

The Therapeutic Effect of Arabic Gum, Purslane and Cress Seeds on Rat Infected with Elevated Uric Acid Levels in the Blood

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Abstract

This study evaluated the therapeutic effect of Arabic gum, purslane and cress seeds powder on rat suffered from hyperuricemia. The biological evaluation, kidney, liver function, oxidative stress and lipid peroxide levels against potassium oxonate were examined. First main group six rats were received basal diet for thirty seven days. Second main group thirty rats received diet with potassium oxonate to elevate uric acid, then diet supplemented with of Arabic gum, purslane and cress seeds powder of each one and their mixture for successive thirty days. Data confirmed that improved role of these plants on kidney, liver function, antioxidants and electrolytes status of animals.

Key Words: hyperuricemia, kidney function, liver enzymes, glutathione peroxidase, electrolytes.

1. Introduction

Hyperuricemia is often the first clinical manifestation of gout and is associated with renal disease. Recently, serum uric acid was found to be an independent risk factor for development of renal insufficiency in a study of 6403 subjects [1]. Hyperuricemic rats, induced with oxonic acid, an inhibitor of uric acid metabolism, and uric acid, also showed impaired renal functions such as concentrating ability, sodium, calcium and phosphate reabsorption, and glomerular filtration [2]. Gum Arabic (GA), a water-soluble dietary fiber rich in Ca(2+), Mg(2+) and K(+), is used in Middle Eastern countries for the treatment of patients with chronic kidney disease. Recent animal experiments shed some light into mechanisms involved in the therapeutic action of GA. According to experiments in healthy mice, GA treatment increases creatinine clearance, enhances renal excretion of antidiuretic hormone ADH, Mg(2+) and Ca(2+), decreases plasma phosphate concentration as well as urinary excretion of phosphate and Na(+). The effects of GA treatment on plasma phosphate concentration, blood pressure and proteinuria may prove beneficial in chronic renal failure and diabetic nephropathy [3]. *Portulaca oleracea* (*Portulacaceae* family), also referred to the common purslane, is listed in the World Health Organization as one of the most used medicinal plants and it has been given the term ‘Global Panacea’. The purslane contains many compounds, including alkaloids, omega-3 fatty acids, vitamins (mainly vitamin A, vitamin C,

THE THERAPEUTIC EFFECT OF ARABIC GUM, PURSLANE AND CRESS SEEDS

and some vitamin B and carotenoids), as well as dietary minerals, such as magnesium, calcium, potassium and iron. It is also rich in coumarins, flavonoids, polysaccharide, cardiac glycosides, and anthraquinone glycosides [4]. The efficiency of using either flax/ pumpkin or purslane/pumpkin seed mixture (components of ω -3 and ω -6) on hyperlipidemia, kidney function and as immunomodulators in rats fed high cholesterol diets were detected [5]. Garden Cress is being cultivated as culinary vegetable in North America, Europe, and all over Asia including India, and in Egypt, Sudan and Saudi Arabia [6]. The edible whole seed is known to have health promoting properties hence; it was assumed that these seeds can serve as raw material for functional foods [7]. Diet fortified at 5% and 10% cress seeds powder helped to improve blood lipid levels as well as reducing hazards on kidney and liver function compared with positive control groups (injected with Cisplatin) which were considered as a major risk factor for renal failure disease. Histopathological kidney observation proved that the last groups “curative & protective groups” fed on basal diet containing cress seeds powder at 10% showed proximal tubules suffering from mild individual cell necrosis and minimal interstitial inflammation [8].

2. Material and methods

2.1 Materials

The present study was carried by using thirty six male white albino rats of an average body weight 150 ± 10 g of (*Sprague Dawley Strain*). They were obtained from the laboratory animal house of faculty of science, Tanta University. Animals were acclimatized to laboratory condition before being used. Rats were fed on basal diet (casein – basal diet) was composed of 12 g of casein (85 % protein); corn oil (10% fat); minerals mixture (4 % minerals); vitamins mixture (1% vitamins); cellulose (4% fiber); and corn starch (71 % starch), and water supply was given *ad-libitum* and checked daily. Composition of mineral mixture according to Hegsted *et al.*, [9]. Composition of vitamin mixture presented as (g/kg) according to Campbell [10]. Potassium oxonate (oxonic acid potassium salt) and uric acid has been used as toxic chemical for kidney injury. It was obtained from Sigma Company for Pharmaceutical and Chemical Industries.

