Academic Sciences Asian Journal of Pharmaceutical and Clinical Research
Vol 4, Suppl 2, 2011 ISSN - 0974-2441

Research Article

ANTI-NEPHROTOXIC EFFECT OF MORIN ON CADMIUM INDUCED NEPHROGENEIC POISONING

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Received: 20 July 2011, Revised and Accepted: 11 October 2011

ABSTRACT

Flavonoids are structurally diverse group of compounds that occur, widely in the plant kingdom. Morin is one of the flavonoids present in the fruits like apple and guava, therefore Morin is an integral part of the human diet, which is present in food in thrust food flavonoids has increased greatly because of antioxidant and free radicals, scavenging abilities the above property of Morin scilipapers scavenges of cadmium regular intake related to delefite some diseases, its present investigation there are considerable evidence like kidney marker analysis of uric acid ,urea, creatinine, ALT, LDH, GGT and ACP and histopathological examination of the kidney tissues it was rats orally administration of Morin (200mg/kg/bodyweight/day)for 20days rats orally administration of cadmium(3.5mg/body weight/day) for continuous for 3 days. It was conclude that the Morin possesses good Nephrotoxic effect against cadmium induced Nephrotoxicity.

Key words: Cadmium, Morin, kidney, marker enzymes.

INTRODUCTION

Cadmium is one of the danger occupational an environmental toxin, it is found in drinking water atmospheric air and even in found product of vegetable origin are main carrier of cadmium compound in food[1]In cadmium- polluted area of Japan renal damage has also been observed in the general population[2]. A higher incidence of proteinuria and beta 2 microglobinuria has been observed in Jintzu river basin in Toyama prefecture and in other area where higher concentration of cadmium have been observed in rice. The increased urinary excretion of beta macroglobulin was strongly related to the residence time in that area and to the cadmium level in urine and blood of affected individuals[3]. As kidney dysfunction progresses mineral, such as calcium and phosphorus may also be lost into the urine which increased excretion of calcium and phosphorus may disturb bone metabolism and kidney stones,[4]. Have been found in exposed workers having been absorbed from the alimentary tract, cadmium forms double combinations with proteinthioneion forming metallothioneins with play an important and liver are considered to be most susceptible organs in the case of exposure to cadmium[5]. Some natural compounds isolated from herbs used traditional Chinese medicine have been previously demonstrated to possess Xanthine oxidase inhibitory activities[6]. In the present investigation Morin which occurs in twigs of Morus Alba, L documented in traditional Chinese medicine literature to treat conditions of gout was demonstrated to expert potent inhibitory action of ureate uptake in rat renal BBMV indicating that this compounds acts on kidney to inhibit ureate reabsorption[6].

MATERIALS AND METHODS

Chemical using

The fine chemicals Lactate, sodium tungstrate TCA. BSA, creatinine, Urea, Folin's phenol. Picric acid, Phosphotungstic acid, sulphuric acid. Amino antipyrene were purchased from Merck companies, Morin and cadmium from sigma chemical USA.

Laboratory animals

Wister strain albino rats weight 200-220g was used. The animals were housed in spacious cages under hygienic condition and maintained on commercial diet containing 21% protein, 5% lipids, 4% crude fiber, 8% ash, 1% calcium, 0.6% phosphorus, 55% Nitrogen free extract enriched with vitamins and minerals. It was supplied by the "Hindustan Lever Limited" (Mumbai). Under the trade name gold mohur feeds and water was made available and libtum. The rats were acclimatized in animal house for ten days before starting the experiments.

Experimental procedure

A total number of 24 rats were taken for this present study while selecting the rats considered carefully being existing with similar age sex (male) and weight of each rats(CPCSEA Approval No:APCAS/IAEC/2010/04).

Experimental design

Group-A Control: Rats orally administered with 0.01N nitric acid (0.5ml /day) daily at 10:30am for 20 days.

Group-B: Rats orally administered with cadmium (3.5 mg/kg body weight/day) dissolved in 0.01N nitric acid daily at 10:30am for 3 days.

