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Anti-inflammatory Effects of Quranic Plants' Mixture: A New Pharmaceutical Product

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Author's contribution

The sole author designed, analyzed and interpreted and prepared the manuscript.

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ABSTRACT

Aims: This work was carried out to determine anti-inflammatory effects of this new pharmaceutical product (Quranic Plants' Mixture) and also to study side effects of this product on many important organs of the body of investigated animals.
Place and Duration of the Study: *In vivo* studies were carried out in the Animal House of the National Research Centre, Dokki, Giza, Egypt (during 21-22 July 2014). Histological studies of investigated animals were done in the Pathology Department Lab, Theodor Bilharz Research Institute, Giza, Egypt.
Study Design: Three different doses of this new pharmaceutical product were tested in this study regarding their anti-inflammatory effects.
Methodology: *In vivo* studies of anti-inflammatory effects of feeding adult female albino rats under investigation with three different doses (2, 4 and 8 g/kg) of this new pharmaceutical product were carried out after 24 hours of inducing inflammation by injecting investigated animals with carrageen. Additionally, weights of many important organs (Brain, Kidney, Liver, Heart, Lung, Spleen, Stomach and Colon) of the body of investigated animals were measured, along with investigations of their histological structures, to examine any bad side effects of this new pharmaceutical product on investigated animals.
Results: *In vivo* studies of anti-inflammatory effects of feeding adult female albino rats under investigation with three different doses (2, 4 and 8 g/kg) of this new pharmaceutical product

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showed that, both edema sizes and weights were decreased in case of feeding these rats with all investigated doses of Quranic plants' mixture. In this regard the highest anti-inflammatory effect was obtained by feeding animals with 8 g/kg of Quranic plants' mixture based on edema weight estimation; however, 2 g/kg of Quranic plants' mixture was found to be the best effective dose by estimating edema sizes of inflammated rats. Weights' estimation and histological investigations of many important organs of the body of investigated animals revealed that, all investigated doses (2, 4 and 8 g/kg) of Quranic plants' mixture have not any bad side effects on many important organs of all examined rats.

Conclusion: These promising results of anti-inflammatory effects of Quranic plants' mixture will add a new safe anti-inflammatory agent in the world of pharmaceutical products; also these results will lead us to more biological and chemical investigations of this new, cheap and safe pharmaceutical natural product of plant origin.

Keywords: Anti-inflammatory effects; edible and medicinal plants; Quranic plants' mixture; histological studies.

1. 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 a mixture of fifteen plants mentioned in the Holy QURAN [1] in different percentages, this mixture is valuable against many dangerous diseases (with no toxicity and too little side effects), results will be published in a series of successive papers [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 A1-Kahf (The Cave): (32); Sûrat Maryam (Mary): (23-26); Sûrat A1-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-Wâqi'ah (The Event): (20, 28-29, 32, 89); Sûrat A1-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].

Results of in vitro studies of the ethanolic extract of the Quranic plants' mixture showed the cytotoxic effect of this extract against both human prostate (PC3) and colon (HCT116) cancer cell lines. Inhibition caused by using 100 µl/ml (this volume is related to 25 µg d.w. of the Quranic plants' mixture) of this extract reached to 36.300±0.085 and 76.300±0.045 against both HCT116 and PC3 cell lines, respectively. IC_{50} of this extract against PC3 cell line equals 44.60 µl/ml (this volume is related to 11.15 µg d.w. of the Quranic plants' mixture), but IC_{50} cannot be detected in case of HCT116 cell line using these investigated concentrations of this extract. In vivo studies of the diuretic effect of daily feeding rats with 2, 4 and 8 g/kg of the Quranic plants' mixture revealed that, the amount of urine increased by increasing the amount of this mixture when compared to the control group. Results of kidney functions and urine analyses showed that, this mixture has not any bad side effects in this regard, moreover, rats feeding with the Quranic plants' mixture have better kidney functions (urea and creatinene are lower in case of rats feeding with these different concentrations of Quranic plants' mixture than those of the control group). Rats fed with this mixture are also having normal urine physical and chemical characters compared to the control group [3].

