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Pathological Studies of Various Levels of Dietary *Momordica charantia* on Wistar Rats

Fahad Abdullah Al-Hizab, Mohammed Salem Moqbel and Seif Mustafa Barakat
Department of Pathology, College of Veterinary Medicine, King Faisal University,
Al-Hassa, 31982 Hofuf, Saudi Arabia

Abstract: The study aimed to evaluate the pathological, haematological and biochemical effects of various levels of dietary *Momordica charantia* (MC) in male Wistar rats. *Momordica charantia* (MC) is claimed to have several medicinal properties and is used as a traditional medicine for the treatment of a wide variety of disorders. The fruits of MC was fed to rats at 2, 5 and 10% of the standard diet for a period of 3 months. Administration of MC fruits at 2 and 5% was not toxic to rats. However, focal cellular swelling and individual cell necrosis of hepatocytes as well as degenerative changes in the renal tubules associated with interstitial nephritis were observed in rats fed with a diet containing 10% MC. These histopathological changes were accompanied clinically by alteration of serum Aspartate aminotransferase (AST), Alanine aminotransferase (ALT), Alkalin Phosphatase (ALP), BUN, creatinine and uric acids. No significant changes were observed in hematological values in all groups.

Key words: Clinicopathology, histopathology, hepatotoxicity, *Momordica charantia*, nephrotoxicity

INTRODUCTION

Over the years medicinal plants are known to contain several compounds used for therapeutic purposes and they may synthesize compounds producing drugs. Many (Rizwana *et al*., 2010) herbal drugs are widely used in the traditional medicine practice in Kingdom of Saudi Arabia for a very long time (Mossa *et al*., 1987).

Several plants were used in human medicine or veterinary practice for therapeutic and/or prophylactic purposes. Moreover the use of herbal medicine is considered as essential part of the primary health care in human and veterinary medicine (Bakhiet and Adam, 1995). Many researcher have indicated the importance of plants constituents including, essential oils, triterpenes, alkaloids, glycosides and saponins in the treatment of various animals diseases (Bakhiet and Adam, 1995; Bep, 1986).

Momordica charantia (MC) (Fig. 1), known as bitter melon is a member of the Cucurbitaceae family. It grows worldwide in tropical areas of Asia, Africa and South America. Ahmed *et al*. (2001) have studied the use of MC as antidiabetic, antiobesty, antimicrobial, anti inflammatory, antihypertensive and anticancer (Abdollahi *et al*., 2010; Batran *et al*., 2006; Khan and Omoloso, 1998; Matsuda *et al*., 1998; Virdi *et al*., 2003).

Fig. 1: *Momordica charantia* fruit

MATERIALS AND METHODS

Plant material: Fresh green whole fruits of *Momordica charantia* (MC) were purchased from local markets in Al-hassa, kingdom of Saudi Arabia. The

Corresponding Author: Fahad Abdullah Al-Hizab, Department of Pathology, College of Veterinary Medicine, King Faisal University, Al-Hassa, 31982 Hofuf, Saudi Arabia

fruits were sliced and then oven dried on 60°C temperature for 24 h. The dried fruits were powdered by an electric mill (0.05 mL), added to the powdered feed at 2, 5 and 10% and then mixed thoroughly by an electrical mixer. The mixure was made as bullets by electrical bullets machine then oven dried on 60°C temperature for 24 h.

Animals: Fourty male wistar albino rats weighing (150-200 g) were housed in hygienic fiber glass cages. Animals were fed on a balanced commercial pellets (obtained from the grain silos and flourmills organization-riyadh). All rats were given two weeks adaptation period with free access to food and water before starting of any experimental procedures.

Experimental design: Fourty rats were allotted at random manner to four groups 10 rats each:

- Group 1: 10 rats were fed untreated diet as control
- Group 2: 10 rats were fed MC at 2% of the diet
- Group 3: 10 rats were fed MC at 5% of the diet
- Group 4: 10 rats were fed MC at 10% of the diet

At the end of experiment, 12 weeks, rats from each group were humanly scarified, blood samples were collected for serobiochemical and hematological analysis, gross lesions were recorded and tissue specimens were collected from liver and kidney for histopathological studies and were fixed in 10 neutral buffered formalin.

