, Nyarko AK, Appiah-Oponga R, Yamthe LR, Addoa P, Asante I, Boyom FF (2015) Ethnopharmacological reports on anti-buruli ulcer medicinal plants in three West African countries. J. Ethnopharmacol. 172: 297-311.

Gupta AK, Sinha S (2007) Phytoextraction capacity of the plants growing on tannery sludge dumpsite. Bioresour. Technol. 98: 1788-1794.

Hain OK, Colin DJ, Rastogi S, Clarke PR (2016) Prolonged mitotic arrest induces a caspase-dependent DNA damage response at telomeres that determines cell survival. Sci. Rep. 6: 26766.

Iyamah PC, Idu M (2015) Ethnomedicinal survey of plants used in the treatment of malaria in Southern Nigeria. J. Ethnopharmacol. 173: 287-302.

Jang DS, Park EJ, Kang YH, Su BN, Hawthorne ME, Vigo JS, Graham JG, Cabieses F, Fong HH, Mehta RG, Pezzuto JM, Kinghorn AD (2003) Compounds obtained from *Sida acuta* with the potential to induce quinone reductase and to inhibit 7,12-dimethylbenz[a]anthracene-induced preneoplastic lesions in a mouse mammary organ culture model. Arch. Pharm. Res. 26: 585-590.

Jindal A, Kumar P, Jain C (2012) Antifungal activity of flavonoids of *Sida acuta* Burm f. against *Candida albicans*. Int. J. Drug Dev. Res. 4: 92-96.

Karou D, Dicko MH, Sanon S, Simpore J, Traore SA (2003) Antimalarial activity of *Sida acuta* Burm f. (Malvaceae) and *Pterocarpus erinaceus* Poir (Fabaceae). J. Ethnopharmacol. 89: 291-294.

Konaté K, Bassolé IM, Hilou A, Aworet-Samseny R, Souza A, Barro N, Dicko MH, Datté JY, M'batchi B (2012) Toxicity assessment and analgesic activity investigation of aqueous acetone extracts of *Sida acuta* Burn f. and *Sida cordifolia* L. (Malvaceae), medicinal plants of Burkina Faso. BMC Complement. Altern. Med. 12: 120.

Mallikarjuna G, Prabhakaran V, Sarat KV (2013) Anticancer activity of *Sida Acuta* Burm f. against nitrosodiethylamine and CCl4 induced hepatocellular carcinoma. Indo Am. J. Pharm. Res. 3: 7477-7483.

Marangos P, Stevense M, Niaka K, Lagoudaki M, Nabti I, Jessberger R, Carroll J (2015) DNA damage-induced metaphase I arrest is mediated by the spindle assembly checkpoint and maternal age. Nat. Commun. 6: 8706.

Nefic H, Musanovic J, Metovic A, Kurteshi K (2013) Chromosomal and nuclear alterations in root tip cells of *Allium cepa* L. induced by alprazolam. Med. Arch. 67: 388-392.

Nguyen-Pouplin J, Tran H, Tran H, Phan Ta, Dolecek C, Farrar J, Tran TH, Caron P, Bodo B Grellier P (2007) Antimalarial and cytotoxic activities of ethno-pharmacologically selected medicinal plants from South Vietnam. J. Ethnopharmacol. 109: 417-427.

Nwankpa P, Chukwuemeka OG, Uloneme GC, Etteh CC, Ugwuezumba P, Nwosu D (2015) Phyto-nutrient composition and antioxidative potential of ethanolic leaf extract of *Sida acuta* in wistar albino rats. Afr. J. Biotech. 14: 3264-3269.

Oboh IE, Onwukaeme DN (2007) Pharmacognostic evaluation of the leaves of *Sida acuta* Burm f. (Malvaceae). J. Phytomed. Ther. 12: 56-65.

Oboh IE, Akerele JO, Obasuyi O (2007) Antimicrobial activity of the ethanol extract of the aerial parts of *Sida acuta* burm f. (Malvaceae). Trop. J. Pharm. Res. 6: 809-813.

Owoeye O, Agboola OS, Gabriel OM, Salami OA (2017) Cisplatin-induced neurotoxicity in rat brain was attenuated by *Sida acuta* ethanol extract. Arch. Basic Appl. Med. 5: 89-94.

