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on Experimental Rats  
with Chronic Renal  
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**Dr. Dalia Mohamed Talatt Abdel-  
khalik**  
Assistant professor  
(Nutrition and food science)  
Home Economic- Fayoum University



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البريد الإلكتروني للمجلة E-mail

## Effect of Enhancing Low Protein and Sodium Diets with Cardamom on Experimental Rats with Chronic Renal Failure

**Dr. Dalia Mohamed Talatt AbdEl-khalik**

Assistant professor (Nutrition and food science)

Home Economic- Fayoum University

### ABSTRACT:

This study aimed to investigate the effect of enhancing low protein and sodium diets with cardamom on experimental rats with chronic renal failure. Forty-eight male albino rats weighing  $190 \pm 10g$  were used in this study, these rats were fed on a basal diet for one week for acclimatization and then were divided into two main groups, the first main group (n=6) fed on a basal diet throughout the experiment and was used as the control negative group, while the second main group (42 rats) fed on a basal diet BD containing 2 % W/W L- arginine (arginine diet AD) for 4 weeks to induce chronic renal failure, and then were divided into seven subgroups (n = 6 rats in each group) as the following. *Subgroup (1):* fed on (arginine diet AD) and used as a positive control group. *Subgroup (2):* fed on a low sodium arginine diet. *Subgroups (3):* fed on a low protein and sodium arginine diet. *Subgroups (4 and 5):* fed on an arginine diet "AD" containing 5 and 10% cardamom, respectively. *Subgroup (6 and 7):* fed on low protein and sodium diets containing 5 and 10% cardamom, in addition to 2% W.W. L arginine respectively. During the experimental period, rats were weighed weekly, and feed intake was recorded daily. At the end of the experimental period (4 weeks), rats were sacrificed and the blood sample was collected from each rat, and was then separated the serum to determine kidney functions, lipid profile, liver enzymes, protein status, glucose, potassium and sodium. The results of this study revealed that serum concentrations of uric acid, urea nitrogen, creatinine, cholesterol, triglycerides, low density lipoprotein-cholesterol LDL-c, very low density lipoprotein-cholesterol VLDL-c, aspartate aminotransferase AST, alanine aminotransferase ALT, alkaline phosphatase ALP, glucose, and potassium were significantly elevated, while serum (high density lipoprotein-cholesterol, protein, albumin, globulin and sodium) in addition to feed intake and body weight gain% were decreased significantly by using L arginine administration in the diet (control positive), as compared the control negative. Treating chronic renal failure groups with low protein and sodium diets containing 5% and 10% cardamom improved all of these above parameters, especially when using low protein and sodium diets containing 10% cardamom. From these results, it could be concluded that low protein and

sodium diets containing cardamom are very important to improve the adverse effects that result from chronic kidney failure in rats.

**Keywords:** low protein diet, low sodium diet, cardamom, rats, chronic renal failure.

**Introduction:**

The existence of kidney damage or an estimated glomerular filtration rate (eGFR) of less than 60 ml/min per 1.73 square meters that lasts for three months or more is referred to as chronic kidney disease (CKD). It is a condition characterized by a gradual loss of kidney function that calls for renal replacement therapy (such as dialysis or transplantation) (Vaidya *et al.*, 2022).

Reduced dietary protein consumption, according to some studies, may aid in the management of chronic kidney disease (CKD), including decreasing the disease's development, enhancing albuminuria, and regulating uremia (Kovesdy & Kalantar-Zadeh 2016 and Kalantar-Zadeh *et al.*, 2016). On the other hand, dietary salt restriction is another aspect of the nutritional treatment for CKD, according to Locatelli and Del Vecchio, (2014) because it makes it possible to better control blood pressure, reduce proteinuria, and manage salt and water retention

The majority of spices have historically had medical and therapeutic benefits on people, but it is presently difficult to discover scientific proof of these effects. There have been various reviews made regarding herbal medicines that use spices. While, there have been various reviews made regarding herbal medicines that use spices. Additionally, the anti-inflammatory and antioxidant properties of spices have been researched (Iyer *et al.*, 2009). Cardamom is one of these spices that contains a wide range of antioxidants. *Elettaria cardamomum* is the scientific name for cardamom, which is a member of the ginger family (Zingiberaceae) (Ammam *et al.*, 2010). The significant antioxidant and therapeutic properties of cardamom have been attributed to its flavonoids, which are mostly terpenoids, according to the findings of several research. According to several researchers, flavonoids work by different mechanisms (Patel *et al.*, 2013).

Cardamom is sometimes referred to as the queen of spices because of its very pleasant aroma and taste. It is particularly prevalent in the Indian subcontinent, where it is used both as a traditional cure for stomachaches and for its aphrodisiac effects. (Kubo *et al.*, 1991).

Only a few research studies have examined the cardamom's effects on human participants. In one such trial, LDL, TG, and total cholesterol were found to be positively affected by cardamom supplementation, along with plasma fibrinolytic activity and serum total antioxidant status (Verma *et al.*, 2012). Cardamom supplementation effectively lowered

blood pressure and enhanced serum total antioxidant status in hypertensive individuals, according to a clinical investigation (Verma *et al.*, 2009).

Wolk, (2017) reported that, protein is frequently linked to many Western dietary practices, which cause mortality and harmful impacts on many chronic diseases, including chronic kidney disease. While, Naber and Purohit, (2021) concluded that also many CKD patients are at risk of hyperkalemia, hyperphosphatemia, chronic metabolic acidosis, bone loss, irregular blood pressure, and edema. These risks may be minimized, and the disease's progression may be slowed through careful monitoring of protein, phosphorus, potassium, sodium, and calcium, symptoms experienced by CKD patients. Therefore, The purpose of this study is to determine the impact of enhancing low protein and sodium diets with cardamom on experimental rats with chronic renal failure.

## Materials and Methods

### Materials

- Casein, minerals, vitamin mixture, choline chloride and L-arginine were purchased from Al-Gomhoria Company for Trading Drugs, Chemicals and Medical Instruments, Cairo, Egypt.

- Cardamom and starch were purchased from the local market, in Cairo, Egypt.

- Adult male albino rats (48) *Sprague Dawley* strain, weighing ( $190 \pm 10$ g) were obtained from the Animal Colony, Food Technology Research Institute, Agriculture Research Center, Giza, Egypt.

