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ANTIPIRETTIC EFFECTS OF QURANI PLANTS' MIXTURE (A NEW PHARMACEUTICAL PRODUCT)

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ABSTRACT

Objective: QURANI plants' mixture is a new pharmaceutical product composed of some edible and medicinal plants (15 plants) mentioned in the Holy Quran (in a certain percentage, according to that is mentioned in Patent no. 1429/2013, presented to the Academy of Scientific Research and Technology, Egypt in 11/9/2013). The main aim of this work is to determine antipyretic effects of this new mixture and to study side effects of this mixture on many important organs of the body.

Methods: *In vivo* studies of antipyretic effects of feeding adult female albino rats under investigation with 2, 4 and 8 g/kg of the QURANI plants' mixture was carried out after 0, 1, 2, 3 and 24 hours of the induction of fever by yeast extract. Important organs (Heart, Brain, Kidney, Liver, Lung, Spleen, Stomach and Colon) weights were checked, in addition to the investigation of their histopathological structures, in order to check any bad side effects of this new pharmaceutical product.

Results: *In vivo* studies of the antipyretic effect of feeding adult female albino rats under investigation with 2, 4 and 8 g/kg of the QURANI plants' mixture showed that, the bodies' temperatures degrees of investigated rats were decreased till reaching to 37° C in case of feeding these rats with all investigated doses of the QURANI plants' mixture. The highest antipyretic effect was obtained by feeding rats with 8 g/kg of the QURANI plants' mixture. Based on weights' estimation and histopathological investigations, it was found that, all investigated doses (2, 4 and 8 g/kg) of the QURANI plants' mixture have not any bad side effects on many important organs (Heart, Brain, Kidney, Liver, Lung, Spleen, Stomach and Colon) of all examined rats.

Conclusion: Results of the antipyretic effect of the QURANI plants' mixture will lead us to more biological and chemical investigations of this new, cheap and safe pharmaceutical natural product.

Keywords: Antipyretic effect, Edible and medicinal plants, QURANI plants' mixture, Histopathological studies.

INTRODUCTION

The presented work is a part of the submitted Patent no. 1429/2013 (A new Pharmaceutical Product from Plants Mentioned in the Holy Quran), presented to the Academy of Scientific Research and Technology, Egypt in 11/9/2013. This patent is aimed at the production of a new, cheap and safe pharmaceutical product, this product is composed of QURANI plants' mixture (15 plants) in different percentages, this mixture is valuable against many dangerous diseases (without toxicity and too little side effects), results will be published in a series of successive papers [1-2].

These 15 plants, those used to prepare this new mixture were cited in the Holy Quran as follows: Sûrat Al-Baqarah (The Cow): (61, 266); Sûrat Al-An'âm (The Cattle): (99, 141); Sûrat Ar-Ra'd (The Thunder): (4); Sûrat An-Nahl: (11); Sûrat Al-Kahf (The Cave): (32); Sûrat Maryam (Mary): (23-26); Sûrat Al-Anbiyâ (The Prophets): (47); Sûrat Al-Mu'minûn (The Believers): (18-20); Sûrat An-Nûr (The Light): (35); Sûrat Ash-Shu'arâ (The Poets): (146-148); Sûrat Luqmân: (16); Sûrat Saba' (Sheba): (16); Sûrat Yâ-Sîn: (33-35, 57); Sûrat As-Sâffât (Those Ranged in Ranks): (146); Sûrat Sâd: (51); Sûrat Az-Zukhruf (The Gold Adornments): (73); Sûrat Qâf: (10); Sûrat At-Tûr (The Mount): (22); Sûrat Ar-Rahmân (The Most Gracious): (10-13, 37, 52, 68); Sûrat Al-Wâq'ah (The Event): (20, 28-29, 32, 89); Sûrat Al-Insân or Ad-Dhr (Man or Time): (17); Sûrat Al-Mursalât (Those Sent Forth): (42); Sûrat An-Naba' (The Great News): (32); Sûrat 'Abasa (He Frowned): (27-31); Sûrat At-Tîn (The Fig): (1-2) (The Holy Quran).

