Aqueous extract of *Monodora myristica* ameliorates cadmium induced hepatotoxicity in male rats.

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Presented by

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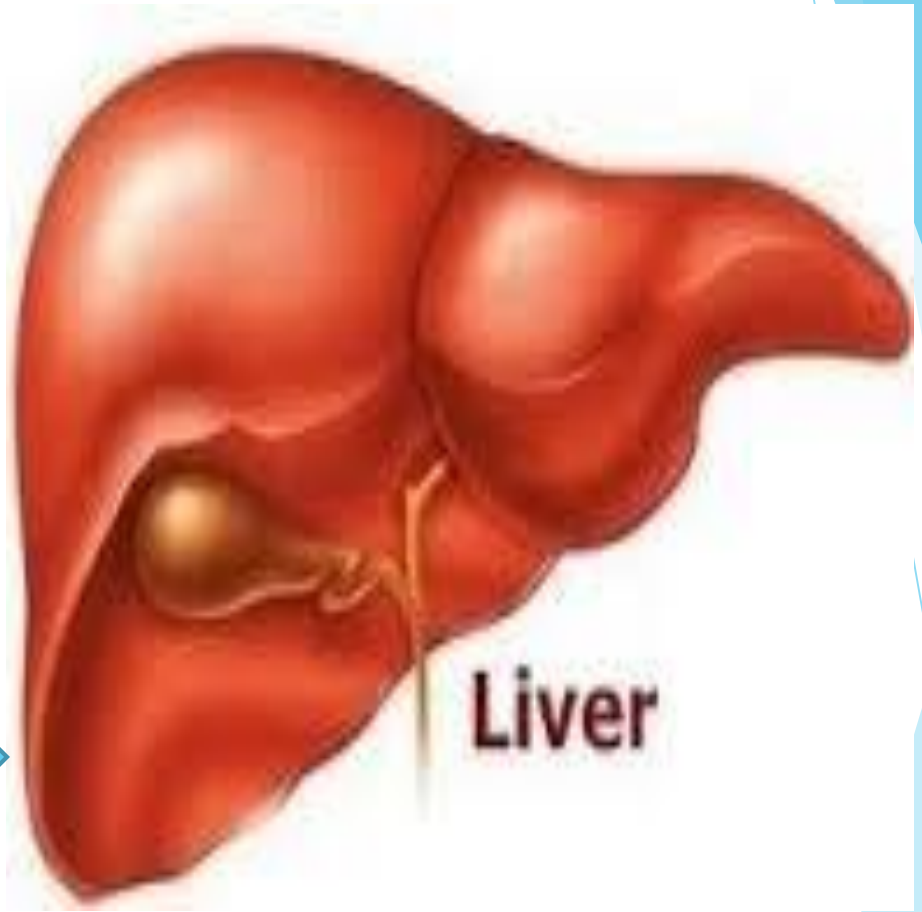
Hepatotoxicity

Drugs

Chemicals

Toxic metals



Symptoms and effect of hepatotoxicity in humans include;

- Fatigue
- Stomach ache
- Skin problems
- Lack of appetite amongst others

Biochemical effect of hepatotoxicity include

- Elevation in serum levels of alanine and aspartate transaminases
- Reduction in antioxidants such as glutathione, superoxide dismutase, catalase and malondialdehyde

Cadmium toxicity

- Cadmium is a pollutant whose continuous accumulation affects various organs such as liver, kidney and testis
- In severe cases cadmium accumulation can lead to death
- Environmental contamination by cadmium (Cd) results from its industrial use and its presence in agricultural fertilizers
- Cd accumulation also occur through smoking and consumption of Cd contaminated sea fish and water

- Cadmium exerts its toxic effects through oxidative damage to cellular organelles by inducing the generation of reactive oxygen species (ROS)

- Inability of the cellular organelles to undergo repair processes can lead to apoptosis or necrosis

- Naturally occurring phytochemicals have been reported to possess hepatoprotective activity required in Cd intoxication therapy

Monodora myristica

- This tropical plant belongs to the *Annonaceae* family
- It is also called calabash, Jamaica or African nutmeg
- This plant is extensively distributed in Africa, Asia, Australia as well as Central and South America
- It is used traditionally in culinary for various delicacies
- For treatment of stomach ache, constipation
- And as carminative, antiseptic and fragrance
- Previous research showed it has antisickling and anthelmintic activity (Raphael et al., 2010; Uwakwe, 2013).