2.2 Methods

2.2.1 Experimental design

Animals were classified into two main groups (6 rats per group). Gr.I: Served as control group, where animals were received basal diet for successive forty days. Gr. II: Thirty rats were received oxonic acid potassium salt 5% and uric acid 2.5% in their diet for successive seven days as an inhibitor of uricase (hyperuricemia rats) according to Yasushi *et al.*, [11]. Subgroup (1): was left as positive control and fed on basal diet only. Subgroup (2):

THE THERAPEUTIC EFFECT OF ARABIC GUM, PURSLANE AND CRESS SEEDS

was supplemented diet with powder 50 g Arabic gum/kg diet. Subgroup (3): was supplemented diet with powder 50 g purslane seeds/kg diet. Subgroup (4): was supplemented diet with powder 50 g cress seeds/kg diet. Subgroup (5): was supplemented diet with powder 60 g mixed plants/kg diet 20 g for each one.

2.2.3 Biological Evaluation

Feed intake, body weight gain (BWG%), feed efficiency ratio (FER) and organs weight relative to body weight % were calculated according to Chapman *et al.*, [12]. During the experimental period, the body weight was recorded every week. Clear separated serum was subjected to the following biochemical analysis. Liver, kidney and heart were removed from each rat, carefully washed with saline solution, dried with filter paper and weighted according to the method described by Drury and Wallington [13].

2.4 Biochemical Analysis

At the end of the experimental period, all rats were sacrificed after fasting 12 hrs. Serum were separated from collected blood samples by centrifugation and used freshly for determination of serum uric acid by Fossati [14], serum urea was measured according to Patton and Crouch [15], serum creatinine was determined according to the method described by Kroll *et al.*[16], aspartate aminotransferase (AST), alanine aminotransferase (ALT) activities were determined according to Reitman and Frankel [17]. Glutathione peroxidase (GSH-Px) was measured by HPLC according to Ellman [18], lipid peroxidation products as nitric oxide (NO) were assayed according to the method of Montgomery and Dymock [19]. Sodium and potassium were assayed according to Henry *et al.*, [20].

2.5 Statistical analysis

Data are presented in tables as means \pm standard deviation (S.D.). Values were statistically analyzed by one-way analysis of variance (ANOVA) according to Armitage and Berry [21] by using SPSS 20 software package. The P values <0.05 were considered significant.

4. Results & Discussion

4.1 Results

4.1.1 Biological evaluation

Data in table 1 showed therapeutic effect of Arabic gum, purslane and cress seeds and their mixture on, body weight gain (BWG %), feed efficiency ratio (FER) of rats suffered from hyperuricemia. Feed intake recorded significant decrease of daily intake in positive group as compared to normal rats group (10.52 ± 0.1 and 6.43 ± 0.2 g/day, respectively). All treated plants showed significant increases ($p \leq 0.05$) as compared to positive group

THE THERAPEUTIC EFFECT OF ARABIC GUM, PURSLANE AND CRESS SEEDS

(9.11±0.4, 9.12±0.2, 9.15±0.3 and 9.17±0.1 g/day, respectively). Body weight gain % illustrated high significant decrease of positive group as compared to normal group (-30.65±0.4 and 25.88±0.3%, respectively). All supplemented diet group showed high significant increase as compared to positive group (18.52±0.5, 18.56±0.8, 18.67±0.8 and 18.99±0.8%, respectively). Feed efficiency ratio (FER) demonstrated high significant decrease in positive group as compared to normal rats (-0.046±0.2 and 0.024±0.4, respectively). All plants showed high significant increase as compared to positive group (0.105±0.3, 0.106±0.6, 0.107±0.6 and 0.109±0.6, respectively). From these results mixture plants group recoded the best values of biological evaluation compared to positive group.

Table 1. Therapeutic effect of Arabic gum, purslane and cress seeds and their mixture on feed intake, body weight gain (BWG %) and feed efficiency ratio (FER) of hyperuricemic rats

Groups	Feed intake (g/day)	BWG%	FER
normal group	10.52±0.1 ^a	25.88±0.3 ^a	0.024±0.4 ^b
positive group	6.43±0.2 ^c	-30.65±0.4 ^c	-0.046±0.2 ^a
Arabic gum 5%	9.15±0.3 ^b	18.67±0.8 ^b	0.107±0.6 ^c
Purslane seeds 5%	9.12±0.2 ^b	18.56±0.8 ^b	0.106±0.6 ^c
Cress seeds 5%	9.17±0.1 ^b	18.99±0.8 ^b	0.109±0.6 ^c
Mixture plants 10%	9.11±0.4 ^b	18.52±0.5 ^b	0.105±0.3 ^c

Mean± SD values, means in the column with different letters are significantly different ($p \leq 0.05$).

