

Cytotoxicity potentials of some medicinal plants in Mindanao, Philippines

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ABSTRACT

*This study aimed to assess the crude ethanolic extracts of five medicinal plants on *Allium cepa* (onion) root tip cells and kidney /liver cells of BALB/c strain mice for cytotoxic potential by observing any possible chromosomal aberrations in order to ensure a relatively safe use of medicinal plants. The five medicinal plants include *Jatropha gossypifolia* Linn. (Tuba-tuba), *Smalanthus sonchifolius* (Yacon), *Chromola enaodorata* (Hagonoy), *Euphorbia cotinifolia* (Malapascuas) and *Tinospora rumphii* (Panyawan) which are commonly used among the indigenous inhabitants of Mt. Nebu, Bukidnon, Philippines. . Result of higher concentration of the extracts (25mg and 35mg) showed more chromosomal abnormalities compared to 5mg and 15mg. These abnormalities include disturbed metaphase, chromosome fragments, vagrant chromosome, chromosome bridge, C-mitosis, binucleated cell and the presence of micronucleus. Among the five plants, only the extract of *S. sonchifolius* did not indicate any abnormalities to the root tips. Histological validation in this study had resulted significant change in liver and kidney tissues of BALB/c strain mice. The result gave a good initial indication for the toxicity of the plants tested but did not necessarily establish a direct link to toxicological effects in humans. Thus, this study recommends further laboratory validation especially in vivo studies.*

Keywords: *Allium cepa* root tips, chromosomal abnormalities, Musmusculus, plant extracts

INTRODUCTION

Plants have shaped the basis of urbane traditional medicine systems [1]. The medicinal use of plants is always been part of human practices and perhaps it is as old as human kind itself. The World Health Organization estimates that up to 80% of the world's population relies on traditional medicinal system [2]. It is used primarily in developing countries for primary health care and is also entering the therapeutics in the developed countries with a large number of bestselling herbal medicines. Herbal medicines escape toxicity testing before they are marketed as drug laws allow traditional medicines a short cut into the market [3]. Despite the profound therapeutic advantages possessed by some of the medicinal plants, some constituents of medicinal plants have been shown to be potentially toxic, mutagenic, carcinogenic and teratogenic [2]. Many reports have revealed that drugs of plant origin are not free from toxic effects and it has also been reported that hepatic failure and even death followed on the ingestion of herbal medicine [4]. It is important to note that most of the traditional medicinal plants have never been the subject of exhaustive toxicological tests such as is required for modern pharmaceutical compounds, and based on their traditional use for long periods of time they are often assumed to be safe [5]. Research has shown that traditional medicinal plants have in vitro mutagenic or toxic and carcinogenic properties, thus it is important to explore medicinal plants for their cytotoxicity. The non-prescription use of medicinal plants is cited today as an important health problem, in particular their toxicity to the kidneys [6]. In fact, there is currently a global reawakening of ethnobotanical surveys of medicinal plants and so as the need for screening specific parts of plants [7]. This makes

cytotoxicity today a major subject in pharmaceutical studies particularly in the area of cancer research [8]. Assessment of the potential role of traditional medicines on chromosomal abnormalities is indeed a significant issue because the damage to the genetic material caused by those plants may lead to critical mutations and therefore also to an increased risk of cancer and other diseases.

In the Philippines, majority of the rural poor especially to those localities that belong to the Indigenous People are suffering from chronic crippling economic disabilities that make mainstream health care unaffordable. And for this reason, indigenous people rely only to trial and error method of using plants for their health care practices [9]. For so many in these areas, health and healing are relegated to alternative forms of treatment like the hand-me-down herbal concoctions and some form of rural alchemy. Hence, a lot of local medicinal plants are being used in such areas without the prescription of an authority. Situations like this raises concern about the potential cytotoxic or mutagenic hazards those people could get resulting from the long-term use of such plants [10]. Moreover, there is scarcity of data on safety and tolerability of the plant when used as a phytomedicine in humans [11].

This present study aims to test the extracts of five medicinal plants on *A. cepa* (onion) to observe the possibility of chromosomal aberrations in the root tip cells. Extracts that lead to the occurrence of chromosomal aberrations are further subjected to an animal organism (white mice). The five medicinal plants include *J. gossypifolia* Linn. (Tubata), *S. sonchifolius* (Yacon), *C. odorata* (Hagonoy), *E. cotinifolia* (Malapascuas) and *T. rumphii* (Panyawan) which are commonly used among the indigenous inhabitants (Lumad) of Mt. Nebu, Bukidnon, Philippines. This study serves as awareness of cytotoxic potential of the plants mentioned to understand the necessity in ensuring a relatively safe use of medicinal plants. It could further be used as reference for future research on genotoxicity of medicinal plants here in the Philippines and thus will lead to a possible discovery of new medicines of such diseases the plant believed to be a cure.

