Asian Journal of Chemistry Vol. 19, No. 2 (2007), 1468-1472

Effect of Short-Term Treatment with *Citrullus colocynthis* L on the Lipid Profile and Other Blood Biochemical Parameters in Albino Rats

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The effect of *Citrullus colocynthis* L aqueous extract in 70% ethanol on blood biochemical parameters including: total cholesterol, triglycerides, total bilirubin, total protein, blood urea, serum creatine kinase (CK), serum lactate dehydrogenase (LDL), serum aspartate aminotransferase (AST) and serum alanine aminotransferase (ALT) were determined after oral administration of the extract to albino rats in a dose of 500mg/kg body weight for 7 d. A total of 20 rats were involved in this study and were divided into two groups. Group (A) a vehicle-treated control and group (B) a treated group with *Citrullus colocynthis* L. Our results demonstrated that administration of *Citrullus colocynthis* L in a dose of 500 mg/kg of body weight for 7 d induces a very significant decrease in total serum cholesterol level. The total cholesterol serum concentration was 180.1 ± 6.96 mg/dL in controls, while 135 ± 6.82 mg/dL in treated rats ($p \leq 0.01$). In addition, a significant decrease in blood levels of both ALT and CK ($p \leq 0.05$) and a significant increase in LDL blood serum level were found ($p \leq 0.01$). Other parameters including, triglycerides, total bilirubin, total protein, blood urea and AST were also tested and their serum levels were found to be unchanged. In conclusion, the lowering effect of *Citrullus colocynthis* L on total cholesterol was very significant and this should be considered in the treatment of high cholesterol blood levels.

Key Words: *Citrullus colocynthis* L, Cholesterol, Triglycerides, Blood urea, Serum aspartate aminotransferase, Serum alanine aminotransferase, Serum lactate dehydrogenase and Serum creatine kinase.

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INTRODUCTION

Desert plants in Jordan and their medicinal usage have been studied over thousands of years. Between 1998-1999, Lev and Amar[1] conducted a survey study in the Kingdom of Jordan which contain selected markets dealing with traditional medicinal substances of ethnic communities throughout the kingdom. This survey included diversified medicinal plants used in the Kingdom and their healing characteristics.

In Jordan, *Citrullus colocynthis* L (Cucurbitaceae), locally known as *Handal* is a well recognized plant in the traditional medicine and was used by people in rural areas as a purgative, antidiabetic and insecticide[2]. Mediterranean *Handal* was also known as effective medicine and was used as traditional medicine by both the old Greeks and Romans. Powder generated from the ripped fruit pulp has been used as purgative acting directly on the gastrointestinal tract a fact demonstrated by Elawad[3]. This plant contains a number of chemical compounds including cucurbitacins A, B, C, D and α-elaterin attributed to its porgative effect[4,5]. Furthermore, components such as saponin and glycoside were also found in this plant possessing a hypoglycimic effect on rabbits[6]. Recently, pharmacological research performed with this plant confirmed its effectiveness in the treatment of induced diabetes mellitus in rats through a signifiacant stimulation of insuline secretion[7]. Toxic effect of this plant seeds and leaves extracts was demonstrated in sheep, and found to be attributed to the administration of higher doses which could eventually lead to death[8]. Moreover, Al-Gaithi *et al.*[9], reported that oral administration of this plant aqueous extract reduces certain biochemical parameters such as AST and LDH, eliminating the toxic effect of streptozotocin-induces diabetes in rats. In this study, our object is to determine the acute effect of oral administration of low doses of this plant extract on the lipid profile and other biochemical parameters using albino rats.

EXPERIMENTAL

Adult male and female albino rats of Sprague Dawley strain, weighing about 300 g were raised in the Animal House Unit, Faculty of Medicine, Jordan University of Science and Technology under controlled temperature of 21 ± 1°C and 12 h light:dark schedule. Food and water were available *add labitum*.

Citrullus colocynthis L plants were collected from Aqaba area, mature black seeds were separated manually from the pulp of the fruits, then the pulp was dried and grinded into powder. Powder was extracted by water-ethanol mixture (70/30 v/v) for 6 h following the instructions published by Nmila *et al.*[7]. This step was repeated three times then the filtrate was pooled and concentrated under vacuum keeping a temperature less than 50ºC. The

concentrate was dissolved in a normal saline and used. The extract, 500 mg/kg, was administered orally to rats using animal feeding intubation's needles.

Rats were divided into two groups of ten rats each. These groups were treated as follows:

Group one were given 500 mg/kg body weight of the crude extract of *Citrullus colocynthis* L dissolved in 2 mL normal saline orally for one week in a daily bases. Group two were given 2 mL normal saline orally every one day for 1 week. 24 h after of the last dose, animals were weighed and autopsied under light ether anesthesia. Blood samples were collected through cardiac puncture for serum analysis using sterile syringes.

Biochemical parameters including: total proteins, total cholesterol, triglycerides, phospholipids, serum aspartete aminotransferase, serum creatine kinase, serum lactate dehydrogenase, total bilirubin, and blood urea were investigated using commercially available diagnostic kits. Concentrations were determined using UV/Visible spectrophotometer. Glucose was determined in the plasma obtained from collected blood sample by using commercially available kits (Promega). Insulin was measured in plasma by double antibodies ELISA, using Medgenix-Ins-ELISA kit (Biosourse Europe S.A).