The following is a simple introduction of some important plants contained in this mixture regarding their medicinal importance and chemical composition. *Punica granatum* L., commonly known as pomegranate, is a fruit-bearing deciduous shrub or small tree, native to Asia and belongs to the family Lythraceae. Different parts of the plant such as bark, leaves, immature fruits and fruit rind have medicinal significance. *P. granatum* has been extensively used as a traditional medicine in many countries for the treatment of

dysentery, diarrhea, helminthiasis, acidosis, hemorrhage and respiratory pathologies. Additionally, this plant is reported to have excellent antibacterial, antifungal, antiprotozoal, anti-tumour, anti-hepatotoxicity, anti-lipoperoxidation and antioxidant properties. *Punica granatum* L. (pomegranate), a high phenolic content fruit, is widely used as an antipyretic and analgesic in Chinese culture. In hematology, pomegranate could reduce the common carotid intima-medium thickness, thus lowering blood pressure and decreasing low-density lipoprotein (LDL) oxidation and the incidence of heart disease. Numerous phytochemical constituents have been reported to be present in different parts of the pomegranate plant making it pharmacologically precious [3-4].

Ficus carica Linn. (Syn: *Ficus sycomorus*; family: Moraceae) is commonly referred as "Fig". Its fruit, root and leaves are used in the native system of medicine in different disorders such as gastrointestinal (colic, indigestion, loss of appetite and diarrhea), respiratory (sore throats, coughs and bronchial problems), inflammatory and cardiovascular disorders. Fig has been traditionally used for its medicinal benefits as metabolic, cardiovascular, respiratory, antispasmodic and anti-inflammatory remedies. Previous reports concerning the nutrient composition of dried figs have indicated that, it has the best nutrient score among the dried fruit, being an important source of minerals and vitamins. The presence of Phytosterols (433 mg/100 g dry basis) has also been reported in fig fruit. The fresh and dried figs also present relatively high amounts of crude fiber (5.5 %, w/w) and polyphenols. Some recent works have reported that, fig antioxidants can protect lipoproteins in plasma from oxidation and produce a significant increase in plasma antioxidant capacity for 4 hours after consumption. Also, showed that, the higher the Polyphenols contents, especially Anthocyanins, in fig fruit, the higher was their antioxidant activity. Treatment with ethanol extract of *Ficus carica* at doses of 100, 200 and 300 mg/kg body wt. decreased the rectal temperature of the rats in a dose dependent manner. The antipyretic effect started as early as the first hour after administration, and the effect was maintained for four hours after its administration [5-14].

Ginger (*Zingiber officinale*), a member of the Zingiberaceae family, is a well-known spice used in the daily diet in many Asian countries. It is a rhizomatous plant grown throughout South-eastern Asia, China and in parts of Japan, Austria, Latin America, Jamaica and Africa. It has been used as a spice and medicine in India and China since ancient times. It was known in Germany and France in the 9th century and in England in 10th century for its medicinal properties. Over three quarters of the world population still rely on plants and plant extracts for health care. Ginger compounds are active against specific type of diarrhea which is leading to cause death in infants in developing countries. Moreover, it has been found that, ginger is effective in treating nausea caused by sea sickness, morning sickness and chemotherapy, though it was found superior over a place for post operative nausea. In addition, it has been reported that, the main ingredients of ginger like volatile oil, gingerol, shogaol and diaryl heptanoids work as antioxidant, anti-inflammatory, anti-lipid, anti-diabetic, analgesic, antipyretic and anti-tumor. Moreover, it is consumed worldwide as flavoring agent which is used extensively in food, beverage, and confectionary industries in the products such as marmalade, pickles, chutney, ginger beer, ginger wine, liquors, and other bakery products. In South India, ginger is used in the production of a candy called Injimirappa meaning ginger candy in Tamil. Currently, there is a growing interest to detect natural compounds characteristics and activities, like plant extracts of herb and spices for the preservation of foods, flavor characteristic and sometimes show antioxidant activity as well as antimicrobial activity [15-28].

MATERIAL AND METHODS

Plant material

Fifteen edible and medicinal plants mentioned in the Holy Quran were purchased from the Egyptian market, these plants were washed carefully with distilled water and surface sterilized by 70 % ethanol for 20-30 seconds, then they cut to small pieces, dried at room temperature (25°C) till complete dryness, then these plants were grinding to give a fine powder, then mixed in a certain percentage [1-2].

Animals and Diet

Thirty six adult female albino rats weighing 125-140 g were obtained from the Animal House of the National Research Centre, Dokki, Giza, Egypt. Animals were divided into six groups, each group consisted of six animals, rats were held (during 20-22 July 2014) in the metabolic cages (at the normal environment in the Animal House of the National Research Centre) and fasted for 19 hours. Then all groups were allowed for water and fed with their normal basal diet (containing 23 % protein). Diet was purchased from Milado Company, Egypt.