MATERIALS AND METHODS

Plant collection and selection

The plant samples (Table 1), were collected from and based on ethnopharmacological use through oral interviews with local communities (indigenous people) during the month of June 2013. The plants were instigated according to the current utilization of these medicinal plants of natives as alternative medicine. Plants were identified and authenticated by the senior botanist, Edgardo C. Aranico at the Department of Biological Sciences, Mindanao State University – Iligan Institute of Technology. Fresh plant parts of *C. odorata*, *J. gossypifolia*, *E. cotinifolia*, *S. sonchifolius*, and *T. rumphii* in which the locals used were collected from transitional forest in Mt. Nebu, Valencia City, Bukidnon – Philippines.

Table 1. Medicinal plants

Scientific Name	Local Name	Common Name	Medicinal Use
<i>C. odorata</i>	Hagonoy	Bitter Bush	*Healing properties: antiseptic, anti-inflammatory
<i>J. gossypifolia</i>	Tuba-Tuba	Jatropha Plant	*Antidote for snakes bites, boiled and used as baths for fevers, treatment for boils and itches
<i>E. cotinifolia</i>	Malapascuas	Red Spurge	*Cathartic properties
<i>S. sonchifolius</i>	Yacon	Peruvian Ground Apple	*Stop bleeding, wound healing, muscle pain and rheumatism, diabetes and kidney problem
<i>T. rumphii</i> Boerl	Panyawan	Makabuhay Plant	*Toothache, stomach ache, abortive properties

Extraction

The various parts of *C. odorata* [stem and leaves], *J. gossypifolia* [leaves], *E. cotinifolia* [stem and leaves], *S. sonchifolius* [stem and leaves], and *T. rumphii* [stem and leaves], were cut into pieces and wrapped with foil then oven-dried for approximately 48 hrs at 40°C. The dried parts were pounded. Fine powdered plant parts were sequentially macerated with ethanol. This assay was carried out according to the principle and protocol previously described by Islam and Kato-Noguchi [12] with slight modifications. A 14.30 g pounded oven-dried plant parts were extracted with 200 ml of 100% (v/v) aqueous ethanol for 48 hrs. The filtrates were stocked in a glass container and set aside at a room temperature before use. Crude extract was also prepared by maceration of powdered oven-dried plant parts into distilled water to further evaluate its effect on mice. The maceration was carried out within 48 hrs and put into a glass container at room temperature before use.

Test organism

For the initial testing of cytotoxic activity of selected plant samples, test organism used was *Allium cepa* Linn. (Onions). Healthy *A. cepa* bulbs that were of the same sizes were purchased from a local market in Iligan City,

Lanao Del Norte. For inhibition activity of plant extracts, *A. cepa* was allowed to grow in each of the plant extract concentrations of 5, 15, 25, 35, 50 mg per 100ml distilled water. The inhibitory activity of plant extracts on the growth of the *A. cepa* roots was observed. For the preparation of *A. cepa* that were used for cytotoxicity of the plant extracts, *A. cepa* samples were allowed to grow simultaneously by soaking them in distilled water with plant extract concentrations for about 5 days in a room temperature. The treatments were arranged in an orderly manner with 3 replicates for each concentration.

Commercially bought 30 female BALB/c strain mice, 18 week old weighing 25-30 g were used to further assess the toxicity of the tested plants. The mice were housed individually in a metal screen cage and kept at room temperature. They were provided with water and food ad libitum. The aqueous plant extracts [0.1, 0.25, 0.50, 0.75 and 1 cc concentration for each plant extracts] were administered orally to the mice using a 1 cc syringe without needle. A control group was established and administered orally once daily with distilled water only. The rest of the groups were given the aqueous extract. They were treated for a span of 20 days and were sacrificed on the following day according to the protocol of Adekilekum *et al.* [13] with little modifications.

Evaluation of cytotoxic activity on onions

Final assay concentration of the dry weight extract was divided into 5 replicates and was initially tested on *A. cepa* set ups. The grown root tips of *A. cepa* were measured and collected. Root tips were cut off at approximately 1 cm (root caps were removed) and then fixed in a fixative solution, fresh cold methanol/glacial acetic acid solution 3:1 (v/v) for 24 hours. Following fixation, the roots were washed with distilled water and treated with 1 N HCl for 15 minutes. Subsequently, root tips were placed on a glass slide and cut into tiny pieces. Acetocarmine was used to stain the root tips and observed under a light microscope and presence of chromosomal abnormalities was examined. The root tips of control group were also prepared along with the experimental onion samples. The percentage length of root tips were determined by reference to the length of the control onions.