Group-C: Rats orally administered with cadmium (3.5 mg/ kg body weight/day) dissolved in 0.01N nitric acid followed by orally administration of Morin (200mg/kg body weight/day) dissolved in 0.9% saline daily at 10:30am for 20 days.

Group-D: Rats orally administered of Morin (200mg/kg body weight/day) dissolved in 0.9% saline daily at 10:30am for 20 days

Sample collection and analysis

On the final day after 20 days treatment of experiment the animal were scarified and the blood sample was collected by carotid bleeding and serum prepared Alkaline phosphatase (ALP) assayed according to the method of Reitman's and Frankel (1975). Values are expressed as IU/L. ALP activity was measured using the method of Kind and King (1954). LDH-king. (1965). URIC ACID (W.T. caraway's et al., 1955) UREA (Nevelson et al., 1951), CEEATININE (Brod and sirota, 1948).

Statistical analysis

The Values were expressed as mean $\pm$ S.E.M, SPSS- 11 version. The data were subjected to statistical analysis using one way analysis of variance (ANOVA) Dunnet's Multiple comparison test to determine the level of significance of individual variations between the control and treatment groups was considered at the level of $P<0.05$

Result and discussion

Influence of Morin on Cadmium Induced Serum Biochemical Changes in the Kidney.

HISTROPATHOLOGICAL EXAMINATION OF RATS KINDE

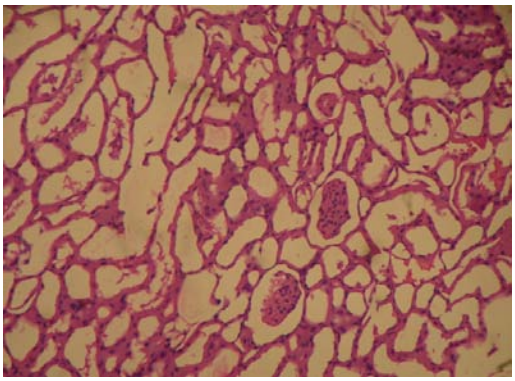
One animal from the treated groups showing maximal activity as indicated by improved biochemical parameters from control,

cadmium control, Morin groups were utilized for this purpose. The animals were sacrificed, and the abdomen was cut open to remove the liver. Then, 5mn thick picric if the liver were fixed in bouin's solution (mixture of 7.0 ml of saturated picric acid ,25ml of 40% formaldehyde and 5ml of glacial acetic acid) for 12 hours and then embedded in paraffin ,using conventional methods , and cut into 5mm thick section and stained, using heamatoxylin Eosin dye, and finally mounted in diphenylxylene. Then the section was observed under microscopes for histopathalogical changes in liver architecture, and their photomicrographs were taken.

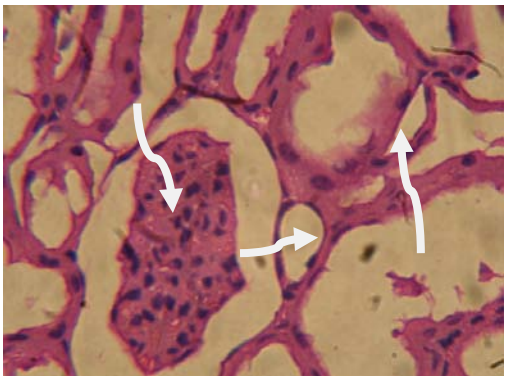
Table 1:

S.No	Parameters	Control	Cadmium induced	Cadmium +morin	morin treated
1	Uric acid in (mg/dl)	3.71±0.06	4.21±0.19**a**	3.7±0.123**ab**	3.55±0.09**bc**
2	Creatinine in (g/dl)	0.483±0.01	1.48±0.01**a**	0.42±0.01**ab**	0.47±0.01**bc**
3	Urea (g/dl)	22.15±0.22	60.32±0.77**a**	23.18±0.55**ab**	21.22±012**bc**
4	ACP (g/dl)	2.18±0.12	3.92±0.19**a**	2.38±0.44**ab**	2.42±0.60**bc**
5	ALP in (U/L)	120.16±1.22	244.83±1.22**a**	116±0.57**ab**	58.4±0.70**bc**
6	LDH in (U/L)	155.8±0.44	240.0±0.19**a**	155.6±0.60**ab**	159.8±0.36**bc**
7	GGT in (U/L)	157.8±1.77	140.12±0.87**a**	155.41±0.77**ab**	153.S38±1.14**bc**

