



## Genotoxic and cytotoxic activities of ethanol leaf extract of *Panicum maximum* Jacq (Poaceae) on root meristem of *Allium cepa* bulb

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### Abstract

There is a growing interest in the therapeutic potential of natural products and the mounting need to ensure their safety and efficacy. *Panicum maximum* Jacq (Poaceae) is one of such medicinal plant used traditionally to treat various diseases in Nigeria. The genotoxic and cytotoxic effects of the leaf extract were investigated using the *Allium cepa* test. The effect of *Panicum maximum* leaf extract on the root meristem cells of *Allium cepa* bulbs was investigated using onion bulbs exposed to varying concentrations of the extract (2.5, 5 and 10 mg/mL) for macroscopic and microscopic analyses. Tap water was used as a negative control and methotrexate (0.1 mg/ml) was used as a positive control. There was a statistically significant ( $p < 0.05$ ) inhibition of root growth depending on the concentration of the extract, compared with the negative control group. All tested concentrations of the extract were observed to have cytotoxic effects on cell division in *A. cepa*. The extract-induced chromosomal aberrations and micronuclei (MNC) formation in *A. cepa* root tip cells were significant ( $p < 0.05$ ) when compared with the control group. The treatment with extract induced further cell death, ghost cells, cell membrane damage, and binucleated cells. These results suggest that the leaf extract of *Panicum maximum* exerts cytotoxic and genotoxic effects on *A. cepa* root meristem cells.

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meristem, apoptosis.

### 1. Introduction

*Panicum maximum* Jacq (Poaceae) is a perennial, tuft grass with a short, creeping rhizome regarded as the most valuable fodder plant and is extensively used to make hay. The stems of this robust grass can reach a height of up to 2 – 3 m. Leaf sheaths were found at the bases of the stems and covered in fine hairs. It is a tropical grass that is widely distributed in Africa and other tropical regions of the world and is usually found along roads and in uncultivated farmlands and fields [1]. The people of Southern Nigeria use the leaves ethnomedically in the treatment of various ailments, such as malaria, microbial infections,

rheumatism pain, inflammation and diabetes. Some of these ethnomedical claims have been validated scientifically. Antidiabetic [2], antimalarial and analgesic [3], antibacterial [4-6], anti-inflammatory and antipyretic [7], antifungal [8], anticancer, antioxidative burst, antileishmanial [9], antidepressant [10], anticonvulsant [11], alpha amylase and alpha glucosidase inhibitory [12] activities of the leaf extracts have been reported. Phytochemical components such as phytol, pentadecanoic, hexadecanoic, dodecanoic and 8,11,14-eicosatrienoic (Z, Z, Z) acids as well as mono



and sesquiterpenes, such as terpinen-4-ol, borneol and germanicol have been reported in the leaf extract [9]. Despite its wide use in traditional medicine for the treatment of various diseases, there is a paucity of scientific information on the safety profile of this plant extract and evidence on the genotoxic and cytotoxic potential of *Panicum maximum* leaf extract. Thus, we investigated the genotoxic and cytotoxic activities of ethanol leaf extract of *Panicum maximum* on the root meristem cells of *Allium cepa* bulbs.

## 2. Materials and methods

### 2.1. Plants collection

The fresh leaves of *Panicum maximum* were collected in May, 2023 at Farmland in Uyo, Uyo LGA, Akwa Ibom State, Nigeria. The plant was identified and authenticated as *Panicum maximum* by a taxonomist, Prof. Margaret Bassey, in the Department of Botany and Ecological Studies, University of Uyo, Uyo, Nigeria. The herbarium specimens were deposited at the Faculty of Pharmacy Herbarium (FPH 76c), University of Uyo, Nigeria. The bulbs of *A. cepa*, which were procured from the Itam market, in Itu LGA of Akwa Ibom State, were equally identified and authenticated, as reported above.

### 2.2. Extraction

The leaves of *P. maximum* were washed and air-dried on a laboratory table for 2 weeks. The dried leaves were pulverized using a mortar and pestle. Powdered leaves (1 kg) were macerated in 95% ethanol for 72 h with intermittent shaking. The liquid ethanol extract obtained by filtration was evaporated to dryness in a water bath at 60 °C. The extract (yield-12.6%) was stored in a refrigerator at 4 °C until used for the experiment reported in this study.