Evaluation of phytochemical toxicity on mice

The mice were sacrificed and the kidneys and liver were collected for histological analysis. The organs were then fixed in 10% formalin solution. Histopathology was evaluated under a light microscope. Photos were taken using Nikon D5100 DSLR camera.

RESULTS AND DISCUSSION

Table 2 showed the cytotoxic and root growth inhibitory effects of various concentrations of crude extract. The effects revealed a significant result that as crude extract concentration increases the root growth decreases. All the concentrations (5, 15, 25, 35, 50 mg/ml) of the medicinal plants produce different types of chromosomal aberrations in the *Allium cepa* such as disturbed metaphase, chromosome fragments, vagrant chromosome, chromosome bridge, C-mitosis, binucleated cell and presence of micronucleus. The result specifically showed that only *S. sonchifoliusextract* showed a normal response to the *Allium cepa* root growth thus, there was no chromosomal aberrations observed. The rest of medicinal plant extracts showed a positive response. It showed in *J. gossypifolia*, *E. cotinifolia*, and *T. rumphii* at 50 mg/ml extracts that there were no roots have grown.

Fig. 1 shows the seven types of aberrations seen in the root cells of the *A. cepa*. Most of the aberrations can be observed in metaphase and anaphase stage of mitotic division which can be viewed evidently as a structural aberration of the chromosome. During metaphase, some cells at this stage seem to be disturbed and sometimes chromosomes are not properly aligned at the center. Some chromosome wanders at a random area in the cytoplasm during both metaphase and anaphase stage of mitotic division and can be easily distinguished as vagrant chromosome and sometime fragmented while some forming chromosome bridges instead of separating at the poles. Furthermore, C-mitosis was observed and unseparated nucleuses were also observed at the telophase stage identified as binucleated cells and cells with micronucleus.

The root growth can be observed to be higher in lower concentrations but then completely inhibited as concentrations are getting higher. Roots of the control *A. cepa* do not have any aberration thus it is reasonable to suggest that the cytological abnormalities seen may be due to the exposure of the experimental onion roots to the extracts. Cells of the treated root tips are observe to have some clumping and stickiness of the chromosomes. According to the study of Nwakanma and Okoli, stickiness usually leads to the formation of the bridges and end up inhibiting metaphase and cytokinesis respectively and thus hampering cell division [14]. Moreover, they stated it in

their research that the ability of some plant extracts can cause DNA depolymerization and partial dissolution of nucleoproteins, breakage and exchanges of the basic folded units of chromatids and the stripping of the protein covering of DNA in chromosomes. In other cases, most chromosome breaking agents also has the ability to affect the synthesis, state or structure of DNA [15].

Table 2: Effect of plant extracts on the root growth and cytology of *A. cepa*

Treatment Conc. (mg/ml)	Phenotypic indices		Chromosomal aberrations						
	No. of dividing cells	Mean root length	Disturbed metaphase	Chromosome fragments	Vagrant chromosome	Chromosome bridge	C-mitosis	Bi-nucleated	Presence of micro-nucleus
Tested plants									
<i>C. odorata</i>									
Control	25	118.67	0	0	0	0	0	0	0
5	12	81.33	0	3	0	0	0	0	0
15	11	69.33	0	0	0	0	0	0	0
25	11	35	2	4	0	1	1	2	0
35	9	18	1	0	0	1	1	1	1
50	5	29	2	1	0	0	5	6	1
<i>J.gossypifolia</i>									
Control	25	118.67	0	0	0	0	0	0	0
5	14	105.33	1	1	0	1	0	1	0
15	13	92.67	1	1	2	1	0	1	2
25	10	54.33	2	2	0	1	5	4	2
35	8	34	4	5	7	5	3	7	9
50	-	-	-	-	-	-	-	-	-
<i>E. cotinifolia</i>									
Control	25	118.67	0	0	0	0	0	0	0
5	15	116.67	0	0	0	0	0	1	0
15	11	88.33	0	0	0	0	0	3	0
25	10	84.67	1	0	0	0	0	3	1
35	10	45	4	0	3	2	0	2	0
50	-	-	-	-	-	-	-	-	-
<i>S. sonchifolius</i>									
Control	25	118.67	0	0	0	0	0	0	0
5	26	108	0	0	0	0	0	0	0
15	23	110	0	0	0	0	0	0	1
25	21	104.33	0	0	0	0	0	0	0
35	24	103.33	1	0	0	0	0	0	0
50	25	107.5	0	0	0	0	0	1	0
<i>T. rumphii</i>									
Control	25	118.67	0	0	0	0	0	0	0
5	10	74.67	1	0	1	0	0	1	1
15	9	70.33	3	0	1	0	1	0	2
25	8	64.33	5	1	3	1	1	6	7
35	7	31	5	4	3	2	5	8	5
50	-	-	-	-	-	-	-	-	-

Aside from the aberrations mentioned, the number of micronuclei and chromosome breakages present among the treated onions are also considerable. While micronuclei can be interpreted as a consequence of clastogenic (chromosome breakage) or aneugenic (chromosome lagging and interference on the spindle behavior) effects [16], chromosome breakages on the other hand are the result of unfinished repair or disrepair of DNA which can result in cell death or a wide variety of genetic alteration or mutation [17]. Natural plant products can, apart from inducing mutations, also modify the action of other known mutagens on the living organisms by stimulating the existing mutagens within the cell, inhibiting the production of mutagens in the cell, synergizing the activity of existing mutagens, or activating the promutagens within the cell into mutagens [16].