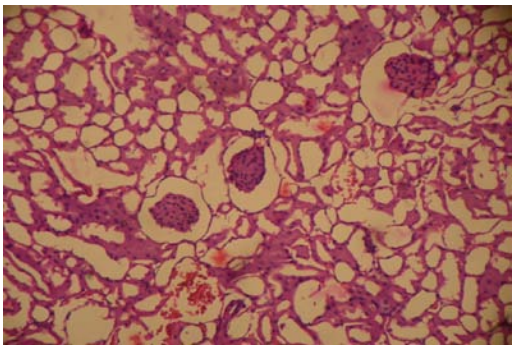
Values were expressed as Mean ± SE for six rats in each group (n: 6)
a- Cadmium induced toxicity group significantly different from the control group.
Ab-cadmium + Morin group significantly different from the control and cadmium group.
Bc-cadmium group significantly different from cadmium Morin group.
All the groups differs from each other significantly p<0.05



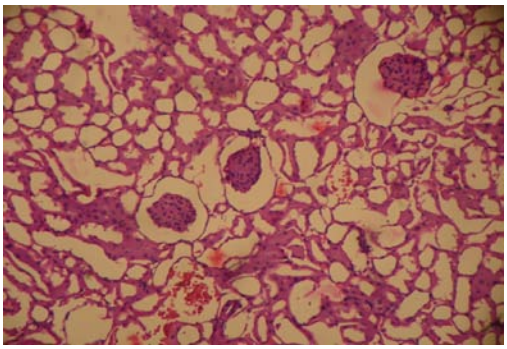
CONTROL -A 10X RAT KIDNEY



CADMIUM INDUCED-B 10X RAT KINDEY



CADMIUM+MORIN -C 10X RAT KINDEY



MORIN TREATED -D 10X RAT KINDEY

Group-A control the rigid cells are seen in rat kindey. Microscope 10x visible eyes
Group-B (Cadmium Induced) The lesions are seen due to kindey damage artitecture that means outer stripe of outer medulla and also cadmium deposition in distal part of the proximal concluted tubule. Microscope 10x visible eyes
Group-C (Cadmium+Morin) the simultaneously treated groups protects the kindey cells froum cadmium action. Microscope 10x visible eyes
Group-D morin treated groups protects the kindey cells from cadmium action Microscope 10x visible eyes .

RESULT AND DISCUSSION

Serial No 1,2,3 and 4 Respresent the levels of creatinine and uric acid in the differnt groups of animals the group-B was administered with cadmium chloride showed elevated levels of creatinine and uric acid due to renal damage. Whereas, the simultaneously administraation of morin and cadmium chloride group-C significantaly ($p<0.05$) showed protective effect compared with

