

# Potential Effects of Food Processing Byproducts on Neurological and Immunological Disorders of Obese Rats

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## ABSTRACT

The present study aims to explore the effect of three byproducts that result from food processing processes, namely onion and bananas peels, and apricot seeds on neurological and immunological disorders of obese rats. Feeding of rats on diet induced obesity (DIO) leads to increase the BW than the control group. At the end of the experiment (8 weeks), rats of the normal group recorded 131.33% of baseline for the BW while obese group was 197.25% of baseline. Replacement of diets starch with banana peel powder (BPP), onion skin powder (OSP), apricot seeds powder (ASP) and their mixture induced significant decreasing on BW of the obese rats which recorded 177.85, 155.41, 173.59 and 144.83% of baseline, respectively. The higher effect on weigh decreasing was recorded for the plant parts mixtures followed by OSP, ASP and BPP, respectively. On the other side data has demonstrated the potency of the selected food processing byproducts including BPP, ROSP, ASP and their mixture to ameliorate the neurological (dopamine and serotonin content and acetylcholine esterase activity) and immunological (serum albumin and tumor necrosis factor- $\alpha$  content, and protease activity) disorders in obese rats. These findings provide a basis for the use of the selected food processing byproducts for the prevention and early treatment of obesity. Also, the data support the benefits of dietary modification, including food processing byproducts supplementation, in alleviating neurological and immunological disorders associated obesity.

**Keywords:** Body weight banana peel, onion skin, apricot seeds, acetylcholine esterase, dopamine, serotonin, albumin, tumor necrosis factor and protease activity.

## INTRODUCTION

Obesity is a complex disease that results from the inappropriate control of the body's energy balance leads to excess adipose tissue mass. Over half of adults are overweight and 19.5% of the adult populations are obese in Organization for Economic Co-operation and Development member countries (OECD, 2017). According to the World Health Organization (WHO), there are more than one billion overweight adults in the world. At least 300 million of them are clinically obese

(WHO, 2006) and of these about 115 million come from developing countries (WHO and Dini, 2006). Egypt, a developing country, is undergoing rapid urbanization changes. This has a direct impact on its people's dietary habits and physical activity patterns. According to national studies, it is common to skip meals and to replace them with daily snacks, and most of these snacks are high in calories and low in nutrients. So, Egypt appeared in No. 8 ranking among the countries of the world where obesity - adult prevalence rate, 30.3% ([http://www.indexmundi.com/egypt/obesity\\_adult\\_prevalence\\_rate.html](http://www.indexmundi.com/egypt/obesity_adult_prevalence_rate.html)).

It is well known that obesity is a risk factor for several malignancies including hepatic, pancreatic, thyroid, uterine and colon cancer and for diabetes mellitus and cardiovascular diseases (Gukovsky *et al.*, 2013; Alzahrani *et al.*, 2014 and Mokdad, 2003). Also, obesity is consequent to a loss of the balance between energy intake and expenditure over long periods of time, and the brain plays a principal role in controlling and inhibiting the pre-potent responses to foods (Morton *et al.*, 2014). On the other side, epidemiologic studies suggest that obesity is known as risk factor for neurodegenerative diseases (Loef and Walach, 2013) such as Alzheimer's disease (AD). AD is a the most prevalent form of dementia which characterized by a cumulative decline in memory, cognitive functions and behavior in the elderly population (Albert *et al.*, 2011). Several studies reported that correlation studies have shown that obesity was associated with decreased brain volume, altered brain structure and function deficits in learning, memory and executive function, alterations and reduction in focal gray matter volume (Pannacciulli *et al.*, 2006 and Pistell *et al.*, 2010).

Epidemiological studies have reported that consumption of plant parts imparts health benefits, e.g. reduced risk of diabetics, obesity, coronary heart disease, stroke, and certain types of cancer (Elhassaneen *et al.*, 2016 a-d; and Elmaadawy *et al.*, 2016). Apart from dietary fiber, these health benefits are mainly attributed to many organic micronutrients including

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phytochemicals, vitamins and others. Food processing in the arab countries represent a large proportion of waste/byproducts was estimated at 18.14 million tons per year and represent remnants of vegetables and fruit processing about 6.14% of this amount ([http://elasaala.blogspot.com/2012/01/blog-post\\_2703.html](http://elasaala.blogspot.com/2012/01/blog-post_2703.html)). Waste in the food processing is characterized by a high ratio of product-specific waste/by-products. Food processing by-products/plant parts could be considered a good source of phytochemicals. They are a large group of plant-derived compounds such as phenolic compounds (phenolic acids and flavonoids), terpenes, volatile oils and nitrogen compounds (indoles), and organosulphur containing compounds hypothesized to be responsible for much of the disease protection including obesity provided by diets high in by-products of fruits, vegetables, herbs, beans, cereals, plant-based beverages etc (Elhassaneen *et al.*, 2016 a-d). We will limit our study here to three of the by-products that result from food processing activities which are onion and banana peels, and apricot seed/kernels\_apricot (*Prunus armeniaca* L.; *Rosaceae* family) is mostly grown in Mediterranean countries, Pakistan, Russia, USA and Iran. Apricot seeds are waste of the apricot processing industry. It is used partially used as apricot seed oil in cosmetics and peeled seeds as a raw material for the processing of persipan (reviewed in Schieber *et al.*, 2001). Apricot seed/kernel oil is a rich source of monounsaturated fatty acids (MUFA) and polyunsaturated fatty acids (PUFA), including mainly oleic (~70%) and linoleic acids, respectively. Additionally, apricot kernel oil could be considered as a good source of different bioactive compounds such as phytosterols and tocopherols (Hassan, 2011 and Taha, 2019). Onion (*Allium cepa* L.) belongs to family, *Alliaceae* and represent one of the most important crop around the world including Egypt. The amount of onion waste produced annually in the European Union is estimated at approximately 450,000 tons. Onion skins are a source of flavour components and fiber compounds and particularly rich in quercetin glycosides, phenolics, carotenoids (Hertog, *et al.*, 1992; Waldron, 200, Elhassaneen and Sanad, 2009, and Hassan, 2015). Banana (*Musa sapientum*) belongs to the family *Musaceae* which has already provided human with food, tools and shelter prior to recorded history (Ngwang, 2015). Its play an important role in the economy and food security of many wet tropical regions in the world (Coulibaly *et al.*, 2007). Peels represent about 30 – 40 g / 100 g of fruit weight. Significant quantities of banana peels equivalent to 40% of the total weight fresh banana are generated as a waste product in industries producing banana based products (Ragab *et al.*, 2016). Banana fruit peel has a broad spectrum of biological activities and include be used as a good

source of antioxidant and antitumor agent (Kumar *et al.*, 2012). In addition to banana peels extracts are promising sources of natural antioxidants total phenol (Kumar, 2015) and Bioactive compounds such as alkaloids, anthocyanin, flavonoids, glycosides, phlobatannins, tannins and terpenoids.