Serious problems and damages on cells by incorrect usage of medicinal plants are possible. And traditional preparation methods take different toxicity levels in aqueous and ethanol extracts are taken into account when choosing the appropriate solvent for the preparation of the remedy [18]. In addition, mutagenicity of certain medicinal plant observed in the earlier studies encourages the necessity of using medicinal plants with specific guidelines, which have a sound basis and relevance to the population concerned [19]. In fact, it would be difficult to openly translate the results of this study to other animal species or directly to man because of genetic variation in response to drugs by different species [20], though some herbal medicine can cause undesired toxic effects to human which ranges from allergic reactions to cardiovascular, hepatic, renal, neurological and dermatological toxic effect [21].

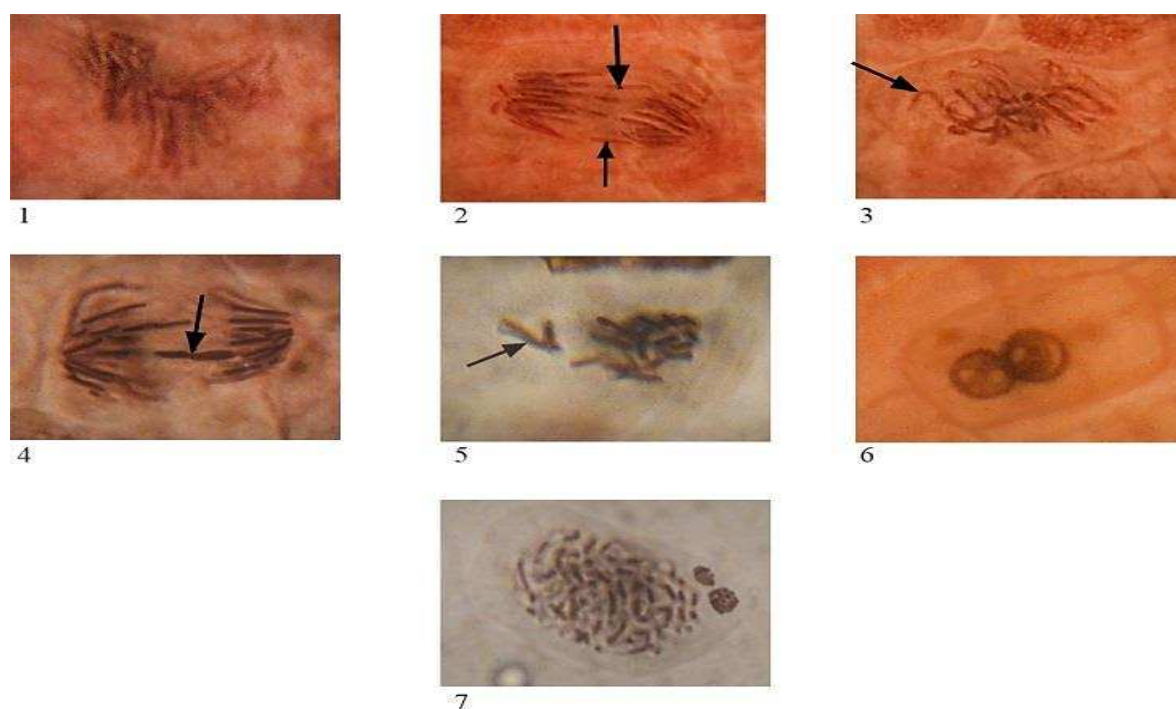


Figure 1. Aberrations at various stages of cell division of *A. cepa* treated with five medicinal plants. 1) Disturbed metaphase, 2) Chromosome fragments, 3) Vagrant chromosome, 4) Chromosome bridge, 5) C-mitosis, 6) Binucleated and 7) Micronucleus
Magnification 100x (cropped). Stain: Acetocarmine

Histological processing of liver and kidney was prepared and was viewed under the microscope. Any remarkable damage on morphological characteristics of both tissues in treatment group were compared to the control group (Table 3 and Table 4). The severity of the damage in liver and kidney tissue was treatment-dependent where an increase of treatment administered to the mice also revealed to be severely damaged. The two vital organs (liver and kidney), were carefully observed microscopically and revealed some histological changes in comparison to the control group that shows normal histological appearance (Fig. 2.)