group-B. Thhis was due to morin effective protective action. The Uric acid is the end product of purine metabolism, it is excreated to large degree by the kidneys and to smaller degree in the intestinal tract by micobial degradation increased levels lead to gout arthritis, impaired renal function and starvation[7]. Hyperuricemia is associated with a number of pathological condition such as gout. Lowering of elevated uric acid levels in blood could be achieved by xanthine oxidase inhibitors of renal ureate reabsorption[8]. The inhibition of morin xanthine oxidase is moderate when compared with allopurinal [9]At high dose of morin, however xanthine oxidase would be signifiicantly inhibited. Creatinine is increased under severe renal dysfunction , reduced renal blood flow, one the treatment with morin scavenging the free radicals [7] treatment with morin produced a significant reduction in creatinine and uric acid due to this antioxidant property of morin is actually an added advantage for this compound as a hyporuicemic agent because the attenuated antioxidant capacity due to the lowering of uric acid levels could be compensated by the natural compound [10]. Urea represents the levels of urea in different groups of rats, the group-B was administered with cadmium chloride showed elevated levels of urea was due to different types of renal damage whereas, the simultaneously administered group-C significantaly ($P<0.05$) showed protective effective compared with group-B this was due to morin effective protective action than the treatment action cadmium chloride induced as kidney dysfunction progresses mineral. Such as calcium and phosphorus may also be lost into the urine which increased excretion of calcium and phosphours may distrub bone metabolism and kidney stones, have been found in exposed workers [11] on the treatment with morin, the antioxidant properties gets reduced the serum urea level to be normal. The levels ACP in different groups of rats,the group-B was administered with cadmium chloride elevated levels of ACP in every part of the damaged kidneys (cartex, medulla and papilla) whereas the simultaneously administered group-C significantly at ($P<0.05$) levels showed protective effect compared with group-B, This was due to morin effective protective action. The increased levels of ACP in the prostatic fraction are associated with prostatic carcinomas and liver diseases hyperparathyroidism and paget's diseases[7] on the treatement with morin produce a significant reduction in serum marker enzymes of ACP. This may be due to an improvement in the secretary mechanism of the renal tubules Morin is to Scavenge the free radicals and increases the levels of antioxidant properties[12].

Serial No 5 and 6 Respresent the levels of ALP, LDH in different group of rats. The group-B was administered with cadmium chloride showed elevated of is ALP and LDH were due to different types of kindey diseases, where as the simultaneously administered group-C significantly ($P<0.05$) showed protective effect compared with group-B. This was due to Morin effective protective action. LDH increases in the renal cortical infarction may mimic pattern of acute myocardial infarction (AMI). Ruleout renal infrection of LDH-1 (less than LDH-2) is increased in the absence of AMI (or) Anemia increased LDH is out of proportion to AST level. It may be slightly increased (LDH-4 and LDH-5) in nephrotic syndrome, LDH-1 and LDH-2 may be increased in nephritis[13] . AST increased in liver diseases such as necrosis, extra hepatic bilary disease, cirohosis and some cases of metastatic cancer and granulomas. It is also increased in renal infarection occasionally and decreased chronic renal dialysis.[7].On treatment with Morin produced a significant reduction in serum marker enezymes such as LDH and AST, Morin which is directed to scavenging the hydroxyl radicals and super oxide annion, highly reactive oxygen species implicated in the inintiation of lipid peroxidation[14]. In LDH Morin reduces the levels due to an early improvement in the secreatary mechanism of renal tupbles [15] Morin reduces the liver diseases, renal infarction and intestinal injury.

Serial No 7 and **Histopathological observation** Reprsent the level of GGT in different group of rats. The group-B as administered with cadmium chloride showed elevated levesl of GTT in every part of kidney diseases, Whereas, the simultaneouly administered group-C significatly ($P<0.05$) showed protective effect compared with group-B. This dueto Morin effective antioxidant proterty. The increased level of GGT might bbe related to increased odiative stress dinduced by cadmiumchloride which also increased in cadmium chloride exposed rats [16]. GGT is elevated primary liver diseases and heights levels of GGT found in abiliary ostrcution, GGT is actively iinfusible by certain drugs hence elevated GGT levels are obtain found in ture hpatotoxicity reactive oxyzen species are least one of signals ijnvlved in increasing GGT tyranscription[17]. On treatment with Morin produce significant reduction is serum enzymes of GGt leads to decreased free radical productionparticularly in present of iron [18]. Histopatholofical observation reveal that cadmium choride treated rats has kindy damage architecture that means outer stripe of outer medulla and cadmium deposition in the distal part of the proximal convoluted tubel . an morin treated is maintained the kidney and nephron morphology against the cadmioum chloride action.

The prsent study celarly derived a conclusion that cadmium chloride (3.5mg/Body Wt,) dissoved in 0.01N nitric acid for 3 days, capable of causing nephrotoxicity but continuous treatment with Morin (200mg/Body Wt,) dissolved inn 0.9% saline continuous 20 days mimic cadmium chloride toxicity.

Aknowledgements

The author expresses due to Adhiparasakthi College of Arts and Science Management.

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