The antipyretic effect of Qurani plants' mixture

Groups of rats were divided as follows: a) Six rats were left as negative control receiving 1 ml saline and fed with their normal basal diet. b) All remaining rats (30 rats) were injected subcutaneously with 10 ml/kg of yeast extract (25 mg/ml w/v) to

induce fever. After the induction of fever, these rats were divided to 5 groups as follows: 1) Group of six rats was given 20 mg/kg paracetamol orally using stomach tube. 2-4) Three groups of rats were feeding with 2, 4 and 8 g/kg of the QURANI plants' mixture, respectively. The last group is non-treated injected group of rats with yeast extract.

Body temperatures were estimated after 0, 1, 2, 3 and 24 hours of inducing fever by yeast extract to all treated groups compared to controls [29]. All animal treatments were conducted according to the Ethics Committee of the National Research Center and in accordance with the recommendations for the proper care and the use of laboratory animals (NIH Publication No. 85-23, revised 1985) in accordance with international ethical considerations.

To study side effects of feeding rats with 2, 4 and 8 g/kg of the QURANI plants' mixture on many important organs, weights of Brain, Heart, Lung, Liver, Kidney, Spleen and Stomach were investigated.

Histopathological study

Heart, Brain, Kidney, Liver, Lung, Spleen, Stomach and Colon were removed. Slices from each organ were fixed in 10 % formalin for 24 hours. Organs were washed in running tap water over night, afterwards, they were dehydrated in ascending grades of alcohol, cleared in xylo, embedded in hard paraffin wax (melting point between 55°C) for 90 minutes, then paraffin wax blocks were prepared. Paraffin sections were cut specially at 8 µm thickness using a rotating microtome. Sections were mounted on slides smeared with egg albumin.

Slides were spread on a hot plate, kept at a temperature of about 40°C later; slides were kept for 2 hours in an incubator at 37°C to dry. Such steps were done to avoid detachment of sections during subsequent of staining. Paraffin sections were used to demonstrate the general histopathological changes by using Haematoxylin& Eosin stain [30].

Statistical analysis

Results were expressed as mean ± SD, they were analyzed by one way ANOVA. The differences between means were tested at P < 0.05 by least significant test (LSD). In all statistical tests, the probability level (P < 0.05) was considered significant. Spearman correlation coefficient was used to determine the relationship between different variables. All analysis was made by SPSS version 16.0 for windows (Statistical package for Social Science, Chicago, USA). Replicate numbers in these experiments are 6 replicates.

RESULTS AND DISCUSSION

The antipyretic effect of the Qurani plants' mixture

Results in Table.1 showed that, the maximum antipyretic effect was obtained by feeding rats with 8 g/kg of the QURANI plants' mixture (Average temperature =37.012±0.010).

Table.1: The antipyretic effect (measured in °C) of the Qurani plants' mixture after 0, 1, 2, 3 and 24 hours of induction of fever by yeast extract {1= Control group of rats, 2= Non-treated injected group of rats with yeast extract, 3, 4, 5 = Groups of rats those feeding with 2, 4 and 8 g/kg of the Qurani plants' mixture, respectively, and 6 = Positive control group of rats (Rats those administered paracetamol, 20mg/kg/day)}, (n= 6 rats).

Time	Groups					
	1	2	3	4	5	6
0 hour	37.280 ±0.040	38.050 ±0.060	37.080 ±0.020	37.200 ±0.020	37.060 ±0.020	37.300 ±0.080
1 hour	37.040 ±0.010	37.700 ±0.050	37.020 ±0.010	37.000 ±0.000	37.000 ±0.000	37.000 ±0.000
2 hours	37.140 ±0.030	37.780 ±0.060	37.020 ±0.010	37.000 ±0.000	37.000 ±0.000	37.020 ±0.020
3 hours	37.220 ±0.080	38.240 ±0.070	37.000 ±0.000	37.000 ±0.000	37.000 ±0.000	37.000 ±0.000
24 hours	37.220 ±0.040	38.240 ±0.060	37.000 ±0.000	37.000 ±0.000	37.000 ±0.000	37.000 ±0.000
Average temperature	37.1800 ±0.050	38.002 ±0.060	37.024 ±0.020	37.040 ±0.010	37.012 ±0.010	37.064 ±0.060

Studies of side effects of feeding rats with the QURANI plants' mixture on some important organs, based on results presented in Table.2, it is clear that, feeding rats with 2, 4 or 8 g/kg of the

QURANI plants' mixture have not any bad side effect on weights of many important organs under investigation (Heart, Brain, Kidney, Liver, Lung, Spleen, Stomach and Colon).

