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Therapeutic Effect Of Methanolic Extract Of Parsely and Celery Leaves in experimentally Hyperuracemic Rats.

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Abstract

Gout is a serious disease affecting men and characterized by abnormal high level of uric acid in the body, resulting in the formation and deposition of urate crystals in the joint and other tissues causing painful inflammation. The present study was conducted to investigate the effect of parsley and celery leaves extract on experimentally oxonated – hyperuracemic rats. For this purpose fifty male albino rats were categorized into five equal groups (N=10/group) as follows: group I (Negative control group), group II (Pot Oxonate Hyperuracemic group), group III (Hyperuracemic rats treated with parsley extract), group IV (Hyperuracemic rats treated with celery extract), group V (Hyperuracemic rats treated with allopurinol). Allopurinol was used as a hypouracemic standard drug. The results revealed that oxonated hyperuracemic rats (group II), characterized by a significant increase in the concentration of uric acid, creatinine, urea, activities of ALT, AST and ALP in serum. In addition to significant changes in the antioxidant damage of hepatic tissue through increased levels of lipid peroxidation (MDA), and decreased in reduced glutathione (GSH) concentration, glutathione peroxidase (GPx) and superoxide dismutase (SOD) activities. On the other hand administration of parsley and celery leaves extracts modulated significant the alterations in most of the previously mentioned parameters into normal ranges. In conclusion, our finding suggests that, the two selected medical plants (parsley and celery leaf extracts) can be considered as a potential source of antioxidants and xanthine oxidase inhibitory agent that might be helpful in the prevention and treatment of gout.

Introduction

Gout is a chronic metabolic disease characterized by increasing the level of uric acid in the blood and the deposition of monosodium urate crystals in joints and other tissues **(Dalbeth and Haskard, 2005 and Corrado et al., 2006)**. Elevated oxidative stress has been reported in gouty patients **(Urano et al., 2002)**. Avoidance of purine-rich foods is important for gout management **(Beneke, 2003)**.

Allopurinol is the only XO inhibitor under the clinical application and has served as a dominant uric acid-lowering agent in the past four decades **(Fels E and Sundy JS 2008)**. However, any severe adverse effects such as hepatitis and allergic reactions limit the clinical use of allopurinol **(Strazzullo P and Puig JG. 2007)** . Therefore, food consumption and especially from natural sources as a botanicals which inhibit xanthine oxidase activity can reduce the formation of uric acid with less frequent side effect are desired.

The two selected medical plants (parsley and celery) are herbs of the Apiaceae family. They are annual or biennial plants Mediterranean countries **(Vovlas, N et al ., 2008 and Vora Sh et al ., 2009)** , the two tested compounds has been reported to be flavonoids rich food **(Nadia A et al ., 2015** and **sipailiene et al ., 2005)** and possesses broad range of medicinal and biological activities including antioxidant **(Wen , T.Q et al ., 2006)** , antimicrobial **(Al-Daraji et al ., 2012 and sipailiene , A et al ., 2005)** , antihepatotoxicity **(Ahmed , B et al ., 2002 and Al-Daraji et al ., 2012)** , anticancer **(pei-wen et al ., 2005)** , hypoglycemic **(Mimica-Dukic , N , et al ., 2007)** and hypolipidemic **(Mansi , K et al ., 2009)**

The present study was designed to evaluate the hypouracemic effect of the selected two herbs materials (parsely and celery leaves methanolic extract) to be used as antigout food stuff or for the development of a safer alternative drug to allopurinol for treatment of gout.

Materials & Methods:

Chemicals

ll chemicals and reagents that used in this study were pure analytical grade and supplied by sigma chemical Co. (USA), biodiagnostic (Egypt).

Preparation of parsley and celery extracts.

Parsely and celery leaves were air dried at room temperature and grind to a fine powder using a blender , the powder plant material (450 gm) for parsely and (363 gm) for celery was extracted separately by erculation with methanol 95% according to method described by **(Emendorfer ,**

2005) , successive addition of methanol to each plant till complete exhausion of the leaves .

A total number of 50 male albino rats, weighing 140-150 grams obtained from the faculty of veterinary medicine, Cairo university were used in this study. The animals were kept under normal laboratory conditions for one week before starting the experiment, and allowed to water and fed on a uniformly basal diet.

The animals were divided into 5 equal groups (10 rats for each). Group I : served as control normal rats , while remaining 40 rats were subjected to hyperuracemia regimen using potassium oxonate as each rats were injected intraperitonialy with potassium oxonate in a dose (250 mg/kg.b.w)

Blood samples and biochemical analysis

Blood samples were collected from each rat in a different group from retinabulbar venous plexus by using fine capillary glass tubes on the 1st , 7th and 14 days of experimental periods. The collected blood sample were centrifuged at 3000 RPM for 10 min to separate serum.