### 2.3. *Allium cepa* test

#### 2.3.1. Root growth inhibition assay

The methods earlier described by Komolafe [13] and Ikechukwu [14] were used in this experiment. Small onion bulbs (*A. cepa*) were processed for the experiment by scarifying the bulbs of the dry scales and bottom base without destroying the root primordia, using a small sharp knife. Stock solution of the extract was prepared by dissolving 20 g of extract in distilled water (200 mL). Various working concentrations of the extract (2.5, 5 and 10 mg/mL)

were prepared from the stock solutions. The test concentrations of the extract (2.5, 5, and 10 mg/mL) prepared in 50 mL beakers were arranged in a series of 5 per test concentration. One *A. cepa* bulb was placed on top of each beaker, with the root primordia downward toward the liquid. Tap water was used as a negative control and methotrexate (0.1 mg/mL) was used as a positive control. After 24 h, the test samples were changed to the control and all the test concentrations. This was continued for 72 h, after which the roots were counted per beaker at all the tested concentrations and the mean root number was calculated. Similarly, the root lengths were measured using a metre rule and the mean root length was calculated. These were also done for the control groups. Several root tips were cut at a length of 10 mm from the bulbs at 8:30 am, and fixed in 3:1 (v/v) ethanol: glacial acetic acid for 24 h according to Ikechukwu *et al.* [14] before putting them in sample bottles and stored in a refrigerator until use.

#### 2.3.2. Microscopy

The root tips were placed in a test tube with 1N HCL and heated at 50 °C for 6 min to hydrolyze and macerate them. Roots were then washed with distilled water. Thereafter, the root tips were placed on microscopic slides on a blank background with forceps and were cut off at terminal tips followed by the addition of two drops of 2% orcein solution and allowed to stand for 2 min to stain properly. Two additional drops of 2% (w/v) orcein stain were added and mixed with the rootlets by knocking and stirring with a stirring spatula. Then a cover slip was placed at 45° to avoid air bubbles. Excess stain was removed with tissue paper by pressing slightly down with the thumb. After that, the cells were squashed by placing a filter paper on a coverslip and pressed lightly with a thumb. Five slides were prepared for each concentration according to Ikechukwu *et al.* [14]. The cover slip was sealed with a clear fingernail polish and each slide was examined under a light microscope at a magnification of × 40. Microphotographs were obtained to detect chromosomal aberrations. The mitotic index and frequency of chromosomal aberration were calculated based on the number of aberrant cells per total cells counted at each concentration of the test extract [15, 16]. Mitotic

**Table 1.** Cytotoxicity of *Panicum maximum* leaf extract on growing roots of onion (*Allium cepa*).

Treatment group	Concentration of extract (mg/mL)	Average root Number $\pm$ S.D	Average root length (cm) $\pm$ S.D
Negative control	Tap water	26.40 $\pm$ 3.82	4.82 $\pm$ 0.12
Methotrexate	0.1	2.10 $\pm$ 0.02 <sup>a</sup>	0.10 $\pm$ 0.01 <sup>a</sup>
	2.5	25.4 $\pm$ 3.68 <sup>a</sup>	3.56 $\pm$ 0.29 <sup>a</sup>
<i>Panicum maximum</i>	5.0	24.4 $\pm$ 4.04 <sup>a</sup>	3.12 $\pm$ 0.14 <sup>a</sup>
	10.0	17.80 $\pm$ 3.55 <sup>a</sup>	1.96 $\pm$ 0.26 <sup>a</sup>

Values are expressed as mean  $\pm$  SEM (n=5). Significant at  $p < 0.05$  when compared to negative control.

inhibition was determined using the following formula:

$$\text{Mitotic index} = \frac{\text{Number of dividing cells}}{\text{Total number of cells}} \times 100$$

The following indices were considered for evaluation of cytotoxicity and genotoxicity: (i) the mitotic index (MI) was calculated as the ratio between the number of mitotic cells and the total number of cells scored, expressed as a percentage and (ii) chromatin aberrations (stickiness, bridges, breaks and polar deviation) were used as endpoints for assessment of cytogenetic effects and micronuclei (MNC) were scored in interphase cells per 500 cells.