### Methods:

**Chemical Composition:** cardamom was chemically evaluated for moisture, fat, protein, fiber, and ash, according to methods of (A.O.A.C., 2000). Sodium and potassium were estimated according to the method given by A.O.A.C, (2005). Cardamom's total flavonoid and phenolic compound contents were assessed according to the methods described by (Crozier *et al.*, 1997 and Pric *et al.*, 1978).

### Biological evaluation

Cardamom was purchased from the local market, in Cairo, Egypt then it was ground in a grinder machine to get the coarse powder to be used as supplementation with the diet. A total of (48) adult male albino rats weighing  $190 \pm 10$ g were fed on a basal diet for one week for acclimatization. Rats were divided into two main groups, **the first main group** (n=6) was fed on a basal diet throughout the experimental period and was used as the control negative group. **The second main group** (42 rats) fed on (arginine diet AD)\* for 4 weeks to induce chronic renal failure, and then were divided into seven subgroups (n =6 rats in each group) as the following. **Subgroup (1):** fed on AD containing 14%

protein, and was used as a positive control group. **Subgroup (2):** fed on a low sodium diet\*\* in addition to 2% W/W L arginine. **Subgroups (3):** fed on a low protein\*\*\* and sodium diet in addition to 2% W/W L arginine. **Subgroups (4 and 5):** fed on an "AD" supplemented with 5 and 10% cardamom, respectively. **Subgroup (6 and 7):** fed on low protein and sodium diets supplemented with 5 and 10% cardamom, in addition to 2% W.W. L arginine respectively.

\* **AD:** Arginine diet (basal diet containing 2% L arginine).

\*\* **Low Sodium Diet:** (the mineral mixture which used in preparing this diet for this group contain 75% from the amount of sodium chloride which used in preparing mineral mix. which used in basal diet).

\*\*\* **Low protein diet:** diet containing 7% protein.

At the end of the experimental period, rats fasted overnight, then the rats were anaesthetized and sacrificed, and blood samples were collected from the aorta in a dry centrifuge tube. The blood samples were centrifuged and serum was separated to assess some biochemical parameters i.e. the uric acid (Fossati *et al.*, 1980), urea nitrogen (Henry *et al.*, 1974), creatinine (Henry, 1974), total cholesterol (Richmond, 1973), triglycerides (Wahalefeld, 1974), high density lipoprotein- cholesterol (HDL-C) (Richmond method, 1973), low-density lipoprotein cholesterol (LDL-c) and (VLDL-c) (Friedwald *et al.*, 1972), Aspartate Amine Transaminase (AST) and Alanine Amine Transaminase (ALT) activities (Reitman and Frankel, 1975), Alkaline Phosphatase (ALP) (Belfield and Goldberg, 1971). Protein (Gomal *et al.*, 1949), albumin (Doumas and Biggs, 1971). Glucose (Trinder, 1969). Sodium (Henry *et al.*, 1974) and potassium (Henry, 1964).

### Statistical analysis

The statistical analysis was carried out by using SPSS, PC statistical software (version 10.0; SPSS Inc, Chicago, USA). The results are expressed as mean  $\pm$  SD. Data were analyzed by one-way analysis of variance (ANOVA). The least significant difference (LSD) test was used to determine the significance of the differences between the means at ( $P < 0.05$ ) (Steel and Torri, 1980).

### Results and Discussion

The chemical composition (on a dry weight basis per 100 g) of cardamom, in addition to potassium, sodium, total flavonoids and total phenolic is shown in Table (1). It is noticed from the data that, the mean value of moisture, protein, fat, ash, dietary fiber and carbohydrate, were 8.12 g, 9.25 g, 8.35 g, 6.90 g, 24.5 g and 42.88g /100g respectively, these results agree with Abera *et al.*, (2019) who found that cardamom contains 8.51 % moisture, 6.72 % ash, 9.29 % crude protein, 10.025 % oleoresin, 8.01 % essential oil, 24.14 % crude fiber and 41.08 % total

carbohydrate. Results in this table showed that, the mean value of potassium and sodium in cardamom was 1065 mg/100g and 17.11 mg/100g, respectively. These findings were in the line with findings of (Abera *et al.*, 2019 and Tawfek and Ali, 2022) who found that cardamom contains 843.28 mg of potassium and 18 mg of sodium per 100 g, respectively.

**Table (1): Chemical composition of cardamom / 100g**

Nutrients	%
Moisture (g)	8.12
Protein (g)	9.25
Fat (g)	8.35
Ash (g)	6.90
Dietary fiber (g)	24.50
Carbohydrate (g)	42.88
Potassium (mg)	1065
Sodium (mg)	17.11
Total flavonoids contents (mg CE/100g)	6.75
Total phenolic compound (mg GAE/100g)	34.55

The values in this table are the average of two estimates.

According to the data in this table, the total flavonoid contents and total phenolic compound in cardamom extracted by using methanol were 6.75 mg CE/100g and 34.55 mg GAE/100g, respectively. These findings were in the line with (Chimbetete *et al.*, 2019) who found that total phenolic content (TPC) (mg GAE/100g) and total flavonoids content (mg CE/100g) in cardamom extracted by water and methanol was (7.55 and 31.24 mg GAE/100g for phenolic content) and (0.31 and 6.33 mg CE/100g for flavonoids content), respectively.

#### **Effect of enhancing low protein and sodium diets with cardamom on feed intake and body weight gain% of chronic renal failure rats.**

The findings in Table (2) demonstrated the impact of low protein and sodium diets containing two levels of cardamom on feed intake (g/day/ each rat) and body weight gain % of experimental rats with chronic renal failure. From these findings it could be shown that, the mean values of feed intake for the positive control group which was fed on a basal diet containing 2% W/W L arginine (arginine diet AD) showed a significant decrease in this parameter  $p \leq 0.05$ , as compared to the control negative group. The data presented in this table revealed that, non-significant changes in the mean values of feed intake between all other groups.