The serum was analyzed for determining the level of uric acid according to the method of (**Fossati P**

Liver homogenate and biochemical assay

At The end of the experimental period, rats were decapitated. The liver was quickly excised and washed with cold saline, Each liver sample was divided into four portions. The first portion was homogenized in cold 1.15% cycle to make 10% (w/v) homogenate and centrifuged at 1000 RPM to remove nuclei and cell debris, then allocated for the measurement of malondaildehyde (MDA) according to the method of (**Albro, p.w., et al., 1988).** The second liver portion was homogenized in 5% Sulphosalicylic acid to make 10% homogenate and immediately used for the determination of reduced glutathione (GSH)

Statistical analysis:

Statistical analysis (**SPSS statics 17.0., 2008**) statistical analysis for collecting data through period SPSS (**statistical package of social science**) data gathered from the study of the survey, mean and standard error were carried out

Animals and experimental design:

once daily for consecutive 14 days , 1 hour before oral administration of test compounds (**yonetani et al ., 1987**) , group II : hyperuracemic rats (positive control) , group III : hyperuracemic rats treated daily for 14 days with parsely leave extract in adose (5 gm/kg b.w) an 1 hour later of inducing hyperuracemia , group IV: hyperuracemic rats treated once daily for consecutive 14 day with celery leave extract in adose (5 gm /kg b.w) and group V hyperuracemic rats treated once daily for 14 days with allopurinol in a dose (5 mg/kg b.w) an hour later of inducing hyperuracemia.

el al 1980), creatinine (**Spencer K and Price CP, 1980),** urea (**Shephard MD and Mezzachi RD, 1983).** Alanine amino transferase (ALT) and aspartate aminotransferase (AST) activities in serum were determined according to (**Reitman, S., and Frankel, S., (1975).** Serum alkaline phosphatase (ALP) activity was measured according to the method of (**Befield A and Goldberg D.M 1971**)

content according to (**Ellman, 1959**). The third portion was homogenized in 5 Mm phosphate buffer 7.4 to make 10 % (w/v) homogenate and centrifuged at 1000 RPM to remove nuclei and cell debris. The aliquoted was used for determination of glutathione peroxidase activity (GP-X) according to the method of (**Rotruk, j.t et al., 1973**) .Determination of superoxide dismutase (SOD) was performed according to the method of (**Nandi, A and Chatterjee, I.B. 1988**). The fourth portion was kept in 10 % formalin for the histopathologically examination according to the method of (**Banchroft et al., 1996**) .

and then followed by invariant and multivariate analysis.The analysis of variance and list significant difference tests were performed after designing and arranging the data (**one way ANOVA).**

Results

Table (1): Effects of parsley, celery and allopurinol on Plasma Uric Acid (mg/dl) in normal, hyperuracemic and treated hyperuracemic subgroups of rats.

Day's number	Groups of rats				
	Normal I	Hyperuracemia II	Hyperuracemic + ParsleyIII	Hyperuracemic + Celery iv	Hyperuracemic +Allopurinol V
1st day	4.13 ± 0.59 b (A)	7.84 ± 0.25 a (A)	3.08 ± 0.54 c (B)	2.40 ± 0.40 c (B)	2.81 ± 0.42 c (A)
7th day	3.12 ± 0.20 c (B)	6.28 ± 0.27 a (B)	4.17 ± 0.52 b (A)	4.20 ± 0.31 b (A)	3.06 ± 0.10 c (A)
14th day	1.80 ± 0.18 b (C)	5.95 ± 2.50 a (B)	2.06 ± 0.26 b (C)	2.48 ± 0.26 b (B)	1.47 ± 0.16 b (B)

- Data are expressed as mean ± standard error (SE).
- Different small letters indicate significant variation between different groups at the same day (rows) at $p \leq 0.05$.
- Different capital letters between parentheses indicate significant variation among different days for the same group of rats (columns) at $p \leq 0.05$.

-LSD value at $p \leq 0.05$ =.96

Table (2): Effects of parsley, celery and allopurinol on Creatinine (mg/dl) in normal, hyperuracemic and treated hyperuracemic subgroups of rats.

Day's number	Groups of rats				
	Normal I	Hyperuracemia II	Hyperuracemic + Parsley III	Hyperuracemic + Celery iv	Hyperuracemic +Allopurinol V
1st day	0.55 ± 0.03 bc (B)	0.64 ± 0.01 a (B)	0.51 ± 0.02 c (A)	0.58 ± 0.02 ab (A)	0.53 ± 0.03 bc (A)
7th day	0.59 ± 0.02 b (AB)	0.69 ± 0.03 a(B)	0.54 ± 0.01 b (A)	0.57 ± 0.02 b (A)	0.55 ± 0.03 b (A)
14th day	0.62 ± 0.02 b (A)	0.80 ± 0.11 a (A)	0.57 ± 0.03 bc (A)	0.60 ± 0.03 bc (A)	0.55 ± 0.05 c (A)

- Data are expressed as mean ± standard error (SE).
- Different small letters indicate significant variation between different groups at the same day (rows) at $p \leq 0.05$.
- Different capital letters between parentheses indicate significant variation among different days for the same group of rats (columns) at $p \leq 0.05$.
- LSD value at $p \leq 0.05$ =.06

Table (3): Effects of parsley, celery and allopurinol on Plasma Urea (mg/dl) in normal, hyperuracemic and treated hyperuracemic subgroups of rats.

