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**Phyto-extracts applied in beef meatballs ameliorates  
hyperglycemia and its complications in alloxan-induced  
diabetic rats**

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**Abstract:** Diabetes mellitus is widely distributed all over the world including Egypt, and nearly one of each 10 person is diabetic. Oxidative stress, lipid toxicity and low- grade inflammation as major causes on diabetic complications. Several strategies to improve diabetic complications have been proposed, because early treatment and prevention play a pivotal role in reducing the population burden of diabetes. Therefore, the present study aims to investigate the effectiveness of three methanolic phyto-extracts by-products (pomegranate peel, red onion skin and eggplant peel) blends in meat balls in modulating hyperglycemia using alloxane-induced diabetic rats. Treatment of animals with aloxane caused a significant increased ( $p \leq 0.05$ ) in serum glucose concentration by the ratio 85.59% compared to normal controls. Supplementation of the rat diets with meatballs (20%) decreased this value which recorded 63.64%. The decreasing rate was elevated with the blending of the meatballs with 0.1% w/w by pomegranate peel methanolic extract (PPME), red onion skin methanolic extract (ROSME) and eggplant peel methanolic extract (EPME) and their mixture which recorded 40.87, 30.49, 34.83 and 21.64%, respectively. The same behaviour was recorded for liver tissue MDA level, the biomarkers of oxidative stress and inflammation in liver. Also, improving in liver and kidney functions in diabetic rats have been induced by different rates as the result of supplementation the diet with meatballs blending with the tested phyto by-products extracts. All of these effects could be attributed to the strong antioxidant activity of these extracts as the result of their high phenolics content. These findings provide a basis for the use of the selected phyto by-products extracts for the prevention and early treatment of T2DM.

**Keywords:** pomegranate peel, onion skin, eggplant peel, antioxidant activity, total phenolics, malonaldehyde, glutathione, liver functions.

## **Introduction**

Diabetes is defined as a state in which homeostasis of carbohydrate and lipid metabolism is improperly regulated by insulin. This results primarily in elevated fasting and postprandial blood glucose levels. If this imbalanced homeostasis does not return to normalcy and continues for a protracted period of time, it leads to hyperglycemia that in due course turns into a syndrome called diabetes mellitus (WHO, 1999 and Tiwari and Madhusudana, 2002). There are two main categories of this disease. Type 1 diabetes mellitus (T1DM) also called insulin-dependent diabetes mellitus (IDDM) and Type 2 (T2DM), the noninsulin-dependent diabetes mellitus (NIDDM). IDDM represents a heterogeneous and polygenic disorder, with a number of non-human leukocyte antigen (HLA) loci (about 20) contributing to the disease susceptibility (Fabregat *et al.*, 2015). T2DM is one of the world's most common chronic diseases as changing lifestyles lead to reduced physical activity and increased obesity (Wild *et al.*, 2004). Early phenomenon of T2DM is insulin insensitivity, which not only has negative metabolic consequences but also contributes subsequent pancreas  $\beta$ -cell exhaustion, resulting in the onset of clinical hyperglycemia (Stumvoll *et al.*, 2005). Thus, understanding the regulation of the insulin response and identifying the related mechanisms are important to early treatment and prevention of T2DM.

Diabetes mellitus is widely distributed all over the world including Egypt, and nearly one of each 10 person is diabetic. In 2006, according to the World Health Organization, at least 171 million people world wide suffer from diabetes (ADA, 2005). The incidence is increasing rapidly and it is estimated that by the year 2030, this number will probably double (ADA, 2005). Therefore, the human population worldwide appears to be in the midst of an epidemic of diabetes. Reports from the World Health Organization (WHO) indicate that diabetes mellitus is one of the major killers of our time, with people in Southeast Asia and Western Pacific as well as Middle East being most at risks (Tiwari and Madhusudana, 2002).