In the positive control group fed on (AD), as opposed to the negative control group fed on a baseline diet, the mean value of body weight gain% (BWG%) reduced considerably  $p \leq 0.05$ . Rats fed either a

low sodium diet or a low protein and sodium diet had their mean BWG% values significantly lower than those of the negative and positive control groups. While rats fed the same meal with 5% cardamom exhibited non-significant deference, rats fed the same diet having 10% cardamom produced a substantial drop in BWG%.against the group that received a positive control (AD). Rats fed low protein, high sodium meals with 5% and 10% cardamom exhibited no significant differences in BWG% compared to rats on a low protein, high sodium diet with just arginine (LPSD).

In this regard, **Omar and Kabil, (2018)** discovered that, compared to rats fed on a baseline diet, rats fed on a diet containing 2% L arginine for 8 weeks to induce chronic renal failure experienced lower mean values of feed intake and body weight increase. Contrarily, giving a group of rats a diet containing 0.7% adenine for 4 weeks to induce chronic renal failure resulted in a much lower mean value of feed intake and body weight growth than feeding the group of rats a baseline diet (**Awad-Allah et al., 2020**). Conversely, a low-protein diet was found to cause weight loss in chronic renal failure rats when compared to a high-protein diet (**Christiane et al.,1999**) . When compared to rats without chronic renal failure, the mean value of feed intake and body weight growth considerably decreased in the chronically ill rats. When compared to a positive control group (chronic renal failure), chronic renal failure groups fed on a diet with low levels of refined and rock salt saw the least drop in feed intake and body weight (**Awad-Allah et al., 2020**).

**Table (2): Effect of enhancing low protein and sodium diets with cardamom on feed intake and body weight gain% of chronic renal failure rats.**

Groups		Parameters	Feed intake g/day/each rat	Body weight gain %
Control (-ve)			17.00 <sup>a</sup> ± 0.790	49.87 <sup>a</sup> ± 1.937
Control (+ve) Basal diet containing arginine (AD)			14.50 <sup>b</sup> ± 0.500	22.20 <sup>b</sup> ± 3.346
Low sodium basal diet containing arginine			14.90 <sup>b</sup> ± 0.418	19.00 <sup>c d</sup> ± 3.391
Low protein and sodium diet containing arginine (LPSD)			14.80 <sup>b</sup> ± 0.570	17.80 <sup>c d e</sup> ± 2.588
AD contain	5% cardamom		14.80 <sup>b</sup> ± 0.670	20.80 <sup>b c</sup> ± 1.483
	10% cardamom		15.30 <sup>b</sup> ± 0.570	18.20 <sup>c d</sup> ± 1.303
LPSD contain	5% cardamom		14.50 <sup>b</sup> ± 0.500	16.60 <sup>d e</sup> ± 1.341
	10% cardamom		14.90 <sup>b</sup> ± 0.418	14.80 <sup>e</sup> ± 1.643

AD: Arginine diet (basal diet containing 2 % W/W L- arginine)

LPSD: low protein sodium diet containing 2 % W/W L- arginine

Mean values in each column with same letters are not significantly different.

**Effect of enhancing low protein and sodium diets with cardamom on kidney functions of chronic renal failure rats.**

The data presented in Table (3) demonstrated the impact of low-protein, low-sodium meals containing two amounts of cardamom on the kidney functions of experimental rats with chronic renal failure, including uric acid, urea nitrogen, and creatinine (mg/dl). The results indicated that the control positive group (arginine diet AD) had significantly higher mean values for uric acid, urea nitrogen, and creatinine than the control negative group, with a p-value of 0.05 for each parameter. Conversely, when rats were given a basal diet containing 2% W/W L-arginine (arginine diet AD) to cause chronic renal failure, the mean values of serum uric acid, urea nitrogen, and creatinine increased relative to the negative control group by approximately 161.35%, 156.99%, and 390.33%, respectively. In this regard, **Rashid et al., (2005)** found that elevated blood uric acid, urea nitrogen, and creatinine levels were symptoms of chronic renal failure caused in rats. These levels have risen, which shows that renal damage has altered the glomerular filtration rate (GFR) and reabsorption mechanisms. The 2% arginine diet was shown to raise the blood levels of creatinine and urea nitrogen by **Yokozawa et al., (2003)**. These findings show that arginine delivery to rats results in the metabolization of guanidino compounds, which build up in the serum and cause renal damage.

**Table (3): Effect of enhancing low protein and sodium diets with cardamom on kidney functions of chronic renal failure rats.**

Groups		Parameters	Kidney functions (mg/dl)		
			Uric acid	Urea nitrogen	Creatinine
Control (-ve)			1.405 <sup>g</sup> ± 0.035	25.133 <sup>f</sup> ± 1.121	0.621 <sup>g</sup> ± 0.033
Control (+ve) Basal diet containing arginine (AD)			3.672 <sup>a</sup> ± 0.068	64.591 <sup>a</sup> ± 3.706	3.045 <sup>a</sup> ± 0.169
Low sodium basal diet containing arginine			3.139 <sup>b</sup> ± 0.070	58.748 <sup>b</sup> ± 3.920	2.610 <sup>b</sup> ± 0.189
Low protein and sodium diet containing arginine (LPSD)			2.889 <sup>c</sup> ± 0.092	53.458 <sup>c</sup> ± 3.849	2.349 <sup>c</sup> ± 0.165
AD containing	5% cardamom		2.515 <sup>d</sup> ± 0.077	50.855 <sup>c</sup> ± 3.300	2.132 <sup>d</sup> ± 0.068
	10% cardamom		2.144 <sup>e</sup> ± 0.087	42.775 <sup>d</sup> ± 3.034	1.672 <sup>e</sup> ± 0.076
LP SD	5% cardamom		2.135 <sup>e</sup> ± 0.074	43.269 <sup>d</sup> ± 3.195	1.744 <sup>e</sup> ± 0.053



10% cardamom	1.695 <sup>f</sup> ± 0.075	33.893 <sup>e</sup> ± 1.148	1.206 <sup>f</sup> ± 0.122
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AD: Arginine diet (basal diet containing 2 % W/W L- arginine)

LPSD: low protein sodium diet containing 2 % W/W L- arginine

Mean values in each column with same letters are not significantly different.

