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RESEARCH ARTICLE

Potentials of *Massularia acuminata* stem bark extracts on Serum enzymes and haematological parameters of aluminium chloride-induced toxicities

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ABSTRACT

Massularia acuminata is a bioactive herbal plant used to treat many diseases since ancient times. The research work estimates the potential different solvent extracts of *Massularia acuminata* on serum enzymes and haematological parameters of animals exposed to aluminium chloride. The ethanolic, methanolic and butanolic extracts of this plant were used against aluminium chloride for their hepato-protective effects against aluminium chloride toxicity in Wistar rats with ascorbic acid as standard. The rats were divided into 10 groups with different doses of all the extract, standard and control. The rats were administrated for 30 days under prescribed laboratory conditions. Blood samples were taken through the cardiac puncture, liver organs were harvested and the ALT, AST, ALP, bilirubin and total protein levels were determined to know the effects of *Massularia acuminata* extracts on liver cells. The results showed a reduction in serum enzymes and aluminium chloride caused a significant decrease in RBC, PCV, Hb, Monocyte and Lymphocyte counts while WBC increased. The results obtained from this study indicate that the solvent extracts of *Massularia acuminata* have an androgenic potential that can suppress the reproductive toxicity caused by aluminium chloride and could be used in the treatment of infertility This study shows therefore that the extracts from *Massularia acuminata* may serve as a potent drug against aluminium chloride toxicity.

Key words: *Massularia acuminata*, aluminium chloride, serum enzyme, haematology, ascorbic acid.

1. INTRODUCTION

About 84% of couples in general population are expected to conceive within one year and about 92% conceive within two years of their intercourse. When a couple fails to conceive even after two years of regular frequent coitus and there is no known reproductive pathology, the couple may be considered infertile [1]. However, the term infertility implies a definitive inability to conceive. Therefore, couples who do not conceive in more than one year should be regarded as sub-fertile. The repeated inability of the male's sexual organs

and factors relating to erection of the copulatory organ to function effectively or a disorder that interfere with his full sexual response cycle is termed male sexual dysfunction (MSD) [2]. MSD is common worldwide among men of all ages, ethnicities, and cultural backgrounds. Although MSD rarely threatens physical health, it can take a heavy psychological toll, bringing on depression, anxiety, and debilitating feelings of inadequacy [3]. Sexual dysfunction in men takes different forms, such as disorders of desire (persistently or recurrently deficient sexual fantasy and desire for sexual activity), disorders of orgasm (persistent or recurrent delay in, or absence of, orgasm after a normal sexual excitement phase), erectile dysfunction (persistent failure to generate sufficient penile body pressure to achieve vaginal penetration and/or the inability to maintain this degree of penile rigidity until ejaculation), disorders of ejaculation (persistent or recurrent ejaculation with minimum sexual stimulation that occurs before, upon, or shortly after penetration and before a person wishes it or a situation where ejaculation does not occur at all) and failure of detumescence (prolonged priapism lasting for more than 4 h). Erectile dysfunction (ED) and premature ejaculation are the two most common complaints of male patients presenting with sexual dysfunction [4-5]. ED is defined as a man's consistent or recurrent inability to attain and/or maintain penile erection sufficient for satisfactory sexual activity [6]. Symptoms include a marked difficulty in obtaining an erection during sexual activity and maintaining an erection until the completion of sexual activity, and a marked decrease in erectile rigidity. MSD is of varied etiology and these include personal life styles (chronic alcohol abuse, cigarette smoking), androgen deficiency, aging population, psychological disorders, side effects of some anti-hypertensive, central agents, psychiatric medications, antiulcer, antidepressants, and anti-androgens. The chronic medical conditions like diabetes, hypertension and pulmonary cancer can also be caused [7].

Humans widely use metals for their day to day use. The ubiquity of its presence in nature has polluted air, water, soil, food, and long-term persistence in the environment. Metals may have serious effect on the male reproductive system directly (they target specific reproductive organs) or indirectly (when they act on the neuroendocrine system) [8]. Metals have been shown to affect spermatogenesis in rodents and humans, which can lead to low sperm count, abnormal sperm morphology and poor semen quality [9-10]. Among all the metals, Aluminium (Al) is the most widely distributed trivalent cation found in its ionic form inside animal and plant tissues. It is the third most prevalent element and the most abundant metal in the earth's crust, representing approximately 8% of total mineral components [11]. Al occurs naturally in the environment and is also released due to anthropogenic activities such as mining and industrial uses, in the production of Aluminium metal and other forms of Al compounds. A variety of Al compounds are produced and used for different purposes, such as in water treatment, papermaking, fire retardant, fillers, food additives, colors and pharmaceuticals.

