

## Potential ameliorative effects of garlic and onion by-products against the toxicity of ibuprofen in rats

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## Abstract:

onion and garlic peels contains several natural compounds that have antioxidant potent such as poly phenols and flavonoids; despite their importance human are not interested to eat these un-edible parts. Ibuprofen is an anti-inflammatory drug, which could affect hepatic, renal and hematological functions in rats. The present study aims to investigate the effect of added onion and garlic by-products (peels) to bread on toxicity of ibuprofen in rats. Twenty five male rats, were divided into two main groups, the first main group (10 rats) divided into two groups, (1) fed on basal diet and (2) fed on basal diet + (25%) of control bread; the second main group (15 rats) was given (40 mg ibuprofen /kg body weight) for 4 weeks; classified into three sub groups as follow: group (3), fed on basal diet as a positive control; groups (4-5), fed on 25% bread with 10 % of onion peel powder (OPP) or garlic peel powder (GPP) respectively.

Biochemical analysis data indicated that ibuprofen induced a significant increased ( $p \leq 0.05$ ) in TG, TC and LDL, also ALT and AST levels compared to normal group. Feeding on 10% of OPB and GPB exhibited a significant improvement ( $p \leq 0.05$ ) in these levels. Also result indicated that ibuprofen significantly ( $p \leq 0.05$ ) raised serum urea and creatinine concentration in control positive group and significant decrease in Hb, Hct and RBCs count comparing with control negative group. On the other side, groups treated with OPB and GPB restored these levels to nearly normal. These results were confirmed with histopathological examination of liver and kidney.

**Keywords:** *Allium* family, peels powder, anti-inflammatory drug, blood parameters, histopathological examination.

## Introduction

Garlic (*Allium sativum*) is one of the earliest of cultivated plants originally from Central Asia. The genus *Allium* belongs to the monocot family Alliaceae, formerly considered part of Liliaceae and Amaryllidaceae. These plants are hardy per-ennials with underground storage organs consisting of true bulbs or less-developed vestigial bulbs attached to rhizomes, the latter known as rhizomatous alliums (Murray, 2005; Kamenetsky and Rabinowitch 2006). The potency of garlic has been acknowledged in the Egyptian medical papyrus dating to about 1550 B.C.E as an effective remedy for a variety of ailments as a remedy for intestinal

disorders, flatulence, worms, respiratory infections, skin diseases, wounds, symptoms of aging and many other ailments (**Amagase et al., 2001; Murray, 2005 and Hanieh et al., 2010**).

Garlic cloves contain thin outer skins (inedible) for protecting the body of each clove (segment) contains pectin (27%), combined rhamnose (1.42%) and galactose (5.6 %), but before it is used as food, the outer skins must be removed (**Mudgal, 2005 and Chitsaz et al., 2018**). Because of large consumption of garlic in daily life garlic peel as a kind of easily available agricultural waste (**Ngah and Hanafiah, 2008 and Liu et al., 2014**). Garlic peels principally consists of cellulose and hemicellulose (**Kallel et al., 2015**). Composed of four to five layers which are divided into several (5–20)sub layers, contains high amount of total dietary fiber , it is similar to fenugreek husk and for soy husk powder (**Naidu et al., 2011 and Tyug et al., 2010** ). Also, garlic husk also contains noticeable fractions of lignin, similar content was found in coconut husk (**Adeyi, 2010**). Garlic straw were contained low lipid 2.66% and high protein content 4.38 % (**Bampidis et al., 2005; Nwinuka et al., 2005 and Kallel et al., 2014** ). Garlic crusts are potentially a rich source of carbohydrate and ash content which similar as cacao pod husk. **Vriesmanna et al., (2011)**.The extract of garlic skins (peels) showed strong antioxidant activity were isolated and identified by (HPLC-PDA) analyses suggested that these compounds were phenylpropanoids, Coumaroyloctopamine, N-trans-feruloyloctopamine, guaiacylglycerol-beta-ferulic acid ether, and guaiacylglycerol-beta-caffeic acid ether were identified as were trans-coumaric acid and trans-ferulic acid (**Ichikawa et al., 2003**). So, today garlic use as effective natural antibiotic (antioxidant, anti-microbial, anti-cholesteremic, anti-bacterial, anti-inflammatory, anti-cancerous and antihypertensive properties) and that causes no environmental or physical side effects (**Hanieh et al., 2010; Mansoub, 2011 and Lee and Gao, 2012**).