Many studies have discovered the protective effect of such plant parts on different complications including serum lipid profile, hyperglycemia, cardiovascular disease, atherosclerosis, liver and kidney functions (Elhassaneen *et al.*, 2016 a-d; and Elmaadawy *et al.*, 2016) in obese experimental animal model. But till now, there are no studies were conducted to explore the effect of these foods processing byproducts consumption on neurological and immunological complications in obese rat. To fill the information gap, the present study was designed to investigate whether consumption of apricot kernels, onion skin, banana peels and their mixture would alleviate neurological and immunological disorders in obesity rat model.

## MATERIAL AND METHODS

### MATERIALS

**By-products:** Yellow onion skin (*Allium cepa* L.) was obtained from the New Beni Suef company for Preservation, Dehydration and Industrialization of Vegetables, Beni Suef Elgudida City, Beni Suef, Egypt; and banana (*Musa sapientum*) and apricot (*Prunus armeniaca* L.) fruits were obtained from Benha City market, Benha Governorate, Egypt, transported to the laboratory and used immediately for peels and seeds powder preparation.

**Chemicals, solvents and buffers:** All chemicals, solvents and buffers (except mentioned on site) were purchased from Al-Gomhoryia Company for Trading Drugs, Chemicals and Medical Equipment's, Cairo, Egypt. Serotonin, dihydroxybenzylamine (DHBA) as internal standard, perchloric acid (HClO<sub>4</sub>), Na<sub>2</sub>HPO<sub>4</sub>, citric acid, Na<sub>2</sub>EDTA, and heptanesulfonic acid (HSA) were purchased from Egyptian agent of Sigma Chemical Co. (St. Louis, MO). The water employed in all solutions was purified through a Nanopure II system (Thermo Fisher Scientific, Waltham, MA)

### METHODS

#### Preparation of by-products peel powder

##### Banana peels powder (BPP)

Banana fruits were washed, peeled and sliced to get the peels then dried in a hot air oven (Horizontal Forced Air Drier, Proctor and Schwartz Inc., Philadelphia, PA) at 55 °C for 14 hours. The dried peels were ground into a fine powder in high mixer speed (Moulinex Egypt, Al-Araby Co., Egypt). The material that passed through an 80 mesh sieve was retained for use.

### Onion peel powder (OPP)

Yellow onion skin peel were washed and then dried in a hot air oven (Horizontal Forced Air Drier, Proctor and Schwartz Inc., Philadelphia, PA) at 60 °C for 12 hours. The dried skins were milled to a fine powder in high mixer speed (Moulinex Egypt, Al-Araby Co., Egypt). The material that passed through an 80 mesh sieve was retained for use.

### Apricot seed powder (ASP)

Unripe apricot fruits were washed, sliced to get the kernels and crushed to extract the seeds. The seeds were treated to remove all toxic substances according to the methods mentioned by Galanakis, (2019) and dried at 60°C for 8 hours in hot air oven (AFOS Mini Smoker, England). Dried parts followed by milling with miller (Retsch Micro Universal Bench Top Grinder, Germany) to produce the proper powder type. The material that passed through an 80 mesh sieve was retained for use.

## Biological Experiments

### Animals

Animals used in this study, adult male albino rats (145±10 g per each) were obtained from Research Institute of Ophthalmology, Medical Analysis Department, Giza, Egypt.

### Basal Diet

The basic/standard diet prepared according to the following recipes as mentioned by AIN, (1993) as follow: casein/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 Diet Induced Obesity (DIO) was prepared according to Research Diets, Inc. NJ, USA, as follow: casein, 80 mesh (23.3%), L-cystine (0.35%), corn starch (8.48%), maltodextrin (11.65%), sucrose (20.14%), soybean oil (2.91%), animal/lamb fat (20.69%), mineral mixture (1.17%), dicalcium phosphate (1.52%), calcium carbonate (0.64%), potassium citrate.1 H<sub>2</sub>O (1.92%), vitamin mixture (1.17%), choline bitartrate (0.23%). The used vitamins and salt mixtures components were constituted according to Campbell, (1963) and Hegsted, (1941), respectively.

### Experimental design

All biological experiments performed a complied with the rulings of the Institute of Laboratory Animal Resources, Commission on life Sciences, National Research Council (NRC, 1996). Rats (n= 36 rats), 145±10 g per each, were housed individually in wire cages in a room maintained at 24 ± 2 °C and kept under normal healthy conditions. 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, the first group (Group 1,

6 rats) still fed on basal diet and the other main group (30 rats) was feed with diet-induced obesity (DIO) (Research Diets, Inc. NJ, USA) for 8 weeks which classified into sex sub groups as follow: group (2), fed on DIO as a positive control; group (3), fed on DIO containing 5 % BPP; group (4), fed on DIO containing 5 % ; OSP, group (5), fed on DIO containing 5 % ASP and group (6): fed on DIO containing 5 % mixture, BPP, OSP and ASP by equal parts. Body weight gain (as percent of initial weight) was assayed every week in rats.

### Blood sampling

At the end of experiment period, eight weeks, blood samples were collected from rats after twelve hours fasting using the abdominal aorta and rats were scarified under ethyl ether anesthetized. Blood samples were received into clean dry centrifuge tubes and left to clot at room temperature then centrifuged for ten minutes at 3000 rpm to separate the serum according to Drury and Wallington, (1980). Serum was carefully aspirate, transferred to clean tubes and stored at -20 °C until use.

