EFFECT OF SOME PLANT EXTRACTS ON HYPERURICEMIA IN EXPERIMENTAL ANIMALS

By

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B.Sc. Agric. Sc. (Agric. Biochemistry), Ain Shams University, 2015

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ABSTRACT

Fatma M.Abo EL-Magd:Effect of Some Plant Extract OnHyperuricemia In Experimental Animal.Unpublished M.Sc. Thesis,Department of Agriculture Biochemistry, Faculty of Agriculture, Ain Shams University,2019.

Hyperuricemia (elevated serum levels of uric acid) is a key risk factor for the development of gout, and has been linked to renal dysfunction, cardiovascular diseases, hypertension, diabetes and metabolic syndrome.Hyperuricemia was induced by oxonic acid or adenineinexperimental rats to evaluate the protective and curative effects of alcoholic extracts from fig leaves, parsley shoots and celery seeds.The rats were randomly divided into 12 groups (n = 5) in two different experiments (protective and curative). The protective experiment included six groups, and the first one served as a normal control group. Before induction of hyperuricemia, three groups of rats were given various plant extracts (celery, parsley or fig) by oral administration using a stomach tube at a dose of 250 mg/kg. A positive control group of rats was administerate orally the hypouricemic drug, allopurinol at a dose of 100 mg/kg. A negative control group did not receive any plant extracts or drugs then it was affected with hyperuricemia. The various plant extracts and the drug were adminesterated for the rats every day for 9 days. On the 10^{th} day, all groups except the normal control received a single dose of oxonic acid (250 mg/kg) by intraperitoneal injection to induce hyperuricemia. After two hours of hyperuricemia induction by oxonic acid injection, blood samples were collected from all rat groups. The curative experiment included six groups, and the first one was fed on a basal diet, and served as a normal control group. Other groups were fed on the basal diet containing adenine (0.5%) for 10 days to induce hyperuricemia. Serum uric acid of these rat groups was determined to

confirm the induction of hyperuricemia. One group of hyperuricemic rats did not receive any plant extracts or drugs, and served as a negative control group. Other three groups of hyperuricemic rats were given various plant extracts (celery, parsley and fig) by oral administration using a stomach tube at a dose of 250 mg/kg. One group of hyperuricemic rats was administerated orally the hypouricemic drug, allopurinol at a dose of 100 mg/kg and served as a positive control group. The various plant extracts and the drug were administerated for these groups daily for another 10 days. At the end of experiment period (20 days), blood samples were collected from all rat groups.The protective and curative effects of various plant extracts were monitored through measurement of uric acid and other blood biochemical analyses for the rats as well as assays of xanthine oxidase activity in their liver tissues. In both experiments, the data showed a significant ($P<0.05$) increase in the levels of uric acid, urea, creatinine and potassium, and a significant ($P<0.05$) decrease in the levels of total calcium in serum of hyperuricemic rats (negative control) compared to the normal control.These results indicated that oxonic acid or adenine causedhyperuricemia and renal dysfunction in the negative control group. The protective and curative effects of various plant extracts were established by appearance the levels ofuric acid and other kidney function tests near to their normal values in serum of rats treated with these plant extracts.Concerning the curative experiment, the data revealed a significant ($P<0.05$) increase in the levels ofalanine aminotransferase (ALT), aspartate aminotransferase (AST), total cholesterol, triglycerides and glucose while the data indicated insignificant ($P<0.05$) differences in these analyses in serum of hyperuricemic rats (negative control) compared to the normal control in the protective experiment. These results indicated that adenine caused other adverse effects which are called metabolic syndrome while oxonic acid did not cause these adverse effects owing to short time of its effect. The curative effects of various plant extracts were also established by restoring the levels of liver enzymes, lipids and glucose to their normal

values in serum of rats treated with these plant extracts. Generally, the different plant extracts possessed protective and curative effects against hyperuricemia in variant efficacies compared to allopurinol. These efficacies were in the following order: fig> allopurinol > celery ≈ parsley. Comparatively, the different plant extracts exhibited inhibitory effects on the activity of liver xanthine oxidase enzyme in variant efficacies compared to allopurinol. These efficacies were in the following order: allopurinol > fig> celery ≈ parsley.It can be noticed that fig extract was the most effective treatment against hyperuricemia while allopurinol was the strongest inhibitor against xanthine oxidase activity. This may be due to that fig extract possessed dual action as hypouricemic agent (inhibition of xanthine oxidase which led to decreasing of uric acid synthesis in liver, and inhibition of uric acid reabsorption in kidney which led to increasing of uric acid excretion in urine) while allopurinol possessed only one action as hypouricemic agent (inhibition of xanthine oxidase which led to decreasing of uric acid synthesis in liver). The hypouricemic activity of fig extract may be ascribed to the presence of flavonoids such as morin while thehypouricemic activity of parsley and celery extracts may be ascribed to the presence of flavonoids such as apeginin, luteolin, quercetin, myricetin and kaempferol in variant percentages.