Day's number	Groups of rats				
	Normal I	Hyperuracemia II	Hyperuracemic + Parsley III	Hyperuracemic + Celery iv	Hyperuracemic +Allopurino V
1st day	52.40 ± 2.72 ab (A)	60.10 ± 4.29 a (A)	43.40 ± 1.80 bc (A)	48.80 ± 3.07 bc (AB)	41.80 ± 2.54 c (A)
7th day	47.10 ± 3.83 bc (A)	58.00 ± 1.91 a (A)	41.70 ± 4.11 c (A)	39.30 ± 3.27 c (B)	48.50 ± 4.26 ab (A)
14th day	52.20 ± 3.52 b (A)	68.60 ± 4.38 a (A)	48.20 ± 1.15 b (A)	50.60 ± 4.45 bc (A)	51.00 ± 5.63 b(A)

- Data are expressed as mean ± standard error (SE).
- Different small letters indicate significant variation between different groups at the same day (rows) at $p \leq 0.05$.
- Different capital letters between parentheses indicate significant variation among different days for the same group of rats (columns) at $p \leq 0.05$.

-LSD value at $p \leq 0.05$ =10.10

Table (4): Effects of parsley, celery and allopurinol on (ALT) Alanine Aminotransferase (U/L)) in normal, hyperuracemic and treated hyperuracemic subgroups of rats.

Day's number	Groups of rats				
	Normal I	Hyperuracemia Ii	Hyperuracemic + Parsley iii	Hyperuracemic + Celery iv	Hyperuracemic +Allopurinol V
1st day	13.70 ± 1.25 bc (A)	17.50 ± 1.02 a (A)	13.50 ± 0.56 bc (AB)	12.10 ± 0.94 c (B)	15.90 ± 1.07 ab (C)
7th day	15.30 ± 1.22 b (A)	17.60 ± 0.70 b (A)	14.90 ± 1.39 b (A)	16.00 ± 0.62 b (A)	24.10 ± 0.95 a (B)
14th day	11.30 ± 0.91 c (B)	15.80 ± 0.49 b (A)	10.90 ± 0.50 c (B)	14.00 ± 0.37 b (AB)	29.00 ± 0.99 a (A)

- Data are expressed as mean ± standard error (SE).
- Different small letters indicate significant variation between different groups at the same day (rows) at $p \leq 0.05$.
- Different capital letters between parentheses indicate significant variation among different days for the same group of rats (columns) at $p \leq 0.05$.

-LSD value at $p \leq 0.05$ =3.75

Table (5): Effects of parsley, celery and allopurinol on plasma Aspartate Aminotransferase (U/L) in normal, hyperuracemic and treated hyperuracemic subgroups of rats.

Day's number	Groups of rats				
	Normal I	Hyperuracemia II	Hyperuracemic + ParsleyIII	Hyperuracemic + Celery iv	Hyperuracemic +AllopurinolV
1st day	52.00 ± 6.16 c (B)	96.33 ± 3.39 a (A)	96.17 ± 5.85 a (A)	82.50 ± 11.70 b (A)	91.67 ± 3.18 a (A)
7th day	53.50 ± 4.06 cd (B)	75.0 ± 6.54 b (B)	56.17 ± 1.17 cd(C)	60.33 ± 2.42 c (B)	86.33 ± 0.33 a (A)
14th day	71.33 ± 4.06 d (A)	90.17 ± 1.85 ab(A)	79.17 ± 4.86 c (B)	81.50 ± 3.16 c (A)	93.0 ± 1.86 a (A)

- Data are expressed as mean ± standard error (SE).
- Different small letters indicate significant variation between different groups at the same day (rows) at $p \leq 0.05$.
- Different capital letters between parentheses indicate significant variation among different days for the same group of rats (columns) at $p \leq 0.05$.

-LSD value at $p \leq 0.05$ =7.84

Table (6): Effects of parsley, celery and allopurinol on (ALP) Alkaline phosphatase activity (IU/L) in normal, hyperuracemic and treated hyperuracemic subgroups of rats.