Aims and objective of study

This research was conducted to investigate the ability of aqueous extract of *Monodora myristica* (MM) to ameliorates cadmium induced hepatotoxicity in Male rats

Objectives

- Phytochemical screening of aqueous extract of MM
- Inducing hepatotoxicity in male experimental rats by maintaining them on cadmium
- Investigating the effect of extract treatment on hepatotoxic rats by measuring the relevant biochemical parameters
- Histological examination of liver to determine

Experimental design

Chemicals of high purity were obtained

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Plant materials were obtained, authenticated

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Plant materials were prepared to obtain aqueous MM extract

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Phytochemical screening of extract

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30 experimental male Wistar albino rats were divided into five groups

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Oral administration of H_2O, $CdCl_2$ solution, MM (at 200 mg/kg and 400 mg/kg) and 20 mg/kg Livolin forte to G1-G5 respectively for 21 days

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Sacrificing and preparation of tissues for biochemical analysis

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Biochemical analysis and histological analysis

Biochemical analysis and histological examination

- Alanine aminotransferase (ALT) and aspartate aminotransferase (AST) activities and serum triglyceride (TG) were measured spectrophotometrically using Randox commercial assay kits
- Glutathione (GSH) activity was determined using method of Beutler et al., 1963
- Catalase activity was ascertained as described by Sinha, 1972
- Superoxide dismutase activity was measured by method of Misra and Fridovich 1972
- Stained pieces liver tissue sections were then observed under a light microscope for histological assessment.

Statistical analysis

Statistical analysis. All data were expressed as mean ±S.D. One-way analysis of variance (ANOVA) was used for the analysis of the biochemical indices. Differences were considered significant at $P<0.05$.

Results

Table 1. Results of the phytochemical screening of *Monodora myristica*

Phytochemicals	Alkaloids	Saponins	Tannins	Flavonoids	Cardiac glycosides	Phenols
Aqueous Extracts	++	++	+	+++	++	+++

+ = present in trace, ++ = moderately present, +++ = abundantly present

Table 2. The effect of *Monodora myristica* on the levels of on liver marker enzyme activities.

Treatment Group	ALT activity (U/L)	AST activity (U/L)
G1	115.61 ± 1.21	121.25 ± 3.78
G2	156.50 ± 1.80	181.17 ± 5.20
G3	139.01 ± 3.79	169.82 ± 3.43
G4	104.12 ± 2.63	136.20 ± 1.57
G5	108.27 ± 0.13	127.27 ± 0.17

Values shown are mean ± S.D. (n = 6). Mean differences are significant ($P < 0.05$) when compared with: [a] G1 (control group), [b] G2 (cadmium only)

Table 3. The effect of *Monodora myristica* on hepatic MDA, serum triglyceride and cholesterol levels.

Treatment Group	MDA (nmole/mg/protein)	Triglyceride (mg/dl)	Cholesterol (mg/dl)
G1	38.93 ± 0.96	124.62 ± 2.23	87.22 ± 5.60
G2	70.66 ± 1.77	175.11 ± 1.05	173.20 ± 1.35
G3	51.75 ± 2.32	154.23 ± 3.14	111.20 ± 8.14
G4	47.21 ± 2.21	139.05 ± 3.19	106.80 ± 6.27
G5	40.82 ± 0.41	126.89 ± 1.69	109.77 ± 0.60

Values shown are mean ± S.D. (n = 6). Mean differences are significant ($P < 0.05$) when compared with: [a] G1 (control group), [b] G2 (cadmium only)

Table 4. The effect of *Monodora myristica* on the levels of liver glutathione and activities of liver catalase and superoxide dismutase.

Treatment Group	GSH (nmole/mg protein)	CAT (unit/min/mg protein)	SOD (unit/min/mg protein)
G1	36.42 ± 0.52	65.83 ± 5.43	27.04 ± 0.05
G2	23.92 ± 0.37	42.73 ± 0.69	15.79 ± 0.06
G3	37.78 ± 0.38	59.66 ± 0.65	24.99 ± 0.13
G4	44.28 ± 0.40	64.31 ± 0.79	35.02 ± 0.08
G5	41.74 ± 0.61	68.02 ± 0.18	31.37 ± 0.79

Values shown are mean ± S.D. (n = 6). Mean differences are significant ($P < 0.05$) when compared with: [a] G1 (control group), [b] G2 (cadmium only)