Results of In vivo studies of the antipyretic effect of feeding adult female albino rats under investigation with 2, 4 and 8 g/kg of the Quranic plants' mixture showed that, the bodies' temperatures degrees of investigated rats were decreased till reaching to 37ºC in case of feeding these rats with all investigated doses of the Quranic plants' mixture. The highest antipyretic effect was obtained by feeding rats with 8 g/kg of the Quranic plants' mixture. Results of organs

weights' estimation and histological investigations revealed that, all investigated doses (2, 4 and 8 g/kg) of the Quranic plants' mixture have not any bad side effects on many important organs (Heart, Kidney, Brain, Lung, Liver, Stomach, Spleen, and Colon) of all examined rats [4].

GC analysis of the ether extract of the Quranic plants' mixture revealed that, it contained 37 volatile compounds. The most dominant compound in this extract is 2-Ethoxy-3-chlorobutane; Area % of this compound is 27.07, this compound is followed by 5-methyl-5-vinyl-1,3-cyclopentadiene; Area % of this compound is 16.71. This extract contained also many other important compounds such as: D-Limonene and 2-á-Pinene; Area percentages of these compounds are 4.72 and 1.38, respectively. Octadecane, 1-chloro - (CAS) and 2-Undecanol (CAS) were found to be the least available compounds in this extract; Area % of these compounds are equaled 0.45 [5].

The main aim of this work is to determine anti-inflammatory effects of this new mixture and to study side effects of this mixture on many important organs of the body.

2. MATERIALS AND METHODS

2.1 Plant Material

Fifteen edible and medicinal plants mentioned in the Holy Quran [1] were purchased from the Egyptian market, these plants were washed carefully with sterile distilled water and surface sterilized by 70% ethanol for 20-30 seconds, then they cut to small pieces, dried at room temperature (25ºC) till complete dryness, then these plants were grinding to give fine powder, then mixed in a certain percentage [6].

2.2 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 21-22 July 2014) in the metabolic cages (at the normal environment in the Animal House of the National Research Centre) and fasted for 16 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.

2.3 Anti-inflammatory Effects of Quranic 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 into the sub-planter surface of the right hind paw with 0.1 ml carragenan (1% w/v in 0.9% NaCl) to induce inflammation. After inducing inflammation these rats were divided to 5 groups as follows: 1) Group of six rats was given 200 mg/kg Ibuprofen orally using stomach tube. 2-4) three groups of rats feeding with 2, 4 and 8 g/kg of Quranic plants' mixture, respectively. 5) The last group is inflammated non-treated group. Paw volumes were measured used differential volume meter, paw weight were measured also using electric balance before and after 24 hours of the injection with carragenan. The mean increase of the hind paw volumes and weight of rats given the Quranic plants' mixture were compared with that of the control inflammated rats [7].

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 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 Quranic plants' mixture on many important organs, weights of Brain, Heart and Lung, Liver, Kidney, Spleen and Stomach were used as indicator.

2.4 Histological 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 xylol, embedded in hard paraffin wax (melting point between 55ºC) 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

40ºC later; slides were kept for 2 hours in an incubator at 37ºC to dry. Such steps were done to avoid detachment of sections during subsequent of staining. Paraffin sections were used to demonstrate the general histological changes by using Haematoxylin& Eosin stain [8].

2.5 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.

3. RESULTS AND DISCUSSION

3.1 Anti-inflammatory Effects of Quranic Plants' Mixture

In vivo studies of the anti-inflammatory effects of feeding adult female albino rats under investigation with 2, 4 and 8 g/kg of Quranic plants' mixture showed that, both edema sizes and weights are decreased in case of feeding these rats with all investigated doses of Quranic plants' mixture. The highest anti-inflammatory effect was obtained by feeding with 8 g/kg of Quranic plants' mixture based on edema weight estimation and 2 g/kg of Quranic plants' mixture based on edema size estimation (Table 1).

3.2 Weights of Some Important Organs of the Body of Investigated Rats

Data in Table 2 shows that, there is not any bad side effects on weights of all examined important organs (Brain, Heart and Lung, Liver, Kidney, Spleen and Stomach) of the body of all rats under investigation by feeding them with 2, 4 and 8 g/kg of Quranic plants' mixture.

3.3 Histological Studies on Some Important Organs of the Body of Investigated Rats

Results of histological studies on important organs of all investigated rats revealed that, inducing inflammation by injecting rats with carragenan, followed by feeding these rats with 2, 4 or 8 g/kg of Quranic plants' mixture have not any bad side effect on the histological structures of these organs (Heart, Brain, Kidney, Liver, Spleen, Stomach, Colon and Lung).