Onion (*Allium cepa* L.) is another member of the Liliaceae family that is largely utilized all over the world in various types of foods, Egypt is one of the top world onion producers with an annual production of more than 2.32 million Tons and it contains small quantities of fat, sugar and vitamins A, C and B complex; it is rich in magnesium, potassium, copper and contains very high content of carbohydrate (88.56%) and low protein (0.88%) (**Gabor *et al.*, 2010; FAO, 2011 and Beatrice, 2017**). Consumed onion fresh or in processed products due to its flavor and health benefits and has increased used as a traditional medicine in the treatment of several disorders (**Ly *et al.*, 2005; Gurushizde *et al.*, 2007 and Yang *et al.*, 2013**).

Onion is has antioxidant activity reduced risk of developing many forms of cancer and cardiovascular due to its high contents phenolic and flavones, especial the outer dry layer of onion have antioxidant properties because the concentration of quercetin (one of the flavonols) is higher in onion peel than in others part (**Huber *et al.*, 2009 and Prakash *et al.*, 2007**).

The flavonoids present in the onion consist of anthocyanins (cyanidin and peonin) and mainly flavonols (quercetin, kaempferol, isorhamnetin and their glycosides). The onion skin has a high content of free and glycosidically bonded quercetin (2-10% w/w) and oxidized quercetin derivatives such as minor flavonols and phenolic compounds (**Griffiths *et al.*, 2002 and Suh *et al.*, 1999**).

Red onion peels can serve as a convenient and cost-effective source of high-value antioxidant nutraceuticals for protection against oxidative stress-related disorders (**Ahmed *et al.*, 2017**). The total phenolic contents and flavonoids of the onion peel extract ranged from 120.19 to 371.62 mg GA/g E and 364.9 to 496.14 mg QE/g E respectively and quercetin, the major flavonoids in onion peel (**Razavi and Kenari, 2016**).

During food processing the onion peel regarded as bio-waste and significant by-products. However, effective utilization of these by-

products is desirable, occasionally used in traditional medicine in treatment of liver ailment and inflammation (**Michał *et al.*, 2013; Ahmed *et al.*, 2017 and Beatrice, 2017**).

Ibuprofen is one of non-steroidal anti-inflammatory drugs (NSAIDs) which most commonly used over-the-counter medications for pain and fever (**Onay *et al.*, 2009**). It's widely considered to have high safety profiles but the frequent and widespread use of ibuprofen and other NSAIDs is likely to increase the prevalence of their adverse effects, ibuprofen particularly is associated with a small increase in systolic blood pressure in hypertensive patients, but chronic exposure and duration of exposure may increase ibuprofen toxicity and affect hepatic, renal and hematological functions by increased urea and creatinine levels at the high dose (40 mg/kg) (**Aprioku *et al.*, 2014**)

So, the objective of this study was to investigate the effect of (garlic or onion) by- products on the alleviation of health complications caused by ibuprofen in rats.

## Materials and Methods

### Materials

#### Garlic and onion by- products

Garlic peel and red onion skin were obtained by special arrangements with some merchants, Minia City, Minia Governorate, Egypt.

### Chemicals

Ibuprofen tablets were purchased from Pharmacy in Minia city, assay kits were purchased from Bio diagnostic, Cairo, Egypt. All other chemicals and solvents were of highest grade commercially available.

## Methods

### Preparation of Garlic and onion peels powder

Peels were separated from the onion and garlic bulbs; washed thoroughly and dried in oven at 40C°. The peels were grinded into well powder using lab blender. Then the powders were kept in the fridge until use (**Beatrice, 2017 and Chitsaz *et al.* 2018**)

## Preparation of Garlic and onion by-products bread

Slices bread were prepared according to **Pojic et al., (2015)** and **Contado et al., (2009)** with some modifications showed in Table (1). Wheat flour was substituted with (10% of GPP or OPP). All the ingredients were mixed in a Braun mixer (type3202, France) for 5 min until they reached optimal consistency. The dough was fermented for 30 min at  $28\pm 1C^{\circ}$ . Divided fermented bread into four a cylinder shape pieces placed in the pan and after 15 min of resting and optimum volume increase. The proofed dough was baked in baking oven at  $220C$ . The baked bread was cooled at room temperature for 1 h. Bread cut to slices and dried on oven at  $100 C^{\circ}$ .

**Table (1):** Formulas composition of onion and garlic by-products bread

Ingredients (g)	Control Bread (CB)	Onion and Garlic by-products bread	
		Onion peel bread (OPB)	Garlic peel bread (GPB)
Wheat flour	500	450	450
Onion peel powder (OPP)	—	50	—
Garlic peel powder (GPP)	—	—	50
Fresh yeast	12.5	12.5	12.5
Vegetable oil	20	20	20
Salt (NaCl)	10	10	10
Water	270	270	270

## Preparation of Ibuprofen

The ibuprofen drugs were powdered and mixed with distilled water in a glass mortar and administered as aqueous suspension **Aprioku et al., (2014)**.