Table 2: Weights (in grams) of some important organs (Brain, Heart and Lung, Liver, Kidney, Spleen and Stomach) of investigated rats {1= Control group of rats, 2= Non-treated injected group of rats with yeast extract, 3, 4, 5 = Groups of rats those feeding with 2, 4 and 8 g/kg of the Qurani plants' mixture, respectively, and 6 = Positive control group of rats (Rats those administered paracetamol, 20mg/kg/day)}, (n= 6 rats).

Organs	Groups					
	1	2	3	4	5	6
Brain	0.910 ±0.120	1.050 ±0.100	1.304 ±0.110	1.286 ±0.100	1.223 ±0.100	1.274 ±0.100
Heart+	1.198	1.668	1.775	1.394	1.736	1.534
Lung	±0.100	±0.130	±0.140	±0.120	±0.130	±0.125
Liver	5.494 ±0.210	6.438 ±0.250	5.890 ±0.220	6.344 ±0.240	5.612 ±0.215	5.738 ±0.235
Kidney	0.409 ±0.070	0.656 ±0.060	0.518 ±0.060	0.494 ±0.060	0.519 ±0.060	0.495 ±0.055
Spleen	0.412 ±0.060	0.413 ±0.050	0.778 ±0.100	0.708 ±0.100	0.520 ±0.060	0.738 ±0.050
Stomach	1.145 ±0.120	1.278 ±0.100	1.554 ±0.130	1.376 ±0.110	1.617 ±0.120	1.367 ±0.150

Histopathological studies on some important organs of investigated rats:

Results of histopathological studies on important organs of investigated rats revealed that, inducing fever by injecting rats with

yeast extract, followed by feeding these rats with 2, 4 or 8 g/kg of the QURANI plants' mixture have not any bad side effect on these organs (Heart, Brain, Kidney, Liver, Lung, Spleen, Stomach and Colon).

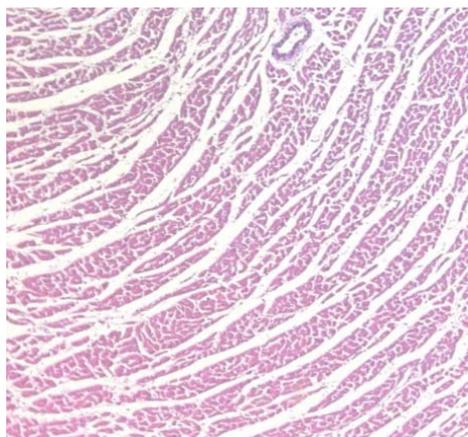


Fig. 1: A photomicrograph of a section in heart of rats fed with 8 g/kg of QURANI plants' mixture showing their normal histopathological structures (Hx \$ E x 100)

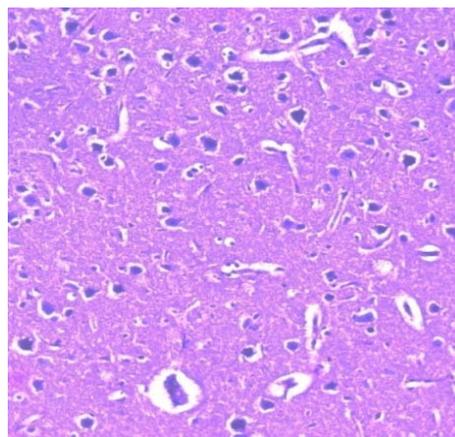


Fig. 2: A photomicrograph of a section in brain of rats fed with 8 g/kg of QURANI plants' mixture showing their normal histopathological structures (Hx \$ E x 200)

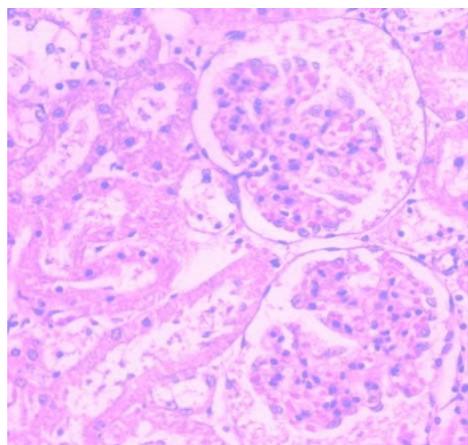


Fig. 3: A photomicrograph of a section in kidney of rats fed with 8 g/kg of QURANI plants' mixture showing their normal histopathological structures (Hx \$ E x 400)