(Figs.1-9) show the normal histological structures of heart, brain, kidney, liver, spleen, stomach, colon and lung of inflammated rats (inflammation was induced by injecting these rats with carragenan) after feeding with 2 g/kg of Quranic plants' mixture as a good anti-inflammatory agent.

Table 1. Anti-inflammatory effects of Quranic plants' mixture after 24 hours of induction of inflammation {1 = Control, 2 = Injected group of rats with carragenan, 3, 4, 5 = Groups of rats those feeding with 2, 4 and 8 g/kg of Quranic plants' mixture, respectively and 6 = Positive control group of rats (administered Ibuprofen, 100 mg/kg)}, (n= 6 rats)

Estimation of inflammation	Groups					
	1	2	3	4	5	6
Weight of paw (gm)	-	0.703±0.090	0.353±0.070	0.393±0.050	0.256±0.020	0.554±0.060
% of change of weight of paw	-	0.000±0.000	49.787±0.453	44.097±0.513	63.585±0.759	21.195±0.202
Volume of paw (Cm^3)	-	0.500±0.004	0.180±0.003	0.220±0.001	0.220±0.002	0.380±0.006
% of change of volume of paw	-	0.000±0.000	64.000±0.309	56.000±0.409	56.000±0.567	24.000±0.203
L.S.D. (0.05)		0.323	1.340	2.000	2.311	0.722
L.S.D. (0.01)		0.538	1.960	3.032	3.501	1.115

Table 2. Weights (gm) of some important organs (brain, heart and lung, liver, kidney, spleen and stomach) of investigated rats after 24 hours of induction of inflammation {1 = Control, 2 = Injected group of rats with carragenan, 3, 4, 5 = groups of rats those feeding with 2, 4 and 8 g/kg of Quranic plants' mixture, respectively and 6 = positive control group of rats (administered Ibuprofen, 100 mg/kg)}, (n = 6 rats)

Organs	Groups					
	1	2	3	4	5	6
Brain	0.910±0.120	1.682±0.120	1.292±0.110	1.440±0.130	1.432±0.109	1.090±0.107
Heart+Lung	1.198±0.100	0.868±0.133	1.365±0.145	1.390±0.122	**1**.359±0.135	1.070±0.129
Liver	5.494±0.210	5.386±0.220	6.077±0.225	5.780±0.**2**35	5.303±0.225	4.374±0.237
Kidney	0.409±0.070	0.494±0.050	0.325±0.062	0.363±0.**0**50	0.395±0.040	0.582±0.056
Spleen	0.412±0.060	0.556±0.040	0.437±0.040	0.416±0.040	0.336±0.060	0.370±0.060
Stomach	1.145±0.120	1.308±0.160	1.508±0.135	1.400±0.115	1.606±0.123	1.425±0.148
L.S.D.(0.05)	1.000	0.722	0.933	1.051	0.971	1.130
L.S.D. (0.01)	1.531	1.220	1.315	1.602	1.401	1.651

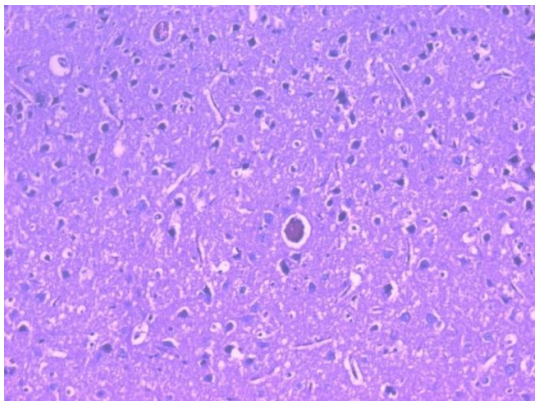

Fig. 1. A photomicrograph of a section in a brain of rat feeding with 2 g/kg of Quranic plants' mixture after 24 hours of the induction of an inflammation showing normal histological structure (Haematoxylin & Eosin stain, x=200)