#### 2.4. Statistical analysis

Data obtained from this study were analyzed statistically using one-way ANOVA followed by Tukey-Kramer multiple comparison tests using the InStat Graphpad software, (San Diego, USA). Differences between the means were considered significant at the 5% level of significance i.e.  $p < 0.05$ .

### 3. Results and discussion

#### 3.1. Physicochemical characterization

The effects of *Panicum maximum* leaf extract on physicochemical parameters (root number and root length) are presented in Table 1. This result shows that all tested concentrations of *Panicum maximum* leaf extract caused significant inhibition of roots' growth compared to the negative and positive control groups. Root number and root length decreased as the leaf extract concentration increased. The mean root lengths in the negative and positive control (methotrexate) groups were  $4.2 \pm 0.12$  and  $0.10 \pm 0.01$  cm respectively. However, mean root length in 10 mg/mL treatment group was observed to have decreased significantly relative to negative control;

$1.96 \pm 0.26$  cm for *Panicum maximum* (Table 1). The mean root lengths in the treatment groups decreased, significantly ( $p < 0.05$ ) relative to the negative control. The root morphology and appearance were normal in the negative control group, but root tips treated with 2.5 mg/mL of *Panicum maximum* leaf extract, appeared slightly yellow and at 5 and 10 mg/mL of *Panicum maximum* leaf extract, the roots tips were observed to appear brownish (Table 1).

#### 3.2. Cytogenetic analysis

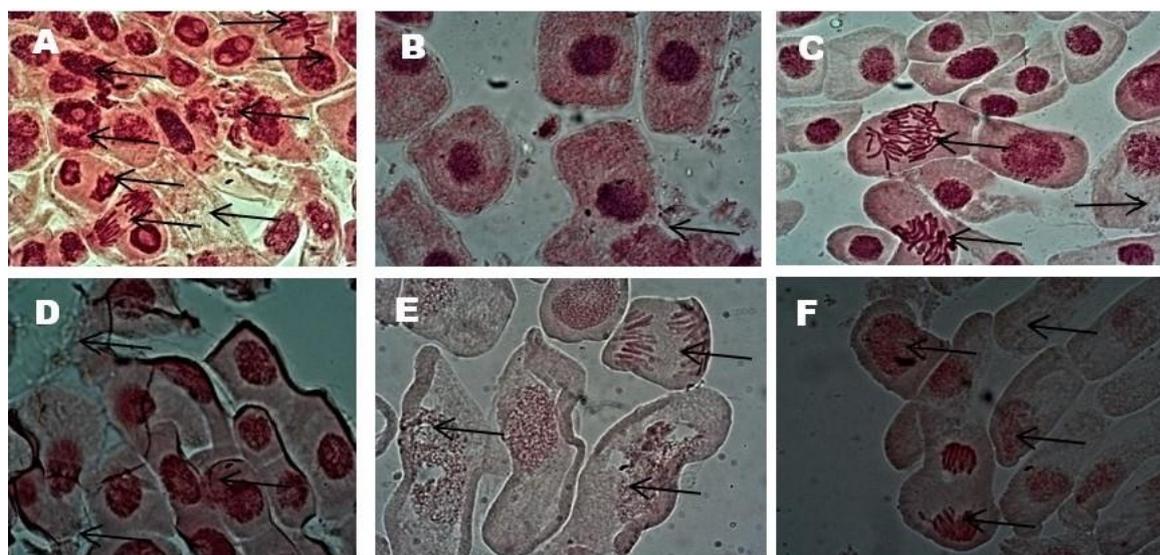
Table 2 shows the effects of the *Panicum maximum* leaf extract on the cytogenetic parameters of *Allium cepa* roots. Cytogenetic analysis showed that the leaf extract caused a concentration-dependent and significant ( $p < 0.05$ ) decrease in the mitotic index relative to that of the negative control group. The leaf extract of *P. maximum* at 2.5 mg/ml and 10 mg/mL had mitotic index of  $14.20 \pm 1.33$  and  $4.80 \pm 3.19$  as compared to  $70.80 \pm 3.22$  recorded in the negative control group (Table 2).

