EFFECT OF MORIN ON MERCURY CHLORIDE INDUCED NEPHROTOXICITY

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INTRODUCTION

During the process of metabolism lot of waste materials and carbon dioxide are produced in the tissues. Apart from these, the residue of undigested food, heavy metals, drugs, toxic substances are also present in the body. Kidney is the versatile organ in the body. It is responsible for excretion of metabolic wastes from the body and for the regulation of acid base balance, water balance, electrolyte balance, blood pressure, calcium level in the body. This sometimes results in toxicity when the metabolite is more toxic than its precursor leads to kidney damage (Sembulingam and Sembulingam, 2004).

Mercury is a widespread environmental and industrial pollutant, which induces severe alterations in the tissues of both animals and men (Stacey and Kappas, 1982). Humans are exposed to these heavy metals through diet and in cases of occupational settings, by inhalation (Goldstein and schnellmann, 1996).

A natural compound Morin, commonly known as Morin hydrate, is used as an effective anti oxidant. Morin has been reported to possess a variety of biological properties against oxidative stress induced including protection of cardiovascular cells, (Wu et al., 1994) glomerular mesengial cells, hepatocytes, oligo dendrocytes and neurons damaged oxidative stress. In this present study an attempt was made to study the effect of Morin on Mercury chloride induced Nephrotoxicity.

MATERIALS AND METHODS

Chemicals used: The fine chemicals Lactate, Sodium Tungstate, TCA, BSA, Creatinine, urea, Folin’s Phenol, Picric acid, Phospho tungstic acid, Sulphuric acid, amino antipyrene used for the present study purchased from Loba, Merck companies. (AR grade). Morin and Mercury purchased from Sigma Chemicals, USA.

Laboratory animals: Healthy adults cross male Wistar albino rats (weight 150-180g) were used throughout the experiment, animals were maintained at 25±2°C with 45-55% relative humidity and 12hr light and dark cycle. They were housed in well ventilated polyurethane cages and had free access to tap water and laboratory pellet (Lipton Pvt. Ltd) feed. The animals purchased from Institute of Veterinary Preventive medicine (IVPM), Ranipet and maintained at Adhiparasakthi college of Arts and science, Kalavai.

Experimental procedure: A total number of 24 male rats were taken for the present study and they were grouped into Group A: Rats administered with 0.9% saline for continuous 15 days. Group B: Rats administered with Mercury chloride (5mg/kg body weight dissolved in 0.9% saline) intraperitoneally for continuous 5 days then saline alone continued from 6th day to 15th day. Group C: Rats administered with Mercury chloride (5mg/kg body weight dissolved in 0.9% saline) intraperitoneally for continuous 5 days along with Morin (200mg/kg body weight dissolved in 0.9% saline) then Morin alone continued from 6th day to 15th day.

ABSTRACT

The present study was carried out to investigate the possible effect of Morin (flavonoid) on Mercury chloride induced nephrotoxicity in rats with the help of serum biochemical markers and histological studies. They clearly derived a conclusion that mercuric chloride (5mg/kg body weight dissolved in 0.9% saline) for continuous five days capable of causing nephrotoxicity, at the same time simultaneous administration of Morin (200mg/kg body weight dissolved in 0.9% saline) with mercuric chloride mimics the toxicity in Group C than post toxicity treatment of Morin (Group D).
The levels of ACP were expressed in KA units/L; Values are mean ± SD for six rats in each group (n=6)

Collection of blood sample: Experimental rats were anesthetized with chloroform. Blood samples were withdrawn by carotid vein bleeding and allowed to clot for 30 minutes by keeping undisturbed at room temperature. Serum was separated by centrifugation at 2500rpm at 30°C for 15 minutes and used for the estimation of serum creatinine by Brod and Sirota, (1948), serum urea by Natelson et al., (1951); Serum uric acid by Caraway’s et al., (1955); acid phosphatase (ACP) by King and Arm strong (1934), lactate dehydrogenase (LDH-E.C.1.1.1.27) by King, (1965) and aspartate transaminase (AST): (E.C.2.6.1.1.) by Reitmann and Frankel (1957) methods.

Statistical analysis: The statistical significance was assessed using one-way analysis of variance (ANOVA) using SPSS 17.0 version (SPSS, Cary, NC, USA) followed by Bonferroni’s multiple comparison test (BMCT). The values are expressed as mean ± SD and considered its significance.

RESULTS AND DISCUSSION

Comprehensive toxicity studies are carried out by animal testing in order to ascertain whether the product exhibit any short term to long term toxicity (Walsh, 2004).

Nephrotoxicity was successfully induced to rats intra peritoneal (i.p) using freshly prepared mercury chloride (5mg/kg body weight dissolved in 0.9% saline) and it shows an elevated levels of various biochemical parameters like creatinine, urea, uric acid and marker enzymes such as ACP, LDH and AST. They were investigated in Control and Experimental groups of rats.