Biochemical analysis: Blood samples were collected for biochemical parameters. Serum was separated by centrifugation of the clotted blood and stored at 20°C till used. Samples were then analyzed for the activities of Aspartate aminotransferase (AST), Alanine Aminotrans Ferase (ALT) and Alkaline Phosphatase (ALP) as well as the cholesterol concentration, total protein, albumin, globulin, total bilirubin, Blood Urea Nitrogen (BUN), uric acid and creatinine using commercial kits (Bio system S.A, Barcelona Spain) and automatically analyzed.

Hematological analysis: For hematological parameters, blood samples were collected in test tubes containing ETDA (Ethylene diamine tetra acetic acid) for determination of Hemoglobin concentration (Hb), Red Blood Cells (RBCs), pPacked Cell Volume (PCV), Mean Corpuscular Volume (MCV), Mean Corpuscular Hemoglobin (MCH), Mean Corpuscular Hemoglobin Concentration (MCHC) and total White Blood Cells (WBCs) using UDIHEM I-FRANCE analyzer.

Histopathological technique: The tissue specimens were trimmed and put in the vaccum infiltrating tissue processing machine (Tissue-Tik VIP 5Jr. Japan) and embedded in paraffin wax by SLEE MPS/C machine, Germany. Specimens waxed blocks were sectioned to 5 μm by LEICA RM 2235 microtome, Germany and then stained with Haematoxylin and Eosin (H and E) for histopathological examination (Kiernan, 1999).

Statistical analysis: Data was statistically evaluated with SPSS 7.5 Software. All results were expressed as mean±SD (Snedecor and Cochran, 1991).

RESULTS AND DISCUSSION

Pathological changes: Neither macroscopic nor microscopic lesions were seen in the liver and kidney tissues of rats fed with 2 and 5% MC. Rats fed with 10% MC showed, macroscopically mild hepatic congestion (Fig. 2). Microscopic examination revealed hepatic congestion, mostly seen in the central veins and portal blood vessels (Fig. 3). In addition, individual cell necrosis was randomly distributed all over hepatic zones (Fig. 4). Renal tissue showed aggregations of mononuclear inflammatory cells mostly lymphocytes and macrophages in interstitial tissues (Fig. 5). Degenerative and nucleic changes were observed within the tubular epithelium mostly in convoluted tubules and collected ducts that was evident by hypereosinophilic cytoplasm and pyknotic nuclei (Fig. 6). Moreover, deposition of homogenous casts in convoluted tubules lumen and congestion of interstitial blood vessels were seen (Fig. 7 and 8).

Fig. 2: Liver of rats fed 10% MC showing congestion

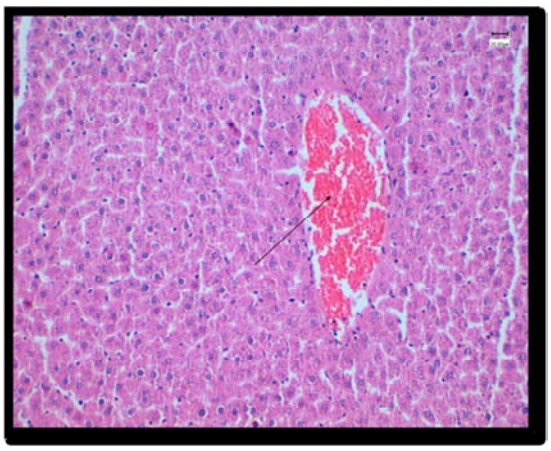

Fig. 3: Liver of rats fed 10% MC showing central vein congestion

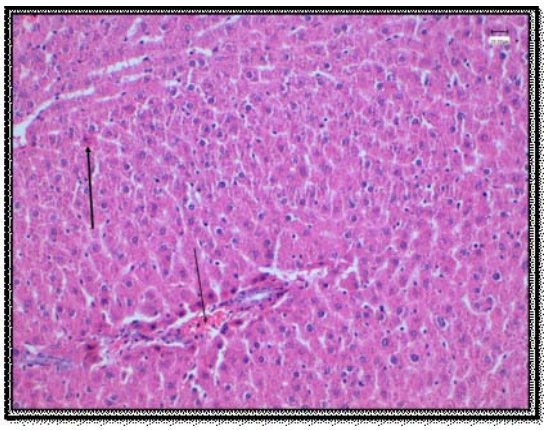

Fig. 4: Liver of rats fed 10% MC showing individual cells necrosis (thick arrow) and congestion of portal blood vessels (thin arrow)