Table 2 showed relative organs weight % of treated and hyperuricemic rats. Kidneys weight % recorded high significant increases ($p \leq 0.05$) of positive group as compared to normal rats (0.57±0.10 and 0.44 ±0.23, respectively). Treated groups showed significant decrease of kidneys weight nearly normal rat's data. Liver weight % showed high significant decrease in positive group as compared to normal group (1.40±1.10 and 2.49 ±0.95, respectively). Rats received supplemented diet recoded significant increase in mixture plants and purslane seeds followed by Arabic gum and cress seeds (2.06±0.34, 2.09±0.16, 2.28±0.14 and 2.36±0.23, respectively).

Table 2. Therapeutic effect of Arabic gum, purslane and cress seeds and their mixture on relative organs weight % of hyperuricemic rats

Groups	Kidney	Liver
normal group	0.44 ±0.23 ^b	2.49 ±0.95 ^a
positive group	0.57±0.10 ^a	1.40±1.10 ^d
Arabic gum 5%	0.48±0.04 ^b	2.28±0.14 ^c
Purslane seeds 5%	0.47±0.07 ^b	2.09±0.16 ^b
Cress seeds 5%	0.49±0.06 ^b	2.36±0.23 ^c
Mixture plants 10%	0.46±0.02 ^b	2.06±0.34 ^b

Mean± SD values, means in the column with different letters are significantly different ($p \leq 0.05$).

4.1.2 Biochemical analysis:

a. Kidney function

The results in table 3 explained kidney function of hyperuricemic rats and supplemented diet with Arabic gum, purslane seeds, cress seeds and their mixture. Uric acid, urea and creatinine results showed extra highly significant increase ($p \leq 0.05$) in positive group (5.14 ± 0.87 , 62.78 ± 3.85 and 0.93 ± 0.25 mg/dL) as compared to normal rats group (2.17 ± 0.42 , 27.65 ± 2.28 and 0.51 ± 0.14 mg/dL). All treated plants recorded significant decrease of serum uric acid, urea and creatinine especially in mixture group as compared to positive group.

Table 3. Therapeutic effect of Arabic gum, purslane and cress seeds and their mixture on kidney function of hyperuricemic rats

Groups	Uric acid mg/dL	Urea mg/dL	Creatinine mg/dL
normal group	2.17 ± 0.42^c	27.65 ± 2.28^c	0.51 ± 0.14^c
positive group	5.14 ± 0.87^a	62.78 ± 3.85^a	0.93 ± 0.25^a
Arabic gum 5%	3.72 ± 0.27^b	31.79 ± 3.43^d	0.62 ± 0.09^b
Purslane seeds 5%	3.38 ± 0.33^b	33.99 ± 2.03^d	0.58 ± 0.15^b
Cress seeds 5%	3.82 ± 0.35^b	36.50 ± 3.48^d	0.67 ± 0.24^b
Mixture plants 10%	3.33 ± 0.23^b	29.25 ± 2.32^{cd}	0.55 ± 0.16^{bc}

Mean± SD values, means in the column with different letters are significantly different ($p \leq 0.05$).

b. liver enzymes

Liver enzymes as aminotransferases ALT and AST in table 4 illustrated significant increases ($p \leq 0.05$) in positive rats group (19.32 ± 1.29 and 25.35 ± 2.72 U/L) as compared to normal rats (14.12 ± 1.05 and 20.49 ± 2.8 U/L). All supplemented diet groups showed significant decreases in ALT and AST enzyme especially mixture group and Arabic gum followed by purslane and cress seeds groups as shown in table 4.

Table 4. Therapeutic effect of Arabic gum, purslane and cress seeds and their mixture on liver enzymes of hyperuricemic rats

Groups	ALT U/L	AST U/L
normal group	14.12 ± 1.05^d	20.49 ± 2.8^d
positive group	19.32 ± 1.29^a	25.35 ± 2.72^a
Arabic gum 5%	15.21 ± 1.16^c	21.46 ± 2.31^c
Purslane seeds 5%	15.96 ± 1.44^b	23.39 ± 2.44^{bc}
Cress seeds 5%	16.29 ± 1.15^b	24.52 ± 2.53^b
Mixture plants 10%	15.13 ± 1.6^c	21.0 ± 1.52^c

Mean± SD values, means in the column with different letters are significantly different ($p \leq 0.05$).