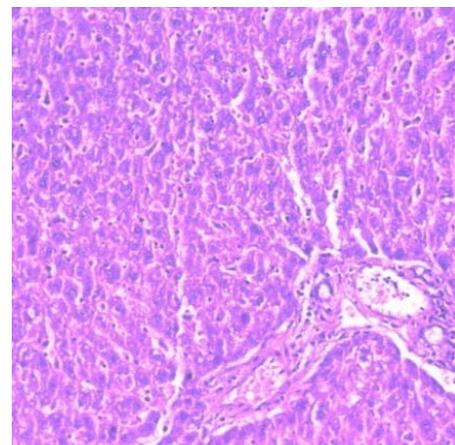


Fig. 4: A photomicrograph of a section in liver of rats fed with 8 g/kg of QURANI plants' mixture showing their normal histopathological structures (Hx \$ E x 200)

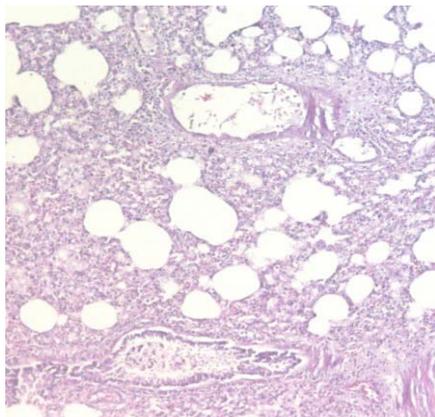


Fig. 5: A photomicrograph of a section in lung of rats fed with 8 g/kg of QURANI plants' mixture showing their normal histopathological structures (Hx \$ E x 100)

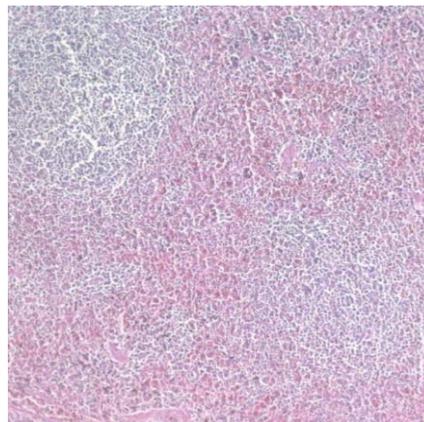


Fig. 6: A photomicrograph of a section in spleen of rats fed with 8 g/kg of QURANI plants' mixture showing their normal histopathological structures (Hx \$ E x 100)

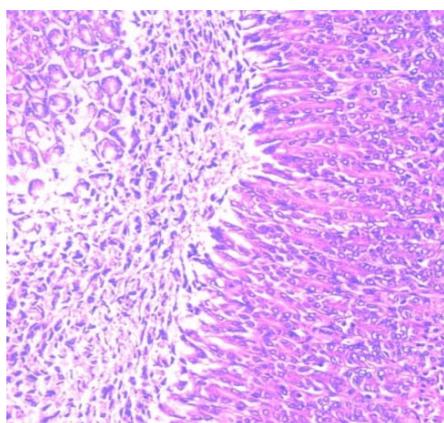


Fig. 7: A photomicrograph of a section in stomach of rats fed with 8 g/kg of QURANI plants' mixture showing their normal histopathological structures (Hx \$ E x 200)

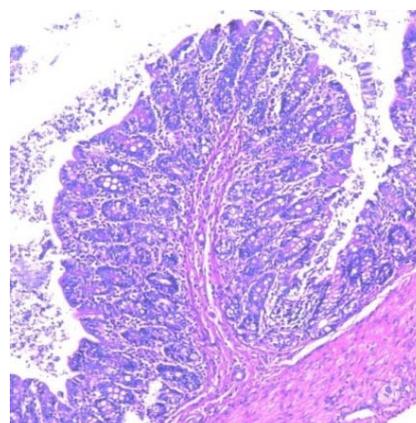


Fig. 8: A photomicrograph of a section in colon of rats fed with 8 g/kg of QURANI plants' mixture showing their normal histopathological structures (Hx \$ E x 100)

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