### Hematological analysis

#### Level of Dopamine and serotonin

Levels of dopamine and serotonin in serum were measured by Elisa methods and LDN kits (Germany).

#### Acetylcholinestrase (AChE) determination

Serum AChE activity (Rappaport units/mL) was assayed according to the colorimetric method mentioned by Gowenlock, (1988).

#### Albumin

Albumin was determined in plasma using kits purchased from El-Nasr Pharmaceutical Chemicals Company, Cairo, Egypt.

#### Protease activity assay

The protease activity was determined according to the method of Rindernecitt *et al.*, (1968). In brief, 100 µl of plasma were added to 40 µl of buffer (150 mM Tris base, 30 mM CaCl<sub>2</sub>, 0.05% Brij 35) and 50 µl of protease substrate (20% Hide powder azure, HPA, 20 % sucrose, 0.05% Brij). The tubes contents were incubated at 37°C with continuous shaking for 2 hours. The reaction was stopped by the addition of 50 µl of 10% TCA and the tubes were stored at 4 °C for about 15 min. After spined the tubes at 8500 rpm for 5 min, the supernatants were transferred to new tubes and the absorbencies were measured at 540 nm. Blank tubes were prepared by the same previous steps without samples addition.

#### TNF-α assay

TNF-α was determined by a sandwich enzyme-linked immunosorbent assay (ELISA), utilizing two monoclonal antibodies directed against separate

antigenic determinants on rat TNF-  $\alpha$ . The kits for the assay were provided by Adlitteram Diagnostic Laboratories Inc. (San Diego, CA, USA).

### Statistical Analysis

All samples analysis were carried in tree times and recorded as mean $\pm$  standard deviation (SD). Statistical analysis was done by using Student *t*-test and MINITAB-12 computer program (Minitab Inc., State College, PA).

## RESULTS AND DISCUSSION

### The effect of selected food processing byproducts on body weight of obese rats

The effect of selected food processing byproducts on body weight of obese rats was shown in Table (1) and Figure (1). From such data it could be noticed that feeding of rats on diet induced obesity (DIO) leads to increase the BW than the control group. At the end of the experiment (8 weeks), rats of the normal group recorded 131.33% of baseline for the body weight while obese group was 197.25% of baseline. Alteration of diets starch with banana peel powder (BPP), onion skin powder (OSP), apricot seeds powder (ASP) and their mixture exhibited significant ( $p \leq 0.05$ ) decreasing on body weight of the obese rats which recorded 177.85, 155.41, 173.59 and 144.83% of baseline, respectively. The higher effect on weigh decreasing was recorded for the plant parts mixtures followed by OSP, ASP and BPP, respectively. The effect of different food processing byproducts including OSP, ASP and BPP in the control of obesity is the main topics of several studies (El-Safty, 2012; Bonet *et al.*, 2015; Elmaadawy *et al.*, 2016; Sayed Ahmed, 2016; Aly *et al.*, 2017; Mahran *et al.*, 2018-a and Saad *et al.*, 2018).

The positive effects of such selected foods processing byproducts regarding the control of the obesity could be attributed to their high level content of different categories of phytochemicals including alkaloids, phenolic acids, anthocyanins, carotenoids, flavonols, organosulfur compounds and phytosterols (Onyeneho and Hettiarachchy, 1993; Rodriguez *et al.*, 1994; Velioglu *et al.*, 1998; Beattic *et al.*, 2005; Bedawy, 2008; Hassan, 2011; Mahran *et al.*, 2018-b and Saad *et al.*, 2018). Also,

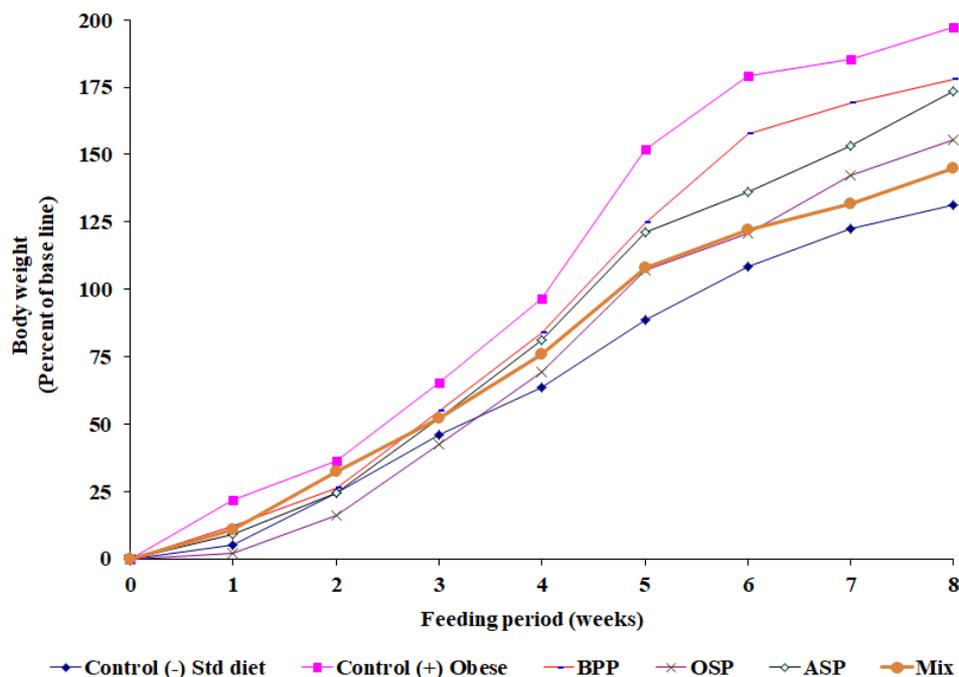
Erdogan-orhan and Kartal, (2010) reported that apricot seeds oil (ASO) is a rich source of monounsaturated fatty acids and polyunsaturated fatty acids, including mainly oleic (about 70%) and linoleic acids, respectively. In addition, ASO could be considered as a good source of bioactive compounds such as tocopherols and phytosterols consisting mainly of the  $\alpha$ -isomer and  $\beta$ -sitosterol, respectively. Due to its high content of essential fatty acids, ASO is considered as a healthy supplement in diet.