Cytogenetic alterations caused by the extracts are shown in Table 3. Chromosomal and cytological alterations were observed in the negative control, methotrexate and *Panicum maximum* leaf extract-treated groups, as shown in Table 3. Analysis of chromosome aberrations observed in the study showed that sticky chromosomes, cell walls and nuclear damage as well as polar deviation were detected in the different concentration treatments, especially at the highest concentration (Table 3) (Figs. 1A and 1B). This difference was significant ( $p < 0.05$ ) when compared to the negative control group. Fragmentation or clastogenic breaks of chromosomes, chromosome bridges and laggards were also observed at high concentrations (5 and 10 mg/mL) of the leaf extract (Table 3 and Fig. 1C). Apoptotic bodies,

**Table 2.** Dividing and total cells counted under microscopic observations and mitotic values in control and treatment concentrations.

Treatment group	Concentration of extract (mg/mL)	Total number of cells	Dividing cells	M.I (%) ± S.E
Negative control	Tap water	500	354	70.80±3.22
Methotrexate	0.1	500	14	2.80±0.10 <sup>a</sup>
	2.5	500	71	14.20±1.33 <sup>a</sup>
<i>Panicum maximum</i>	5.0	500	53	10.60±2.14 <sup>a</sup>
	10.0	500	24	4.80±3.19 <sup>a</sup>

Values are expressed as mean ± SEM (n=5). Significant at p < 0.05 when compared to negative control.



**Figure 1.** Photomicrograph showing the mitotic and chromosomal aberrations of *Allium cepa* root meristem cells after *Panicum maximum* leaf extract treatments under light microscope X40 magnification. Arrows indicate (A) fragmented chromosomes, apoptotic bodies, polar deviation, sticky chromosomes, cell wall and nuclear damage (B) cell wall and nuclear damage (C) sticky chromosome, bridge, laggard, cell wall damage (D) cell wall damage and binucleated cell (E) polar deviation, membrane and nuclear damage (F) dead cell, cell wall and nuclear damage, sticky chromosome, polar deviation.

dead cells and binucleated cells were also observed (Figs. 1D and 1E) in the extract-treated groups. It was generally observed that these abnormalities increased with increasing concentrations of the extracts. A concentration-dependent and statistically significant ( $p < 0.05$ ) increase in total aberrant cells (aberrant cells include bridge, laggard and stickiness), compared with the negative control was observed (Table 3). However, the methotrexate-treated group (positive control) showed the highest number of aberrant cells (Table 3). Genotoxic activities of the extract were further demonstrated by the induction of micronuclei in the root tip meristem cells of *A. cepa*, which was not concentration-dependent as the groups treated with methotrexate and 2.5 mg/mL of *Panicum maximum*

had a higher number of cells with micronuclei in the experiment, compared to the negative control, which was statistically significant ( $p < 0.05$ ) (Fig. 1(A)). In addition, cells with membrane and nucleus damages (Fig. 1F) were observed at various frequencies. Also, apoptotic cells (Fig. 1E) were detected in the group treated with the leaf extract.

In this study, the toxic effects of *Panicum maximum* leaf extract were assessed by evaluating the growth and morphology of the roots of onion bulb. The root growth was inhibited by various concentrations of the extract relative to the control group, as observed in this study. The root growth inhibition assay is considered a standard model for the assessment of cytotoxic and genotoxic potentials of various

**Table 3.** Chromosomal and mitotic aberrations in the root meristematic cells of *Allium cepa* after treatment of extract of *Panicum maximum*.

Treatment group	Concentration of extract (mg/mL)	Chromosome breaks (%) ± S.E	Stickiness (%) ± S.E	Polar deviation (%) ± S.E	Aberrant cells (%) ± S.E	MNC (%) ± S.E
Negative control	Tap water	-	0.11±0.08	0.31±0.04	1.05±0.56	-
Methotrexate	0.10	3.23±1.38 <sup>a</sup>	34.12±2.38 <sup>a</sup>	15.23±2.34 <sup>a</sup>	51.12±3.42 <sup>a</sup>	3.12±0.56 <sup>a</sup>
<i>Panicum maximum</i>	2.5	-	16.38±1.26 <sup>a</sup>	-	28.29±3.27 <sup>a</sup>	1.04±0.22 <sup>a</sup>
	5.0	0.14±0.08 <sup>a</sup>	22.48±6.32 <sup>a</sup>	1.25±0.69 <sup>a</sup>	34.48±3.81 <sup>a</sup>	0.45±0.08 <sup>a</sup>
	10.0	0.82±0.02 <sup>a</sup>	32.02±4.25 <sup>a</sup>	2.74±0.56 <sup>a</sup>	40.35±4.18	0.64±0.33 <sup>a</sup>