Several strategies to improve diabetic complications have been proposed, because early treatment and prevention play a pivotal role in reducing the population burden of diabetes. Benefits of pharmaceutical factors to treat the disease aggressively early have been recommended, but medications may have unwanted side effects. Also, the cost of administering modern antidiabetic drugs is beyond the reach of most

people in the low income group and those living in the rural areas (Jevas, 2011). Thus, the therapeutic approach of several traditional medicinal systems is more holistic. The fundamental mechanisms of these medicinal systems are still unexplainable using modern tools. The medicinal preparations in traditional medicines contain a variety of herbal and non herbal ingredients that are thought to act on a variety of targets by various modes and mechanisms (Tiwari and Madhusudana , 2002; and Matsui *et al.*, 2006 and Elhassaneen *et al.*, 2016). Thus, there has been a growing interest in herbal remedies that can be but have been difficult to maintain over a long term introduced into the general population with the least side effects and the maximal preventive outcome (Matsui *et al.*, 2006). In this context, many phytochemicals naturally occurring in plant foods would be desirable options. Amongst all of these bioactive compounds flavonoids, phenolic compounds, organosulfur compounds and anthocyanins are represent the central position. Such compounds has been reported to improve diabetic status by decreasing oxidative stress (Dias *et al.*, 2005 and Coskun *et al.*, 2005) or by reducing the disturbance of hepatic gene expressions (Kobori *et al.*, 2009).

Extensively studied sources of such natural compounds are fruits and vegetables, seeds, cereals, berries, wine, tea, onion bulbs, olive oil and aromatic plants. Attempts are also made to identify and evaluate these bioactive compounds in agricultural by-products, ethnic and traditional products, herbal teas, cold pressed seed oils, exudates resins, hydrolysis products, not evaluate fruits and edible leaves and other raw materials rich in antioxidant phenols that have nutritional importance and/or the potential for applications in the promotion of health and prevention against damages/complications caused by many diseases including diabetes mellitus. Amongst of these agricultural by-products, pomegranates (*Punica granatum* L.) peel, red onion (*Allium cepa* L.) skin and eggplant (*Solanum melongena*) peel are producing in large quantities in food-processing plants.

Pomegranate peel (PP) has been used extensively in the folk medicine of many cultures (Longtin, 2003 and Yunfeng *et al.*, 2006). Many studies found that PP had the highest antioxidant activity among the peel, pulp and seed fractions of 28 kinds of fruits commonly consumed in China (Guo *et al.*, 2003). Also, Singh *et al.*, (2002) reported that methanol extract of PP had much higher antioxidant capacity than that of seeds. Furthermore, PP extract could effectively protect (after oral

administration) against CCl<sub>4</sub> induced hepatotoxicity, in which ROS damage was intensively involved (Murthy *et al.*, 2002). It seems, therefore, that PP may be a rich source of natural antioxidants and worthy of further study.

The major by-products resulting from industrial peeling of onion bulbs are brown skin, the outer two fleshy leaves and the top and bottom bulbs. The outer dry layers of onion bulbs (Onion skin, OS), which are not edible and removed before processing, have been shown to contain a wide spectrum of polyphenolic components (Singh *et al.*, 2002). Also, it is a source of flavour components and fiber compounds and particularly rich in flavonoids including quercetin glycosides (Hertog *et al.*, 1992 and Waldron, 2001). Since quercetin from onions and their skins is rapidly absorbed and slowly eliminated, it could contribute significantly to antioxidant defense (Hollman *et al.*, 1997). For this reason and others, OS extracts used successfully in many different technological and therapeutic applications. For example, Elhassaneen *et al.*, (2016-a) improved the bioactive compounds content and antioxidant properties in crackers with the incorporation of OS powder. Also, OS extracts could effectively protect against CCl<sub>4</sub> and benzo(a)pyrene induced hepatotoxicity (Elhassaneen *et al.*, 2016-b).

Eggplant, one of the most widespread vegetable consumed around the world. The most widely cultivated varieties are elongated ovoid or slender type in a dark purple skin. Eggplant is ranked as one of the top ten vegetables in terms of oxygen radical scavenging capacity due to the fruit's phenolic constituents (Cao *et al.*, 1996). Anthocyanins, an important group of naturally occurring pigments of red and/or purple colored fruits, are the main phenolic compounds in eggplant peel which provide a myriad of health benefits. For example, Nanda *et al.*, (2013) reported that eggplant extract may lower blood glucose level of DM rats near to normal. Also, Esther *et al.*, (2013) reported that the inhibition of starch hydrolyzing enzymes and antioxidant activities suggested the potential use of eggplants in the dietary management or control of postprandial hyperglycemia associated with type- 2 diabetes (T2DM). Furthermore, Sepideh *et al.*, (2016) found that eggplant, due to containing compounds with antioxidant properties, can reduce free radicals and thereby improve memory deficits caused by diabetes.