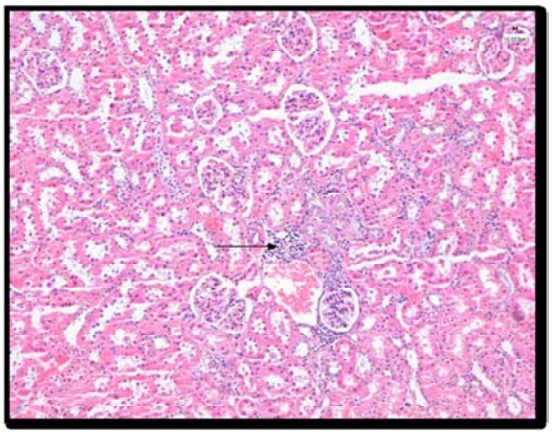

Fig. 5: Kidney of rats fed 10% MC showing aggregation of inflammatory cells in interstitial tissue (arrow)

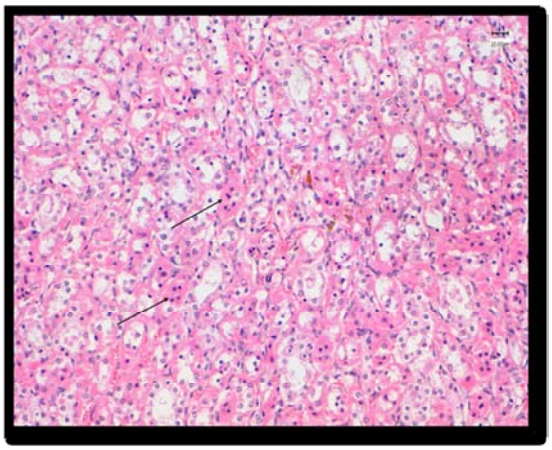

Fig. 6: Kidney of rats fed 10% MC showing individual cells necrosis (arrows), notice hyper eosinophilic cytoplasm and pyknotic nucleus

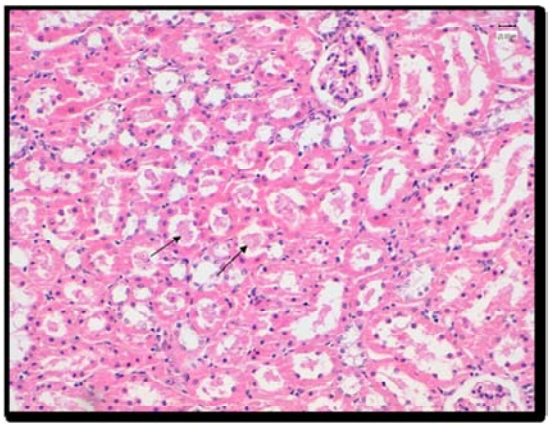

Fig. 7: Kidney of rats fed 10% MC showing homogenous casts in convoluted tubules (arrows)

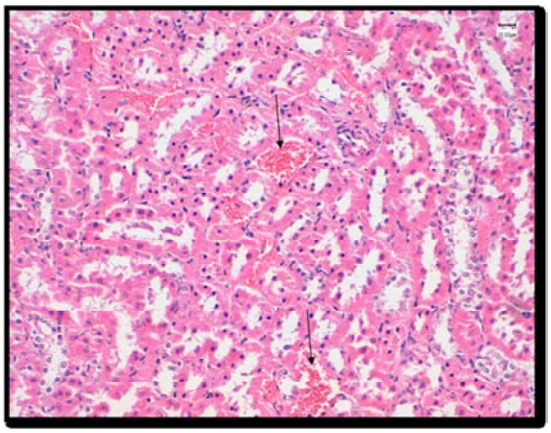

Fig. 8: Kidney of rats fed 10% MC showing congestion of intertubular blood vessels (arrows)

Table 1: Effect of *Momordica charantia* (MC) on hematological parameters in rats for 3 months

Haematological parameters	G1 control	G2 (2% MC)	G3 (5% MC)	G4 (10% MC)
WBC (10^3 μL^{-1})	16.09±0.90^a	18.09±1.76^a	14.43±1.44^a	15.97±1.05^a
LYM (10^3 μL^{-1})	9.70 ±0.50^a	11.69±1.29^a	9.94±1.37^a	10.62±0.86^a
MON (10^3 μL^{-1})	0.60±0.34^a	0.90±0.43^a	0.36±0.19^a	0.40±0.23^a
NEU (10^3 μL^{-1})	5.79±0.54^a	5.49±0.51^a	4.13±0.37^a	4.93±0.31^a
RBC (10^6 μL^{-1})	8.93 ±0.25^a	9.22±1.26^a	8.52±0.22^a	9.49±0.22^a
HGB (g dL^{-1})	14.34±0.43^a	14.24±0.75^a	14.39±0.36^a	14.66±0.22^a
MCV (fl)	53.25±1.18^a	53.75±2.21^a	53.56±0.41^a	52.50±1.02^a
MCH (pg)	16.09±0.42^a	14.41±1.49^a	15.70±0.15^a	15.45±0.20^a
MCHC (g dL^{-1})	30.38±0.74^a	29.36±3.37^a	29.26±0.18^a	29.38±0.50^a
PLT (10^3 μL^{-1})	621.88±66.18^a	630.25±214.95^a	542.33±78.48^a	574.38±59.87^a