## Experimental animals

Normal male albino rats, weight  $150 \pm 10g$  per each were obtained from Faculty of Pharmacy, Nahda University, Beni- Suef.

## Basal Diet

The basic diet prepared according to the following formula as mentioned by **AIN, (1993)** as follow: protein (10%), corn oil (10%), vitamin mixture (1%), mineral mixture (4%), choline chloride (0.2%), methionine (0.3%),

cellulose (5%), and the remained is corn starch (69.5%). The used vitamin mixture component was that recommended by **Campbell, (1963)** while the salt mixture used was formulated according to **Hegsted *et al.*, (1941)**.

### Experimental design

Twenty five adult male albino rats were housed individually in wire cages in a room maintained at  $25 \pm 2$  °C and kept under normal healthy condition in the biological laboratory of Chemistry Department, Faculty of Agriculture, Minia University. All rats were fed on basal diet for one- week before starting the experiment for acclimatization. After one week period, the rats were divided into two main groups as following:

- First main group (10 rats) was divided into two sub groups as follow:
  - Group (1): fed on basal diet as a negative control.
  - Group (2): fed on basal diet (75%) + control bread (25%).
- Second main group (3-5) (15 rats) was given (40 mg ibuprofen /kg body weight) daily by oral according to **Aprioku *et al.*, (2014)**, divided into equal three sub groups as follow:
  - Group (3): fed on basal diet as a positive control.
  - Group (4): fed on basal diet (75%)+ bread containing 10% onion peel powder (25%).
  - Group (5) fed on basal diet (75%) + bread containing 10% garlic peel powder (25%).

The body weight of each rat was recorded every week. Animals were dissected and liver, kidney; lungs and spleen were excised, washed in ice-cold saline, wiped with filter paper and weighted.

### Biochemical analysis of serum

#### Blood samples

Blood samples were collected at the end of experiment period, 4 weeks; from the retro-orbital plexus (**Schermer, 1967**) from all animals of each group after anesthesia by diethyl ether. Suitable volumes of fresh blood were immediately taken in heparinized tube for hematological examination.

The other part of blood samples was allowed to coagulate at room temperature, and centrifuged at 3000 rpm for 15 min at 4°C. The obtained serum was used to assessment of liver, kidney function tests and lipid profile.

## Hematological analysis

Blood collected in heparinized tube was analyzed for white blood cells (WBCs) and red blood cells (RBCs), as described by **Dacie and Lewis (1984)** while hemoglobin concentration (Hb) was measured according to **VanKampen and Zijlstra (1961)**. HCT (%) was determined by centrifuging blood in heparinized micro hematocrit tube (capillary tubes of 1mm internal diameter and 7.5 cm length) for 5 minutes at 15000 rpm (**Dacie and Lewis, 1991**).

## Biochemical analysis

Different tested parameters in serum were determination using specific methods as follow: Glutamic oxaloacetic transaminase (GOT) glutamic pyruvic transaminase (GPT) according to **Reitman and Frankel, (1957)**, urea and creatinine according to **Fawcett and Scott, (1960) and Murrly, (1984)**, respectively.

Total cholesterol (TC), HDL-c and TG were determined according to the methods of **Allain et al., (1974)**, **Burstein et al., (1970)** and **Fassati and Prencipe (1982)**, respectively. LDL-cholesterol and very low density lipoprotein cholesterol VLDL-c were assayed according to the equations of (**Friedewald et al., 1972**) as follow:  $VLDL-c = TG/5$  and  $LDL-c = TC - HDL-c - VLDL-c$

## Histopathological examination

Autopsy samples were taken from the livers and kidneys of rats in different groups and fixed in neutral buffered formalin10%. Cleaning using tap water then serial dilutions of absolute ethyl alcohol for dehydration, embedded in paraffin .Sections 4-5 microns thick were prepared, collected on glass slides, deparaffinized and stained by hematoxylin and eosin stain for histopathological examination (**Banchroft et al., 1996**).

## Statistical analysis

Experimental results were expressed as means  $\pm$  SD of three parallel measurements. Analysis of variance was performed by ANOVA procedures. Graph Pad Prism® was used for statistical calculations Graph Pad Software, San Diego, CA, USA (**Motulsky, 1999**).