All of the previous studies confirmed the use of plants for the treatment of common diseases such as diabetes is very common. In line

with the WHO expert committee on diabetes which recommends that traditional methods of management of diabetes should be further investigated. Also considering the economic resource constraints and cheapness of these phyto-products, this present study was designed to determine the effects of three phyto-extracts and their mixture bended in beef meatballs on alloxane-induced diabetic rats. Also, their possible mechanisms of action, for possible use in the control of hyperglycaemia characteristic of diabetes mellitus will be in the scope of this investigation.

### **Materials and Methods**

#### **Materials**

**Plant parts:** Pomegranate and eggplant fruits used for their peels preparation from Zagazig local markets, Zagazig City, Egypt. Red onion skin (ROS) was obtained with special arrangements from the New Beni Suef company for Preservation, dehydration and Industrialization of Vegetables, Beni Suef Elgudida City, Nile East, Beni Suef, Egypt;

**Meat samples:** Rose meat samples were obtained from the Egyptian local markets, transported to the lab, cutted into small pieces using sharp knife and mincing using electrical mixer (Moulinex Egypt, Al-Araby Co., Egypt) and used for meatballs processing.

**Experimental animals:** Normal male albino rats (140±10g) were obtained from Research Institute of Ophthalmology, Medical Analysis Department, Giza, Egypt.

**Chemicals:** Alloxan, used for induction of diabetes mellitus among rats, Folin-Ciocalteu reagent, *o*-phosphoric acid, serine borate buffer (SBB), N-1-(pyrenyl) maleimide (NPM), dithiothreitol (DTT) and reduced glutathione (GSH) were obtained from Sigma Chemical Co., St. Louis, Mo. Casein, as main source of protein from Morgan Company for Chemicals. Cairo, Egypt and Vitamins and salts mixtures, all organic solvents and other chemicals were of analytical grade were purchased from El-Ghomhorya Company for Drugs, Chemicals and Medical instruments Trading, Cairo, Egypt.

**Equipments:** Throughout this study a SP Thermo Separation Products Liquid Chromatography (Thermo Separation products, San Jose, CA, USA) was used with a Consta Metvic 4100 pump, a Spectra Series AS100, Spectra System UV 1000 UV/Visible Spectrophotometer Detector, Spectra System FL 3000 and a PC 1000 system software. The columns used (Alltech, Deerfield, IL, USA) were a Spherosorb ODC-2 (5 µm, 150 x 4.6 mm I.d.) for glutathione fractions.

### **Methods**

#### **Preparation of plant parts powder and extracts**

Pomegranate peel (PP), red onion skin (ROS) and eggplant peel (EGP) were washed and then dried in a hot air oven (Horizontal Forced Air Drier, Proctor and Schwartz Inc., Philadelphia, PA) at 55 °C until arriving by the moisture in the final product to about 8%. 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. Powders of the selected plant parts were used for their different types extracts according to the method of Amin *et al.*, (2004) with some modifications. In aqueous extraction, 20 g from dried plant +180 ml deionized water were homogenized and transferred to a beaker and stirred at 200 rpm in an orbital shaker (Unimax 1010, Heidolph Instruments GmbH & Co. KG, Germany) for 1 h at room temperature. The extract was then separated from the residue by filtration through Whatman No. 1 filter paper. The remaining residue was re-extracted twice, and then the two extracts were combined. The residual solvent of aqueous extract was removed under reduced pressure at 55°C using a rotary evaporator (Laborata 4000; Heidolph Instruments GmbH & Co. KG, Germany). In organic solvents extraction, the same previous extraction procedure was carried out by using different organic solvent separately including 80% (v/v) methanol, 80% (v/v) ethanol and 100% hexane as an extraction medium. The yield of the extracts were weighted and evaluated to use the high yield one.

