التأثير الوقائي للكركم واكليل الجبل على وظيفة الكلى والجهاز المناعي ضد ارتفاع حمض البوليك في الجرذان

إعداد

د. سوزان عبد الرحمن سعد & د. سوزان سامي ابراهيم

كلية الاقتصاد المنزلى – قسم التغذية وعلوم الأطعمة – جامعة الأزهر

suzansaad@azhar.edu.eg

Suzansamiibraheim@azhar.edu.eg

مجلة البحوث في مجالات التربية النوعية

معرف البحث الرقمي DOI: 10.21608/jedu.2020.40694.1056

المجلد السادس العدد 27 . مارس 2020

الترقيم الدولي

P-ISSN: 1687-3424 E- ISSN: 2735-3346

موقع المجلة عبر بنك المعرفة المصري https://jedu.journals.ekb.eg/

موقع المجلة http://jrfse.minia.edu.eg/Hom

العنوان: كلية التربية النوعية . جامعة المنيا . جمهورية مصر العربية

التأثير الوقائي للكركم واكليل الجبل على وظيفة الكلى والجهاز المناعي ضد ارتفاع حمض البوليك في الجرذان

د.سوزان عبد الرحمن سعد & د.سوزان سامي ابراهيم

المستخلص العربي

ارتفاع حمض البوليك في الدم هو عامل الخطر الرئيسي والأساسي للإصابة بالنقرس وقد يؤدي ذلك إلى تطور أمراض مشتركة مختلفة. ولهذا أجريت هذه الدراسة لتقييم التأثير الوقائي لمساحيق الكركم وإكليل الجبل على وظائف الكلى والجهاز المناعي ضد فرط حمض البوليك لدى الفئران. تم استخدام ثلاثين فأرً ذكر ألبينو وزنها 130 ± 20 جرامًا في هذه الدراسة . قسمت إلى ست مجموعات متساوية(5 فئران في كل مجموعة) الاولي كانت المجموعة الضابطة السالبة ، والثانية كانت المجموعة الضابطة الموجبة (+) والتي تغذت على النظام الغذائي الأساسي لمدة أربعة أسابيع تلتها التغذية على نظام غذائي أساسي يحتوي على5, 2%حمض بوليك و 5٪ حمض أوكسونيك لمدة سبعة أيام لإحداث الإصابة بارتفاع حمض البوليك في الدم ، بينما أعطيت الأربع مجموعات الأخرى غذاء مدعم بالكركم (1٪، 2٪) و إكليل الجبل (1٪ ، 2٪) لمدة أربعة أسابيع متبوعة بالتغذية على النظام الغذائي الأساسي محتوي على5, 2% حمض البوليك و5 ٪ حمض الأكسونيك لمدة سبعة أيام (كتجربة وقائية).في نهاية فترة التجربة(35 يوم) تم حساب كلا من المأخوذ الغذائي ، النسبة المئوية لوزن الجسم المكتسب ، معدل كفاءة الغذاء والوزن النسبي للكلية .وتم تقدير الكرياتينين ،اليوريا ، حمض البوليك ، الألبومين ، الجلوبيولين والبروتين الكلي في المصل. كذلك تم تقدير مستويات الإنزيمات المضادة للأكسدة في أنسجة الكلى (Super Oxide Dismutase (SOD) ، (Glutathione Peroxidase (GP_X) ، (Catalase (CAT)، كما تم تقدير الغلوبولين المناعي (IgG، IgM) في المصل و Interleukin -6 (IL6)في نسيج الكلى، وخلصت النتائج التي تم الحصول عليها إلى أن استخدام الكركم وإكليل الجبل أدى إلى تحسن في كل المؤشرات المذكورة أعلاه. أفضل النتائج سجلتها المجموعات التي تناولت جرعات عالية (2٪) من كلا من الكركم وإكليل الجبل وفقًا للنتائج ، يمكن استخدام الكركم و إكليل الجبل لتحسين وظائف الكلى والجهاز المناعي والحماية من فرط حمض البوليك في الفئران.