## Results and Discussion

### Effect of additive onion and garlic by-products to bread on body weight gain and relative organs weight

Data from Table (2) explain that there were no significant differences among groups in all relative weight organs except the spleen in group treated with ibuprofen compared to control negative or control +CB groups. Result shows decrease on body weight gain of rats treat with ibuprofen. Our results was agree with **Collier *et al.*, (2018)** who reported that the addition of ibuprofen led to significant changes in food consumption and body weights trended to slightly lower values. While ameliorate occurred in (BWG) when rats feed on OPB and GPB may due to dietary containing garlic skin had significant impact on protein , also onion peel contains very high amount of carbohydrate (88.56%) (**Ifesan, 2017 and Chitsaz *et al.*, 2018**).

**Table (2): Effect of OPB and GPB on body weight gain and relative organs weight in the experimental rat groups treated to ibuprofen\***

Value	Control (-)	Control +CB	Control (+)	onion and garlic by-products bread	
				OPB	GPB
<b>BWG %</b>					
Mean	28.90	31.66	23.18 <sup>ab</sup>	28.54	28.27
SD	2.389	9.09	1.50	8.46	3.48
<b>Liver %</b>					
Mean	4.77	5.10	5.34	4.74	4.80
SD	0.30	0.34	0.18	0.53	0.45
<b>Kidney %</b>					
Mean	0.96	0.94	1.03	0.88	0.93
SD	0.05	0.03	0.04	0.08	0.07
<b>Spleen %</b>					
Mean	0.65	0.73	1.14 <sup>ab</sup>	0.66 <sup>c</sup>	0.71 <sup>c</sup>
SD	0.08	0.03	0.08	0.03	0.09

\*CB, control bread; OPB, onion peel bread; GPB, garlic peel bread. Means are significantly different at  $P \leq 0.05$  (<sup>a</sup> different from control group; <sup>b</sup> different from control +CB group; <sup>c</sup> different from control (+) group.

## Effect of additive onion and garlic by-products to bread on liver functions

AST and ALT enzymes are indicate to that destruction of the liver because of cellular harm. In Table (3) were shown that enzymes are increased in group treat with ibuprofen compared with control group and found improvement in enzymes level when rats feed on OPB and GPB, these because onion had anti-inflammatory agent and good source of antioxidants **Adesso et al .,(2016)** and could able to amelioration of inflammation and hyperlipidemia (**Liao and Lin, 2015**). On another side garlic peel contain bioactive compounds and that consumption lead to prohibit the release of mentioned enzymes into the plasma (**Chitsaz et al., 2018**).

**Table (3): Effect of OPB and GPB on liver enzymes marker in the experimental rats treated to ibuprofen intoxication\***

Value	Control (-)	Control - CB	Control (+)	onion and garlic by-products bread	
				OPB	GPB
<b>AST (IU/L)</b>					
Mean	93.33	93.33	155.7 <sup>ab</sup>	109.30 <sup>abc</sup>	100.00 <sup>c</sup>
SD	5.77	3.51	5.51	0.58	4.58
%of change	0.00	0.00	66.83	17.11	7.14
<b>ALT (mg/dl)</b>					
Mean	39.03	43.33	66.93 <sup>ab</sup>	44.53 <sup>c</sup>	39.90 <sup>c</sup>
SD	5.24	4.86	2.90	1.75	5.46
%of change	0.00	11.01	71.48	14.09	2.23

\*CB, control bread; OPB, onion peel bread; GPB, garlic peel bread .Means are significantly different at  $P \leq 0.05$ (<sup>a</sup> different from control group; <sup>b</sup> different from control +CB group; <sup>c</sup> different from control (+) group.

Our results accordance with these from **Emamat et al.,(2016)** who studied the effects of onion consumption on inflammatory features of nonalcoholic fatty liver disease, indicate that onion consumption can be effective in NAFLD management when it is combined with a healthy diet at percent 7%.

## Effect of additive onion and garlic by-products to bread on kidney function

Urea and creatinine were assessed as markers of renal functions. Data in Table 4 show the urea level was significantly elevated in group treated ibuprofen compared to normal control and control +CB groups. Data agree with **Insel, (1996)** who confirmed that NSAIDs affect renal physiology may lead to acute intrarenal haemodynamic changes with possible deterioration of renal. The serum level of creatinine were significantly increased in group treated with ibuprofen compared to control group, result agree with **Udegbunam et al., (2008)** who suggested decreased renal function due to increase significantly creatinine level in rabbits treated with ibuprofen 30 mg/kg .While concomitant treatment of GPB or OPB with ibuprofen reversed the alteration in urea and creatinine level towards normal levels when compared to ibuprofen alone. Several studies have explained the importance of garlic and its peels, for example **El-Demerdash et al., (2005)** and **Ola-Mudathir et al.,(2008)** who explained that garlic could prevention and treatment of several diseases, these due to dietary phytochemicals, antioxidant properties and ability to modulate the detoxification systems.