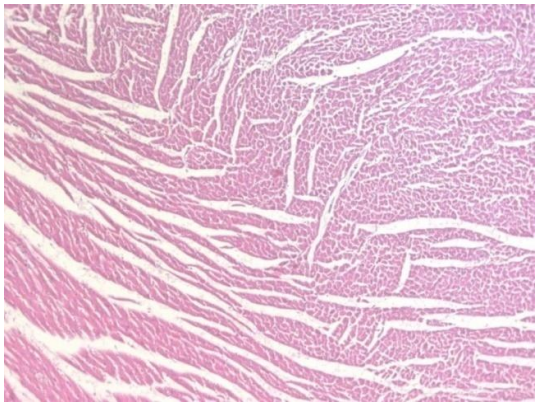

Fig. 2. A photomicrograph of a section in a heart of rat feeding with 2 g/kg of Quranic plants' mixture after 24 hours of the induction of an inflammation showing normal histological structure (Haematoxylin & Eosin stain, x=100)

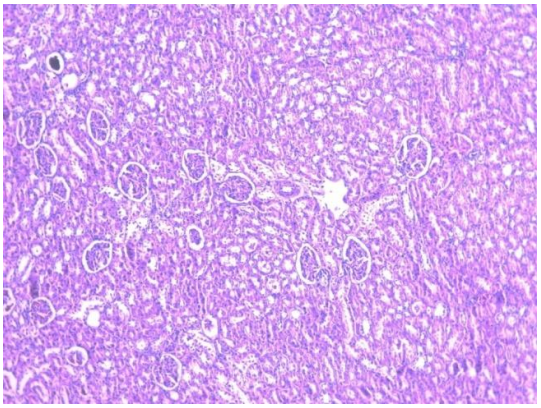

Fig. 3. A photomicrograph of a section in a kidney of rat feeding with 2 g/kg of Quranic plants' mixture after 24 hours of the induction of an inflammation showing normal histological structure (Haematoxylin & Eosin stain, x=100)

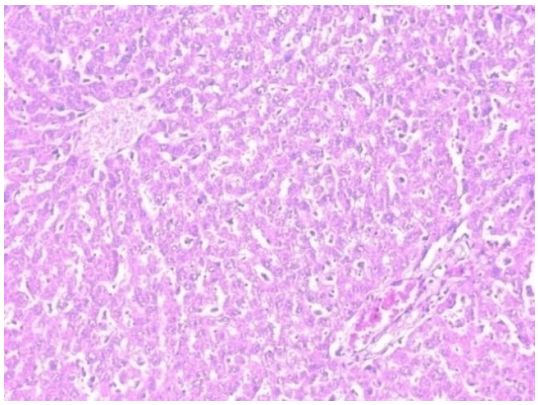

Fig. 4. A photomicrograph of a section in a liver of rat feeding with 2 g/kg of Quranic plants' mixture after 24 hours of the induction of an inflammation showing normal histological structure (Haematoxylin & Eosin stain, x=400)

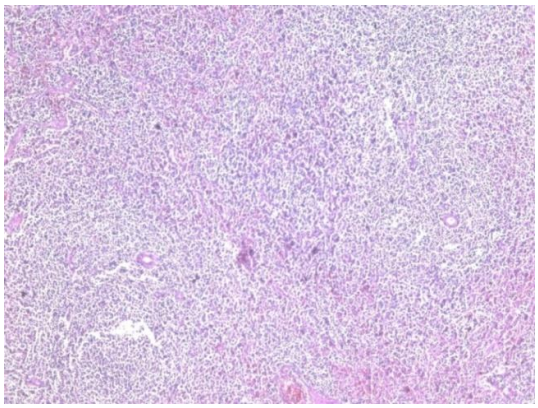

Fig. 5. A photomicrograph of a section in a spleen of rat feeding with 2 g/kg of Quranic plants' mixture after 24 hours of the induction of an inflammation showing normal histological structure (Haematoxylin & Eosin stain, x=100)

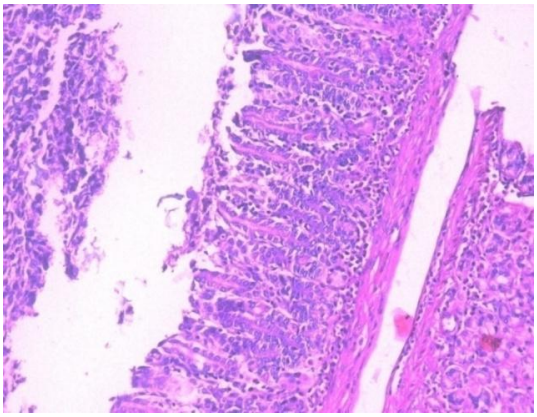

Fig. 6. A photomicrograph of a section in a stomach of rat feeding with 2 g/kg of Quranic plants' mixture after 24 hours of the induction of an inflammation showing normal histological structure (Haematoxylin & Eosin stain, x=200)