Compared to the positive control group fed on AD (a basal diet containing 2% W/W L-arginine), treating chronic renal failure groups with (a low sodium diet or low protein and sodium diet) significantly decreased the mean values of serum uric acid, urea nitrogen, and creatinine  $p \leq 0.05$ . On the other hand, the group that was treated with a low-protein and low-sodium diet had a significant decrease in kidney function compared to the group that was treated with a low-sodium diet only. In the stages of CKD preceding the start of renal replacement therapy, a low-protein diet (0.6g/kg/day) becomes a crucial therapeutic strategy in the stages of CKD that precede the start of renal replacement therapy because it delays kidney failure, improves uremic symptoms, reduces serum phosphorus levels and proteinuria, and improves metabolic acidosis and insulin resistance (**Fouque and Aparício, 2007 and Ikizler, 2009**). On the other hand, **Locatelli and Del Vecchio, (2014)** mentioned that, since it provides for better management of sodium and water retention, blood pressure regulation, and a decrease in proteinuria. **Lambers et al., (2012) and Giordano et al., (2014)** reported that, dietary sodium and protein limitation should be a staple in the nutrition management of all patients with proteinuria, and it has been shown to be helpful even in overt diabetic nephropathy.

Feeding groups of rats that were suffering from chronic renal failure on (arginine diets containing two levels of cardamom) or (low protein and sodium diets containing the same levels of cardamom 5% and 10%) showed a significant reduction in the mean values of uric acid and urea nitrogen and creatinine at ( $p < 0.05$ ), as compared with the positive control group. The mean values of these parameters decreased gradually with increasing the levels of cardamom. The group treated with a low-protein, low-sodium diet containing 10% cardamom showed the greatest improvement in kidney function; their mean values for serum uric acid, urea nitrogen, and creatinine were lower than those of the positive control group by approximately 53.84 %, 47.53 % and 60.39 % than that of the positive control group, respectively. In this respect, **Ballabh et al., (2008)** reported that cardamom has been used in traditional medicine to treat renal and bladder diseases. **Elkomy et al., (2015)** reported that, co-administration of cardamom and gentamicin helps reduce the nephrotoxicity that gentamicin causes. **Verma et al., (2015)** found a

significant decrease in blood urea nitrogen and serum creatinine following the beneficial effect of an alcoholic seed extract of *A. cardamomum*. This was because the kidney's glomerular function had improved and a positive nitrogen balance was maintained.

#### **Effect of enhancing low protein and sodium diets with cardamom on lipid profile of rats suffering from chronic renal failure.**

The impact of a low-protein, low-sodium diet with cardamom on the lipid profile of experimental rats with chronic renal failure, including cholesterol, triglycerides, high density lipoprotein cholesterol (HDL-c), low and very low density lipoprotein cholesterol (LDL-c and VLDL-c), is shown in Table (4). The mean value of serum cholesterol, triglycerides, LDL-c, and VLDL-c increased significantly  $p < 0.01$ , while HDL-c decreased in the positive control group fed on a basal diet containing 2% W/W L arginine (Arginine diet AD), as compared to the negative control group. In this regard, **Litvinova et al., (2015) and Venho et al., (2002)** indicated that L-arginine is engaged in a variety of physiological processes connected to metabolic disorders and cardiovascular disorders. According to **Abd El-Megeid et al., (2009)**, feeding adult rats a basal diet containing 2% L-arginine increased the mean value of serum cholesterol, triglycerides, low and very low density lipoprotein cholesterol, and decreased high density lipoprotein cholesterol when compared to the healthy control rats.

In comparison to the positive control group (AD), feeding chronic renal failure rats a low sodium diet with arginine decreased all lipid parameters, with the exception of HDL-c. On the other hand, feeding chronic renal failure rats on a low protein and sodium diet containing arginine improved all lipid profiles in comparison to the positive control group (AD) and low sodium diet group. In this regard, **Sanders, (2009)** reported that According to this, dietary sodium raises blood pressure (BP) and cardiovascular diseases (CVDs), including stroke, myocardial infarction, and cardiac hypertrophy. While it has been noted by **Graudal et al., (2017)** that sodium restriction has positive benefits in lowering blood pressure and related comorbidities.

**Table (4): Effect of enhancing low protein and sodium diets with cardamom on lipid profile of rats suffering from chronic renal failure.**

Parameters	Lipid profile (mg/dl)				
	Ch	Tg	HDL-c	LDL-c	VLDL-c
Control (-ve)	79.838 <sup>g</sup> ± 1.465	36.195 <sup>f</sup> ± 1.564	48.481 <sup>a</sup> ± 3.048	24.118 <sup>f</sup> ± 2.748	7.239 <sup>f</sup> ± 0.313
Control (+ve) Basal diet containing arginine (AD)	150.021 <sup>a</sup> ± 3.703	74.714 <sup>a</sup> ± 3.410	21.954 <sup>f</sup> ± 2.140	113.124 <sup>a</sup> ± 4.290	14.942 <sup>a</sup> ± 0.681
Low sodium basal diet containing arginine	143.408 <sup>b</sup> ± 1.640	70.571 <sup>b</sup> ± 2.880	24.033 <sup>f</sup> ± 1.877	105.260 <sup>b</sup> ± 2.155	14.114 <sup>b</sup> ± 0.576

Low protein and sodium diet containing arginine (LPSD)		137.685 <sup>c</sup> ± 2.419	67.966 <sup>b</sup> ± 3.717	26.855 <sup>e</sup> ± 1.976	97.237 <sup>c</sup> ± 3.213	13.593 <sup>b</sup> ± 0.743
AD containi	5% cardamom	131.794 <sup>d</sup> ± 3.189	61.180 <sup>c</sup> ± 3.779	33.188 <sup>d</sup> ± 1.956	86.370 <sup>d</sup> ± 3.704	12.236 <sup>c</sup> ± 0.755
	10% cardamom	117.564 <sup>e</sup> ± 2.743	53.443 <sup>d</sup> ± 2.931	37.901 <sup>c</sup> ± 1.252	68.975 <sup>e</sup> ± 1.209	10.688 <sup>d</sup> ± 0.586
LPSD containi	5% cardamom	121.081 <sup>e</sup> ± 3.160	52.820 <sup>d</sup> ± 2.909	39.795 <sup>c</sup> ± 1.180	70.722 <sup>e</sup> ± 3.892	10.563 <sup>d</sup> ± 0.582
	10% cardamom	107.021 <sup>f</sup> ± 7.365	44.974 <sup>e</sup> ± 2.601	44.548 <sup>b</sup> ± 2.278	53.478 <sup>f</sup> ± 5.938	8.994 <sup>e</sup> ± 0.520

Ch: Cholesterol

Tg: Triglyceride

AD: Arginine diet (basal diet containing 2 % W/W L- arginine)

LPSD: low protein sodium diet containing 2 % W/W L- arginine

Mean values in each column with same letters are not significantly different.