Values are expressed as mean ± SEM (n=5). Significant at p < 0.05 when compared to negative control.

compounds, including phytoconstituents of medicinal plants [17]. The inhibition of root growth as observed in this study could have resulted from the growth inhibitory activities of some allelochemicals in the extract as well as the prevention of cell division processes prominent at the root tip of *A. cepa* exposed to different concentrations of the extract [18]. This observation was in agreement with the observations of Akpan *et al.* [19] on the growth inhibitory effect of extracts of *Zea mays* husk and *Saccharum officinarum* leaves on *A. cepa* roots.

Cyto- and genotoxicity were also determined by assessing cytological parameters such as the mitotic index and number of chromosome abnormalities, including chromosome breaks, stickiness, and polar deviations. The mitotic index (MI) of *A. cepa* meristematic cells treated with the extract was significantly decreased relative to control. The inhibition of root growth increased with a decrease in mitotic index. The reduction of mitotic index below 22% in comparison to the negative control can have a lethal impact on the organism [20, 21], while a decrease below 50% usually has sub-lethal effects [22, 23], which is called the cytotoxic limit value [24]. Mitotic index measures the proportion of cells in the M phase of the cell cycle and its inhibition can be interpreted as cellular death or a delay in cell proliferation kinetics [25]. The reduction in mitotic activity could be due to inhibition of DNA synthesis or blocking in the G2 phase of the cell cycle, preventing the cell from entering mitosis [26]. The mito-depressive effects of some herbal extracts, including the ability to block the synthesis of DNA and nucleus proteins, have been reported earlier [27, 28]. Several other herbal extracts have been reported to inhibit mitosis [14, 29, 30]. The

decreased mitotic index in *A. cepa* roots treated with *Panicum maximum* leaf extract was probably due to either disturbance in the cell cycle or chromatin dysfunction induced by extract DNA interactions. The results suggest that the tested extract concentrations have inhibitory and mito-depressive effects on root growth and cell division in *A. cepa*. These findings also indicate that the extract possesses the potential to prevent DNA synthesis and reduce the number of dividing cells in roots due to the cytotoxic activities of its phytoconstituents.

Chromosomal aberrations (CA) are changes in chromosomal structure resulting from a break or exchange of chromosomal material. Most CA observed in cells are lethal, but there are many related aberrations that are viable and can cause genetic effects, either somatic or inherited [31]. Various chromosomal aberrations such as stickiness, bridge formation, fragmented chromosomes, laggards and polar deviations were observed in the present study. These aberrations might have resulted from the effect of the extract on spindle formation processes, resulting in cell division disturbances. Chromosome bridges indicate clastogenic effects due to chromosome breaks, and laggard chromosomes which, can result in lethal effects [32]. The presence of stickiness in metaphase cells and bridges might have resulted from improper folding of chromosome fibers, which connect the chromatids by means of subchromatid bridges. Sticky chromosomes have a highly toxic, irreversible effect and probably leading to cell death. Stickiness has been attributed to the effect of pollutants and chemical compounds on the physicochemical properties of DNA, proteins or both, on the formation of complexes with phosphate groups

in DNA, DNA condensation or the formation of inter- and intra-chromatid cross links [33, 34]. The observation of sticky metaphase supported the toxic effects of the extract. The bridges observed in this study might have been caused by the breakage and fusion of chromatids and subchromatids [17]. The presence of chromosome fragments is an indication of chromosome breaks, and can be a consequence of anaphase/telophase bridges [35].