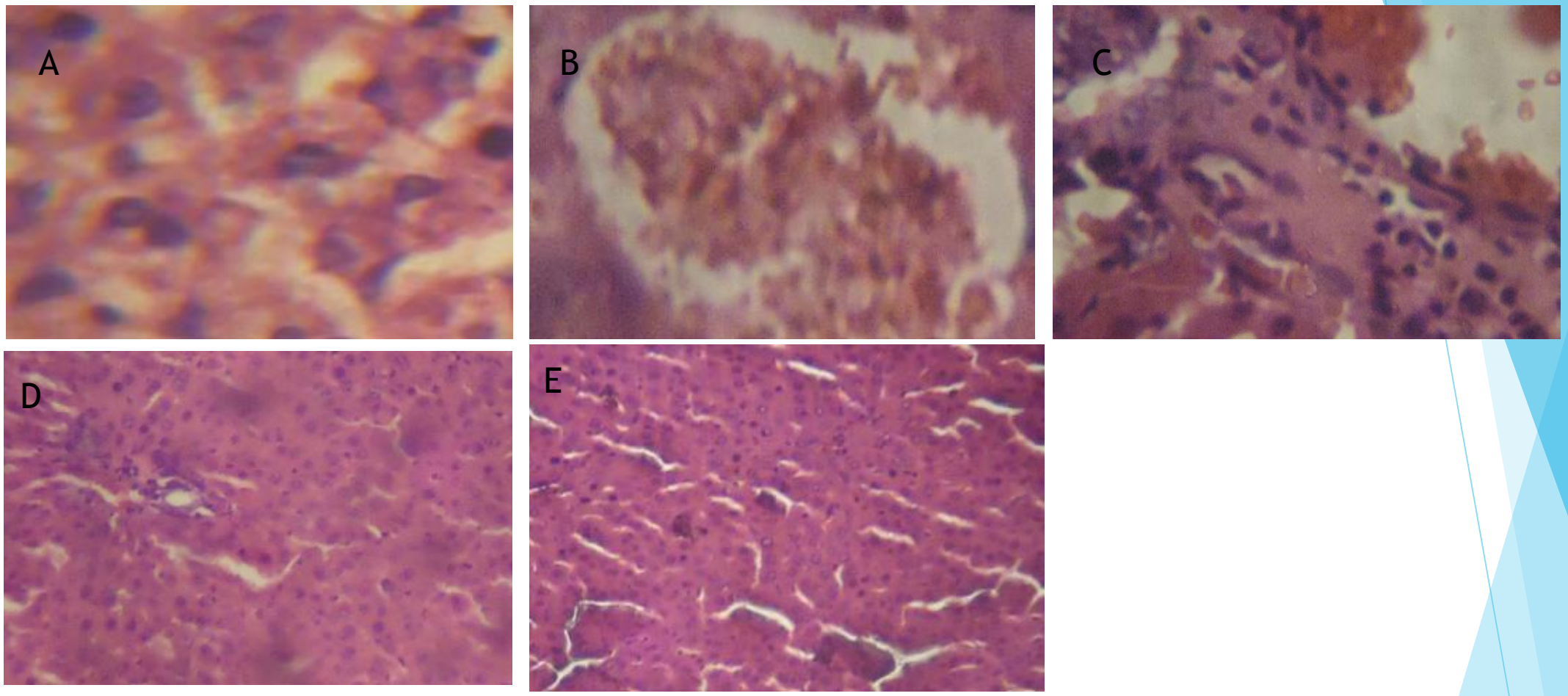

Figure 1. Histological examination of rat livers stained with hematoxylin and eosin (×400)

(A) G1: showing no abnormal morphological alteration;

(B) G2: showing extensive morphological disruption;

(C) G3: showing moderate degeneration of hepatocytes and kupper cells;

(D) G4: showing mild periportal hepatic necrosis hepatic;

(E) G5: showing very mild degeneration of hepatocytes and kupper cells.

Discussion and conclusion

These results demonstrates that aqueous extracts of MM is effective in the amelioration of hepatic damages arising from cadmium-induced toxicity, indicating that the antioxidant bio-constituents of MM play an important role in the prevention of liver toxicity possibly by inhibiting bioaccumulation of free radicals in animal models.

Recommendations

Further research is required to identify and isolate the bioactive component of MM responsible for its hepatoprotective property and hence the exploration of the plant active substance in drug and nutraceutical formulation for liver toxicity.

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THANK YOU!