Such phytochemicals groups have been shown to impact gene expression and cell (including adipocyte) function through one or several of the following mechanisms, interacting with several transcription factors of the nuclear receptor superfamily, interfering with the activity of other transcription factors, modulating signaling pathways which are associated with inflammatory and oxidative stress responses, and extra-genomic actions such scavenging of reactive species (Constance *et al.*, 2003; Bray, 2004; Bonet *et al.*, 2015, Elmaadawy *et al.*, 2016; Sayed Ahmed, 2016 and Mahran *et al.*, 2018-a) . Subsequently, all of these mechanisms participate to their action control of adipocyte function, adiposity and obesity.

**Table 1. The effect of selected food processing byproducts on body weight gain (g) of obese rats\***

Groups	Feeding period (weeks)								
	0	1	2	3	4	5	6	7	8
Control (-) Std diet	151.02	158.57	187.72	220.36	247.06	285.11	314.97	335.79	349.35 <sup>e</sup>
Control (+) Obese	151.02	183.63	205.53	249.45	296.82	380.49	421.40	430.83	448.91 <sup>a</sup>
Banana peel powder (BPP)	151.02	164.99	187.60	229.94	273.60	334.26	356.69	382.60	413.18 <sup>b</sup>
Onion skin powder (OSP)	151.02	154.26	175.40	214.98	255.81	312.52	333.49	366.03	385.72 <sup>c</sup>
Apricot seeds powder (ASP)	151.02	169.22	190.46	233.44	277.77	339.35	388.81	406.35	419.61 <sup>b</sup>
Mixture (BPP+ OSP+ASP)	151.02	167.18	199.69	229.61	265.63	314.11	335.19	350.10	369.75 <sup>d</sup>

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



**Fig. 1.** The effect of selected food processing byproducts on body weight gain (Percent of baseline) of obese rats\*

\*BPP, banana peel powder; OSP, onion skin powder; ASP, apricot seeds powder and Mix, mixture of BPP, OSP and ASP by equal parts.

### The effect of selected food processing byproducts on neurological complications of obese rats

#### a) Serum neurotransmitters (dopamine and serotonin)

The effect of selected food processing byproducts in neurotransmitters, dopamine and serotonin of obese rats were shown in Table (2) and Figure (2). Such data indicated that obesity induced a significant ( $p \leq 0.05$ ) decreasing in dopamine (-14.93%) and serotonin (-13.91%) levels compared to the normal group. Alteration of BPP, OSP, ASP and their mixture exhibited significant ( $p \leq 0.05$ ) increasing on serum dopamine and serotonin levels by the ratio of -10.34, -6.95, -7.96 and -5.07%; and -11.48, -8.62, -10.97 and -5.93%, respectively. The highest improvement in neurotransmitters disorders induced by obesity in rats were recorded for the byproducts mixture treatment followed by OSP, ASP, and BPP, respectively.

Dopamine and serotonin (catecholamines) are neurotransmitters that are produced in different zones of the body including of the abdomen, back and brain. Dysfunction of the dopamine and serotonin system has been implicated in different nervous system diseases such as a complicated with obesity (Nam *et al.*, 2018).

Several studies reported that dopamine and serotonin as neurotransmitters involved in the regulation of food intake and body weight (Lam *et al.*, (2010). Also, Nam *et al.*, (2018) investigated relationship between obesity and the availabilities of striatal dopamine and extra-striatal serotonin transporters. They also found that obesity has an effect on midbrain serotonin transporter availability and body mass index was correlated with pontine serotonin transporter availability but not with striatal dopamine transporter availability. On the other side, Morton *et al.*, (2014) reported that brain plays a critical role in controlling and inhibiting the prepotent responses to foods.

Our data revealed that variety of bioactive compounds such as found in the present selected food processing byproducts i.e. BPP, OSP, ASP and their mixture that demonstrate neurological disorders potential amelioration effects. That decreasing in neurotoxic effects was depending on the type of the food processing byproducts applied. Neurological disorders treatment is described as the ability of bioactive compounds such antioxidants, to promote healthy neurological functions. Certain bioactive compounds have been shown in experimental studies to have neurostimulating properties; that is, they appear to

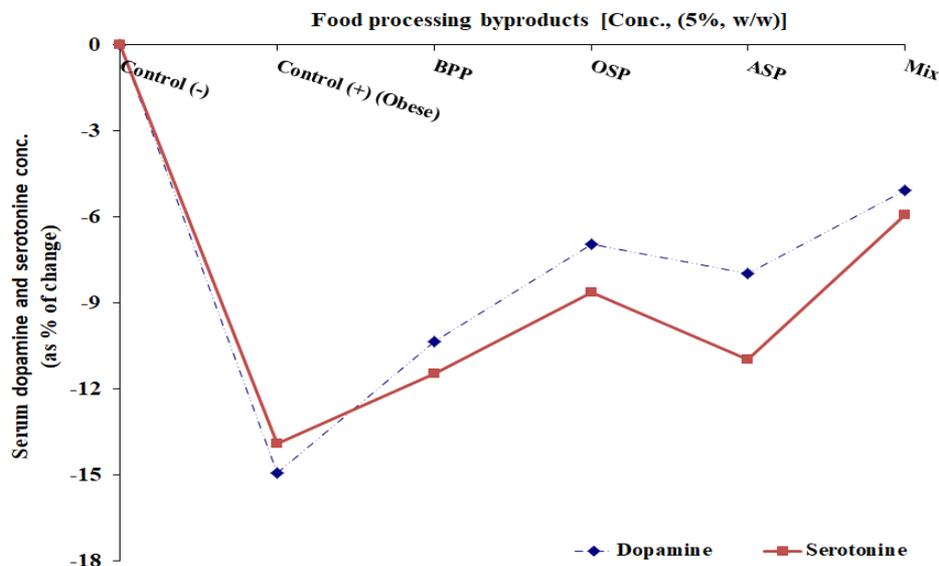
help stimulate neurotransmittance mechanisms by activating catecholamine's transmitters such dopamine and serotonin (Mousseau, and Baker, 2012; and Hugo *et al.*, 2016). To interpret such mechanism, L'opez-P'erez *et al.*, (2015) mentioned that dopamine is breakdown enzymatically to its inactive metabolites by different enzymes mainly monoamine oxidase (MAO). The inhibition of MAO which could be induced by obesity and/or obesity complications has been considered as an adjunctive therapy in neurodegenerative disorders. Such phenomena was observed by in Alzheimer's and Parkinson's diseases (Mousseau and Baker, 2012).