c. Oxidative stress markers (enzymatic antioxidants) and lipid peroxidation parameters

As an indicator to assay oxidative stress markers of rats group, serum glutathione peroxidase (GSH-Px) showed significant decreases ($p \leq 0.05$) in positive group as compared to normal group (17.04 ± 2.47 and 28.09 ± 2.73 ng/ml). Treated plants groups recorded significant increases values as compared to positive group. Lipid peroxidation assay as serum nitric oxide (NO) showed significant increases ($p \leq 0.05$) in positive group compared to normal rats (120.69 ± 5.89 and 70.03 ± 4.88 mmol/L). Supplemented rats group recorded significant decreases values as compared to positive group, the best results found in mixture group and Arabic gum followed by purslane and cress seeds groups as shown in table 5.

Table 5. Therapeutic effect of Arabic gum, purslane and cress seeds and their mixture on Glutathione peroxidase (GSH-Px) and nitric oxide (NO) of hyperuricemic rats

<i>Groups</i>	<i>GSH-Px ng/ml</i>	<i>NO (mmol/L)</i>
normal group	28.09±2.73^a	70.03±4.88^d
positive group	17.04±2.47^c	120.69±5.89^a
Arabic gum 5%	22.53±3.43^b	94.37±3.92^c
Purslane seeds 5%	24.35±1.45^b	99.65±3.19^b
Cress seeds 5%	25.03±3.90^b	100.42±3.29^b
Mixture plants 10%	21.99±3.01^b	92.11±4.07^c

Mean± SD values, means in the column with different letters are significantly different ($p \leq 0.05$).

d. Electrolytes parameters

Serum electrolytes found in table 6 recorded significant decreases ($p \leq 0.05$) in sodium values of positive group compared to normal rats (115 ± 3.5 and 137 ± 3.1 mEq/L). High significant increases values in treated plant groups compared to positive group were showed in sodium levels. But, potassium level recorded high significant increases values ($p \leq 0.05$) in positive group compared to normal group (6.6 ± 0.3 and 3.8 ± 0.4 mEq/L). All supplemented diet groups showed significant decreases in potassium levels especially mixture group and Arabic gum followed by purslane and cress seeds groups.

THE THERAPEUTIC EFFECT OF ARABIC GUM, PURSLANE AND CRESS SEEDS

Table 6. Therapeutic effect of Arabic gum, purslane and cress seeds and their mixture on serum electrolytes of hyperuricemic rats

Groups	Sodium mEq/L	Potassium mEq/L
normal group	137±3.1 ^d	3.8±0.4 ^d
positive group	115±3.5 ^a	6.6±0.3 ^a
Arabic gum 5%	123±2.3 ^b	4.2±0.3 ^c
Purslane seeds 5%	125±2.4 ^b	5.5±0.1 ^b
Cress seeds 5%	130±3.2 ^c	5.7±0.1 ^b
Mixture plants 10%	120±1.2 ^b	4.0±0.2 ^c

Mean± SD values, means in the column with different letters are significantly different ($p \leq 0.05$).

4.2 Discussion

The present study investigated therapeutic effect of Arabic gum, purslane and cress seeds for rats suffered from hyperuricemia. Uric acid is the insoluble end product of purine metabolism. Approximately two-thirds of body uric acid comes from the breakdown of endogenous purines, with the remainder from dietary purines. It is predominantly excreted through the kidney, and a substantial amount is excreted through the gut. Elevated serum uric acid is one of the major risk factors for gout [22]. Hyperuricemia is a very common condition, being usually caused by an unhealthy lifestyle that is mainly represented by a poor diet exceeding in purine nucleotides, protein, alcohol, and carbohydrates intake [23]. The results showed significant decrement of feed intake, body weight gain % and feed efficiency ratio as agreement with Yasushi *et al.*, [11] who found body weight of hyperuricemic rats was much less than that of control rats. Hyperuricemia may prevent an increase in body weight and low body weight as compared to normal rats may be partially due to the loss of appetite [24]. In this regard treated rats with Arabic gum, purslane and cress seeds modified the appetite hens, improved biological assay and relative organs weight ratio to reach the level of healthy rats. Hyperuricemia may cause uric acid precipitation in joints and tissues, evaluation of renal function by appropriate formulas and non-pharmacological treatment should be taken into consideration in all patients with hyperuricemia [25]. This research might soon lead to a new possible therapeutic approach regarding hyperuricemia, via a direct decrement in uric acid-related clinical events and complications. Today, medicinal herbs are considered as the most important natural and functional foods. Some herbs have the highest levels of antioxidants such as catalase, superoxide dismutase, vitamin E, vitamin C, glutathione, polyphenols, carotenoids, selenium, alpha-linoleic acid, omega fatty acids, and unsaturated fatty acids, etc. In addition, a significant amount of minerals, group B vitamins, essential amino acids, etc. and are found in some of them [26, 27]. Studies have shown that natural antioxidants reduce the risk of chronic diseases and promote health through prevention of oxidative stress [28]. The