Data in this table revealed that feeding groups of rats that were suffering from chronic renal failure on arginine diets containing (5% and 10% cardamom) improved all lipid parameters, as compared to the groups which were fed on (AD "control positive", low sodium diet, and low protein and sodium diet), especially the group which treated with 10% cardamom. On the other hand, feeding chronic renal failure groups on low protein and sodium diets that are containing (5% and 10% cardamom) led to higher improvement in lipid parameters, as compared to other treated groups. The group with chronic renal failure that was treated with a low protein, low sodium diet that also contained 10% cardamom had the greatest improvement in their lipid profiles.

In this respect, **Rahman et al., (2017)** reported that Cardamom fruit is used to treat gastrointestinal diseases, dyspepsia, debility, anorexia, asthma, bronchitis, and renal and vesicular calculi.

Cardamom's effects on human beings have been the topic of certain investigations. One such study showed that cardamom supplementation favorably changed the atherogenic lipid profile such as LDL, TG, and total cholesterol increased plasma fibrinolytic activity, and enhanced serum total antioxidant status (**Verma et al., 2012**). Another research by **Verma et al., (2009)** found that moderately hypertensive participants taking 3 g of green cardamom per day for 12 weeks had a reduction in blood pressure without any changes in their plasma levels of cholesterol or triglycerides. On the other hand, **Rahman et al., (2017)** found that supplementing with cardamom powder prevented the development of obesity-related peritoneal fat deposition in rats fed a high-carb, high-fat diet.

Cardamom contains essential oils as well as other bioactive substances that are significant sources of flavonoids, alkaloids, terpenoids, anthocyanins, and phenolic compounds like 1,8-cineole,

terpinyl acetate, limonene, terpinolene, and myrcene (Noumi *et al.*, 2018). These compounds have a protective effect against cardiovascular disease CVD by lowering blood pressure (Verma *et al.*, 2009).

#### **Effect of enhancing low protein and sodium diets with cardamom on liver enzymes of rats suffering from chronic renal failure.**

The data presented in Table (5) demonstrated the impact of low-protein, high-sodium diets containing two concentrations of cardamom (5% and 10%) on liver enzymes, including aspartate aminotransferase (AST), alanine aminotransferase (ALT) activities, and alkaline phosphatase ALP (U/l) of experimental rats with chronic renal failure. From these findings, it could be shown that the mean values of AST, ALT, and ALP for the control positive group fed on a basal diet containing 2% W/W L arginine (arginine diet AD) showed a significant increase  $P \leq 0.05$  in all parameters  $p < 0.05$ , as compared to the control negative group. Feeding rats on (arginine diet AD) to induce chronic renal failure led to increasing the mean values of serum AST, ALT and ALP by about 108.04 %, 248.30 %, and 29.93 % compared to the negative control group.

These findings are in parallel with Kabil, (2011) and Shahhat, (2007) who established that liver enzyme levels are elevated in rats with chronic renal failure brought on by L-arginine. Other investigations indicated that L arginine delivery caused albuminuria as a result of kidney damage and/or protein reabsorption tubular blockage (Huang *et al.*, 2021 and Peters *et al.*, 1999). However, Yokozawa *et al.*, (2003) showed that chronic renal failure is linked to the impairment of several organ disturbances, particularly liver functions as seen by an increase in ALT and AST enzymes.

Treating chronic renal failure groups with (a low sodium diet or low protein and sodium diet) decreased the mean values of serum AST, ALT, and ALP significantly  $p \leq 0.05$ , as compared to the positive control group fed on AD (a basal diet containing 2 % W/W L- arginine). In this regard, it was noted by Wang and Bowman, (2013) that excessive consumption of sodium (Na) is a widespread issue around the world. Increased risk of a number of metabolic disorders, including obesity (Zhang *et al.*, 2018), dyslipidemia (Baudrand *et al.*, 2014), and non-alcoholic fatty liver disease (NAFLD), is associated with high sodium consumption (Shen *et al.*, 2019). On the other side Watanabe, (2014) reported that protein-restricted diets have been utilized to treat chronic renal failure in Japan. According to Kuntz, (2001), feeding rats with chronic renal illness LPD led to a considerable improvement in their AST and ALT activity.

Comparing the chronic renal failure groups to the positive control group, which received treatment with an arginine diet including 5% and

10% cardamom, led to a substantial reduction in AST, ALT, and ALP (p 0.05). (arginine diet AD only). On the other hand, as compared to the group receiving the same diet but only containing 5% cardamom, the mean levels of AST, ALT, and ALP in the chronic renal failure group fed on an arginine diet including 10% cardamom reduced considerably p ≤ 0.05.

**Table (5): Effect of enhancing low protein and sodium diets with cardamom on liver enzymes of chronic renal failure rats.**

Parameters		Liver enzymes (U/l)		
		AST	ALT	ALP
Control (-ve)		57.263 <sup>g</sup> ± 1.295	19.328 <sup>f</sup> ± 1.023	180.590 <sup>g</sup> ± 3.739
Control (+ve) Basal diet containing arginine (AD)		119.130 <sup>a</sup> ± 3.486	67.320 <sup>a</sup> ± 4.147	234.647 <sup>a</sup> ± 3.440
Low sodium basal diet containing arginine		109.846 <sup>b</sup> ± 2.797	63.070 <sup>b</sup> ± 2.758	222.283 <sup>b</sup> ± 2.715
Low protein and sodium diet containing arginine (LPSD)		107.601 <sup>b</sup> ± 2.518	60.705 <sup>b</sup> ± 3.221	218.442 <sup>c</sup> ± 2.885
AD containing	5% cardamom	99.985 <sup>c</sup> ± 2.136	54.691 <sup>c</sup> ± 3.565	206.281 <sup>d</sup> ± 3.210
	10% cardamom	90.453 <sup>d</sup> ± 2.260	47.729 <sup>d</sup> ± 2.903	191.115 <sup>f</sup> ± 3.424
LPSD containing	5% cardamom	89.125 <sup>d</sup> ± 1.884	47.643 <sup>d</sup> ± 2.362	196.850 <sup>e</sup> ± 2.935
	10% cardamom	77.392 <sup>f</sup> ± 1.818	39.156 <sup>e</sup> ± 2.000	189.756 <sup>f</sup> ± 2.860

AD: Arginine diet (basal diet containing 2 % W/W L- arginine)

LPSD: low protein sodium diet containing 2 % W/W L- arginine

Mean values in each column with same letters are not significantly different.