Beside MAO inhibitors, hydrogen peroxide ( $H_2O_2$ ) production as the results of oxidative stress (OS) induced by obesity and/or its complications could be a co-factor could be helped in neurodegenerative disorders (Hugo *et al.*, 2016). Neurons have different antioxidant systems, for example, catalase (CAT) and glutathione (GSH), to cope with  $H_2O_2$  production. In similar studies, Mahran *et al.*, (2018) and Elbasouny *et al.*, (2019) reported that different plant parts including the selected food processing byproducts inducing the different antioxidant systems in live cells such serum

**Table 2. The effect of selected food processing byproducts on serum dopamine and serotonin of obese rats\***

Value	Control (-) Std diet	Control (+) Obese	Food processing byproducts Conc. (5%, w/w)			
			Banana peel powder (BPP)	Onion skin powder (OSP)	Apricot seeds powder (ASP)	Mixture (BPP + OSP + ASP)
Serum dopamine level (pg/ml)						
Mean	89.2 <sup>a</sup>	75.89 <sup>c</sup>	79.99 <sup>bc</sup>	83.01 <sup>b</sup>	82.11 <sup>b</sup>	84.69 <sup>b</sup>
SD	5.65	6.11	4.78	8.10	5.21	7.55
% of Change	0.00	-14.93	-10.34	-6.95	-7.96	-5.07
Serum serotonin level (ng/ml)						
Mean	220.32 <sup>a</sup>	189.67 <sup>d</sup>	195.03 <sup>c</sup>	201.32 <sup>bc</sup>	196.15 <sup>c</sup>	207.25 <sup>b</sup>
SD	18.98	19.36	9.23	14.23	15.25	11.45
% of Change	0.00	-13.91	-11.48	-8.62	-10.97	-5.93

\* Means in the same row with different superscript letters are significantly different at  $p \leq 0.05$ .



**Fig. 2. The effect of selected food processing byproducts on serum dopamine and serotonin concentration (as % of change) of obese rats\***

\*BPP, banana peel powder; OSP, onion skin powder; ASP, apricot seeds powder and Mix, Mixture of BPP, OSP and ASP by equal parts

glutathione (GSH) and antioxidant enzymes including CAT which cope H<sub>2</sub>O<sub>2</sub> and neutralization/prevents MAO inhibitors. Also, the study of Thomsen, (2013) reviewed that OS and H<sub>2</sub>O<sub>2</sub> have been implicated as the underlying factors in the initiation and progression of Parkinson’s disease. Increases in endogenous H<sub>2</sub>O<sub>2</sub> in the dorsal striatum attenuated electrically evoked dopamine release and also decreased basal dopamine levels. The present data with the others suggested that the highest therapeutic effect was recorded for the mixture of the selected food processing byproducts could be attributed to the antagonism effects of their content of different categories bioactive compounds. Such observation was confirmed by the

studies of Elmaadawy *et al.*, (2016); Sayed Ahmed, (2016) and Mahran *et al.*, (2018-a).

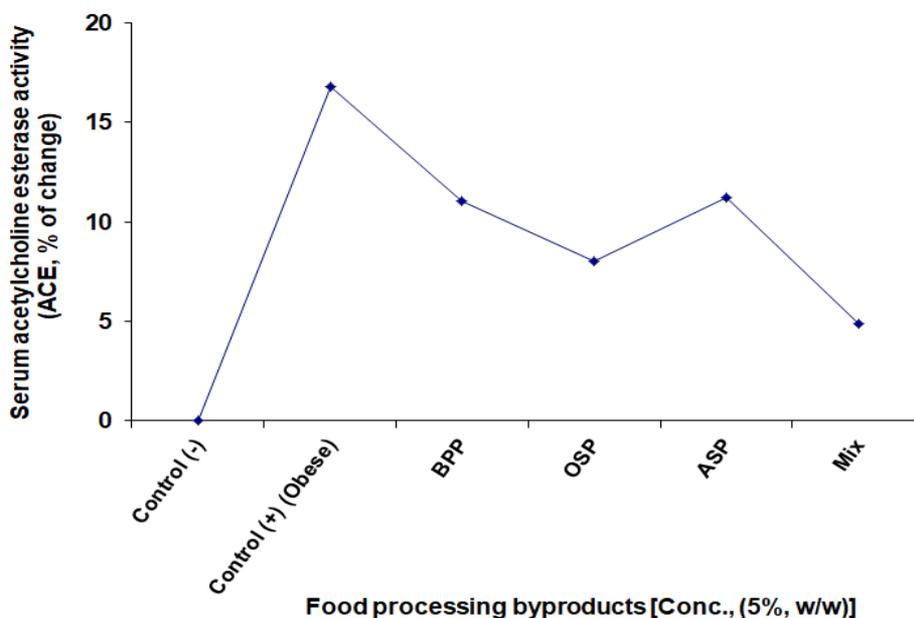
**b. Serum acetylcholine esterase (AChE) activity**

The effect of selected food processing byproducts in serum AChE activity of obese rats was shown in Table (3) and Figure (3). Such data indicated that obesity induced a significant (p≤0.05) increasing in serum AChE (16.80%) level compared to the normal group. Alteration of BPP, OSP, ASP and their mixture exhibited significant (p≤0.05) decreasing on serum AChE levels by the ratio of 11.06, 8.04, 11.22 and 4.91%, respectively. The highest improvement in serum AChE activity induced by obesity in rats was recorded for the byproducts mixture treatment followed by OSP, BPP, and ASP, respectively.