All animals (mice) in all treatment with different doses including control group were observed throughout the conduct of the study. An apparent behavioral change during the course of the study seems to be normal in all treatment groups as compared to the control group. However, by histological validation conducted in this study, it has been cleared that there were significant change in liver and kidney tissues and even to its individual cells. Surprisingly, test group with treatment of the *S. sonchifolius* showed normal morphological characteristics in all treatment groups. Evidently, liver damage, usually noticeable as a result of cellular disarray, dispersed cells, cytoplasm vacuolation, nuclear/cellular apoptosis and necrosis, damaged sinusoid, and cellular rupture. Generally, liver processes all absorbed nutrients and elements from the food taken. Cells will die as a result of necrosis and apoptosis when they encounter toxins, notorious agents injuries [22] which can be implicated also as genetic mechanism and cellular response to present toxins in plants involving in the cascade and/or succession of activated enzymes in the liver [13] and kidney [23]. Knowing that the liver plays a significant role in biotransformation, metabolism as well as detoxification, thus any alteration in the function directories of its biomarkers may be used to monitor the level of injury by the plant extract before biopsy [24]. The activities of liver's functional enzymes will react to the direct protective action of natural toxins in the plant extracts which results to the liver injury, improved hepatic antioxidant status, lower lipid peroxidation, and lower serum activity of liver function and hepatocellular damage [25]. This is further emphasized in the study of [26] on the establishment of mean lethal dose of crude extract that the microscopic lesions of vital organs like liver and coagulative necrosis of hepatocytes could be attributed to the increasing amount of bioactive compounds.

Moreover, kidney was also considered vital organ in digestion of food since it serves as a filtering machine of absorbed nutrients and elements and blood. This present study revealed that kidney also has marked inflammatory changes to the tissues and cellular damage compared to the control group. Tissue damage in the kidney could be

attributed to the synergistic antioxidant activity of phytochemicals such as flavonoids, tannins, saponins, etc, present in tested plants (*J. gossypifolia* Linn. (Tuba-tuba), *S. sonchifolius* (Yacon), *C. odorata* (Hagonoy), *E. cotinifolia* (Malapascuas) and *T. rumphii* (Panyawan) [27] are responsible for kidney tissue destruction.

The result of this study concerning the medicinal plants tested is an eye opener not only to be cautious but also to the urgency in collaborating with the native doctors/healers in the Philippines to loosen the medicinal secrets of herbs used among the local, to document discoveries especially on its alternative form of usage and then validate it using modern techniques. This could be used for future research on genotoxicity of medicinal plants in the country that leads to a possible discovery of new medicines of such diseases those plants believed to be a cure.

Table 3. Histological characteristics of the liver of mice treated with medicinal plants at different concentrations and the control

Treatment group (cc)	Morphological Characteristics			
	Hepatocytes	Central Vein	Sinosoid	Bile Duct
Control Group	Slightly compressed cells, spaces between the hepatic plate	Elongated ovoid shape	Less spaces between the hepatic plate and less sinusoidal beading	Proliferation of the bile duct, cells aligned properly
Tested Plants				
<i>C. odorata</i>				
0.1	Slightly compressed cells, spaces between the hepatic plate and binucleated	Elongated ovoid shape	Less spaces between the hepatic plate and less sinusoidal beading	Proliferation of the bile duct, cells aligned properly
0.25	Slightly expanded cytoplasm, cytoplasm vacuolation	Elongated ovoid shape	Less spaces between the hepatic plate and less sinusoidal beading	Proliferation of the bile duct
0.50	Compress, swelling cells and expanded cytoplasm	Circular, ruptured wall	Less sinusoidal beading	Proliferation and distorted bile duct
0.75	Compressed, swelling cells, cellular rupture, and granules are present	Irregular severely ruptured wall	Severe sinusoidal beading	Distorted bile duct
1	Compressed, swelling cells, cellular rupture, apoptotic cells, and granules are present	Irregular severely ruptured wall	Severe sinusoidal beading and dilation between the hepatic plate	Distorted bile duct
<i>J. gossypifolia</i>				
0.1	Slightly expanded cytoplasm, cytoplasm vacuolation	Elongated ovoid shape	Less spaces between the hepatic plate and less sinusoidal beading	Proliferation of the bile duct, cells aligned properly
0.25	Slightly expanded cytoplasm	Elongated ovoid shape	Less spaces between the hepatic plate and less sinusoidal beading	Proliferation of the bile duct
0.50	Compressed, swelling cells, cellular rupture, and granules are present	Irregular severely ruptured wall	Severe sinusoidal beading	Distorted bile duct
0.75	Dispersed, swelling cells, cellular rupture, apoptotic cells, and granules are present	Irregular severely ruptured wall	Severe sinusoidal beading	Distorted bile duct
1	Dispersed, swelling cells, cellular rupture, and granules are present	Irregular severely ruptured wall	Severe sinusoidal beading and dilation between the hepatic plate	Distorted bile duct
<i>E. cotinifolia</i>				
0.1	Compressed, regular shape	Elongated ovoid shape	Less spaces between the hepatic plate and less sinusoidal beading	Proliferation of the bile duct, cells aligned properly
0.25	Compressed, regular shape	Elongated ovoid shape	Less spaces between the hepatic plate and less sinusoidal beading	Proliferation of the bile duct, cells aligned properly
0.50	Compressed, regular shape	Elongated ovoid shape	Severe sinusoidal beading	Distorted bile duct
0.75	Compressed, swelling cells, cellular rupture, apoptotic cells, and granules are present	Irregular severely ruptured wall	Severe sinusoidal beading and dilation between the hepatic plate	Proliferation of the bile duct
1	Dispersed, swelling cells, cellular rupture, apoptotic cells, cytoplasmic vacuolation. and granules are present	Irregular severely ruptured wall	Severe sinusoidal beading and dilation between the hepatic plate	Distorted bile duct
<i>S. sonchifolius</i>				
0.1	Compressed, regular shape	Elongated ovoid shape	Less spaces between the hepatic plate and less sinusoidal beading	Proliferation of the bile duct, cells aligned properly
0.25	Compressed, regular shape	Elongated ovoid shape	Less spaces between the hepatic plate and less sinusoidal beading	Proliferation of the bile duct, cells aligned properly
0.50	Compressed, regular shape	Elongated ovoid shape	Less spaces between the hepatic plate and less sinusoidal beading	Proliferation of the bile duct, cells aligned properly