Statistical analysis: Student's t test was used to determine the significance of the differences between various groups. The results were expressed as mean ± S.E[10].

RESULTS AND DISCUSSION

Effect of the crude extract on serum cholesterol and triglycerides in normal rats: Administration of 500 mg/kg body weight of the crude extract of *Citrullus colocynthis* L resulted in a highly significant decrease in the total serum cholesterol level ($p < 0.01$), with no evident changes in serum triglyceride levels when compared with the control group.

Effect of the crude extract on key hepatic enzyme in rats: Administration of a crude extract of *Citrullus colocynthis* L showed that serum AST concentration was not altered when compared with the control group. In contrast, ALT concentration was significantly increased when compared with the control group ($p < 0.01$).

Effect of the crude extract on key cardiac enzymes in rats: Administration of a crude extract of *Citrullus colocynthis* L showed a highly significant decrease in creatine kinase CK ($p < 0.05$) and a highly significant increase in lactate dehydrogenase LDH serum levels ($p < 0.001$).

Effect of the crude extract on total serum proteins in rats: Oral administration of the crude extract has no effect on the serum total protein concentration.

TABLE
SERUM BIOCHEMISTRY OF *C. colocynthis* FED ALBINO RATS
(MEAN OF 10 ANIMALS ± S.E.)

Treatment Group	Cholesterol mg\dL	Triglyceride mg\dL	AST IU\L	ALT mg\dL	CK IU\L	LDL U\L	Total Protein mg\dL	Total Bilirubin mg\dL	Urea mg\dL
Control	180.1	94.5	123.38	48.6	427	784	7.2	0.39	62
	±6.96	±5.62	±7.66	±2.72	±3.51	±19.4	±1.31	±0.17	±3.66
Treatment Group	135[b]	86.0[d]	121.78[d]	26.4[a]	342.1[a]	1570[b]	6.8[d]	0.43[d]	64[d]
	±6.82	±4.83	±4.33	±1.96	±9.6	±26.6	±2.1	±0.21	±4.11

When Gr.2, were compared with controls Gr.1
$p \leq 0.05$ = a, $p \leq 0.01$ = b, $p \leq 0.001$ = c, $p \leq$ ns = d

Effect of the crude extract on blood total bilirubin and urea concentrations: Oral administration of the crude extract did not altered the serum concentration of neither total bilirubin nor urea.

A positive correlation between cholesterol plasma concentration and the risk of coronary heart disease has been widely demonstrated by the lipid research Clinics Primary Prevention Trails[11]. In order to find good means to decrease plasma cholesterol level with minimal toxicity, the effect of *Citrullus colocynthis* L on the lipid profile was tested in albino rats of Sprague Dawley strain. To test for toxicity we did include additional blood biochemical parameters such as, total bilirubin, total protein, blood urea, serum creatine kinase (CK), serum lactate dehydrogenase (LDL), serum aspartate aminotransferase (AST) and serum alanin aminotrasferase (ALT). Our results demonstrated that acute oral administration of this extract significantly decreased the total serum cholesterol with no changes in triglycerides levels. In order to explain the hypocholesterolemic effect that usually obtained using various drugs, different mechanisms were suggested including; inhibition of HMG-CoA reductase, the key regulatory enzyme in cholesterol biosynthesis, decrease in cholesterol absorption by the intestinal wall and/or induction of LDL receptors within the peripheral tissue[12]. The mechanism by which *Citrullus colocynthis* L extract decreased the blood cholesterol level in our study will be tested in the future work. Concerning the side effects of this plant extract on the body systems[13] showed that the administration of *Citrullus colocynthis* L with other plant extracts resulted in an anti-oxidative, anti-proliferative, and other biochemical effects pointing to a great potential of hepatoprotective and tumouristetic actions of this combination[13]. On the other hand, oral administration of *Citrullus colocynthis* L fruits in combination with *Rhazya strica* leafs was found to have diversified clinical manifestation accompanied by enterohepatonephrotoxicity in Najdi sheep[14,15]. Barth *et al.* 2002) demonstrated that in certain concentration, the *Citrullus colocynthis* L extract has no hepato-toxic effect when incubated with liver

slices obtained from adult rats. In this study we demonstrated that AST serum levels as well as total bilirubin, total protein, blood urea were found to be unchanged. In addition, a significant reduction in the serum levels of ALT and CK is observed. Based on these results we might conclude that the administered dose of *Citrullus colocynthis* L extract was not toxic. The significant decrease in serum ALT and CK as well as the increase in LDL levels obtained in our results indicated that this plant could have an inhibitory effect on the expression of CK and ALT and induction effect on LDL that should be explained.

We can conclude that administration of *Citrullus colocynthis* L extract to albino rats reduces the serum blood cholesterol levels with no obvious toxicity. Therefore, this plant might have a very important application in decreasing the risk of high cholesterol on the coronary arteries.

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(*Received*: 17 January 2006; *Accepted*: 20 September 2006) AJC-5116