**Table3. The effect of selected food processing byproducts on serum acetylcholine esterase (ACE, Rappapor U/mL) of obese rats\***

Value	Control (-) Std diet	Control (+) Obese	Food processing byproducts (5%, w/w)			
			Banana peel powder (BPP)	Onion skin powder (OSP)	Apricot seeds powder (ASP)	Mixture (BPP + OSP + ASP)
Mean	67.45 <sup>c</sup>	78.78 <sup>a</sup>	74.91 <sup>a</sup>	72.87 <sup>ab</sup>	75.02 <sup>a</sup>	70.76 <sup>ab</sup>
SD	4.11	9.65	5.86	7.43	5.67	7.11
% of Change	0.00	16.80	11.06	8.04	11.22	4.91

\* Means in the same row with different superscript letters are significantly different at p≤ 0.05.



**Fig. 3. The effect of selected food processing byproducts on serum acetylcholine esterase (as % of change) of obese rats\***

\*BPP, banana peel powder; OSP, onion skin powder; ASP, apricot seeds powder and Mix, mixture of BPP, OSP and ASP by equal parts

AChE represent an acetylcholine hydrolyzing enzyme that is accountable for the termination of cholinergic response. An increased AChE activity in brain excite memory deficits as well as oxidative stress (Melo *et al.*, 2003). In present study, obesity induced increase in AChE activity. This observation is confirmed in several previous studies (Paes *et al.*, 2006 and Zahra *et al.*, 2017). They also found that long-term of pomegranate extracts feeding reduce the AChE activity. The increasing of AChE activity could be attributed to  $Ca^{2+}$  influx-mediated oxidative stress caused by Amyloid beta peptides. Our data with the other explain the mechanism of anticholinesterase activity of food processing byproducts which may be due to antioxidant activities of their bioactive compounds such as phenolics, alkaloids and carotenoids. Such compounds protect of neural cell from OS insults by different mechanisms. One of these mechanisms is preventing the influx of  $Ca^{2+}$  despite high levels of ROS, increasing intracellular GSH and directly lowering levels of ROS (Ishige *et al.*, 2001). These findings highlight the neuroprotective effects of food processing byproducts and one of mechanisms is the inhibition of AChE and the stimulation of antioxidant activities.

### **The effect of food processing byproducts on serum immunological parameters of obese rats**

#### **a- Serum albumin content and protease activity**

The effect of selected food processing byproducts in immunological complications, serum albumin and protease activity, of obese rats were shown in Table (4) and Figure (4). Such data indicated that obesity induced a significant ( $p \leq 0.05$ ) decreasing in albumin (-13.54%) and protease activity (-21.71%) levels compared to the normal group. Alteration of BPP, OSP, ASP and their mixture exhibited significant ( $p \leq 0.05$ ) increasing on serum dopamine and serotonin levels by the ratio of -10.34, -6.95, -7.96 and -8.80, -8.13, -10.56 and -4.24%, and -19.68, -16.52, -18.78 and -14.47%, respectively. The highest improvement in immunological disorders induced by obesity in rats was recorded for the byproducts mixture treatment followed by OSP, ASP, and BPP, respectively.

In general, it is knowing that albumin is an important metal binding protein and sacrificial antioxidant that can bind metals (copper tightly and iron weakly) to its surface serving as a target for their related free radical reactions. Thus, albumin inhibits copper ion dependent lipid peroxidation (Gutteridge and Wilkins, 1983). It was reported that hypo-albuminaemia is most frequent in the presence of advanced chronic liver diseases. Hence decline in albumin can be deemed as a useful index of the severity of cellular dysfunction in

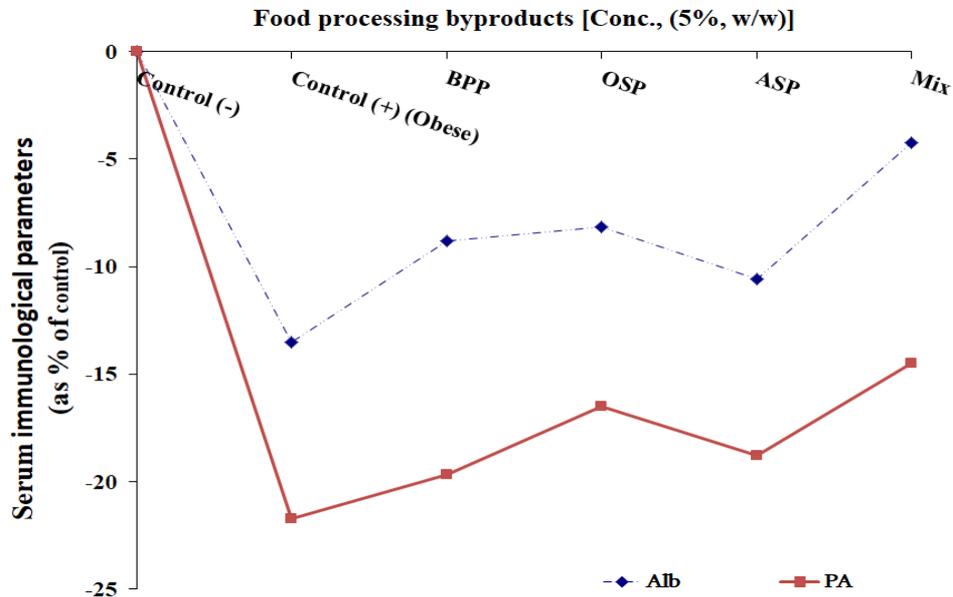
chronic liver diseases. So, it is worthy to report that feeding with some food processing byproducts such BPP, OSP and ASP produced significant ( $p \leq 0.05$ ) improvement in serum albumin compared to obese group. Such observations are in accordance with that reported by Sayed Ahmed, (2016) who found that pretreatment with plant parts such potato, onion and mango peels, and cauliflower leaves (contains almost the bioactive compounds found in the tested byproducts) the produced significant ( $p \leq 0.05$ ) improvement in serum albumin compared to normal group. On the other side, several studies revealed that proteases enzymes could play an important role in immunological functions and humoral host defense (Troll and Kennedy, 1993; Elhassaneen, 1996 and Elmaadawy *et al.*, 2016). Another studies highlighted the direct relationship between protease expression and protozoal virulence have implicated proteases as being involved in pathogenicity. In similar studies, protease activity was found decreased in obesity and its complications as found in the present study (Elmaadawy *et al.*, 2016, Aly *et al.*, 2017 and Elbasouny *et al.*, 2019). Also, co-treatment of  $CCl_4$  and plant parts extracts exhibited therapeutic effects through increasing the immunotoxic effects i.e. albumin level and protease activity in liver cells