Rats with chronic renal failure were fed a low-protein, low-sodium diet supplemented with cardamom (5% and 10%), which resulted in a substantial drop in AST, ALT, and ALP when compared to the positive control group. As opposed to the groups treated with arginine diets (AD) including (5% and 10% cardamom), these treatments reduced the mean levels of AST, ALT, and ALP. The information in this table showed that the chronic renal failure group, which was given a low-protein, low-sodium diet supplemented with 10% cardamom, saw the greatest drop in liver enzymes.

**Abdel-Wahab and Ali, (2005)** observed that clove and cardamom therapy significantly reduced the liver enzymes in the serum. This is explained by the antioxidants found in clove and cardamom, which have phenolic chemicals that have the ability to scavenge free radicals. Additionally, following five weeks of consumption of 2% clove and 2%

cardamom. **Sadeek and Abd El-Razek, (2010)** demonstrated that iron-overloaded rats had significantly lower blood levels of AST, ALT, ALP, and total bilirubin ( $p < 0.05$ ). Cardamom improved liver function by restoring normal liver weight and ALT, AST, and ALP plasma activity. (**Parmar et al., 2009**). Similarly, enhanced hepatic function was measured with cardamom extract in alcohol-induced liver damage (**Morita et al., 2003**). On the other side **Rahman et al., (2017)** found that supplementing with cardamom powder protected liver impairment by reducing the activity of the AST, ALT, and ALP enzymes in obese rats.

**Effect of enhancing low protein and sodium diets with cardamom on protein status of rats suffering from chronic renal failure.**

The findings in Table (6) showed the impact of low protein and sodium diets containing two levels of cardamom (5% and 10%) on protein status, including serum protein, albumin, and globulin (g/l) of experimental rats with chronic renal failure. From these results, it could be observed that the mean values of these parameters for the control positive group fed on a basal diet containing 2 % W/W L- arginine (arginine diet AD) showed a significant decrease  $p < 0.05$ , as compared to the control negative group fed on basal diet. The data in this table revealed that the mean value of serum protein, albumin, and globulin of the control positive group decreased by about 18.21%, 22.41 %, and 13.48%, respectively than that of the negative control group. On the other hand, low sodium basal diet containing the same level of L-arginine led to a significant increase ( $p \leq 0.05$ ) in all parameters, except serum globulin in comparison with the positive control group. The data in this table demonstrated that feeding chronic renal failure rats on a low protein and sodium diet containing L-arginine (LPSD) caused a significant decrease  $p \leq 0.05$  in serum protein and albumin. While serum globulin showed non-significant change, when compared to the chronic renal failure group treated with a low sodium diet. However, this treatment recorded a significant increase ( $p \leq 0.05$ ) when compared to the control chronic renal failure group (positive control group).

When compared to the positive control group, the chronic renal failure group fed on AD containing 5% and 10% cardamom showed significantly higher mean values for serum protein, albumin, and globulin, especially when 10% cardamom was utilized. Serum protein, albumin, and globulin levels were significantly lower in the chronic renal failure groups treated with a low-protein, low-sodium diet containing 5 and 10% cardamom compared to the same groups given AD containing the same quantities of cardamom. Arginine diets or low protein, low sodium meals including the two amounts of cardamom (5% and 10%),

according to the results in this table, increased the protein status in the blood of rats with chronic renal failure.

Accordingly, **Yu and Paetau-Robinson, (2006)** came to the conclusion that CRF is linked to an elevated level of albumin mRNA breakdown in the liver of CRF rats. The decrease in the levels of mRNA for hepatic lipase activity in chronic renal failure may be caused by one of several causes. According to double-blind research, cutting salt consumption from 10 to 5 grams per day results in a 20% decrease in urine protein output. A later double-blind trial revealed that persons with moderate hypertension who reduced their salt consumption even further—from 9.7 to 6.5 per day—experienced a decrease in urine albumin excretion (**Swift et al., 2005**) and (**He et al., 2009**). On the other hand, **Rao and Nammi, (2006)** observed that oral administration of alcoholic A. cardamomum seed extracts increased the levels of total protein owing to the activation of many m-RNA molecules' attachment to the ribosome.

**Table (6): Effect of enhancing low protein and sodium diets with cardamom on protein status of rats suffering from chronic renal failure.**

Groups		Parameters	Protein status (g/l)		
			Protein	Albumin	Globulin
Control (-ve)			7.838 <sup>a</sup> ± 0.109	4.203 <sup>a</sup> ± 0.127	3.635 <sup>ab</sup> ± 0.140
Control (+ve) Basal diet containing arginine (AD)			6.410 <sup>g</sup> ± 0.132	3.261 <sup>e</sup> ± 0.057	3.145 <sup>e</sup> ± 0.164
Low sodium basal diet containing arginine			7.335 <sup>c</sup> ± 0.076	4.095 <sup>a</sup> ± 0.163	3.240 <sup>de</sup> ± 0.162
Low protein and sodium diet containing arginine (LPSD)			6.712 <sup>f</sup> ± 0.049	3.310 <sup>e</sup> ± 0.065	3.402 <sup>cd</sup> ± 0.061
AD containing	5% cardamom		7.136 <sup>d</sup> ± 0.084	3.636 <sup>d</sup> ± 0.108	3.500 <sup>bc</sup> ± 0.116
	10% cardamom		7.536 <sup>b</sup> ± 0.069	3.785 <sup>c</sup> ± 0.130	3.751 <sup>a</sup> ± 0.134
LPSD containing	5% cardamom		6.859 <sup>e</sup> ± 0.064	3.588 <sup>d</sup> ± 0.069	3.270 <sup>de</sup> ± 0.094
	10% cardamom		6.866 <sup>e</sup> ± 0.032	3.945 <sup>b</sup> ± 0.195	2.921 <sup>f</sup> ± 0.183

AD: Arginine diet (basal diet containing 2 % W/W L- arginine)

LPSD: low protein sodium diet containing 2 % W/W L- arginine

Mean values in each column with same letters are not significantly different.