Owoeye O, Salami OA (2017) Monosodium glutamate toxicity: *Sida acuta* leaf extract ameliorated brain histological alterations, biochemical and haematological changes in wistar rats. Afr. J. Biomed. Res. 20: 173-182.

Oyeyemi IT, Yekeen OM, Odusina PO, Ologun TM, Ogbaide OM, Olaleye OI, Bakare AA (2015) Genotoxicity and anti-genotoxicity of aqueous and hydro-methanol extracts of *Spondias mombin* (L), *Nymphaea lotus* (L) and *Luffa cylindrica* (L) using animal bioassays. Interdiscipl. Toxicol. 8: 184-192.

Oyeyemi IT, Bakare AA (2013) Genotoxic and anti-genotoxic effect of aqueous extracts of *Spondias mombin* L., *Nymphea lotus* L. and *Luffa cylindrica* L. on *Allium cepa* root tip cells. Caryologia 66: 360-367.

Putshaka JD, Akyengo O, Akinwande OE (2015) Phytoremediation of heavy metals from flood plains of tannery waste water streams in Challawa Industrial Estate- Kano. Am. J. Chem. Applicat. 2: 52-56.

Pieme C, Penlap VN, Ngogang J, Costache M (2010) *In vitro* cytotoxicity and antioxidant activities of five medicinal

plants of Malvaceae family from Cameroon. Environ. Toxicol. Pharmacol. 29: 223-228.

Qin R, Wang C, Chen D, Björn LO, Li S (2015) Copper-induced root growth inhibition of *Allium cepa* var. agrogarum L. involves disturbances in cell division and DNA damage. Environ. Toxicol. Chem. 34: 1045-1055.

Ruan L, Li M, Xing Y, Hong W, Chen C, Chen J, Xu H, Zhao W, Wang J (2019) Hepatotoxicity and hepatoprotection of *Polygonum multiflorum* Thund. As two sides of the same biological coin. J. Ethnopharmacol. 230: 81-94.

Samal AC, Chakraborty S, Mallick A, Santra SC (2017) An investigation of lead in urban environment of Kolkata city, India. Int. J. Exp. Res. Rev. 12: 31-37.

Sharma S, Sharma S, Vig, AP (2018) Antigenotoxic potential of plant leaf extracts of *Parkinsonia aculeata* L. using *Allium cepa* assay. Plant Physiol. Biochem. 130: 314-323.

Shetty A, Venkatesh T, Suresh PS, Tsutsumi R (2017) Exploration of acute genotoxic effects and antigenotoxic potential of gambogic acid using *Allium cepa* assay. Plant Physiol. Biochem. 118: 643-652.

Sreedevi CD, Latha PG, Ancy P, Suja Sr, Shyamal S, Shine VJ, Sini S, Anuja GI, Rajasekharan S (2009) Hepatoprotective studies on *Sida acuta* Burm f. J. Ethnopharmacol. 124: 171-175.

Subramanya MD, Pai SR, Upadhya V, Ankad GM, Bhagwwat SS, Hedge HV (2015) Total polyphenolic contents and *in vitro* antioxidant properties of eight *Sida* species from Western Ghats, India. J. Ayurveda Integr. Med. 6:24-28.

Taie HAA, El-Yazal MAS, Ahmed SMA, Rady MM (2019) Polyamines modulate growth, antioxidant activity, and genomic DNA in heavy metal-stressed wheat plant. Environ. Sci. Poll. Res. 26: 22338-22350.

Thondawada M, Mulukutla S, Rama K, Raju S, Dhanabal SP, Wadhwania AD (2016) *In vitro* and *in vivo* evaluation of *Sida acuta* burm f. (Malvaceae) for its anti-oxidant and anti-cancer activity. Der Pharma Chem. 8: 96-402.

Welz AN, Emberger-Klein A, Menrad K (2018) Why people use herbal medicine: insights from a focus-group study in Germany. BMC Complement. Altern. Med. 18: 92.

Zhu L, Xiao F, Yu Y, Wang H, Fang M, Yang Y, Sun H Wang L, Sheng Y (2016) KSP inhibitor SB743921 inhibits growth and induces apoptosis of breast cancer cells by regulating p53, Bcl-2, and DTL. Anticancer Drugs 27: 863-872.