الكلمات المفتاحية : ارتفاع حمض البوليك – الكركم – اكليل الجبل - الجهاز المناعي – وظائف الكلى

THE PROTECTIVE EFFECT OF CURCUMA AND ROSEMARY ON KIDNEY FUNCTION AND IMMUNE SYSTEM AGAINST HYPERURICEMIA IN RATS

Dr.Suzan A.E. Saad and Dr.Suzan S. Ibraheim

ABSTRACT

Hyperuricemia is the major and primary risk factor of symptomatic gout, the clinical significance of which has been identified as the development of various co morbidities. So that; this study was conducted to evaluate the protective effect of curcuma and rosemary powders on kidney function and immune system against hyperuricemia in rats. Thirty male albino rats weighing 130 ± 20 g used in this study and divided into equal six groups (5 rats each),the first kept as negative control group (v -) control received basal diet throughout the experiment period, while second was the (v +) control group which fed on basal diet for four weeks followed by feeding on basal diet contains 2.5% uric acid and 5% oxonic acid for seven days to induce hyperuricemia, while the four others groups given diets supplemented with curcuma (1% , 2 %) , rosemary (1 %, 2%) for four weeks followed by feeding on basal diet contains 2.5% uric acid and 5% oxonic acid for seven days **(as a protective experiment)** . At the end of the experimental period (35 days), the feed intake (FI), body weight gain % (BWG %) , feed efficiency ratio (FER) and relative kidneys weight were calculated . Serum creatinine, urea , uric acid , albumin, globulin and total protein were determined. Antioxidant enzymes level in kidney tissues Super Oxide Dismutase (SOD), Glutathione Peroxidase (GP_X) and Catalase (CAT) were estimated. Also, serum immunoglobulins (IgG and IgM) and Interleukin -6 (IL6) in kidney tissues were estimated . The obtained results concluded that using curcuma and rosemary improved all above biological and biochemical parameters. The best results found by using high doses (2%) of curcuma and rosemary . According to the results, curcuma and rosemary could be used for improving kidney functions , immune system and protect from hyperuricemia in rats

Key words: Hyperuricemia - curcuma - rosemary- immune system – kidney function

INTRODUCTION

Hyperuricemia is an elevated uric acid level in the blood. The normal upper limit is 6.8mg/dL, and anything over 7 mg/dL is considered saturated, and symptoms can occur .This elevated level is the result of increased production, decreased excretion of uric acid, or a combination of both processes(**Barkas *et al.*, 2018)**. Hyperuricemia, is the condition closely associated with gout due to the deposition of monosodium urate crystals in peripheral joints and soft tissues **(El-Kafoury *et al.*, 2019).** Elevation of serum uric acid is evident throughout all regions of the world where it has been measured but considerable regional variation exists**(Smith** and **March**,**2015**). It is a very common disorder, being caused by an harmful lifestyle that is mainly denoted by diet exceeding in purine nucleotides, protein, alcohol, and carbohydrates intake **(Hemdan** and **Abdulmaguid, 2018).**

Some reports indicated the protective effect of medicinal herbs such as rosemary and turmeric rhizome against oxidative reactions . These substances may catch and neutralize free radicals, preventing spread of oxidation process (**Gharejanloo *et al.*, 2017).**

Curcuma (*Curcuma longa* Linn), which is commonly known as a turmeric, is a perennial herb that belongs to the Zingiberaceae (ginger) family **(Soleimani *et al.*, 2018)**. The pharmacological activity of turmeric has been attributed mainly to curcuminoids consists of curcumin and two related compounds demethoxycurcumin and bisdemethoxycurcumin **(Paramasivam *et al.*, 2009).** Curcuma has been used to treat respiratory problems, liver disorders, anorexia, and rheumatism. It has antioxidant , anti-inflammatory, anti-cancer , anti-microbial , hepato-protective , reno-protective, thromboinhibitory, cardio-protective and hypoglycemic effects which has been confirmed by advanced researches **(Sefidan and Mohajeri, 2013)**. Also it has achieved the potential therapeutic interest to cure immune related, metabolic

diseases and cancer due to a vast number of biological targets and virtually no side effects **(Siviero *et al.*, 2015).**

Rosemary (*Rosmarinus officinalis* L.) is belongs to the family Lamiaceae (Labiatae) .It is an important plant that grows in Egypt and in many countries of the world. It has also been used in ancient medicine to treat common diseases such as cold, flu and anemia (**Ugulu *et al.*, 2009)**. It is a well-known aromatic plant used as spice, flavoring agent in food processing and in different medicinal purposes .It is used as a drug with strong antioxidant properties for eliminating the generated free radicals, reinforce the antioxidant system and prevent oxidative stress. It is composed of dried leaves and flowers constitutes a particularly interesting source of biologically active phytochemicals as it contains a variety of phenolic compounds including carnosol, carnosic acid, rosmanol, 7-methyl-epirosemanol, isorosmanol, rosmadial and caffeic acid. Rosemary and its constituents especially caffeic acid derivatives such as rosmarinic acid have a therapeutic potential in prevention of bronchial asthma, spasmogenic disorders, peptic ulcer, inflammatory diseases, hepatotoxicity, atherosclerosis, ischemic heart disease, cataract and cancer **(Ragab *et al.*, 2020)**

Therefore, this study aimed to investigate the protective effect of curcuma and rosemary powders on hyperuricemia , kidney functions and immune system in male albino rats.