**Table (4): Effect of feeding OPB and GPB on kidney function in the experimental rats treated to ibuprofen intoxication\***

Value	Control(-)	Control + CB	Control (+)	onion and garlic by-products bread	
				OPB	GPB
<b>Urea (mg/dl)</b>					
Mean	40.97	42.00	57.67 <sup>ab</sup>	44.33 <sup>c</sup>	43.33 <sup>c</sup>
SD	1.53	1.00	2.52	1.53	1.53
%of change	0.00	2.51	40.76	8.20	5.76
<b>Creatinine (mg/dl)</b>					
Mean	0.65	0.61	0.75 <sup>ab</sup>	0.65 <sup>c</sup>	0.64 <sup>c</sup>
SD	0.03	0.03	0.03	0.02	0.02
%of change	0.00	6.15	15.38	0.00	1.54

\*CB, control bread; OPB, onion peel bread; GPB, garlic peel bread .Means are significantly different at  $P \leq 0.05$  (<sup>a</sup> different from control group; <sup>b</sup> different from control +CB group; <sup>c</sup> different from control (+) group

## Effect of additive onion and garlic by-products to bread on cholesterol, triglycerides and lipoprotein levels

The effect OPB and GPB consumption on blood lipid profile parameters of ibuprofen rats groups were shown in Table(5) from such data it could be noticed that ibuprofen induced significant increased ( $P \leq 0.05$ ) in TG(73.82%),TC (50.44%) and LDL (115.71 %) while significant decreased ( $P \leq 0.05$ ) in HDL (39.12) compared to normal group .These increases in levels of (TG), (TC) and (LDL) concentrations are well-known as risk factors for oxidative stress (**Kim *et al.*, 2013**). On other hand consumption of OPB and GPB induced significant improvement on blood lipid profile through decreasing the TC and LDL by the ratio of 18.46 and 26.11%; 39.31 and 55.6 % respectively; the opposite direction was observed for the HDL levels. That result in the line with **Lee *et al.*, (2013)** who reported that onion peel extracts significantly decreased blood triglyceride. May due to that onion had anti oxidative effect (flavonoids and phenolic content) ;the major flavonoids of mature onion bulbs and probably their peeling wastes are quercetin 3,4-O-diglucoside and quercetin 40-O-monoglucoside, accounting for more than 85% of the total flavonoids(**Elhassaneen *et al.*, 2016** and **Lee *et al.*, 2015**).

**Table (5): Effect of OPB and GPB on blood lipids profile concentration in the experimental rats exposed to ibuprofen**

Value	Control(-)	Control + CB	Control (+)	onion and garlic by-products bread	
				OPB	GPB
<b>Triglycerides(TG ,mg/dl)</b>					
Mean	104.33	113.00	181.35 <sup>ab</sup>	145.00 <sup>abc</sup>	161.00 <sup>abc</sup>
SD	1.53	100	0.58	1.53	1.00
%of change	0.00	8.31	73.82	38.98	54.32
<b>Total cholesterol(TC, mg/dl)</b>					
Mean	122.49	123.7	184.27 <sup>ab</sup>	145.10 <sup>abc</sup>	154.47 <sup>abc</sup>
SD	1.53	2.08	2.00	2.52	2.52
%of change	0.00	0.99	50.44	18.46	26.11
<b>High density lipoprotein (HDL ,mg/dl)</b>					
Mean	45.99	42.50	28.00 <sup>ab</sup>	38.60 <sup>abc</sup>	35.71 <sup>abc</sup>
SD	5.32	1.46	0.78	3.48	1.45
%of change	0.00	-7.59	-39.12	-16.07	-22.35
<b>low density lipoprotein (LDL ,mg/dl)</b>					
Mean	55.63	58.60	120.00 <sup>ab</sup>	77.50 <sup>abc</sup>	86.56 <sup>abc</sup>

Value	Control(-)	Control + CB	Control (+)	onion and garlic by-products bread	
				OPB	GPB
SD	1.6	1.2	2.00	1.6	1.4
%of change	0.00	5.34	115.71	39.31	55.60
Very low density lipoprotein (VLDL ,mg/dl)					
Mean	20.87	22.60	36.27 <sup>ab</sup>	29 <sup>abc</sup>	32.20 <sup>abc</sup>
SD	0.33	0.20	0.12	0.31	0.20
%of change	0.00	8.29	73.79	38.96	54.29

CB, control bread; OPB, onion peel bread; GPB, garlic peel bread .Means are significantly different at  $P \leq 0.05$  (<sup>a</sup> different from control group; <sup>b</sup> different from control +CB group; <sup>c</sup> different from control (+) group.