0.75	Compressed, regular shape	Elongated shape	ovoid	Less spaces between the hepatic plate and less sinusoidal beading	Proliferation of the bile duct, cells aligned properly
1	Dispersed, regular shape	Elongated shape	ovoid	Less spaces between the hepatic plate and less sinusoidal beading	Proliferation of the bile duct, cells aligned properly
<i>T. rumphi</i>					
0.1	Compressed, regular shape	Elongated shape	ovoid	Less spaces between the hepatic plate and less sinusoidal beading	Distorted bile duct
0.25	Slightly expanded cytoplasm, cytoplasm vacuolation	Irregular severely ruptured wall	shapes	Less spaces between the hepatic plate and less sinusoidal beading	Distorted bile duct
0.50	Slightly expanded cytoplasm	Irregular severely ruptured wall	shapes	Severe sinusoidal beading and dilation between the hepatic plate	Distorted bile duct
0.75	Dispersed, swelling cells, cellular rupture, apoptotic cells, cytoplasmic vacuolation. and granules are present	Irregular severely ruptured wall	shapes	Severe sinusoidal beading and dilation between the hepatic plate	Distorted bile duct
1	Dispersed, swelling cells, cellular rupture, apoptotic cells, cytoplasmic vacuolation. and granules are present	Irregular severely ruptured wall	shapes	Severe sinusoidal beading and dilation between the hepatic plate	Distorted bile duct, necrosis to some cells

Table 4. Histological characteristics of the kidney of mice treated with medicinal plants at different concentrations and the control