#### **Effect of enhancing low protein and sodium diets with cardamom on serum glucose, potassium and sodium of chronic renal failure rats.**

The effect of enhancing low protein and sodium diets with cardamom on serum glucose (mg/dl) and serum potassium and sodium

(mmol/l) of experimental rats with chronic renal failure is presented in Table (7).

#### **Serum glucose:**

From these findings, it could be shown that the control positive group's mean blood glucose values were significantly higher than those of the control negative group when they were fed a base diet containing 2% W/W L arginine (arginine diet AD). Treating rats with an arginine diet (AD) to induce chronic renal failure increased the mean values of serum glucose by about 75.69 % compared to the negative control group. In this respect, **Jia et al., (2015)** reported that, patients and animals with renal impairment frequently exhibit glucose intolerance. **Massry, (2011) and Liao et al., (2012)** suggest that peripheral insulin resistance and/or impaired insulin secretion are suggested to be the root causes of reduced glucose metabolism. Since diabetes and insulin resistance in chronic kidney disease (CKD) are linked, insulin sensitivity may decline as a result of renal disease.

Rats fed either a low sodium diet or a low protein and sodium diet containing L-arginine caused non-significant changes in serum glucose, as compared to the positive control group (AD). According to WHO recommendations, **Suckling et al., (2016)** found a moderate decrease in dietary sodium intake in T2DM patients, which decreased blood pressure and albuminuria without changing the fasting glucose and glycosylated haemoglobin levels.

Treating rats with AD containing 5 and 10% cardamom induced a significant decrease  $p \leq 0.05$  in serum glucose, when compared to the positive control group fed on an arginine-only diet ( $125.673 \pm 3.676$  mg/dl and  $109.667 \pm 5.227$  mg/dl vs.  $141.785 \pm 3.278$  mg/dl), respectively. The mean value of serum glucose decreased gradually with increasing the level of cardamom in the diet. The same pattern was observed when adding 5% and 10% cardamom in a low protein and sodium diet in feeding the experimental rats with chronic renal failure, as shown in this table. The groups treated with an arginine diet with 10% cardamom came in second place in terms of blood glucose, followed by the groups fed a low protein, low sodium diet with 5% and 10% cardamom.

**El-Yamani, (2011)** researched the hypoglycemic impact of cardamom as one of the spices that possess antioxidant components and found that it lowers blood glucose levels. Cardamom supplementation enhances glucose metabolism and reduces the development of oxidative stressors in rats fed a high carbohydrate, high-fat diet (**Rahman et al., 2017**). The results of this study are also confirmed by earlier studies, which showed that cardamom reduced insulin resistance, hyperglycemia,



and glucose intolerance in rats (Azimi *et al.*, 2014) and (Nitasha *et al.*, 2015). Cardamom's antioxidant, anti-inflammatory, and hypolipidemic properties may all help with diabetes (Aghasi *et al.*, 2018).

#### Serum potassium and sodium:

Data in this table showed that, the mean value of serum potassium in the positive control group which was fed on an arginine diet (AD) increased significantly  $p \leq 0.05$ , while the mean value of serum sodium decreased significantly  $p \leq 0.05$ , as compared to the negative control group fed on basal diet. Feeding rats on an arginine diet increased the mean value of serum potassium by about 84.19% and decreased the mean value of serum sodium by about 20.61% than that of the negative control group fed on the basal diet. According to Singh *et al.*, (2017), renal diseases result in elevated potassium K and reduced sodium Na due to poor glomerular filtration rate and passive back diffusion through damaged tubular cells. Low blood sodium levels and high serum potassium levels in renal illness are indicative of chronic renal failure (CRF). Aldosterone and the renin-angiotensin system, glomerular filtration, and reduced reabsorption are to blame for this. Furthermore, animals fed an L-arginine diet to cause chronic renal failure had higher mean potassium and lower mean salt levels in their serum compared to healthy rats on a baseline diet, according to Fakher El Deen, (2022).

**Table (7): Effect of enhancing low protein and sodium diets with cardamom on serum glucose, potassium and sodium of chronic renal failure rats.**

Parameters		Glucose mg/dl	Potassium	Sodium
			mmol/l	
Control (-ve)		80.703 <sup>e</sup> ± 2.426	3.263 <sup>f</sup> ± 0.089	145.366 <sup>a</sup> ± 1.598
Control (+ve) Basal diet containing arginine (AD)		141.785 <sup>a</sup> ± 3.278	6.010 <sup>a</sup> ± 0.151	115.410 <sup>g</sup> ± 1.136
Low sodium basal diet containing arginine		138.273 <sup>a</sup> ± 3.545	5.416 <sup>b</sup> ± 0.230	122.840 <sup>e</sup> ± 2.834
Low protein and sodium diet containing arginine (LPSD)		141.000 <sup>a</sup> ± 4.018	4.866 <sup>c d</sup> ± 0.239	127.240 <sup>d</sup> ± 1.058
AD contain	5% cardamom	125.673 <sup>b</sup> ± 3.676	5.077 <sup>c</sup> ± 0.223	120.340 <sup>f</sup> ± 1.240
	10% cardamom	109.667 <sup>c</sup> ± 5.227	4.721 <sup>d</sup> ± 0.199	123.840 <sup>e</sup> ± 2.440
LPSD contain	5% cardamom	112.112 <sup>c</sup> ± 4.026	4.706 <sup>d</sup> ± 0.160	130.410 <sup>c</sup> ± 1.506
	10% cardamom	100.717 <sup>d</sup> ± 3.870	4.099 <sup>e</sup> ± 0.100	136.240 <sup>b</sup> ± 1.597

AD: Arginine diet (basal diet containing 2 % W/W L- arginine)

LPSD: low protein sodium diet containing 2 % W/W L- arginine

*Mean values in each column with same letters are not significantly different.*

Comparing the treated rats to the positive control group, low sodium diets and low protein and sodium diets with L-arginine caused a substantial drop in the mean values of blood potassium and a rise in the mean values of serum sodium. As opposed to the positive control group and the group treated with a low sodium diet alone, rats fed with a low protein and high sodium diet had higher mean blood sodium values and reduced mean serum potassium values, both of which were statistically significant. In comparison to the positive control group, adding cardamom (5% and 10%) to arginine diet AD or low protein and sodium diets considerably lowered the mean value of blood potassium and significantly raised the mean value of serum sodium ( $p < 0.05$ ). In contrast, giving rats a low-protein, high-sodium meal that contained 5% and 10% cardamom resulted in a fall in blood potassium and an increase in sodium compared to other treatment groups.