THE THERAPEUTIC EFFECT OF ARABIC GUM, PURSLANE AND CRESS SEEDS

kidney functioning capacity was assessed in this study by measuring the levels of uric acid, urea creatinine and electrolytes in the serum of the rats. The abnormal functioning of the organ in relation to these electrolytes was affected. Kidneys remove metabolic wastes such as urea, uric acid, creatinine and ions, so optimum chemical composition of body fluids is maintained. The concentrations of the metabolites increase in blood during renal diseases or renal damage may due to high activities of xanthine oxidase, lipid peroxidation [29].

Arabic gum (AG), a water-soluble dietary fiber rich in Ca^{2+} , Mg^{2+} and K^{+} , is used in Middle Eastern countries for the treatment of patients with chronic kidney disease. Recent animal experiments shed some light into mechanisms involved in the therapeutic action. AG treatment increases creatinine clearance, enhances renal excretion of antidiuretic hormone (ADH), Mg^{2+} and Ca^{2+} , decreases plasma phosphate concentration as well as urinary excretion of phosphate and Na^{+} , decreased expression of intestinal Na^{+} , plasma urea concentration in mice [30]. AG aqueous extract (0.5 g/kg/day) significantly ($P < 0.05$) lowered the serum enzyme activities of ALT, AST, ALP and antioxidant studies showed decreased the activities of hepatic SOD, CAT and GPx [31]. Arabic gum pretreatment significantly reduced the formation of nitric oxide synthesis as measured by serum nitrate. So, AG is effective in protecting mice against acetaminophen-induced hepatotoxicity. This protection may involve the reduction of oxidative stress [32]. Purslane seeds are preventing oxidative stress and chronic inflammation, improvement of fat metabolism. Purslane and cress seeds increase weight gain as they are found to contain high percent of fat as alpha linolenic acid; which could give it nutritional advantages. Confirmed in the previous studies by Dkhill *et al.* [33] showed that purslane administration at 1.5mg/kg purslane aqueous juice for 12 days caused significant decrease in urea and creatinine. Schaefer *et al.* [34] have recommended many medicinal plants used already in traditional medicine, experimental and clinical, and nephroprotective effects among them rich in PUFAs and antioxidant compounds in animals. The antioxidant enzymes such as GPx, GR, SOD, and GST take part in maintaining glutathione homeostasis in tissues. Also, increased levels of GPx, GR, GST, CAT, and SOD were found to correlate with elevated glutathione level and depressed MDA and NO in rats, thus showing the antioxidant activity of purslane [35]. From the previous studies by Mona *et al.*, [36] they published feeding acute renal failure with garden cress seeds powder at 5% & 10% in curative groups and in protective groups improved the body weight gain, feed intake and feed efficiency ratio, blood lipid levels as well as reducing hazards on kidney and liver function compared with positive control groups (injected with Cisplatin) which were considered as a major risk factor for renal failure disease. Histopathological kidney observation showed proximal tubules suffering from mild individual cell necrosis and minimal interstitial inflammation. The present results are in agreement with those Lamiaa *et al.*, [37] who suggests that both flax/pumpkin and purslane/pumpkin seed mixtures had anti-

THE THERAPEUTIC EFFECT OF ARABIC GUM, PURSLANE AND CRESS SEEDS

atherogenic hypolipidemic and immunomodulator effects which were probably mediated by unsaturated fatty acids (including alpha linolenic acid) present in seed mixture. These plants in our study have high nutritional values and oxidative stress properties as biological scavengers of free radicals and could prevent diseases. So as to, they showed therapeutic effects against potassium oxonate against elevated serum uric acid levels and other biochemical disturbances.

5. Conclusions

This study focus on therapeutic improvement of Arabic gum, purslane and cress seeds and their mixture against potassium oxonate induced disturbances in blood serum uric acid levels of rats. These plants illustrated their possible role on moderated high levels of kidney function and other biochemical data.

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THE THERAPEUTIC EFFECT OF ARABIC GUM, PURSLANE AND CRESS SEEDS

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