Previously, Aluminium has been considered on an indifferent element from a toxicological point of view for a long time. Although Al is present in trace amounts in the biological material, it does not appear to be an essential element and is usually considered to have harmful effects on general health [11]. Aluminium is known as a neurotoxin that can cause certain diseases such as Alzheimer disease, dialysis dementia, Parkinson's and amyotropic lateral sclerosis. In addition, to its neurotoxicity [12], it also affects other body structures like the skeletal system [13], brain tissue, bone, blood cells, liver and kidney [14]. The sources of Al are specially corn, yellow cheese, salt, herbs, spices, tea, cosmetics, Aluminium ware and containers. Also, Al is widely used in antacid drugs, as well as in food additives and toothpaste [15]. Environmental pollution with the different Aluminium containing compounds, especially those in industrial waste water, exposes people to higher than normal levels of Al. This study estimates the potential of ascorbic acid and different solvent extracts of *Massularia acuminata* on serum enzymes and hematological parameters of animals exposed to aluminum chloride. This study was undertaken to assess the effects of aqueous extract of *Massularia acuminata* on the hematological parameters of rats pretreated with aluminium chloride.

2. MATERIALS AND METHOD

2.1. Plant sample

Fresh bark of *Massularia acuminata* was obtained locally from an open forest at Owo (7.1989° N, 5.5932° E) in Ondo state, and was authenticated by a taxonomist at Adekunle Ajasin University, Nigeria.

2.2. Preparation of plant extract

The plant stem was cut with a sterile knife into pieces and then oven-dried at 40°C until a constant weight was obtained. The pieces were then pulverized with an electric blender (Blender/Miller III, model MS-223, China). The powdered material was stocked in a plastic container from which 200 g each was separately extracted in 500 ml of distilled water for 48 hrs at room temperature with constant shaking. The extract was filtered with filter paper and filtrate was concentrated on a steam bath to give between 5.48 and 5.60 g of the brownish black slurry (residue) which is equivalent to a % yield of 2.74±0.05 g. The residue was reconstituted in distilled water to give the required dose of 100mg/kg body weight while higher doses of 300 and 500 mg/kg body weight were also used. The reconstituted aqueous extract was administered orally to all animals in the various groups using metal oropharyngeal cannula.

2.3. Experimental *Animals*

Twenty five (25) male wister rats of average weight 140±30 g were obtained from the Institute of Medical Research and Teaching (IMRAT) at the University Teaching Hospital Ibadan, Oyo state, Nigeria and were allowed to acclimatize to experimental condition for two weeks. They were housed and grouped in a temperature and humidity controlled environment under a 12 hrs light/dark cycle, with their normal rat pellet ration (Top Feeds,

Table 1. Experimental procedure

Groups	
Group 1	Control
Group 2	Aluminum chloride (34 mg/kg)
Group 3	Ascorbic = Ascorbic acid (200 mg/kg)
Group 4	Ascorbic acid (200 mg/kg) + Aluminum chloride (34 mg/kg)
Group 5	Ethanolic extract of *Massularia acuminata* (50 mg/kg) + Aluminium chloride (34 mg/kg)
Group 6	Ethanolic extract of *Massularia acuminata* (100 mg/kg) + Aluminium chloride (34 mg/kg)
Group 7	Methanolic extract of *Massularia acuminata* (50 mg/kg) +Aluminium chloride (34 mg/kg)
Group 8	Methanolic extract of *Massularia acuminata* (100mg/kg)+Aluminium chloride (34 mg/kg)
Group 9	Butanolic extract of *Massularia acuminata* (50 mg/kg) + Aluminium chloride (34 mg/kg)
Group 10	Butanolic extract of *Massularia acuminata* (100 mg/kg)+Aluminium chloride (34 mg/kg)

Nigeria) and portable water available ad libitum.