Day's number	Groups of rats				
	Normal I	Hyperuracemia ii	Hyperuracemic + Parsley iii	Hyperuracemic + Celery iv	Hyperuracemic +Allopurinol V
1st day	64.50 ± 2.73 c (A)	88.17 ± 4.69 a (A)	72.0 ± 1.53 b (A)	74.83 ± 3.66 b (A)	77.50 ± 0.99 b (A)
7th day	34.83 ± 1.28 c (B)	61.50 ± 5.37 a (B)	29.00 ± 1.35 c (B)	33.83 ± 1.58 c (B)	42.17 ± 4.52 b (C)
14th day	33.0 ± 3.06 bc (B)	58.67 ± 2.60 a (B)	35.83 ± 4.73 b (B)	27.83 ± 2.44 c (B)	61.83 ± 7.13 a (B)

- Data are expressed as mean ± standard error (SE).
- Different small letters indicate significant variation between different groups at the same day (rows) at $p \leq 0.05$.
- Different capital letters between parentheses indicate significant variation among different days for the same group of rats (columns) at $p \leq 0.05$.

-LSD value at $p \leq 0.05$ =5.86

Table (7) (MDA) concentration (μM/mg protein), (GSH) concentration (NM/mg), (GPX) concentration (NM/mg), (SOD) concentration (U/g protein) in liver homogenates in normal, hyperuracemic and treated hyperuracemic subgroups of rats.

Groups / Parametrs	Normal I	Hyperuracemia II	Hyperuracemic + Parsley III	Hyperuracemic + Celery iv	Hyperuracemic +Allopurinol V
Mda	0.72 ± 0.13 d	3.19 ± 0.18 a	0.98 ± 0.16 cd	2.49 ± 0.32 ab	1.79 ± 0.19 Bc
Gsh	4.72 ± 0.35 ab	3.52 ± 0.22 b	5.83 ± 0.41 a	5.26 ± 0.41 a	4.93 ± 0.41 Ab
Gpx	129.90 ± 19.0 ab	66.60 ± 7.15 b	218.30 ± 35.4 a	209.40 ± 33.9 a	134.20 ± 11.0 ab
Sod	89.50 ± 16.9 ab	82.90 ± 12.9 ab	136.90 ± 17.3 c	124.10 ± 20.9 ac	57.30 ± 8.19b

- Data are expressed as mean ± standard error (SE).
- Different small letters indicate significant variation between different groups at the same day (rows) at $p \leq 0.05$.the comparison between groups carried out by using one way ANOVA followed by LSD.

Histopathological examination

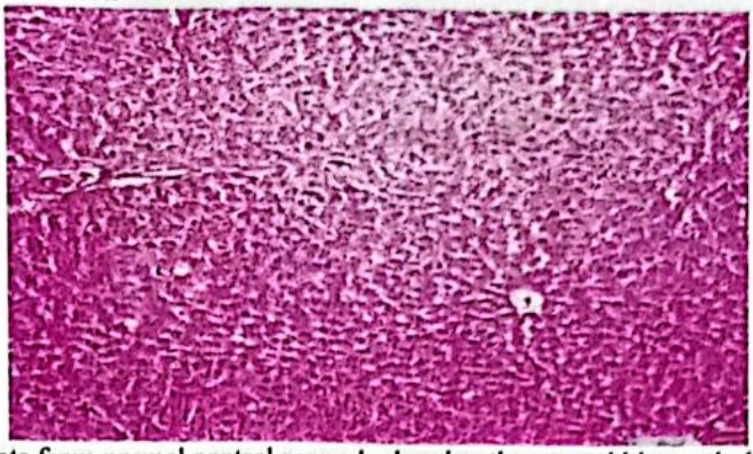

Photo (I) liver of rats from normal control group 1, showing the normal histopathological structure of the hepatic lobule (H and E X 400).

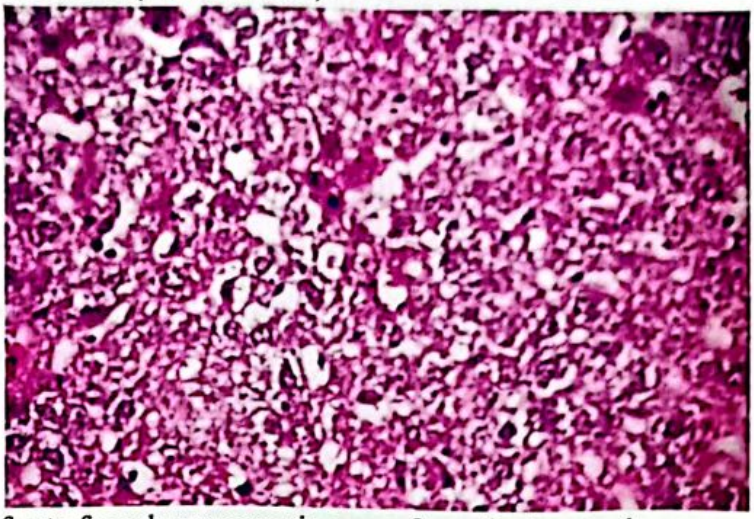

Photo (II) liver of rats from hyperuracemic group 2 received potassium oxonate showing massive, diffuse destruction of hepatic cells. Necrosis is present among hepatic lobule (H& E X 400).