Treatment group (cc)	Morphological Characteristics		
	Renal Cells	Corpuscles	Tubules
Control Group	Normal shape, properly aligned and well-defined nucleus	Normal Bowman's Space, glomerular podocytes remain intact	Well-defined proximal and distal tubules, uriniferous tubules
Tested Plants			
<i>C. odorata</i>			
0.1	Normal shape, properly aligned and well-defined nucleus	Normal Bowman's Space, glomerular podocytes remain intact	Well-defined proximal and distal tubules, uriniferous tubules
0.25	Normal shape, properly aligned and well-defined nucleus	Normal Bowman's Space, glomerular podocytes remain intact	Well-defined proximal and distal tubules, uriniferous tubules
0.50	Nuclear hypertrophy, cell misalignment, cytoplasmic vacuolation, swelling,	Shrinkage, Dilation, and distortion of glomerulus, distension of Bowman's capsule	Well-defined proximal and distal tubules, uriniferous tubules
0.75	Dispersed cells, Nuclear hypertrophy, cell misalignment, cytoplasmic vacuolation, swelling	Shrinkage, Dilation, and distortion of glomerulus, distension of Bowman's capsule	Cellular hypertrophy, shrinkage on convoluted tubules
1	Dispersed cells, Nuclear hypertrophy, cell misalignment, cytoplasmic vacuolation, swelling	Shrinkage, Dilation, and distortion of glomerulus, distension of Bowman's capsule,	Cellular hypertrophy, shrinkage on convoluted tubules, dispersed cells, distorted proximal and distal tubules
<i>J. gossypifolia</i>			
0.1	Normal shape, properly aligned and well-defined nucleus	Shrinkage, Dilation, and distortion of glomerulus, distension of Bowman's capsule	Well-defined proximal and distal tubules, uriniferous tubules
0.25	Dispersed cells, Nuclear hypertrophy, cell misalignment, cytoplasmic vacuolation, swelling	Shrinkage, Dilation, and distortion of glomerulus, distension of Bowman's capsule	Cellular hypertrophy, shrinkage on convoluted tubules
0.50	Dispersed cells, Nuclear hypertrophy, cell misalignment, cytoplasmic vacuolation, swelling	Shrinkage, Dilation, and distortion of glomerulus, distension of Bowman's capsule	Cellular hypertrophy, shrinkage on convoluted tubules, dispersed cells
0.75	Dispersed cells, Nuclear hypertrophy, cell misalignment, cytoplasmic vacuolation, swelling	Shrinkage, Dilation, and distortion of glomerulus, distension of Bowman's capsule	Cellular hypertrophy, shrinkage on convoluted tubules, dispersed cells
1	Dispersed cells, Nuclear hypertrophy, cell misalignment, cytoplasmic vacuolation, swelling	Shrinkage, Dilation, and distortion of glomerulus, distension of Bowman's capsule	Cellular hypertrophy, shrinkage on convoluted tubules, dispersed cells, distorted proximal and distal tubules
<i>E. cotinifolia</i>			
0.1	Normal shape, properly aligned and well-defined nucleus	Normal Bowman's Space, glomerular podocytes remain intact	Well-defined proximal and distal tubules, uriniferous tubules
0.25	Normal shape, properly aligned and well-defined nucleus	Normal Bowman's Space, glomerular podocytes remain intact	Well-defined proximal and distal tubules, uriniferous tubules
0.50	Normal shape, properly aligned and well-defined nucleus	Normal Bowman's Space, glomerular podocytes remain intact	Well-defined proximal and distal tubules, uriniferous tubules
0.75	Dispersed cells, Nuclear hypertrophy, cell misalignment, cytoplasmic vacuolation, swelling	Shrinkage, Dilation, and distortion of glomerulus, distension of Bowman's capsule	Cellular hypertrophy, shrinkage on convoluted tubules, dispersed cells
1	Dispersed cells, Nuclear hypertrophy, cell misalignment, cytoplasmic vacuolation, swelling	Shrinkage, Dilation, and distortion of glomerulus, distension of Bowman's capsule	Cellular hypertrophy, shrinkage on convoluted tubules, dispersed cells, distorted proximal and distal tubules
<i>S. sonchifolius</i>			
0.1	Normal shape, properly aligned and well-defined nucleus	Normal Bowman's Space, glomerular podocytes remain intact	Well-defined proximal and distal tubules, uriniferous tubules
0.25	Normal shape, properly aligned and well-defined nucleus	Normal Bowman's Space, glomerular podocytes remain intact	Well-defined proximal and distal tubules, uriniferous tubules

0.50	Normal shape, properly aligned and well-defined nucleus	Normal Bowman's Space, glomerular podocytes remain intact	Well-defined proximal and distal tubules, uriniferous tubules
0.75	Normal shape, properly aligned and well-defined nucleus	Normal Bowman's Space, glomerular podocytes remain intact	Well-defined proximal and distal tubules, uriniferous tubules
1	Normal shape, properly aligned and well-defined nucleus	Normal Bowman's Space, glomerular podocytes remain intact	Well-defined proximal and distal tubules, uriniferous tubules
<i>T. rumphii</i>			
0.1	Normal shape, properly aligned and well-defined nucleus	Normal Bowman's Space, glomerular podocytes remain intact	Well-defined proximal and distal tubules, uriniferous tubules
0.25	Nuclear hypertrophy, cell misalignment, cytoplasmic vacuolation, swelling,	Shrinkage, Dilation, and distortion of glomerulus, distension of Bowman's capsule	Cellular hypertrophy, shrinkage on convoluted tubules, dispersed cells, distorted proximal and distal tubules
0.50	Dispersed cells, Nuclear hypertrophy, cell misalignment, cytoplasmic vacuolation, swelling	Shrinkage, Dilation, and distortion of glomerulus, distension of Bowman's capsule	Cellular hypertrophy, shrinkage on convoluted tubules, dispersed cells, distorted proximal and distal tubules
0.75	Dispersed cells, Nuclear hypertrophy, cell misalignment, cytoplasmic vacuolation, swelling	Shrinkage, Dilation, and distortion of glomerulus, distension of Bowman's capsule	Cellular hypertrophy, shrinkage on convoluted tubules
1	Dispersed cells, Nuclear hypertrophy, cell misalignment, cytoplasmic vacuolation, swelling	Shrinkage, Dilation, and distortion of glomerulus, distension of Bowman's capsule	Cellular hypertrophy, shrinkage on convoluted tubules, dispersed cells, distorted proximal and distal tubules