### Effect of additive onion and garlic by-products to bread on some blood parameters

The effect of ibuprofen, **OPB** and **GPB** on Hb, Hct, WBCs and RBCs count were shown in Table (6). Results obtained in the same table revealed significant decrease of Hb, Hct, and RBCs count in ibuprofen group, that change about 60.19, 57.06 and 49.23%, respectively, this result is same line with **Gomaa, (2017)** who reported that treatment with ibuprofen showed significant decrease in RBCs count, Hb content and Hct%. But this result does not agree with **Udegbum et al., (2008)** who explained that treat by ibuprofen did not affect the RBC and HB of the rabbits. The difference in results may be due to the differences in the dose of ibuprofen and diet. On other hand results show increase change of WBCs count with treatment by ibuprofen about 55.34% compared to control group. These results agree with **Aprioku et al., (2014)** who reported that ibuprofen effect on hematological functions and toxicity depend to dose and chronic use ,While groups feeding on OPB and GPB shown increased in RBCs count about 4.21,5.49 respectively compared with control (+) about 2.96, data in the same Table show increase in WBCs count in control(+); on other hand consumption of OPB and GPB restored it to nearly normal levels. Result is also supported by another study by **Thanikachalam et al., (2010)** who found that increase in the RBCs and in WBCs count with the administration of garlic peel which might indicate an immunostimulant effect. These results explain that OPB and GPB can lowering or slowing down oxidative stress induced by ibuprofen, may be due to that OPB and GPB as antioxidant nutraceuticals have several phenolic compounds (ferulic, coumaric and caffeic) can serve

for protection against oxidative stress-related disorders (Ichikawa *et al.*, 2003 and Ahmed *et al.*, 2017).

**Table (6): Effect of OPB and GPB on some blood parameters in the experimental rats exposed to ibuprofen\***

Value	Control(-)	Control + CB	Control (+)	onion and garlic by-products bread	
				OPB	GPB
<b>HB (mg/dl)</b>					
Mean	14.57	13.93	5.80 <sup>ab</sup>	9.93 <sup>abc</sup>	13.32
SD	1.55	0.90	0.92	0.31	1.41
%of change	0.00	-0.48	-60.19	-31.85	-8.58
<b>HCT(mg/dl)</b>					
Mean	33.37	33.40	14.33 <sup>ab</sup>	28.33 <sup>abc</sup>	30.83 <sup>abc</sup>
SD	0.82	0.68	0.30	0.48	0.79
%of change	0.00	-0.09	-57.06	-15.10	-7.61
<b>RBCs (10<sup>6</sup>)</b>					
Mean	5.83	5.72	2.96 <sup>ab</sup>	4.21	5.49 <sup>c</sup>
SD	0.81	0.65	0.29	0.44	0.80
%of change	0.00	-1.89	-49.23	-27.79	-1.00
<b>WBCs (10<sup>3</sup>)</b>					
Mean	10.30	10.63	16.00 <sup>ab</sup>	12.27 <sup>c</sup>	10.70 <sup>c</sup>
SD	1032	0.76	0.30	0.83	0.20
%of change	0.00	3.20	55.34	19.13	3.88

\*CB, control bread; OPB, onion peel bread; GPB, garlic peel bread. Means are significantly different at  $P \leq 0.05$  (<sup>a</sup> different from control group; <sup>b</sup> different from control +CB group; <sup>c</sup> different from control (+) group).