Table 2: Effect of *Momordica charantia* (MC) on serobiochemical parameters in rats for 3 months

Biochemical parameters	G1 control	G2 (2% MC)	G3(5% MC)	G4 (10% MC)
ALT (IUL^{-1})	40±2.85^a	39±1.96^a	42.88±3.07^a	58.56±2.12^b
AST (IUL^{-1})	67.54±3.73^a	69.18±3.53^a	80.64±5.21^a	116.98±10.83^b
ALP (IUL^{-1})	131.11±6.16^a	153.72±10.84^a	154.94±7.22^a	198.06±8.10^b
T. Bilirubin (mg dL^{-1})	0.30±0.00^a	0.29±0.01^a	0.29±0.01^a	0.28±0.01^a
Cholesterol (mg dL^{-1})	60.78±2.53^a	62.67±4.64^a	61.50±3.60^a	63.56±6.16^a
T. Protein (g dL^{-1})	7.77±0.15^a	7.42±0.11^a	7.70±0.17^a	7.90±0.12^a
BUN (mg dL^{-1})	18.67±0.71^a	21.56±1.31^a	22.75±1.06^a	27.22±0.32^b
Creatnin (mg dL^{-1})	0.40±0.04^a	0.40±0.04^a	0.43±0.04^a	0.60±0.04^b
Uric acid (mg dL^{-1})	4.81±0.72^a	5.13±0.46^a	5.17±0.49^a	9.99±1.56^b

Values are mean±standard error; different letters between group means values are significant ($p \leq 0.05$)

Hematological changes: No significant changes were observed in the values of WBCs, RBCs, HGB, MCV, MCH, MCHC and PLT in all treate d and control groups (Table 1). Effect of Momordica Charantia (MC) on hematological parameters in rats for 3 months values are mean±standard error different letters between group means values are significant ($p = 0.05$).

Serobiochemical changes: As shown in Table 2, rats fed on the 10% of MC diets (Group 4), showed a significant increase in the activity of ALT, AST, ALP, BUN, creatinine and uric acids ($p = 0.05$). No significant changes in the concentration of cholesterol, total bilirubin and total protein.

CONCLUSION

In this study, we investigated the pathological and iochemical effects of feeding *Momordica charantia* uits to male Wistar rats. No clinical signs were bserved in all treated rats, this may suggested that the MC fruits doses given to the rats in this study are relatively safe. This finding is consistent with the results obtain by Platel *et al.* (1993).

No significant changes were observed in the values of WBCs, RBCs, HGB, MCV, MCH, MCHC and PLT in all treated and control groups. This finding is in agreement with (Rathi *et al.*, 2002; Husna *et al.*, 2013) observed significant differences only in Red Blood Cells Count (RBC) and Packed Cell Volume (PCV) percentage.

The increased activities of enzymes ALT, AST and ALP are indicative of hepatocellular leakage, organelles injury and loss of the functional integrity of the cell membranes (Rajagopal *et al.*, 2003; Rajesh and Latha, 2004). Moreover, the increased in creatinine, BUN and uric acid indicates renal tissue injury (Mardani *et al.*, 2014).

In our study, the increased of ALT, AST, ALP, creatinine, BUN and uric acids agree with studies of Ataman and Idu, 2007; Mardani and Nasri, 2014). On the other hands the changes obtained in biochemical parameters in this study disagree with Batran *et al.* (2006). The histopathological changes in liver and kidney tissues observed in this study are consistent with the finding of and some histopathological changes obtained in the present study are in harmony with other studies of Ng *et al.* (1994). The pathological and serobiochemical observations obtained in our study indicate that MC fruits may be hepatotoxic and nephrotoxic to rats at higher doses. However, it is difficult at this stage to explain the mechanism in which the plant injured these organs.

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