The frequencies of total chromosome aberrations increased significantly following exposure to the extract indicating clastogenic activity. The obstruction of different phases of cell division and disorganisation of chromosom arrangement at different stages of cell division may be responsible for the increased chromosomal aberrations. These aberrations might have resulted from the activities of the genotoxic constituents of the extract, such as inhibition of DNA synthesis or spindle formation [36].

Micronuclei were observed in this study, especially at the lowest concentrations. The frequency of cells with micronuclei is a good indicator of the cytogenetic effects of the tested chemicals. Micronuclei (MNC) often results from the acentric fragments or lagging chromosomes that fail to incorporate into the daughter nuclei during telophase of the mitotic cells and can cause cellular death due to the deletion of primary genes [37, 38]. Previous studies suggesting MNC-induced effect of various plant extracts such as *Azadirachta indica* [39], *Psychotria* species [40], *Lavandula stoechas* and *Ecballium elaterium* [41, 42], *Hippocratea africana* [29], *Setaria megaphylla* [27, 30], *Heinsia crinata*, *Lasianthera africana* and *Justicia insularis* [14], *Solanum anomalum* fruit [43], *Croton zambesicus* [44], *Stachytarpheta cayenensis* [45] and *Stigma maydis* [46] have been documented.

In this study, membrane-damage cells were observed in all the treated groups. These results indicated the potential of the extract to exert cytotoxic effects over certain concentrations such as membrane damage. Multinucleated and binucleated cells were observed in extract-treated groups. This is due to the prevention of cytokinesis or cell plate formation. Microtubules have been implicated in cell plate formation by the extract, resulting in inhibition of cytokinesis. Ghost cells are dead cells in which the outline remains

visible, but whose nucleus and cytoplasmic structures are not stainable [42, 47]. Some ghost cells were observed at various frequencies in this study, especially in the 10 mg/mL treated groups. This could have resulted from the activities of the phytochemical constituents of the extract leading to nuclear damage and the prevention of cytoplasmic structures. In addition, the extract also induced DNA damage, cell death and/or apoptosis at various frequencies. Cell death is a basic biological process occurring in living organisms. The cell death is induced by high concentrations of toxins, stress, heavy metals, chemicals and others [48]. The findings of this study support earlier reports on the cytotoxic potential of leaf extracts by Okokon et al. [9].

Phytochemical components such as phytol, pentadecanoic, hexadecanoic, dodecanoic, and 8, 11, 14-eicosatrienoic (Z, Z, Z) acids, as well as mono and sesquiterpenes such as terpinen-4-ol, borneol and germanicol have been reported on the leaf extract of *Panicum maximum* [9]. The phytochemical constituents of this extract may have been responsible for the observed effects in this study. The terpenes present in this extract may have contributed to the observed cytotoxic and genotoxic activities in this study. It has been reported that terpenes especially monoterpenes extracted from various plant sources have shown high cytotoxic potential [49].

#### 4. Conclusions

The results of this study show that the leaf extract of *Panicum maximum* can induce cytogenetic alterations (cytoplasmic shrinkage, nuclear condensation, DNA fragmentation, membrane blebbing, cytoskeleton alterations and appearance of apoptotic bodies) and cell death in the root tips of *A. cepa*, suggesting cytotoxic and genotoxic activities of the extract. However, proper use of this plant in ethnomedicine is recommended and high doses should be avoided, as it can cause cytotoxic and/or genotoxic effects.

#### Disclaimer (artificial intelligence)

Author(s) hereby state that no generative AI tools such as Large Language Models (ChatGPT, COPILOT, etc.) and text-to-image generators were utilized in the preparation or editing of this manuscript.

## Authors' contributions

Conceptualization, J.E.O., C.C.O.; methodology, J.E.O.; software, U.F.U.; validation, C.C.O., J.E.O.; formal analysis, C.C.O., J.E.O., U.F.U.; investigation, K.E. resources, C.C.O., U.F.U., J.E.O., K.E.; data curation, K.E.; writing – original draft preparation, J.E.O.; writing – review & editing, C.C.O., U.F.U.; visualization, K.E., U.F.U., C.C.O.; supervision, J.E.O., C.C.O., U.F.U.; project administration, J.E.O.

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## Availability of data and materials

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## Conflicts of interest

The authors declare no conflict of interest.

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