In this regard, **Locatelli and Del Vecchio, (2014)** revealed that dietary sodium restriction is another component of nutritional treatment for CKD since it improves control of salt and water retention, blood pressure regulation, and proteinuria decrease. According to **Arjan et al., (2013)**, sodium restriction increases long-term cardiovascular and renal protection even without improving blood pressure control, amplifying the effectiveness of the rennin-angiotensin-aldosterone system (RAAS)-blockade.

According to **Adams et al., (1994)** an increase in dietary protein consumption caused a significant rise in proteinuria, renal morphologic damage, and glomerular filtration rate (GFR). Patients with chronic renal failure, however, are unable to react appropriately to changes in salt consumption. the amount of sodium excreted daily by CRF patients is fixed (60–100 mmol), and even if dietary sodium intake is controlled, this amount will still be eliminated (**Morikawa, 2002**).

Green cardamom can serve as a substantial source of natural antioxidants, according to research by **Bhatti et al., (2010)**. On the other hand, **Kuemmerle et al., (1999)** found that antioxidant therapy increased glomerular filtration rate and renal functioning while significantly reducing proteinuria.

## **Conclusion**

In conclusion, based on the findings of the current study, enhancing low protein and sodium diets containing cardamom are very important to improve the adverse effects that result from chronic kidney failure in experimental rats. All of these effects could be attributed to the

high antioxidant activities as the result of high levels of phenolic compounds.

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#### المستخلص:

الهدف من هذه الدراسة هو بحث تأثير تعزيز النظم الغذائية منخفضة البروتين والصوديوم بالحبهان على فئران التجارب المصابة بالفشل الكلوي المزمن. استخدم في هذه الدراسة ٤٨ فأراً من فئران الالبينو اوزانهم (١٩٠ ± ١٠ جم)، تم تغذية هذه الفئران علي غذاء اساسي لمدة أسبوع للتأقلم علي الوجبات الجافة، تم بعد ذلك تقسيم هذه الفئران الي مجموعتين رئيسيتين، المجموعة الرئيسية الأولى (عددها ٦ فئران) تم تغذيتها علي غذاء أساسي طوال فترة التجربة واستخدمت كمجموعة ضابطة سلبية، في حين تم تغذية المجموعة الرئيسية الثانية (عددها ٤٢ فأراً) لمدة اربعة أسابيع علي غذاء اساسي يحتوى علي ٢٪ وزن/ وزن ارجينين لإحداث الفشل الكلوي المزمن، تم بعد ذلك تقسيم فئران المجموعة الرئيسية الثانية الي سبعة مجموعات فرعية (٦ فئران لكل مجموعة) علي النحو التالي: المجموعة الفرعية الاولى: تم تغذيتها علي وجبة الارجينين وأستخدمت هذه المجموعة كمجموعة ضابطة مصابة. المجموعة الفرعية الثانية: تم تغذيتها علي غذاء منخفض الصوديوم ". المجموعة الفرعية الثالثة: تم تغذيتها علي غذاء منخفض البروتين والصوديوم . المجموعات الفرعية الرابعة والخامسة: تم تغذيتهم علي وجبات الارجينين المحتوية علي ٥٪ و ١٠٪ حبهان ، علي التوالي. المجموعات الفرعية السادسة والسابعة: تم تغذيتهم علي غذاء منخفض البروتين والصوديوم يحتوى علي ١٠٪ و ١٠٪ حبهان بالاضافة الي الارجينين، علي التوالي. خلال فترة التجربة تم وزن الفئران اسبوعيا، وتم حساب المتناول من الغذاء يوميا. في نهاية فترة التجربة (٤ اسابيع)، تم ذبح الفئران وتم تجميع

عينات الدم من كل فأر وتم فصل مصل الدم (السيرم) لتقدير وظائف الكلي، صورة دهون الدم، وانزيمات الكبد، وحالة البروتين، ومستوى الجلوكوز، والبوتاسيوم والصوديوم. نتائج هذه الدراسة اشارت الي أن مستويات تركيز حامض اليوريك و نيتروجين اليوريا و الكرياتينين و الكولسترول والجلسريدات الثلاثية وكولسترول الليبوبروتينات منخفضة الكثافة و كولسترول الليبوبروتينات منخفضة الكثافة جدا ومستويات انزيمات الكبد AST, ALT and ALP و الجلوكوز و البوتاسيوم ازدادت معنويا، علي العكس من ذلك حدث انخفاض معنويا في مستويات كولسترول الليبوبروتينات عالية الكثافة و البروتين والاليومين والجلوبيولين والصوديوم هذا بالاضافة الي المتناول من الطعام والنسبة المئوية للزيادة في الوزن وذلك في المجموعة المعاملة بالارجينين (المجموعة الضابطة المصابة)، مقارنة بالمجموعة الضابطة الغير مصابة. معاملة المجموعات المصابة بالفشل الكلوي المزمن بوجبات منخفضة البروتين والصوديوم والمحتوية علي ٥٪ و ١٠٪ حبهان احدثت تحسنا في كل التقديرات السابقة وخاصة عند استخدام الوجبة منخفضة البروتين والصوديوم المحتوية علي ١٠٪ حبهان. من هذه النتائج يمكن الاستنتاج أن الأنظمة الغذائية منخفضة البروتين والصوديوم المحتوية على الهيل مهمة جدًا لتحسين الآثار الضارة الناتجة عن الفشل الكلوي المزمن.

**الكلمات المفتاحية:** نظام غذائي منخفض البروتين ، نظام غذائي منخفض الصوديوم ، حبهان ، فئران ، فشل كلوي مزمن