Table 1 depicts the level of body weight of rats at the interval of 15 days. The weight which was decreased during mercury chloride induced Nephrotoxicity (Group B) rats showed their weight increase towards their initial weight effectively in the Morin treatment group (Group D) where as in the simultaneous administered group did not show much elevation in Group C, this was due to Morin effective protective action Significantly (p < 0.01).

Free radicals restrain an atom with an unpaired electron in their outlet orbit which is deleterious and can damage cellular molecules and lead to decreases in body weight. (Larajinha, 1996). The effect of Morin against mercury chloride related toxicity is suppressed can be attributed to its free radical scavenging capacity and antioxidant activity.

Table 2 Represents the level of creatinine and uric acid in different groups of rats. The group - B was administered with mercury chloride showed elevated level of creatinine and uric acid due to renal damage. Where as the simultaneously administration of Morin and Mercury chloride (Group C) significantly (p < 0.01) showed protective effect compared with group B. This was due to Morin effective protective action.

Uric acid is the end product of purine metabolism. It is excreted to a large degree by the kidneys and to a smaller degree in the intestinal tract by microbial degradation. Increased levels lead to gout arthritis, impaired renal function and starvation (Rajendran, 2002). Hyperuricemia is associated with a number of pathological conditions such as gout. Lowering of elevated
uric acid level in blood could be achieved by xanthine oxidase inhibitors of renal urate reabsorption. (Rott and Agudelo, 2003).

The inhibition of Morin on xanthine oxidase is moderate when compared with allopurinal (Ferman et al., 2002). At high dose of Morin, however xanthine oxidase would be significantly inhibited.

Creatinine is increased under severe renal dysfunction, reduced renal blood flow, on the treatment with Morin scavenging the free radicals (Rajendran, 2002).

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 hypouricemic agent because the attenuated antioxidant capacity due to the lowering of uric acid level could be compensated by this natural compound (Campion et al., 1987).

Table 2 also represents the level of urea in different groups of rats. The group-B was administered with Mercury chloride showed elevated level of urea was due to different types of renal damage. Whereas the simultaneously administered group significantly (p < 0.05) showed protective effect compared with group B. This was due to Morin effective protective action than the treatment action.

Mercury induced changes in serum urea nitrogen (SUN) (Sharratt and Frazer, 1963). Because of renal reserve and compensation only severe injury resulting in 50-75% reduction in GFR can cause SUN. (Goldstein and Schnellmann, 1996). On the treatment with Morin, the antioxidant property gets reduced the serum urea level to be normal.

Table 3 represents the levels of ALP, LDH, and AST in different groups of rats. The group-B was administered with mercury chloride showed elevated level of is ALP, LDH, and AST were
due to different types of kidney diseases. Whereas the simultaneously administered group significantly (pd* 0.01) 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). Rule out renal infection 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 Nephritic syndrome. LDH-1 and LDH-2 may be increased in nephritis (Kemp and Laursen, 1960).

AST increased in liver diseases such as necrosis, extra hepatic biliary disease, cirrhosis and in some cases of metastatic cancer and granulomas. It is also increased in renal infarction occasionally and decreased in chronic renal dialysis (Rajendran, 2002).

On treatment with Morin produced a significant reduction in serum marker enzyme such as LDH and AST. Morin which is directed to scavenging the hydroxyl radical and super oxide anion, highly reactive oxygen species implicated in the initiation of lipid per oxidation (Denda et al., 1989). In LDH, Morin reduces the level due to an early improvement in the secretory mechanism of renal tubules (Kok et al., 2000). Morin reduces the liver diseases, renal infarction and intestinal injury. Table 4 represents the level of ACP in different groups of rats. The group B was administered with Mercury chloride showed elevated level of ACP in every part of the damaged kidneys (cortex, medulla and papilla). Where as the simultaneously administered group significantly (pd* 0.05) 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 in liver diseases, hyperparathyroidism and Paget’s disease (Rajendran, 2002). On the treatment with Morin produce a significant reduction in serum marker enzyme of ACP. This may be due to an improvement in the secretory mechanism of the renal tubule. Morin is to scavenge the free radicals and increases the level of antioxidant properties (Kitazawa et al., 2004).

Histological observation reveal that mercury chloride treated rats has kidney damage architecture (Fig. 2) that means outer stripe of outer medulla and mercury deposition in the distal part of the proximal convoluted tube (PCT) (Stephen sparrow et al., 2009). Morin treated is maintained the kidney and nephron morphology against the mercury chloride action (Fig. 3).

The present study clearly derived a conclusion that mercuric chloride (5mg/kg body weight dissolved in 0.9% saline) for continuous five days capable of causing Nephrotoxicity, at the same time simultaneous administration of Morin (200mg/kg body weight dissolved in 0.9% saline) with (5mg/kg body weight dissolved in 0.9% saline, i.p.) mimic mercuric chloride toxicity in Group C than post treatment of Morin (Group D).

REFERENCES


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