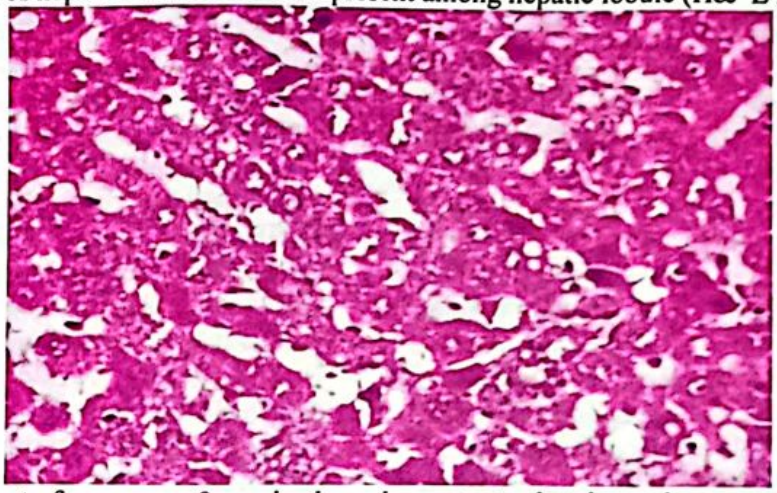

Photo (III) liver of rats from group 3 received parsley extract, showing enlargement of scattered hepatic cells (hepatomegalocytosis) as a trial healthy cells to regenerate to compensate the damage cells (H and E X 400).

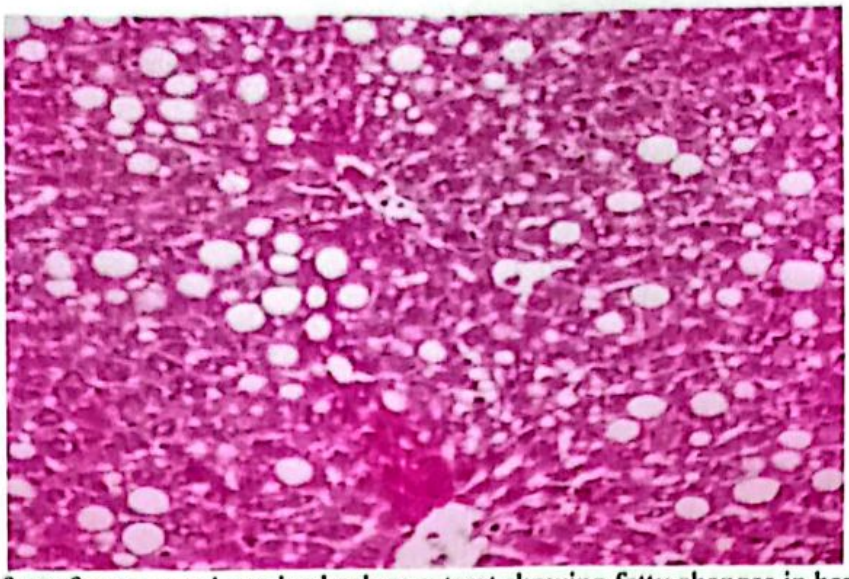

Photo (IV) liver of rats from group 4 received celery extract showing fatty changes in hepatocytes (H & E X 400).

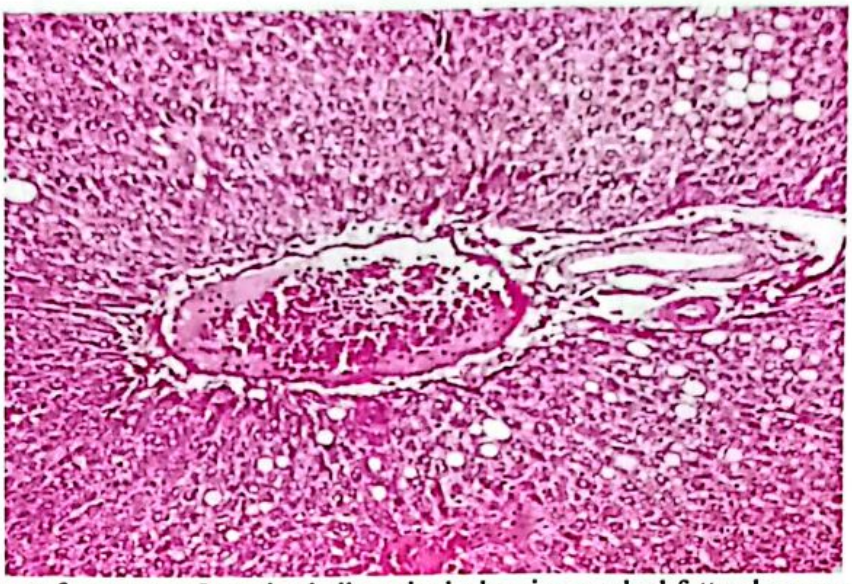

Photo (V) liver of rats from group 5 received allopurinol, showing marked fatty changes with fatty vacuoles in hepatic cells. Slight fibrosis surrounding portal area with congestive of portal vein (H& E 400).