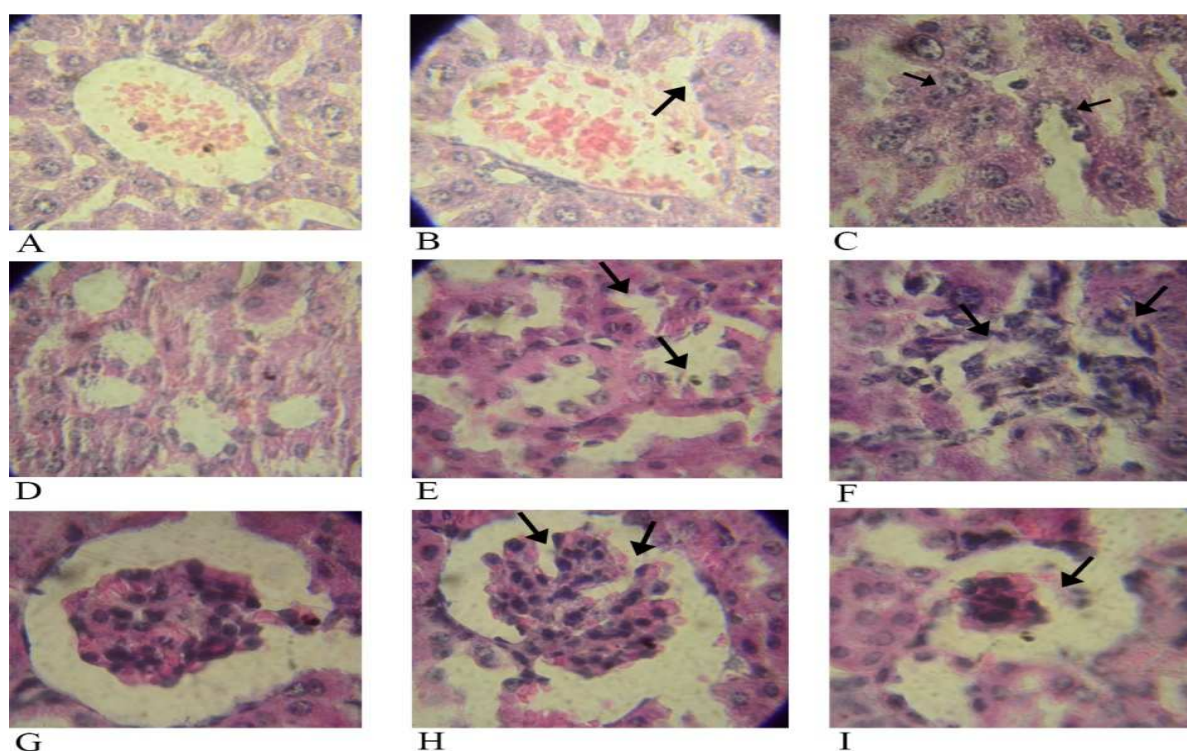


Figure 2. Histological morphology of liver (A-F) and kidney (G-I) sections from mice treated with crude extracts. (A) Normal central vein, (B) ruptured wall of central vein, (C) damage tubules (right arrow) and necrosis to some cells (left arrow), (D) normal liver bile ducts, (E) damaged bile duct (upper arrow) and ruptured sinusoids (lower arrow), (F) irregular shaped cells and apoptotic cells, (G) normal glomerulus, (H and I) glomerular atrophy and distension of Bowman's capsule

CONCLUSION

It is clear from the results that only *S. sonchifolius* showed a normal response to the *Allium cepa* root growth with no indication of any cytotoxic potentials. *C. odorata*, *J. gossypifolia*, *E. cotinifolia* and *T. rumphii* on the other hand are those medicinal plants whose extracts contributed chromosomal aberrations to the *A. cepa* root tips as well as changes to the liver and kidney tissues of BALB/c strain mice. The actual plant ingredients responsible for the observed chromosomal abnormalities were not determined in this study but these observations therefore call for caution in the freehand use and unguided consumption of herbal provisions because of their cytotoxic and possible genotoxic effects on the individuals relying so much on it. The results does give a good initial indication for the toxicity of the plants tested but does not necessarily establish a direct link to toxicological effects in

humans. These findings might not really be a limitation for the use of medicinal plants for primary health care purposes, as there are mechanistic ways by which the body system repair damage DNAs. Thus, the researchers recommend to have further laboratory validation especially in vivo studies.

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