2.4. Experiment *procedure*

The experiment was conducted on different extracts and doses. All these doses were grouped accordingly with Ascorbic acid and control for the experiment (table 1).

2.5. Animal *Sacrifice and Tissue Harvesting*

The animals were subjected to fasting over-night and were sacrificed next morning. Blood samples were collected directly from the eyes of the animals using capillary tubes, poured into an EDTA bottle and taken to the laboratory for the haematological test. Tissues which include the pancreas, liver, intestinal crypt and kidney were excised from all the subjects (animals) into well labelled eppendorf tubes containing normal saline across the groups. Tissues were then stored under the temperature of -70°C for 24 hours.

2.6. Haematological *Tests*

Coulter counter model S-plus: coulter counter model S-plus, an automated Full blood count machine provides the following haematological parameters: Red blood cell, white blood cell, haemoglobin, platelet count and Red blood cell indices (PCV, MCH, MCV, MCHC). The blood sample is allowed to pass the aperture and then closed by a stopper. The device then measured the value of each parameter electrically. Haemoglobin was determined photometrically by passing a beam of light through the lysed solution and measuring the absorbance by photometric device.

2.7. Statistical *analysis*

Data were expressed as the mean of three replicates ± SEM. Means were analysed using a one-way analysis of variance (ANOVA) and complemented with Student's t-test. Post-test analysis was carried out using Duncan Multiple Range Test and Tukey's Multiple Comparison

Test to determine significant differences in all the parameters. The graphs were plotted with Graph pad prism 7. Differences with values of P < .05 were considered statistically significant.

3. RESULTS AND DISCUSSION

This study was conducted to assess and compare the incidence and severity of haematological changes during Aluminium chloride induction and treatment with solvent extracts of *Massularia acuminata* at the dose level of 50 mg/kgbw, 100 mg/kgbw for each extracts respectively and ascorbic acids at the dose of 200 mg/kg body weight. The results from Table 2 shows that there is no significant difference in the total protein level between

Table 2. Effects of *Massularia acuminata* extracts on the Total protein and Bilirubin level of experimental animals.

GROUPS/PARAMETERS	TOTAL PROTEIN	BILIRUBIN
Control	3.23 ± 0.00^{a}	717.00 ± 1.91^{b}
Toxicant (34 mg/kg)	3.23 ± 0.00^{a}	706.15±9.52^{ab}
Ascorbic acid (200 mg/kg)	3.23 ± 0.00^{a}	695.23±11.45^{ab}
Ascorbic acid (200 mg/kg) + Toxicant (34 mg/kg)	3.24 ± 0.01^{a}	717.00±1.91^{b}
Ethanolic extract (50 mg/kg) + Toxicant (34 mg/kg)	3.23 ± 0.00^{a}	706.15±9.52^{ab}
Ethanolic extract (100 mg/kg) + Toxicant (34 mg/kg)	3.23 ± 0.00^{a}	684.38±1.97^{a}
Methanolic extract (50 mg/kg) + Toxicant (34 mg/kg)	3.24 ± 0.01^{a}	695.23±11.45^{ab}
Metanolic extract (100 mg/kg) + Toxicant (34 mg/kg)	3.23 ± 0.00^{a}	706.15±9.52^{ab}
Butanolic extract (50 mg/kg)+ Toxicant (34 mg/kg)	3.23 ± 0.00^{a}	684.38±1.97^{a}
Butanolic extract (100 mg/kg)+ Toxicant (34 mg/kg)	3.23 ± 0.00^{a}	695.23±11.45^{ab}

Table 3. Effects of *Massularia acuminata* extracts on the AST, ALT and ALP level of experimental animals