Discussion

Gout is a common disease with a worldwide distribution and continues to be a health problem.It is often associated with elevated serum levels of uric acid. The most common symptoms of gout are painful arthritis, joint inflammation caused by deposition of insoluble crystals of sodium urate (**Chen LX and Schumacher HR 2008**). Allopurinol, the most common xanthine oxidase inhibitors (**Hawkes, T.R et al., 2008**), but has the unwanted side effect such as hypersensitivity problems. Therefore, alternative treatments are required (**Sasiporn Sarawek, 2007**). The leaves of some flavonoids rich plant as parsley (Petroselinum crispum) and celery (Apium graveolen) have been used traditionally as a diuretic and for treatment of rheumatism and jaundice (**Karim, A and M. K. Bhatty (1976) and D. Hoffmann (2010**). The major constituents of the two studied herbs are flavonoids and phenol compounds, which may show xanthine oxidase inhibition and antioxidant activity in our present study.

Effects of hyperuracemia and supportive treatment on kidney function (uric acid, creatine, urea).

Our reported results tables (1,2,3) revealed a highly significant increase in serum levels of uric acid, creatinine and urea as an indicator of kidney function in potassium oxonate –treated hyperuracemic rats (group II) all over the experimental periods in comparison with normal control rats. Treatment of hyper -uracemic rats with parsley, celery and allopurinol (group III, IV,

V) respectively succeeded in restoring the levels of uric acid , creatinine and urea to value nearing the range of normal rats at all points of experimental periods.

These findings are in accordance with the previous studies reported by **(Aml and Alaa 2013, Nabila M. Rashwan., 2012)** as they found administration of parsley extract induced significant decrease in the elevated levels of uric acid, creatinine and urea in the serum when compared with gentamicin – treated rats.**Chuang Wang et al., (2012)** reported that Quercetin (major falvonoids constituents of parsley extract) and allopurinol improve renal dysfunction and hyperuracemia in STZ – treated rats.

In addition, our results were also supported by **(Hala, E.M El-Kewawy et al., 2013 and Noor Sami Aboud et al., 2014)** as they recorded that

Effects of hyperuracemia and supportive treatment on hepatic enzyme activities (ALT, AST ALP).

Our results tables (4,5,6) displayed a significant rise in liver function, enzyme activities (ALT, AST and ALP) in Hyperuracemic rats (group II) after 1th, 7th and 14th days when compared with the normal control group. Treatment of hyperuracemic rats with both parsley and celery extract (group III & IV) respectively succeeded in restoring the levels of these enzyme activities to nearly the normal range. These results agree with those reported by other authors **(Kolarovic, J et al., 2009 and Popovic, M et al., 2006)** as they reported that treatment of rats of cadmium exposure with parsley extract, showed significant decrease in serum AST & ALP activities compared to the positive control group. In

Effects of hyperuracemia and supportive treatment on hepatic malondialdehyde (MDA).

Result in table (7) revealed that a significant rise in hepatic MDA concentration in hyperuracemic rats in comparison to non treated normal. Treatment of hyperuracemic rats with parsley (group III), celery (group IV) and allopurinol (group V) for a 14 day period showed significant decrease in the liver MDA level when compared with hyperuracemic rats (group II), but still higher than the normal control groups as reported in table (7).Our results supported by **(Fatemeh H, et al., 2011)** as they showed that Oral administration of parsley to hyperuricemic rats induced a significant reduction in the elevated levels of MDA as

Effects of hyperuracemia and supportive treatment on hepatic reduced glutathione (GSH)

administration of celery extracts proved to have some ameliorating effect against renal dysfunction as serum uric acid, creatinine and urea levels were corrected in celery treated group of rats compared with positive control group.