MEATERIALS AND METHODS

Materials

The experimental herbs (curcuma and rosemary) brought from local market “Harraz for herbs, oils and natural extracts”, Cairo, Egypt. Uric acid and oxonic acid were obtained from El-Gomhorya Company for Trading Drugs, Chemicals and Medical Instrumenys, Cairo Egypt.

Animals:

Thirty male albino rats of *Sprague Dawley* strain (130± 20 g) were obtained from the laboratory animal house of Ophthalmic Research Institute, Giza, Egypt.

Experimental Design

Thirty matured male albino rats weighing between 130-150g were kept in individual stainless steel cages under hygienic conditions and fed one week on basal diet for adaptation. Preparation of basal diet according to **Reeves *et al* ., (1993)** then divided into two main groups as follow: First main group (5 rats): negative control (-ve) control: fed on basal diet only throughout the experimental period. Second main group (25 rats): Positive control (+ve) control: fed on basal diet for four weeks then fed on basal diet contains 2.5% uric acid and 5% oxonic acid for one week to induce hyperuricemia according to **Spencer *et al.*, (1976)** which divided into 5 equal groups as follow: group (2) kept as positive control (+ve) . Groups (3 and 4): fed on basal diet supplemented with 1% and 2% curcuma respectively for four weeks then fed on basal diet contains 2.5% uric acid and 5% oxonic acid for one week. Groups (5 and 6): fed on basal diet supplemented with 1% and 2% rosemary respectively for four weeks then fed on basal diet contains 2.5% uric acid and 5% oxonic acid for one week. During the experimental period (five weeks), feed intake and body weights for every rat were recorded twice weekly. At the end of the experiment, the animals were fasted overnight, then the rats were anaesthetized and sacrificed, and blood samples were collected from the hepatic portal vain. Blood samples were taken and centrifuged (3000 r.p.m/15 min.) to obtain the serum.

Biological evaluation

Feed intake (FI), body weight gain% (BWG %) and kidney organs' weight per body weight were calculated according to **Chapman *et al*., (1959).** The feed efficiency ratio (FER) was calculated according to **Hosoya (1980).**

Biochemical analysis:

Serum creatinine, urea and uric acid were determined according to **Murray and Kaplan, (1984); Kaplan, (1984) and Fossati *et al*., (1980)**, respectively. Total protein, albumin and globulin were determined as method described by **Weichselbaum (1946), Bartholomev and Delany (1966) and Coles (1974)** respectively. Antioxidant enzymes levels i.e :Glutathione peroxidase (GPx), Super Oxide Dismutase (SOD), Catalase (CAT), were estimated in kidney tissue according to the methods of **Paglia and Valentine, (1967) ;Nishikimi *et al* ., (1972) and Aebi, (1984)** respectively . Also**,** Immunoglobulins G and M (IgG and IgM) were determined by direct ELISA according to **Manohars and Selvakumaran, (2012)**. Interleukin-6, (IL-6) level in kidney tissue homogenate was estimated by using Rat IL-6 Immunoassay kit from R&D Systems Inc. The United States of America (USA) be of the same mind with **Hibi *et al*.,(1996).**

Statistical analysis

Statistical analysis was carried out using one way analysis of variance (ANOVA) test followed by Duncan test through the program of statistical packages for the social science (SPSS) version 16. Results were expressed as mean± SD. The differences among means at $p \leq 0.05$ are considered significant **(Snedecor and Cochran, 1989).**

RESULTS

Table (1) showed a significant change in feed intake, body weight gain % and feed efficiency ratio in all treated groups compared with (-ve) control. These parameters declined in **(**+ve) control while enhanced in treated groups particularly in high dose groups. The best results recorded by the groups which treated with Rosemary 2% followed by Curcuma 2%.

Table (2) indicated to significant increase in relative kidneys weight in (+ve) control group as compared to (-ve) control group. All treated groups with herbs showed non-significant difference when compared with (-ve) control group. The high levels of curcuma and rosemary recorded the best results.