## Histopathological results

### Liver

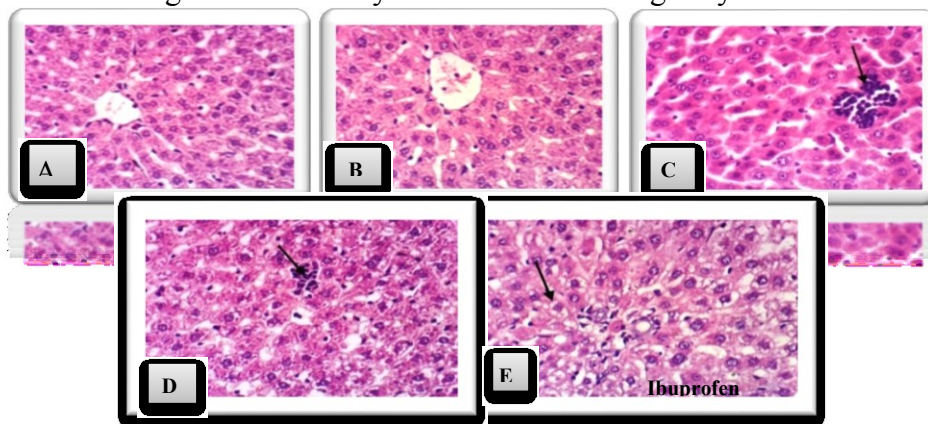
Table (7) & figure (1) revealed that the main findings in liver structure of groups were presence of a wide range of inflammatory and degenerative changes with significant differences between the group which submitted to ibuprofen only and the other groups that have been treated with garlic peel bread or onion peel bread. OPB and GPB groups showed a significant decrease in Vacuolation and Portal fibroplasia. Also Focal hepatic necrosis associated with inflammatory cells infiltration had changed in groups that received bread with onion/garlic peel powder.

**Table (7): Histopathological findings in livers from rats of different groups.**

Lesions	Control (-)	Control +CB	Control (+)	onion and garlic by-products bread	
				OPB	GPB
Kupffer cells activation	-	-	+	-	-
Apoptosis of hepatocytes	-	-	-	-	-
Vacuolation (or hydropic) of hepatocytes	-	-	++	++/+	+
Focal hepatic necrosis associated with inflammatory cells infiltration	-	-	++	-	-
Sinusoidal leukocytosis	-	-	+	-	-
Portal fibroplasia	-	-	++	+/-	+

CB, control bread; OPB, onion peel bread; GPB, garlic peel bread .sign (-): no change; (+): mild change ;(++) : moderate change and (+++): severe change

Our results are nearly similar to that of **Emaraa et al.,(2015)** who studied effect of garlic peel extract on rats liver fibrosis; and found that rats treated with garlic extract revealed marked reduction in both the inflammatory reactions and degenerative changes ,as well as, reduction of fibrosis , also added that garlic contains organosulfur compounds which affect not only via its antioxidant properties, but also, through its effect on the tissue transglutaminase enzyme involved in collagen synthesis



**Figure (1):** Liver histological structure of (A), control; (B), control + CB; ( C), positive control ;  
(D), OPB and (E), GPB groups (H&E 400).

## Kidney

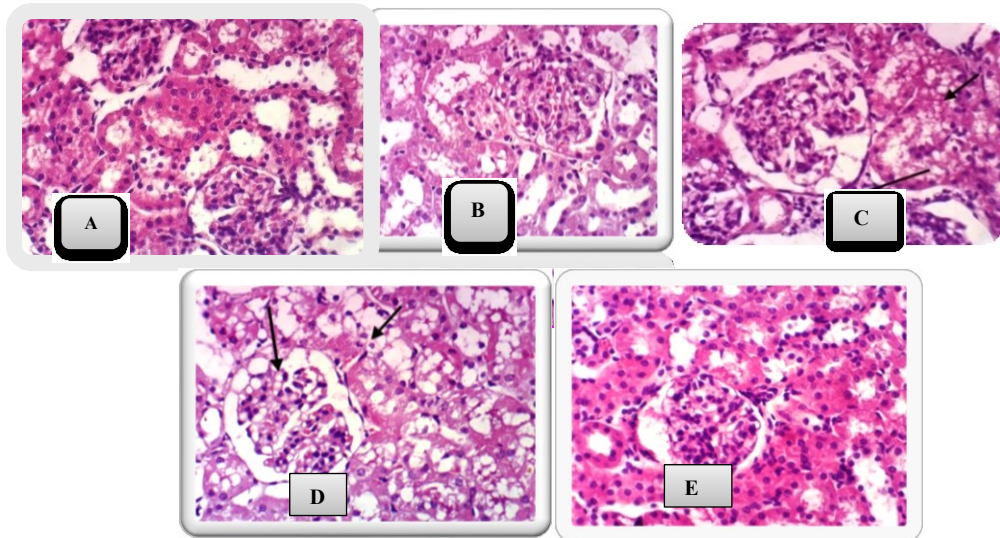
Results of histological study in Table (8) & Figure (2) supported the results of biochemical parameters. Microscopically, kidneys of rats from control and (control +CB) groups revealed the normal histological structure of renal parenchyma. In contrary, kidneys of rats from ibuprofen group showed proteinaceous materials in the lumen of some renal tubules and severe vacuolation of epithelial lining renal tubules and interstitial inflammatory cells.

Table (8) : Histopathological findings in Kidney of rats of different groups.