Keywords: Adenine, Allopurinol, Celery, Fig, Hyperuricemia, Oxonic acid, Parsley,Rats, Uric acid, Xanthine oxidase.

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Finally, words are not enough to express how I am grateful to my parents **Mohamed Abo El – Magd** and **Amal Hamdy** , my brother **Ahmed Abo El- Magd and** all my Family who encouraged me to accomplish sucss in my life, especially my husband **Mohamed Reda.**

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LIST OF ABREVIATIONS

AST : Aspartat aminotransferase
ALT : Alanine aminotransferase
ALB : Albumin
H : Hour
HSE : Hibiscus sabdarffia extract
MSU : Mono sodium urate
OX : Oxonic acid
XO : Xanthin oxidase
ROS : Reactive oxygen species
sUr : Serum urate
TC : Total cholesterol
T.G : Triglycrides
TLS : Tumor lysis syndrome
URAT I : Urate –anion transporter
U.A : Uric acid
XDH : Xanthin dehydrogenase

INTRODUCTION 1:

Hyperuricemia is considered the first step for kidney,heart ,liver diseases and increased risk factor with the continued use of drugs which are used as anti-hyperuricemia.This risk may sometimes reached death. Many fact2ors contribute to hyperuricemia, including genitecs, hypertension, hypothyroidism, insulin resistance, renal insufficiency, diet , use of diuretics, obesity, and consumption of alcoholic beverages which is considerd the most important.

Causes of hyperuricemia can be classified into four functional types:

1. increased production of uric acid ,that includes high level of purine in the diet and increasing purine metabolism.
2. decreased excretion of uric acid,refers to kidney disease.
3. competition for excretion between uric acid and other molecules because of some drugs.
4. mixed type including high level of alcohole and/as fructose in diet and starvation**(Nuki and Smikin, 2006)**.

Drugs used for anti hyperuricemia can be classified into three types namely:

1. Drugs reduce serum uric acid by inhibitingxanthin oxidase which transferxanthin and hypoxanthin to uric acid such as "allopurinol-feboxostate".
2. Drugs increaseexectetion of uric acid in urine by block of tubular which reabsorbance of uric acid and back it to blood ,using this drugs lead to increas of uric acid in urine and decrease it in blood.
3. Drugs decrease uric acid in blood by injected uricase which mitabolised of uric acid to allontine .

Since the use of the first type of medication according to studies has a side effect on kidney, liver and symptoms of allergy and

rash and may lead to death but the allopurinol is the most common, cheapest and least side effect .

The second type of medication has adverse effects on the kidney, which causes the stress of the kidney to get rid of uric acid and also lead to the formation of stones at the same time the most expensive and least expensive.

The third type of medication, which is used to metabolize theuric acid itself enzyme has been shown on the patients symptoms of severe sensitivity and is used in cases that deal with chemotherapy,which causes the demolition of cells and the exit of DNA and blood conversion to uric acid.

The fourth type is the pain killers, which have no effect on the reduces level of blood acid, but reduce the pain and inflammation caused by the deposition of acid in the joints of the hands and feet and cartilage and other side effects.

From here began research and studies to find safer alternatives to human health and cheaper price and more prevalent in the markets, ancient research used plant extracts of garlic, parsley, celery, melochic and others to reduce uric acid.

Celery (Apiumgraveolersdulce) is abiannial plant, belongs to the Umbelliferae family. The celery plant cultivated in the Mediterranean region and its Arabic name is Karafs. Celery seeds contain several substances including volatile oils; flavonoids, antioxidants that give plants their colors and may protect cells from damage; coumarins, chemicals that help thin the blood; and linoleic acid, an omega-6 fatty acid. Celery seed is used for treating arthritis and gout, and to help reduce muscle spasms, calm the nerves, and reduce inflammation.

Celery provides an excellent source of vitamin B1, B2, B6, C and fiber. It's a very good source of folic acid, potassium, and calcium **(Hanaa et al., 2015)**.