In respect to allopurinol as hypouracemic drug. Our result table (1) showed that treatment of hyperuracemic rats with allopurinol (group V), caused a decrease in serum uric acid concentration significantly lower than the hyperuracemic rats (groups II) and the level even reached to the level lower than the normal control value at intervention.These findings are similar to that reported by **(Sirirat R et al., 2007 and Qing-Hua H and Ling-Dong K 2013)** as they reported that allopurinol treatment produced a significant lowering effect in serum uric acid and serum creatinine level in hyperuracemic rats.

addition, these findings were closed related to the previously reported by **(Jabbar A. A et al., 2012)** as they found that treatment of diabetic rats with celery extract and insulin normalized the ALT &AST activities compare with diabetic animal. On the other hand the gained results showed that administration of allopurinol for treatment of hyperuracemic rats (group V) caused a significant elevation in ALT & AST activities at 7^{th} day and 14^{th} day, while the ALP increased significantly at all different time points of the experimental periods when compared with the normal control group and these indicated hepatotoxicity by allopurinol and is confirmed by histopathologically examination (photo V).

compared with hyperuraeemic rats (group II) and a normal control group. These results agreed and similar to that reported by **(Doha A. And Sahar Y 2008)** as they illustrated that administration of celery extract caused significant reduction in liver MDA levels after 6 hours from potassium oxonate injection in rats. The studies which have been done by **(Alshabanah, O.A et al., 2012)**. Comes into agreement with our finding as they reported that oral administration of allopurinol to hyperuracemic rats induced a significant reduction in the elevated levels of liver (MDA).

The obtained result in table (7) revealed that a significant decrease in hepatic GSH concentration in hyperuracemic rats in comparison to non treated normal group. Treatment of hyperuracemic rats with parsley, celery and allopurinol (group III, IV, V) respectively, for a 14 day period, showed increases in the liver GSH concentration higher than the hyperuracemic rats (group II) and normal control (group I). According to **Fejes et al ., (1998)** who demonstrated that because of flavonoids which are the potent constituent in parsely and celery leafs are suggested to scavenge free radical or increase the production of hepatic glutathione (GSH) and glutathione s-transfereas.Our results table (7) showed that treatment of hyperuracemic rats with allopurinol (group V) daily for 14 day , lead to asignificant increase in heptic GSH content compared with hyperuracemic rat (group II) and increased slighty higher than the control group . Our reported results are in accordance with those reported by **(Zafer Sand Suleyman D 2005)** as they stated that the antioxidant allopurinol has beneficial effect on renal GSH levels.

Effects of hyperuracemia and supportive treatment on hepatic glutathione peroxidase (GPx)

Our results in a table (7) showed that highly significant decrease in hepatic GPX concentration in hyperuracemic rats in comparison to non treated normal group. treatment with extract of parsely and celery (group III&IV) respectively showed highly significant increases the liver GPx activity higher than the hyperuracemic (group II) and normal rats after 14 days at the end of experimental period.Treatment of hyperuracemic rats with allopurinol (groupV) for 14 days showed significant increase in GPx activity when compared with hyperuracemic rats (group II) and restoring GPx to its normal range.Our results was in agreement with **(Parul L and Deepak K 2007)** who reported that phytochemical and flavonoids as apotent constituent of parsely and celery extract increased GPx activity which is the first line of defence directly involved in neutralization of ROS and has a protective effect against hepatotoxicity, and also **(Md. Abu Taher S et al ., 2015)** showed that allopurinol treatment restored the antioxidant enzyme catalase and GPx activities in plasma and tissue near normal compared to control rats.

Effects of hyperuracemia and supportive treatment of hepatic superoxide dismutase (SOD) activity.

Results in table (7) demonstrated that non significant decrease in hepatic SOD concentration in hyperuracemic rats in comparison to non treated normal group. Treatment of hyperuracemic rats with extracts of parsley (group III) and celery (group IV) showed significant increase in the liver SOD activity higher than hyperuracemic rats and normal control group. On the other hand, treatment of hyperuracemic rats with allopurinol (group V) decreased the liver SOD activity, but non significantly lower than the hyperuracemic rats (group II) and normal control after the 14 day period. **(Hassan A and Abdel-Wahhab M 2006)** demonstrated that the protective effect of possibly extract might be due to the higher content of flavonoids it has been indicated that treatment with parsely increases the levels of SOD activity in rats. The most accepted explanation of the obtained data is reported by **(Nadia, N et al., 2013)** who reported that oral administration of celery was able to improve the levels of endogenous antioxidants (SOD) in the liver. Our result was also supported by **(Renata C and Allan S 1988)** his study assessed whether xanthine oxidase inhibition with allopurinol affords maximal protection against reperfusion-induced arrhythmias or whether the simultaneous addition of more general free radical scavengers and antioxidants such as superoxide dismutase (SOD) can increase protection beyond that afforded by allopurinol alone.