Lesions	Control(-)	Control +CB	Control (+)	onion and garlic by-products bread	
				OPB	GPB
Vacuolation of renal tubular epithelium	-	-	+++	+/-	++/+
Vacuolation and congestion of glomerular tuft	-	-	+++	+/-	+/-
inflammatory cells infiltration	-	-	++	-	-
proteinaceous materials in the lumen of some renal tubules	-	-	++	-	-

CB, control bread; OPB, onion peel bread; GPB, garlic peel bread. sign (-): no change; (+): mild change ;(++) : moderate change and (+++): severe change





**Figure (2):** Kidney histological structure of (A), control; (B), control + CB; ( C), positive control ;  
(D), OPB and (E), GPB groups (H&E 400).

Results of **Kause *et al.*, (2005)** and **Onay *et al.*, (2009)** proved that high dose of ibuprofen affect hepatic and carry a risk of loss of renal function by reduced renal plasma flow caused by a decrease in prostaglandins and acute interstitial nephritis which is characterized by the presence of an inflammatory cell infiltrate in the interstitial of the kidney.

In conclusion, data of the present study revealed that when onion and garlic by-products (peel powder 10%) administration with ibuprofen significantly alleviation of cholesterol, triglyceride and LDL-C levels as well as ALT and AST activities and ameliorate most inflammatory and fibrotic changes in livers and kidneys tissues.

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## التأثيرات التحسينية المحتملة للمنتجات الثانوية للبصل والثوم ضد سمية الإيبوبروفين في الفئران

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تحتوي قشور البصل والثوم على العديد من المركبات الطبيعية التي لها تأثير مضاد للأكسدة مثل البولي فينول والفلافونويد وعلى الرغم من أهميتها لا يهتم الإنسان بتناول هذه الأجزاء . الإيبوبروفين هو دواء مضاد للالتهابات، يمكن أن يؤثر على وظائف الكبد والكلية وأمراض الدم في الفئران. هدفت الدراسة الحالية إلى دراسة تأثير إضافة النواتج الثانوية للبصل والثوم (القشور) على سمية الإيبوبروفين في الفئران. تم تقسيم خمسة وعشرون من ذكور الفئران إلى مجموعتين أساسيتين، المجموعة الأساسية الأولى (١٠ فئران) وقسمت إلى مجموعتين، (١) تتغذى على النظام الغذائي القاعدي، (٢) تتغذى على النظام الغذائي + (٢٥ ٪ من وجبة الخبز). المجموعة الرئيسية الثانية (١٥ فأر) تم إعطاؤها (٤٠ ملجم من الإيبوبروفين / كجم من وزن الجسم) لمدة ٤ أسابيع ، وصنفت إلي ثلاث مجموعات فرعية على النحو التالي: المجموعة (٣) تم تغذيتها على النظام الغذائي (المجموعة المعاملة بالإيبوبروفين) ، مجموعة (٥،٤) تغذت على ٢٥ ٪ خبز مضاف إليه نسبة ١٠ ٪ من مسحوق قشر البصل (OPP) أو مسحوق قشر الثوم (GPP) على التوالي. أشارت بيانات التحليل الكميائي إلى أن الإيبوبروفين تسبب في زيادة ملحوظة ( $p \leq 0.05$ ) في مستويات الجليسيريدات الثلاثية والكليسترول والبروتينات الدهنية منخفضة الكثافة، وكذلك نشاط مستويات إنزيمات الكبد (AST,ALT) مقارنة بالمجموعة الضابطة. أظهرت التغذية على ١٠ ٪ من الخبز المضاف له قشور البصل (OPB) والخبز المضاف له قشور الثوم (GPB) تحسنا ملحوظا ( $p \leq 0.05$ ) في هذه المستويات. كما أشارت النتيجة إلى أن الإيبوبروفين رفع تركيز مصل اليوريا والكرياتينين في المجموعة المعاملة بالإيبوبروفين وخفضت في مستويات الهيموجلوبين والهيماتوكريت و كرات الدم الحمراء مقارنة مع المجموعة الضابطة. على الجانب الآخر ، المجموعات التي تناولت الخبز المضاف له قشور البصل و الثوم تحسنا ملحوظا ( $p \leq 0.05$ ) في هذه المستويات إلى وضعها الطبيعي تقريبا ، هذه النتائج تم تأكيدها من خلال الفحص النسيجي للكبد والكلية.

**الكلمات المفتاحية:** عائلة *Allium* ، مسحوق القشور، العقاقير المضادة للالتهابات، مؤشرات الدم، فحص الأنسجة.