Table (3) revealed that, significant increase in kidney function parameters; i.e (uric acid , urea and creatinine) in (+ve) control group compared with (-ve) control group. While, these parameters decreased in all treated groups especially at high doses of herbs. The best improvement was recorded by the groups which treated with Rosemary 2% followed by Curcuma 2%.

Table (4) showed significant decrease in serum protein parameters; i.e (total protein, albumin and globulin) in (+ve) control group. While, these parameters increased in all treated groups especially at high doses (2%) of rosemary and curcuma.

Table (5) indicated that ; SOD, GPX and CAT levels reduced in (+ve) control group compare with (-ve) control. However, these levels restored in treated groups, in particular for Rosemary 2% and 1% then Curcuma 2%.

Table (6) revealed that IgG and IgM levels diminished in (+ve) control group. While, Interleukin-6 (IL-6) level was increased in (+ve) control group when compared with (-ve) control. However, the reverse recorded for treated groups, especially for the groups treated with Rosemary 2% and 1% then Curcuma 2%.

Table (1): Effects of curcuma and rosemary powders on feed intake, body weight gain and feed efficiency ratio in hyperuricemic rats (mean±SD)

Parameters / Groups	FI(g)	BWG (%)	FER
(– ve) Control	17.6 ±1.14 [a]	26.03±0.58 [a]	0.062±0.002 [a]
(+ ve) Control	13.2±0.25 [e]	18.26±0.95 [e]	0.042±0.002 [c]
Curcuma 1%	14.56±0.19 [d]	22.50±0.52 [d]	0.05±0.002 [b]
Curcuma 2%	15.46±0.17 [c]	23.23±0.37 [c]	0.053±0.004 [b]
Rosemary 1%	13.92±0.08 [d]	22.38±0.25 [d]	0.050±0.003 [b]
Rosemary 2%	16.64±0.38 [b]	24.82±0.14 [b]	0.061±0.002 [a]

Means in the same column with completely different letters are significantly different at $p \leq 0.05$.

Table (2): Effects of curcuma and rosemary powders on relative kidney weight in hyperuricemic rats (mean±SD)

parameters / Groups	Relative kidney weight (g/100 g. B.Wt.)
(– ve) Control	0.72±0.04 [b]
(+ ve) Control	0.91±0.09 [a]
Curcuma 1%	0.82±0.08 [ab]
Curcuma 2%	0.77±0.11 [b]
Rosemary 1%	0.80±0.06 [ab]
Rosemary 2%	0.78±0.13 [ab]

Means in the same column with completely different letters are significantly different at p≤0.05.

Table (3): Effects of curcuma and rosemary powders on kidney functions in hyperuricemic rats (mean±SD)

Parameters / Groups	Uric Acid(mg/dl)	Urea(mg/dl)	Creatinine (mg/dl)
(– ve) Control	0.62±0.04 [d]	27.2±1.64 [d]	0.60±0.07 [c]
(+ ve) Control	3.4±0.38 [a]	52.6±2.70 [a]	0.98±0.13 [a]
Curcuma 1%	1.98±0.31 [b]	36.4±3.65 [b]	0.72±0.04 [bc]
Curcuma 2%	0.98±0.26 [c]	31.2±3.56 [cd]	0.68±0.08 [c]
Rosemary 1%	1.08±0.16 [c]	32.8±4.44 [bc]	0.82±0.08 [b]
Rosemary 2%	0.66±0.05 [d]	27.6±0.55 [d]	0.66±0.11 [c]

Means in the same column with completely different letters are significantly different at p≤0.05.

Table (4): Effects of curcuma and rosemary powders on serum proteins (T.P, Alb and Glb) in hyperuricemic rats (mean±SD)

Parameters / Groups	T.P mg/ dl	Alb mg/ dl	Glb mg/ dl
(– ve) Control	5.4±0.16 [a]	4.08±0.20 [a]	1.72±0.25 [a]
(+ ve) Control	3.66±0.26 [d]	3.24±0.05 [c]	0.58±0.08 [d]
Curcuma 1%	4.5±0.23 [bc]	3.34±0.11 [c]	0.88±0.16 [c]
Curcuma 2%	4.74±0.18 [b]	3.74±0.05 [b]	1.14±0.17 [bc]
Rosemary 1%	4.28±0.36 [c]	3.44±0.25 [c]	1.02±0.18 [bc]
Rosemary 2%	4.6±0.35 [bc]	3.92±0.11 [ab]	1.16±0.25 [b]

Means in the same column with completely different letters are significantly different at p≤0.05.