GROUPS/PARAMETER	AST	ALT	ALP
Control	121.59 ± 5.53^{abc}	97.71 ± 1.69^{abc}	6.44± 2.43^{a}
Toxicant (34 mg/kg)	123.29±5.07^{abc}	100.03 ±5.04^{c}	9.20±0.92^{a}
Ascorbic acid (200 mg/kg)	132.97±1.72^{bc}	92.45 ±2.12^{abc}	11.96 ±2.43^{a}
Ascorbic acid (200 mg/kg) + Toxicant (34 mg/kg)	122.27±5.89^{abc}	87.95±7.67^{abc}	14.72 ±1.84^{ab}
Ethanolic extract (50 mg/kg) + Toxicant (34 mg/kg)	85.39±35.18^{a}	91.26±1.72^{abc}	16.56±0.00^{b}
Ethanolic extract (100 mg/kg) + Toxicant (34 mg/kg)	152.35±5.01^{c}	84.19 ±4.47^{a}	26.64±8.07^{b}
Methanolic extract (50 mg/kg) + Toxicant (34 mg/kg)	131.78 ±18.18^{bc}	98.34±2.41^{c}	24.84±10.45^{b}
Metanolic extract (100 mg/kg) + Toxicant (34 mg/kg)	124.31±4.18^{abc}	96.46±1.97^{bc}	15.64±3.32^{a}
Butanolic extract (50 mg/kg)+ Toxicant (34 mg/kg)	125.50±8.75^{abc}	93.02±1.27^{abc}	12.88±3.68^{a}
Butanolic extract (100 mg/kg)+ Toxicant (34 mg/kg)	95.25±6.64^{ab}	85.69 ±2.76^{ab}	10.12±3.32^{a}

Values are given as Mean ± SEM for each group. Different alphabets are used to indicate statistical significance at ($p \leq 0.05$) when compared to control and ascorbic acid

groups of experimental animals and equally shows that there is significant decrease in the bilirubin level of animals treated with low dosage of ethanolic extract and high dosage of butanolic extract of *Massularia acuminata*.

The result in Table 3 shows that there is no significant difference in the AST level between all groups. There is more significant damage to the organs of the group administered with aluminium chloride with butanolic and ethanolic extracts of *Masularia acuminata* showing a potent intervention in salvaging the animals against damage from aluminium toxicity. Also, that there is significant increase in the ALP level of animals treated with low and high dosage of ethanolic extract and high dosage of *Massularia acuminata* methanolic extract. There is significant decrease in the ALT level of animals treated with lower dosage of *Massularia acuminata* ethanolic extract.

Haematological disorders have attained epidemic proportions worldwide. As a result, many people turn to medicinal plants for treatment thereby boosting and enhancing health. Aluminium has detrimental effects on body systems, including the reproductive one. *Massularia acuminata*, a plant commonly used as chewing sticks due to its antimicrobial activity has been reported to have many therapeutic properties such as antioxidant and aphrodisiac potentials [16-17].

The table 4 shows different effects from all the group's combinations on wister rats. The result when compared with control and ascorbic acid shows that the methanolic extract with both the

Table 4. The effects of extracts of *Massularia acuminata* on haematological parameters of rats treated with Aluminium chloride.

Groups	WBC	HGB	RBC	PLT	MCV
Grp1	3.73±0.12^{d}	13.3±0.06^{d}	6.68±0.01^{d}	110±1.73^{d}	68.2±0.06^{b}
Grp2	3.63±0.13^{d}	14.27±0.03^{f}	6.94±0.01^{f}	398.67±0.88^{h}	60.13±0.07^{b}
Grp3	4.9±0.12^{e}	12.7±0.06^{c}	6.78±0.01^{e}	265.67±0.33^{f}	64.17±0.09^{b}
Grp4	2.47±0.03^{b}	14.6±0.12^{g}	7.63±0.01^{h}	438.33±0.67^{i}	56.1±0.06^{b}
Grp5	7.7±0.06^{g}	13.57±0.03d^{e}	7.15±0.01^{g}	146.67±0.67^{e}	36.3±15.4^{a}
Grp6	2.4±0.06^{b}	11.93±0.03^{b}	6.08±0.01^{c}	39.0±0.58^{b}	57.8±0.06^{b}
Grp7	5.17±0.09^{f}	13.6±0.06d^{e}	5.75±0.03^{b}	356.0±0.58^{g}	66.5±0.06^{b}
Grp8	2.87±0.03^{c}	14.4±0.06^{g}	7.75±0.03^{h}	356.0±0.58^{g}	54.6±0.06^{b}
Grp9	2.07±0.07^{a}	8.60±0.25^{a}	4.62±0.06^{a}	27.0±0.58^{a}	56.5±0.12^{b}
Grp10	2.37±0.07^{b}	13.8±0.06^{e}	7.10±0.03^{g}	94.4±0.06^{c}	53.73±0.03^{b}

Values are given as Mean ± SEM for each group. Different alphabets are used to indicate statistical significance at ($p \leq 0.05$) when compared to control and ascorbic acid

doses had better effect than others.