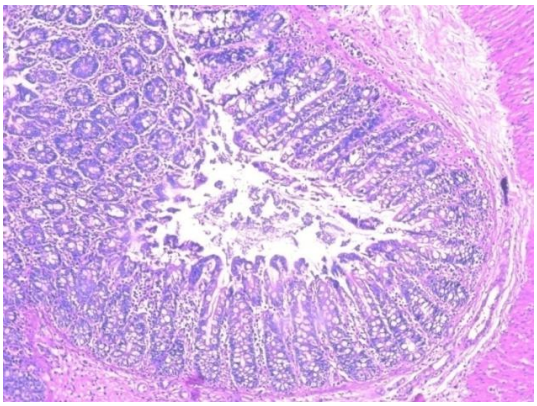

Fig. 7. A photomicrograph of a section in a colon of rat feeding with 2 g/kg of Quranic plants' mixture after 24 hours of the induction of an inflammation showing normal histological structure (Haematoxylin & Eosin stain, x= 100)

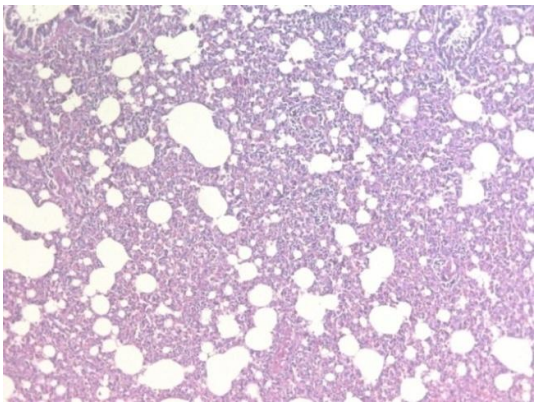

Fig. 8. A photomicrograph of a section in a lung of an inflammated non treated rats after 24 hours of the induction of an inflammation showing pneumonia as a side effect (Haematoxylin & Eosin stain, x=100)

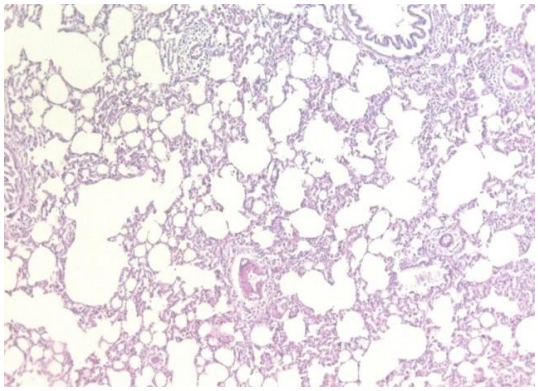

Fig. 9. A photomicrograph of a section in a lung of rat feeding with 4 g/kg of Quranic plants' mixture after 24 hours of the induction of an inflammation showing that, good effect on treating pneumonia was obtained using this dose (Haematoxylin & Eosin stain, x=100)

It is well observed from histological studies included in this work that, pneumonia was occurred as a side effect of inducing inflammation (inflammation was induced by injecting rats with carragenan into the sub-planter surface of the right hind paw), this side effect was treated by all investigated doses of Quranic plants' mixture. 4 g/kg of Quranic plants' mixture was found to be the best dose in this regard (Figs. 8 and 9).

4. CONCLUSION

These promising results of anti-inflammatory effects of Quranic plants' mixture will add a new safe anti-inflammatory agent in the world of pharmaceutical products; also these results will lead us to more biological and chemical investigations of this new, cheap and safe pharmaceutical natural product of plant origin.

ETHICAL CONSIDERATIONS

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 use of laboratory animals (NIH Publication No. 85-23, revised 1985) in accordance with international ethical considerations.

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COMPETING INTERESTS

Author has declared that no competing interests exist.

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