Table (5) : Effects of curcuma and rosemary on antioxidant enzymes levels in kidneys tissues of hyperuricemic rats (mean ± SD)

Parameters / Groups	SOD (U/mg)	GPX (ng/mg)	CAT (ng/mg)
(– ve) Control	42.8±5.02 [a]	36.4±2.61 [a]	67±5.24 [a]
(+ ve) Control	23±4.64 [e]	20.8±4.44 [e]	39.2±4.15 [e]
Curcuma 1%	30.8±2.08[c]	26.6±2.51[c]	50.8±5.02[c]
Curcuma 2%	33.5±4.06 [cd]	29.2±2.17 [cd]	54.4±5.86 [cd]
Rosemary 1%	37.6±2.79 [bc]	32±3.94 [bc]	59.2±3.35 [bc]
Rosemary 2%	40.6±1.95 [ab]	35.2±1.79 [ab]	63.8±3.42 [ab]

Means in the same column with completely different letters are significantly different at p≤0.05.

Table (6) : Effects of curcuma and rosemary on IgG , IgM and interleukin-6 (IL-6) of hyperuricemic rats (mean±SD)

Parameters / Groups	IgG (mg/dl)	IgM (mg/dl)	IL-6(pg/ml) kidney
(– ve) Control	754.4±28.25 [a]	51.4±4.28 [a]	231.4±38.49 [e]
(+ ve) Control	527.2±16.65 [d]	22±4.12 [d]	436.2±23.12 [a]
Curcuma 1%	628.2±18.75 [c]	35±4.69 [c]	382±21.00 [b]
Curcuma 2%	676.6±19.76 [b]	36.2±5.76 [c]	335.8±21.98 [c]
Rosemary 1%	691±34.80 [b]	44.2±3.49 [b]	289.4±40.27 [d]
Rosemary 2%	703.6±8.32 [b]	45.8±3.83 [ab]	268.8±27.30 [de]

Means in the same column with completely different letters are significantly different at $p \leq 0.05$.

Discussion

Oxonic acid-induced hyperuricemia has been widely studied in recent years **Kurra *et al.*, (2015).** Oxonic acid inhibiting uricase enzyme causing reduction in uric acid excretion and higher plasma uric acid levels**(El-Kafoury *etal.*,2019).** In the current study, the results showed that hyperuricemia caused reduction in body weight as compared to normal rats, thus may be due to the beating of appetite according to **Hemdan and Abdulmaguid(2018)** who observed significant decrement of feed intake, body weight gain % and feed efficiency ratio while increase in relative kidney weight in hyperuricemic rats . In this regards; treated with curcuma and rosemary adapted the appetite for rats, improved biological evaluation and relative kidneys weight ratio to reach the level of normal rats , it could be due to improve palatability of the trial diet and effect on appetizing promoter according to **Gharejanloo *et al.*, (2017).**

In this study, we used diet supplemented with 2.5% uric acid and 5% oxonic acid (as inhibitor for hepatic unease activity) through seven days according to **Spencer *et al.*, (1976)** to induce hyperuricemia**.** The (+ve) control group which received 2.5% uric acid and 5% oxonic acid recorded an increase in creatinine, urea and uric acid .These results are in agreement with previous results reported by **Kensara (2013).** Currently, researchers have noticed the essential roles of many natural antioxidants (vitamins and phytochemicals) in foods; they can serve as a defensive line against oxidative damage **(Farid *et al.*, 2019).** Administration of rosemary and curcuma at high dose (2 %) caused significantly decrease in creatinine, urea and uric acid. These results agree with **Hassanen *et al.*, (2019)** who reported that hesperidin and ellagic acid are the major phenolic and flavonoid constituents in rosemary powder that lead to a significant decrease in serum creatinine and urea. Also, these results agree with Saidi ***et al.*, (2019)** who indicated that curcuma administration causes a significant reduction in uremia and serum creatinine; additionally, it provides nephronprotective effect against free radicals through motivation of antioxidant enzymes.

The obtained findings, showed significant decrease in serum protein parameters (total protein, albumin and globulin) in (+ve) control group. Low blood protein values in rats with raised uric acid; where uric acid is tightly merged to α1-α2 globulin. The link of the other protein is loose, allowing glomerular uric acid to be filtered as stated by **El-Kewawy and Morsy (2019).** While, these parameters increased in all treated groups especially at high doses of rosemary and curcuma, perhaps it may due to scavenging free radicals as reported by **El Kholy *et al* (2013)**. These results in line with **Refaat *et al.*, (2019)** who demonstrated that the highest increase in protein parameters concentrations were observed at the groups fed on basal diet supplemented with a mixture of rosemary and garlic. These results are in consonance

with **Saidi *et al.*, (2019)** who reported that; there was a potent effect for curcuma in raising serum protein and albumin levels.