Blood parameters are key factors in diagnosing the actual physiological status of organisms. An organism must keep its blood composition and constituents relatively constant under natural conditions to function properly [18]. The parameters measured were red blood cell, packed cell volume, haemoglobin, white blood cell count, platelet count, monocytes and lymphocytes. The normal range of these parameters can be altered by the ingestion of some medicinal plants [19]. In this study, the administration of solvent extracts of *Massularia acuminata* were examined on the haematological parameters of rats treated with aluminium chloride. Changes in haematological parameters are likely to be influenced by any disease condition including Alzheimer disease, dialysis dementia, Parkinsonism [12], aluminium chloride also affects other body structures e.g. the blood cells causing microcytic anaemia [20]. It has been shown by a study that aluminium chloride induced reproductive toxicity, altering the metabolism of testis and epididymis, leading to a reduction in fertility rate in mice [21]. These can affect health of mankind with various clinical presentations. *Massularia acuminata* has been reported to increase fertility due to its androgenic potential with lower dose seems more effective than higher dose [7] According to Isaac *et al*., (2013) red blood cell is involved in the transport of oxygen and carbon dioxide in the body. Thus, a reduced red blood cell count in the toxicant group implies a reduction in the level of oxygen that would be carried to the tissues as well as the level of carbon dioxide returned to the lungs which may probably have been caused by the toxicant (aluminium chloride) [22]. The highest red blood cell count was observed at the treatment level with 100 mg of plant extract, meaning that the extracts was able to improve the toxic effect of aluminium on red blood cell when compared with the aluminium treated group indicating that the plant extract may contain compounds or phytochemical that increases the production of red blood cells, since the plant works effectively at lower dose more than higher dose. However, there is no much significant difference between the treated group and the control group. Haemoglobin (Hb) is the oxygen-carrying component in the blood and its concentration can be used as good indicator of anaemia. The decrease in Hb corresponds with the decrease in dissolved oxygen; an indication that the decrease in haemoglobin resulted in haemodilution. The reduction may be due to increased rate of breakdown of red blood cells and reduction in the rate of formation of red blood which may probably have been caused by the toxicant. However, treatment with plant extract shows slight significant increase in the haemoglobin count compare to the toxicant group. But there was no significant difference in the haemoglobin count in the treatment group compared to the control group.

Packed Cell Volume (PCV) is used to determine the ratio of plasma to corpuscles in the blood as well as the oxygen-carrying capacity of the blood [24]. The significant decrease in Packed Cell Volume (PCV) of the toxicant group may be attributed to the toxic effect of aluminium chloride on the blood causing anaemia and haemodilution. However, there was slight

significance increase in the groups treated with plant extract compared to the toxicant group, but there was no much significant difference between the treated group and the control group. Since haemoglobin and hematocrit (PCV) profiles relate to the total population of red blood cells in the blood, it could thus imply that the extract may stimulate the production of erythropoietin in the stem of cells of rat [24]. Erythropoietin is a glycoprotein hormone which stimulates stem cells in the bone marrow to produce red blood cells [25]. Erythropoietin affects the oxygen-carrying capacity of the blood and the amount of oxygen delivered to the tissues since red blood cells and hemoglobin are very important in transferring respiratory gases [26].

It may also suggest that the plant extracts can cause polychethermia. Previous studies have indicated that an increase in the count of erythrocytes and PCV is suggestive of polycythermia and positive erythropoiesis [27]. Moreover, studies by Esenowo *et al*., (2010) suggested that the leaves of Peristrophe bicalculata (Retz) are capable of increasing erythrocyte counts in experimental animals [28]. They confirmed the use of Peristrophe bicalculata (Retz) leaves in restoring lost blood during excessive bleeding, who worked on *Baphia nitida* (Lodd) also reported similar results [29]. Therefore, the aqueous extracts of *Massularia acuminata* can be used to restore lost blood during excessive bleeding as observed, the mechanism leading to the increase in erythrocyte count is probably mediated by the anti-oxidant property of the extracts [30]. The presence of antioxidant phytochemicals like flavonoids and tannins in the aqueous extracts of *Massularia acuminata* may be responsible for the hemopoietic stimulating effects. This is in line with previous research that showed that prophylactic and therapeutic oral administration of anti-oxidant supplements in plant extracts significantly increased cells of hemopoietic origin in animals exposed to potentially lethal dose of radiation [30]. Flavonoids, tannins and terpenes have been found to protect erythrocytes from oxidative damage. Further Ren *et al*., (2003) reported that flavonoids have various benefits for human health due to its anti-oxidant and free-radical scavenging activities as well as anti inflammatory, antiviral, and anticancer properties [31].