(Elhassaneen *et al.*, 1997 and Elhassaneen and Tawfik, 2001). In the present study, the selected food processing byproducts i.e. ASP, ROSP, BPP and their mixture exhibited immune-modulatory potential. Immunomodulation is described as the ability of a nutrient, herb, or other substance to promote healthy immune function (Haider *et al.*, 2019). Certain phyto-bioactive compounds (such as found in ASP, ROSP and BPP) have been shown in experimental studies to have immune-stimulating properties; that is, they appear to help stimulate viral defense mechanisms by activating immune cells such as macrophages, lymphocytes (T and B-cell, and natural killer cell), and the cytokines (e.g., interleukin, interferon, and tumor necrosis factor) (Roesler, 1991 and Suresh and Vasudevan, 1994). That decreasing rate in immunotoxic effects was depending on the type of the food processing byproducts applied. With this manner, Singh *et al.*, (2004) reported that the positive immune effects of five extracts/fractions of red onion peel which could attributed to their content of phenolics and flavonoids subsequently antioxidant and free radical scavenging activities. The present data with the others suggested that the highest therapeutic effect was recorded for the mixture of the selected food processing byproducts which could be attributed to the antagonism effects as the result of different phyto-bioactive compounds (Elmaadawy *et al.*, 2016; Sayed Ahmed, 2016 and Aly *et al.*, 2017)

**Table 4. The effect of selected food processing byproducts on immunological parameters of obese rats\***

Value	Control (-) Std diet	Control (+) Obese	Food processing byproducts (5%, w/w)			
			Banana peel powder (BPP)	Onion skin powder (OSP)	Apricot seeds powder (ASP)	Mixture (BPP + OSP + ASP)
Serum albumin level (Alb, g/L)						
Mean	51.42 <sup>a</sup>	44.46 <sup>c</sup>	46.89 <sup>ab</sup>	47.24 <sup>ab</sup>	45.99 <sup>bc</sup>	49.24 <sup>a</sup>
SD	5.21	4.15	1.99	5.02	4.11	7.26
% of Change	0.00	-13.54	-8.80	-8.13	-10.56	-4.24
Serum protease activity (PA, U/L)						
Mean	3.57 <sup>a</sup>	2.79	2.87 <sup>bc</sup>	2.98 <sup>bc</sup>	2.90 <sup>bc</sup>	3.05 <sup>b</sup>
SD	0.47	0.32	0.30	0.22	0.19	0.22
% of Change	0.00	-21.71	-19.68	-16.52	-18.78	-14.47

\* Means in the same row with different superscript letters are significantly different at  $p \leq 0.05$ .



**Fig. 4. The effect of selected food processing byproducts on immunological parameters concentration (as % of control) of obese rats\***

\*BPP, banana peel powder; OSP, onion skin powder; ASP, apricot seeds powder and Mix, mixture of BPP, OSP and ASP by equal parts

**b-Tumor necrosis factor- $\alpha$  (TNF- $\alpha$ )**

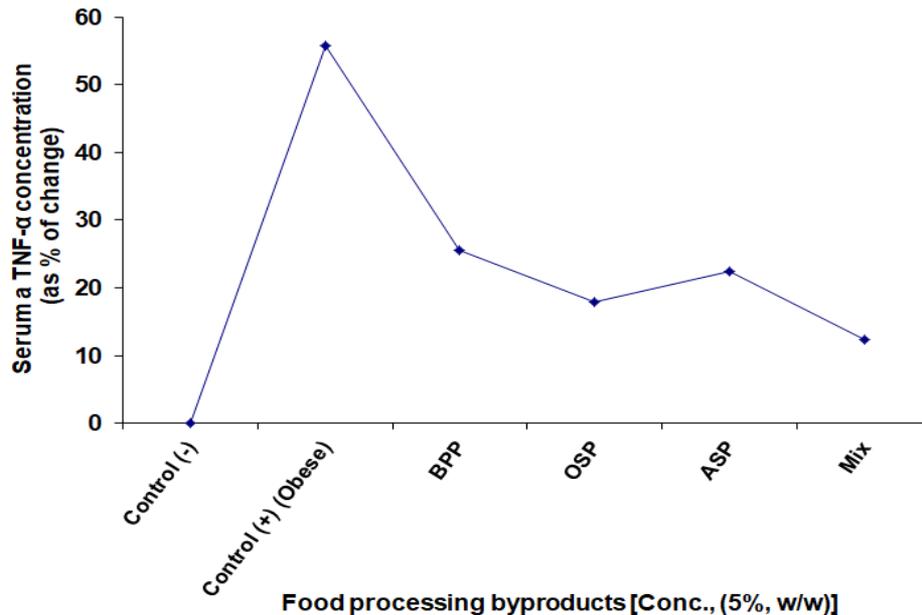
The effect of selected food processing byproducts in serum tumor necrosis factor- $\alpha$  (TNF- $\alpha$ ) obese rats was shown in Table (3) and Figure (3). Such data indicated that obesity induced a significant ( $p \leq 0.05$ ) increasing in serum TNF- $\alpha$  (55.81%) level compared to the normal group. Alteration of BPP, OSP, ASP and their mixture

exhibited significant ( $p \leq 0.05$ ) decreasing on serum TNF- $\alpha$  level by the ratio of 25.58, 17.83, 22.48 and 12.40%, respectively. The highest improvement in serum TNF- $\alpha$  induced by obesity in rats was recorded for the byproducts mixture treatment followed by OSP, BPP, and ASP, respectively.