The current investigation indicated that SOD, GP_X and CAT levels in kidney' tissue agree with **El-Kewawy and Morsy (2019)** who showed that the hyperuricemic rats had significantly lower SOD, CAT and GP_X values of kidney' tissue that may be due to toxicity caused by cracks in the body . Hyperuricemia increase the production of oxygen free radicals according to **Soliman *et al.*, (2020)**. On the other hand, all previous parameters levels restored in treated groups as compared to (+ve) control, in particular for (Rosemary 2%, 1% and curcuma 2% respectively). Under normal conditions, there is a natural defense system provided by several enzymes such as (SOD), (CAT) and (GP_X). The use of antioxidant rich food have greatly importance since many diseases have been related with oxidative stress according to **Hassanen, (2015)** who demonstrated that rosemary contains characteristic polyphenolic compounds. The most vital function of these compounds can either motivate endogenous antioxidant defense systems or scavenge reactive species. The results of this study corresponding with **Saidi *et al.*, (2019)** who reported that treatment with *Curcuma longa* restored the oxidative stress parameters (GSH, GPx, GST, and CAT) that revealed the potent antioxidants activity of curcuma. These biological effects of turmeric have been attributed to its constituent curcumin that has been widely studied for its antioxidant, anti-inflammatory, antiangiogenic, wound-healing and anti-cancer effects **(Sadeek *et al.*, 2010).**

Also, the present study showed decrease in IgG and IgM levels in (+ve) control group. While, IL-6 level was increased in (+ve) control group. IL-6 is pro-inflammatory factors which is expressed in injury and inflammation sites that

subsequently initiate the release of other pro-inflammatory cytokines and inflammatory mediators. These signs were due to potassium oxonate that caused the hyperuricemia, increased oxidative stress; which has a potential effect on the function of B cells *in vivo* as a result of consequently decrease in IgM and IgG levels. Also, gout takes part in many pathogenic with other inflammatory disorders, like a rapid rising in the produce of pro-inflammatory cytokines, such as IL-6 according to **El-Kewawy and Morsy , (2019)**. However, the reverse recorded for treated groups, especially for (Rosemary 2% and1%) then (Curcuma 2%). These results agreement with **Ghozlan *et al.*, (2019)** who conducted that feeding diet with rosemary significantly increase the serum immunoglobulins (IgG and IgM). Also, **Moore *et al.*, (2016)** summarized the existing *in vitro* and *in vivo* studies concentrating on the anticancer effects of rosemary extract and the rosemary extract polyphenols carnosic acid and rosmarinic acid, and their effects on key signaling molecules.

Also, the obtained results were in agreement with the finding of **Çiftçi (2011)** who demonstrated that curcumin increases IgG and IgM levels in rats due to curcumin which can be considered to prevent inflammation by its direct actions on several pro- inflammatory molecules. Also **Wu *et al.*,(2017)** indicted that glycerol-induced acute kidney injury increased expression of IL-6 which was significantly diminished after curcumin treatment.

Conclusion

In conclusion, the findings of the present study confirmed that curcuma and rosemary powders had hypouricemic effect , improving serum creatinine, urea , uric acid and serum proteins . Also, improve antioxidant enzymes , immunoglobulins(IgG and IgM) and Interleukin – 6 levels in male rats.

References

Aebi, H. (1984): Catalase in vitro.Methods Enzymol, 105: 121-126.

Barkas, F.; Elisaf, M.; Liberopoulos, E.; Kalaitzidis, R. and Liamis, G. (2018) : Uric acid and incident chronic kidney disease in dyslipidemic individuals. Curr Med Res Opin.;34(7):1193-1199.

Bartholomev,R.J. and Delany, A. (1966): Proc Aust. Assoc. Biochemists.1, 214.

Chapman, D.G.; Castilla, R. and Cambell, A.J. (1959): Evaluation of protein in food. In Method for the Documentation of protein Efficiency Ratio. Can. J. Biochem. Physiol., 37; 679-686.

Ciftci, O. (2011): Curcumin prevents toxic effects of 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) on humoral immunity in rats. Food and Agricultural Immunology,22(1):31-38.