White Blood Cells (WBCs) defend the body against toxic and foreign substances and produce antibodies. The highest white blood cell count was observed at the toxicant group, there was a significant increase in the WBC count in the toxicant group compared to the control group. The experimental changes observed here was in agreement with the finding, that reported that infection is indicated only by an increased level of leukocytes (particularly polymorphonuclear leukocytes) and their products (e.g., leukocyte elastase) [32]. A high WBC count may indicate acute infection, inflammation, or tissue damage.

The solvent extract of *Massularia acuminata* shows no effectiveness in lowering the white blood cell count of the experimental suggesting that the plant extract may not have immune boosting properties. Also, there was no significance difference in the groups treated

with the plant extract and the control group. As regards the differential count of white blood cells, the Monocytes and Lymphocytes decreased significantly as compared between the toxicant group and the control. The decreased Monocytes and Lymphocytes may be associated with the nature of immunological challenge to which the rats were exposed at the period of experiment and due to the effect of aluminium chloride toxicity. It was observed that the toxicant group recorded a slight significantly lower monocyte and lymphocyte counts compared with the control and the groups treated with aqueous extract of *Massularia acuminata*. The result correlates with the previous reports which show lower lymphocyte and monocyte count in rats treated with aluminium chloride [33]. The lower monocyte count may be associated with the suppression of monocyte chemotactic migration by the toxicant. However, there was a significant increase in monocytes and lymphocytes count of groups treated with the plant extract compared to the toxicant group. An increase in lymphocytes counts may be associated with enhanced release of lymphocytes from lymphomyeloid tissues. This could be an adaptive mechanism to burst the immune system of the rats and give it the positive survival value needed in the sub lethal toxic environment or possibility of leukaemia due to prolonged toxic insult. But there was no much significance difference observed between the control group and the groups treated with the plant extract. Blood platelets are implicated in blood clotting. Low platelet concentration suggests that the process of clot-formation (blood clotting) will be prolonged resulting in excessive loss of blood in the case of injury. The observed decreased in the platelet count in the toxicant group was caused by the toxicant. The experimental changes observed here was in agreement with the finding by Tona *et al.,* (2001), who reported that thrombocytopenia leads to low production of blood clotting due to the anaemic condition in the rat, this is as a result of the treated aluminium chloride which causes a sharp drop in platelets by destroying the red blood cells [34]. Thrombocytopenia is a condition in which there is a low blood platelet count. Platelets (thrombocytes) are colourless blood cells that help blood clot. Platelets stop bleeding by clumping and forming plugs in blood vessel injuries. Thrombocytopenia often occurs as a result of a separate disorder, such as leukaemia or an immune system problem or it can be a side effect of taking certain medications which can affects both children and adults. The aqueous extract of *Massularia acuminata* shows no effectiveness in improving the platelet count of the experimental animals when compared to the control group. This may suggest that the extracts may not have the potential to be developed as plant based therapeutic agents for thrombocytopenia.

4. CONCLUSION

In conclusion, this study supports the claim that aluminium chloride, like most of other forms of aluminium is capable of causing damage to animals by inducing reproductive toxicity and exerting a significant adverse effect on the steroidogenesis, changing their pathological and physiological status. This fact was established by performing some tests on the haematological parameters of rats that have

been treated with aluminium chloride. This study gives a documented evidence of such investigation in rats whose physiology is comparable and predicted to that of human. Thus, the result of this study indicates that the aqueous extract of *Massularia acuminata* has an androgenic potential that can suppress the reproductive toxicity caused by aluminium chloride and could be used in the treatment of infertility.

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6. CONFLICT OF INTEREST

The authors have declared that there is no conflict of interest.

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