The histopathological examination of liver tissue confirmed our laboratory findings. Photo (1) the liver sections of rats from control non treatment group, showed the normal histological structure of the hepatic lobule.Photo (2) liver tissue from oxonate–hyperuracemic rats revealed pathological alterations in the form of massive, diffuse destruction of hepatic cells. Necrosis in present among hepatic lobules. Photos (3) the liver sections of treated hyperuracemic rats with parsley (hyperuarcemic rat + parsley extract), showed enlargement of scattered hepatic cells (hepatomegalocytosis) as a trial of healthy cells to regenerate to compensate the damage cells, and this indicated that possibly exhibited a significant protective and curative effect against hepatocyte damage. Photo (4) liver section of treated hyperuracemic rats + celery extracts) revealed a slight fatty change in hepatocytes. Photo (5) liver

section of treated hyperuracemic rats with allopurinol (hyperuracemic rats + allopurinol) showed many pathological changes in the form of marked fatty changes with fatty vacuoles in hepatic cells , slight fibrosis surrounding portal area , dilatation and congestion of portal vein , and thus indicate that allopurinol has serious side effects and this results was in agreement with (Strazzullo P and Puig JG 2007) who recorded that allopurinol has some adverse effect such as hepatitis . In conclusion our results suggest that the protective effect of Parsley and celery leaves extracts could be attributed to the hypouracemic and antioxidative potential of flavonoids , the major components of the plant extracts. such hypouracemic action of two tested medical plant make apossible safer alteration for allopurinol .

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الملخص العربى

التاثير العلاجى لمستخلص أوراق البقدونس والكرفس فى الجرذان المصابة تجريبيا بارتفاع حمض البوليك

المسعيد ثابت عوض ، محمد ورده ، جوزيف لطيف فايق

يعتبر مرض النقرس من الأمراض الخطيره التى تصيب الأنسان ويتصف بأرتفاع مستوى حمض البوليك فى الجسم والذى يؤدى الى تكوين وترسيبات من بلورات اليوريت فى المفاصل واللأنسجه المختلفه بالجسم والتى تسبب التهابات مؤلمة. تهدف هذه الدراسة الى معرفه تاثير المستخلص الكحولى لأوراق نباتات البقدونس والكرفس كمصادر غذاء طبيعيه غنيه بالفلافونيدات و البوليفينولات على الجرذان المصابه تجريبيا بالنقرس بواسطة حقن ماده أوكسانات البوتاسيوم بجرعه (250 ملج /كجم من وزم الجسم) داخل البريتون مره يوميا ولمده أسبوعين – وقد اجرينا الدراسة على عدد خمسون من ذكور الجرذان من سلاله الالبينو والتى قسمت الى خمس مجموعات متساوية (عشرة جرزان لكل مجموعة) - المجموعة الأولى : استخدمت كمجموعه ضابطه وغير مصابة – المجموعة الثانيه : مصابة تجريبيا بارتفاع حمض البوليك – المجموعة الثالثه : مصابة ومعالجه باوراق البقدونس – المجموعة الرابعة مصابة ومعالجه بمستخلص أوراق الكرفس – المجموعة الخامسة مصابة ومعالجه بعقار اللألوبيرنول وقد تمت المعالجه مرة واحده يوميا ولمده أسبوعين . وقد كشفت النتائج على ان حقن الجرزان بماده أوكسانات البوتاسيوم أدى الى حدوث أرتفاع معنوى فى نسبة حمض البوليك فى الدم وزيادة معنوية فى وظائف الكلى (كرياتينين واليوريا) وأيضا أدى الى زيادة معنوية فى نشاط أنزيمات الكبد (ALT, AST, ALP) . اما فى أنسجه الكبد فقد حدثت زيادة معنوية فى مستوى المالون داى الدهيد مع أنخفاض معنوى فى مستوى الجلوتاثيون المختزل ونشاط انزيمات الاكسدة (الجلوتاثيون بيروكسيديز و السوبر أوكسيد ديسميوتيز) – كما أثبتت النتائج أيضا ان العلاج بمستخلص أوراق البقدونس والكرفس أدى الى انخاض معنوى فى الزياده الحاصله فى مستويات حمض البوليك والكيرياتينين واليوريا وفى نشاط أنزيمات الكبد (ALT, AST, ALP) فى مصل الدم – وقد لوحظ أيضا ان العلاج بمستخلص هذه النباتات أدى ايضا الى انخفاض معنوى فى مستوى المالون داى الدهيد فى أنسجه الكبد هذا بالأضافة أنه حدثت زيادة معنوية فى مستوى الجلوتاثيون المختزل ونشاط انزيمات الجلوتاثيون بيروكسيديز و السوبر أكسيد ديسميوتيز – كما لوحظ أيضا تحسن ملحوظ فى أنسجه الكبد عند الفحص الهستوباثولوجى وخاصة فى المجموعة الثالثة المعالجة بمستخلص اوراق البقدونس – نستنتج من هذه الدراسة ان نباتات البقدونس والكرفس لها القدرة على خفض حمض البوليك فى الدم و أعادته الى المستوى الطبيعى فى خلال أسبوعين وكذلك لها تأثير كمضدات للأكسده وبذلك ننصح باستخدام هذه النباتات بكثرة فى الغذاء وبمحاوله استخدام هذه النباتات فى تحضير أدويه للعلاج من النقرس مستقبلا.