Coles, E.H. (1974): Liver Function: In Veterinary Clinical Pathology, 2nd Ed. W.B. Saunders Company. Philadelphia: 202-215.

ELKafoury,B.M.; Ahmed ,M.A.; Hammouda ,G.A.; ElKady , A. H.; Lasheen, N.N. (2019): Possible role of l -carnitine in improvement of metabolic and hepatic changes in hyperuricemic and hyperuricemic—Fructose- supplemented rats. Physiol Rep. 2019;7e14282. https ://doi.org/10.14814/ phy2.14282 .

El-Kewawy, H.E. and Morsy, G.M.(2019): Beneficial role of quinoa and *Nigella sativa* seeds as antihyperuricemia in rats. Bulletin of the National Nutrition Institute of the Arab Republic of Egypt. (53) 63:84.

El Kholy, W.; Serag, H.; zakaria, A. and El Metwaly, A. (2013): The Potency of Some Natural Products on Dimethyl Benz (A)antheracene(DMBA) Induced Hepatotoxicity in Rats. The Egyptian Journal of Hospital Medicine. 53: 1036– 1048.

Farid, H. E.A.; Alnahdi, H.S.; Ayaz, N.O. and Abozid, M.M.(2019): Protective role of rosemary against trichroacetate- induced toxicity in kidney of male rats. Bioscience research, 2019 16(3):2430-2438.

Fossati, P.; Prencipe, L. and Berti, G. A. (1980): New direct colorimetric procedure for uric acid in serum and urine. Clinical Chemistry, 26(2):227-231.

Gharejanloo, M. ; Mehri, M. and Shirmohammad , F.(2017): Effect of Different Levels of Turmeric and Rosemary Essential Oils on Performance and Oxidative Stability of Broiler Meat. Iranian Journal of Applied Animal Science. 7(4) : 655-662.

Ghozlan , S. A.; El-Far,A. H.; Sadek,K.M.; Abourawash, A. A. and AbdelLatif, M.A. (2017): Effect of Rosemary (*Rosmarinus Officinalis*) Dietary Supplementation in Broiler Chickens Concerning immunity, Antioxidant Status, and Performance. , AJVS. 55 (1):152-161.

Hassanen, N.H.M. (2015):Protective Effect of Nutmeg and Rosemary on Oxidative Stress in Hypercholesterolemic Rats. International Journal of Nutrition and Food Sciences. 4(4) : 465-476. doi: 10.11648/j.ijnfs.20150404.18

Hassanen , N. H.M. ; Fahmi , A.; Shams-Eldin , E and Abdur-Rahman, M. (2019) : Protective effect of rosemary (*Rosmarinus officinalis*) against diethylnitrosamine-induced renal injury in rats. Biomarkers, 25(24):1-30

Hemdan, D.I. and Abdulmaguid, N. Y.M. (2018): The Therapeutic Effect of Arabic Gum, Purslane and Cress Seeds on Rat Infected with Elevated Uric Acid Levels in the BloodInternational Information Institute, 21(3): 1249-1260.

Hibi M; Nakajima K and Hirano T (1996): "IL-6cytokinefamilyand signal Transduction: a model of the cytokine system," Journal of Molecular Medicine, 74(1): 1–12 .

Hosoya, N. (1980): Determination of feed efficiency ratio . Cited in Hosoya, N .; Inami , S. and Goto , S., eds. Nutrition Experiments Using Small Animals. Daiichi Shuppan, Tokyo, Japanese, pp:71.

Kaplan, A. (1984): Urea. Clin Chem., 1257- 1260 and 437 and 418.

Kensara, O. A. (2013): Protective effect of vitamin C supplementation on oxonate-induced hyperuricemia and renal injury in rats. International Journal of Nutrition and Metabolism. 5(4): 61-68,

Kurra,V.; Vehmas, T. ; Eräranta, A.; Jokihaara,J.; Pirttiniemi,P.; Ruskoaho,H.; Tokola,H.; Niemelä, O. ; Mustonen,J. and Pörsti ,I.(2015): Effects of oxonic acid-induced hyperuricemia onmesenteric artery tone and cardiac load inexperimental renal insufficiency. BMC Nephrol.; 16: 35. doi: 10.1186/s12882-015-0033-5

Manohars S and Selvakumaran R (2012): Estimation of serum immunoglobulin E (IgE) level in allergic asthma and allergic rhinitis patients before and after treatment. Euro. J. Experiment Biol. 2: 2199-2205.