**Table 5. The effect of selected food processing byproducts on serum TNF- $\alpha$  concentration (ng/L) of obese rats\***

Value	Control (-) Std diet	Control (+) Obese	Food processing byproducts (5%, w/w)			
			Banana peel powder (BPP)	Onion skin powder (OSP)	Apricot seeds powder (ASP)	Mixture (BPP + OSP + ASP)
Mean	1.29 <sup>c</sup>	2.01 <sup>a</sup>	1.62 <sup>ab</sup>	1.52 <sup>b</sup>	1.58 <sup>b</sup>	1.45 <sup>bc</sup>
SD	0.10	0.21	0.17	0.09	0.14	0.11
% of Change	0.00	55.81	25.58	17.83	22.48	12.40

\* Means in the same row with different superscript letters are significantly different at  $p \leq 0.05$ .



**Fig. 5. The effect of selected food processing byproducts on serum TNF- $\alpha$  concentration (as % of change) of obese rats\***

\*BPP, banana peel powder; OSP, onion skin powder; ASP, apricot seeds powder and Mix, mixture of BPP, OSP and ASP by equal parts

In general, TNF- $\alpha$  is a pro-inflammatory cytokine, and plays an important role in initiating the tissue inflammatory reaction (Kim *et al.*, 2003). TNF- $\alpha$  functions including increases vascular permeability, promotes leukocyte adhesion of vascular endothelial cells, stimulates IL-1 production by vascular endothelial cells endothelin, and other inflammatory mediators, leading to tissue inflammation and damages endothelial cells. On the other side, TNF- $\alpha$  stimulates neutrophil degranulation "outbursts," which produces reactive oxygen species (ROS), proteases and lipids, leading to tissue damage (Gao, 1999 and Elhassaneen *et al.*, 2016-e). Additionally, in inflammatory reactions, TNF- $\alpha$  is synthesized and secreted by mononuclear macrophages, by autocrine and paracrine mechanisms, releasing IL-1, IL-6, and IL-8, causing a "cascade effect" and aggravating tissue damage (Bentrem and Joehl, 2003). Data of the present study indicated that serum TNF- $\alpha$

levels in food processing byproducts treated groups are significantly lower than in obese group. ( $P \leq 0.05$ ). This data with others suggests that food processing byproducts may prevent development of obesity complications related to immunity probably by reducing vascular permeability and the release of inflammatory cells, inflammatory mediators and inflammatory cell infiltration relieving edema, and inhibiting generation of IL-1, IL-6, and IL-8 (Elhassaneen *et al.*, 2016-e). This observation was confirmed by Junzhang *et al.*, (2014) who reported that brown algae bioactive compounds (such found in BPP, OSP and ASP) may prevent the development of radiation esophagitis, perhaps by inhibiting the generation and release of the inflammatory response factors including TNF- $\alpha$ .

In conclusion, the present study has demonstrated that the potency of the selected food processing byproducts including BPP, OSP and ASP to ameliorate

the neurological and immunological complications /disorders in obese rats. Improving the neurological complications includes increasing the serum neurotransmitters (dopamine and serotonin) level and decreasing the acetylcholine activity. While, improving the immunological complications includes increasing the albumin level and protease activity in serum. These findings provide a basis for the use of the selected food processing byproducts in the prevention and early treatment of obesity. Also, the data support the benefits of dietary modification, including bioactive compounds in food processing byproducts supplementation, in alleviating the conventional neurological and immunological disorders associated obesity. Finally, more research must be done on the future to elucidate the realized benefits from dietary plant parts intake, such food processing by products, on obesity disease and its complications.

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## الملخص العربي

### الآثار المحتملة للنواتج الثانوية لمصانع الأغذية على الاضطرابات العصبية والمناعية للفئران المصابة بالسمنة

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تليها، OSP ، ASP ، BPP على الترتيب. على الجانب الآخر، أظهرت النتائج فاعلية النواتج الثانوية المختارة لمصانع الأغذية وخليطها تحسين وظائف الجهاز العصبي (محتوى الدوبامين والسيروتونين ونشاط انزيم أستيل كولين استريز) والمناعة (محتوى الألبومين وعامل نخر الورم- ألفا في السيرم ونشاط انزيم البروتيز) في الفئران البدنية. توفر هذه النتائج أساساً لاستخدام المنتجات الثانوية لمصانع الأغذية للوقاية والعلاج المبكر من السمنة. كما تدعم تلك النتائج فوائد تعديل النظام الغذائي، بما في ذلك مكملات النواتج الثانوية لمصانع الأغذية، في التخفيف من الاضطرابات العصبية والمناعية المرتبطة بالسمنة.

الكلمات المفتاحية: وزن الجسم، قشر الموز، قشر البصل، بذور المشمش، انزيم الأستيل كولين استريز، الدوبامين، السيروتونين، الألبومين، نشاط انزيم البروتيز، عامل نخر الورم.

أجريت الدراسة الحالية بهدف استكشاف تأثير ثلاثة من النواتج الثانوية الناتجة عن تصنيع الأغذية وهي قشور البصل والموز وكذلك بذور المشمش على الاضطرابات العصبية والمناعية للفئران المصابة بالسمنة. أوضحت النتائج أن تغذية الفئران المصابة بالسمنة التي يسببها النظام الغذائي المحث للسمنة (DIO) إلى زيادة وزن الجسم مقارنة بالمجموعة الضابطة السالبة. وفي نهاية التجربة (٨ أسابيع) سجلت الفئران من المجموعة الضابطة السالبة زيادة مقدارها ١٣١.٣٣٪ من خط الأساس، كما أدى استبدال نشا الوجبات بمسحوق قشر الموز (BPP) ، ومسحوق قشر البصل (OSP) ، ومسحوق بذور المشمش (ASP) ومخلوطهم (ASP + OSP + BPP بأجزاء متساوية) إلى انخفاض كبير في وزن الجسم للفئران التي تعاني من السمنة المفرطة وذلك بنسبة ١٧٧.٨٥ ، ١٥٥.٤١ ، ١٧٣.٥٩ و ١٤٤.٨٣٪ من خط الأساس على التوالي. كما تم تسجيل التأثير الأعلى على انخفاض الوزن للمجموعة التي تغذت على المخلوط من أجزاء النبات