Moore, j.; Yousef , M. and Tsiani, E.(2016): Protective effect of rosemary (*Rosmarinus officinalis*) against diethylnitrosamine-induced renal injury in rats. Nutrients, 8(731) :1-32.

Murray, R. L. and Kaplan, A. (1984): Creatinine. Clin Chem., 1261-1266 and 418.

Nishikimi, M.; Roa, N.a. and Yogi,K.(1972): Biochem. Bioph. Res. Common, 46:849-854.

Paglia, D.E. and Valentine,W.N.(1967): Studies on quantitative and qualitative characterization of erythrocyte glutathione peroxidase. J. Lab.Clin. Med.,70:158-169.

Paramasivam, M.; Poi, R.; Banerjee, H. and Bandyopadhyay, A. (2009): High performance thin layer chromatographic method for

quantitative determination of curcuminoids in Curcuma longa germplasm. Food Chem. 113:640-644.

Ragab, M. R. ; Abdelhamid, O.M. ; Said, A.M. and Farrag, R. A.A.(2020): protective effect of rosemary on liver cirrhosis induced experimentally in rats. World journal of pharmacy and pharmaceutical sciences,9(1): 413-423.

Reeves, P.G., Nielsen, F.H. and Fahmy, G.C. (1993): Final report of American Institute of Nutrition adhoc writing committee on the reformulation of AIN-76A rodent diet. Journal of Nutrition, 123: 1939-1951.

Refaat ,O.G.p; Rabeh , N.M. and Ezzat , A.A. (2019): Influence of Rosemary and Garlic on some Haematological parameters and Immunological Functions on Cirrhotic Liver Rats . Egypt. J. of Nutrition and Health. 14 (1): 1-16.

Sadeek, E.A. Abd El-Razek, F. H. (2010): The Chemo-Protective Effect of Turmeric, Chili, Cloves and Cardamom on Correcting Iron Overload-Induced Liver Injury, Oxidative Stress and Serum Lipid Profile in Rat Models. Journal of American Science. 6 (10): 702- 712.

Saidi , M.; Aouacheri, O.; Saka,S. ; Tebboub ,I. and Ailane, L. (2019): Nephron-protective effects of curcuma on oxidative damage and oxidative stress in rat under sub-chronic poisoning of chromium. International Journal of Biosciences. 15(1): 241-250.

Sefidan, A. M. and Mohajeri, D. (2013): Preventive Effects of Turmeric (*Curcuma longa linn*) on Renal Ischemia-Reperfusion Injury in Rats. Adv. Biores., 4 (4): 40-46.

Siviero, A.; Gallo, E. and Maggini ,V. (2015): Curcumin, a golden spice with a low bioavailability. J Herb Med. 5:57-70

Smith, E. and March, L.(2015): Global Prevalence of Hyperuricemia: A Systematic Review of Population-Based Epidemiological Studies [abstract]. Arthritis Rheumatol. 67 (suppl 10).

Snedecor, George, W. and Cochran, William, G. (1989): Statistical Methods. Eighth Edition, Iowa State University Press.

Soleimani, V.; Sahebkar, A. and Hosseinzadeh, H. (2018): Turmeric (Curcuma longa) and its major constituent (curcumin) as nontoxic and safe substances: Review. *Phytotherapy Research*, *32*(6), 985–995.

Soliman,M.M.;Nassan,M.;Aldhahrani,A.andMohamed,M.A. (2020): Molecular and histological study on the ameliorative impacts of *Petroselinum Crispum*and *ApiumGraveolens*against experimental hyperuricemia . Scientific Reports . 10:9512.

Spencer,H.W. ; Yarger , W.E. and Robinson, R.R.(1976): Alterations of renal function during dietary-induced hyperuricemia in the rat. Kidney International, Vol. 9 (1976) p. 489—500.

Ugulu, I.; Baslar, S.; Yorek, N. and Dogan, Y. (2009): The investigation and quantitative ethnobotanical evaluation of medicinal plants used around Izmir province. Turkey J Med Plants Res, 3, 345-367.

Weichselbaum, T.F. (1946): An accurate and rapid method for the determination of protein in small amount of blood.serum and *plasma .Am .J .Clin Path, (16):40.*

Wu,J.; Pan, X.; Fu, H.; Zheng,Y.; Dai, Y.; Yin, Y.; Chen, Q.; Hao,Q.; Bao, D. and Hou , D. (2017): Effect of curcumin on glycerol-induced acute kidney injury in rats. SCieNTiFiC Reports . 7: 10114 . 1-11 . DOI:10.1038/s41598-017-10693-4.