#### **Meatballs manufacture**

##### **Meatballs formulation**

Egyptian-style meatballs were formulated as follow: 80% minced beef (~20% fat content), 14.5% potato powder, 5% water and 0.5% salt. A set of 5 treatment samples differing only by the plant parts methanol extract added were prepared as follow: beef meatballs formula (control samples), beef meatballs formula + 0.1 % (w/w) pomegranate peel

methanol extract (PPME), beef meatballs + 0.1 % (w/w) red onion skin methyl extract (ROSME), beef meatballs + 0.1 % (w/w) eggplant peel methyl extract (EPME) and beef meatballs + 0.1 % (w/w) mixture, PPME+ ROSME+ EPME by equal parts. Plant parts were used at the recommended concentrations as previous mentioned by the studies of Elhassaneen *et al.*, (2016).

#### **Beef meatballs processing**

Beef meatballs were prepared in a pilot plant resembling to commercial processing conditions. All ingredients were homogenized in a bowl mixer with a spiral dough hook (Moulinex Egypt, ElAraby Co., Egypt) during 5 min. For each treatment, the corresponding plant part extract was added at the concentrations suggested, and then mixed again for 5 min. Meatballs were formed by hand (15 g, 2-3 cm in diameter) and then subjected to a two stage cooking process. First, the meatballs were flash fried into sunflower oil at 190 °C for 30 seconds to seal the surface of the ball and produce the characteristic browned look. They were then thoroughly cooked in a forced draught oven (Zanussi, Italy) at 250 °C during 4 min to reach an internal temperature of 72 °C in the center of the meatball. The temperature was monitored using an Omega digital thermometer (Omega Engineering, Inc., Stamford, CT) with a chromel–alumel (Omega K) thermocouple probe positioned in the geometric center of the product samples. When the endpoint temperature was achieved, the samples were immediately placed in a chiller (4 °C) to reach a product temperature below 12 °C. Three replications of this experiment were made.

#### **Chemical analysis**

##### **Antioxidant activity**

Antioxidant activity of the selected plant parts extracts and standards ( $\alpha$ -tocopherol, BHA, and BHT; Sigma Chemical Co., St. Louis, Mo) was determined according to the  $\beta$ -carotene bleaching method following a modification of the procedure described by Marco (1968). For a typical assay, 1mL of  $\beta$ -carotene (Sigma) solution, 0.2 mg/mL in chloroform, was added to round-bottom flasks (50 mL) containing 0.02 mL of linoleic acid (J.T. Baker Chemical Co., Phillipsburg, NJ) and 0.2 mL of Tween 20 (BDH Chemical Co., Toronto, On). Each mixture was then dosed with 0.2 mL of 80% MeOH (as control) or corresponding plant extract or standard. After evaporation to dryness under vacuum at room temperature, oxygenated distilled water (50 ml) was added and the

mixture was shaken to form a liposome solution. The samples were then subjected to thermal autooxidation at 50 °C for 2 h. The absorbance of the solution at 470 nm was monitored on a spectrophotometer (beckman DU-50) by taking measurements at 10 min intervals, and the rate of bleaching of  $\beta$ -carotene was calculated by fitting linear regression to data over time. All samples were assayed in triplicate. A 50 g per letter of  $\alpha$ -tocopherol in 80% methanol was used as the control. Antioxidant activity was expressed as antioxidant activity (AA) and calculated as percent inhibition relative to control using the Al-Saikhan *et al.*, (1995) equation [AA= (R<sub>control</sub> - R<sub>sample</sub>) / R<sub>control</sub> x 100, where R<sub>control</sub> and R<sub>sample</sub> were the bleaching rates of beta-carotene in reactant mixture without antioxidant and with plant extract, respectively].

#### **Total phenolics**

Total phenolics of the selected by-products extracts were determined by using Folin-Ciocalteu reagent (Singleton and Rossi, 1965). A 100  $\mu$ l of each extract was mixed with 0.75 mL of Folin-Ciocalteu reagent (previously diluted 10-fold with distilled water) and allowed to stand at 22 °C for 5 min; 0.75 ml of sodium bicarbonate (60 g.L<sup>-1</sup>) solution was added to the mixture after 90 min at 22 °C, absorbance was measured at 725 nm. Results are expressed as gallic acid and equivalents (GAE).

#### **Biological experimental**

##### **Animals**

Animals used in this study, adult male albino rats (130-150 g per each) were obtained from Helwan Station, Ministry of Health and Population, Helwan, Cairo, Egypt.

##### **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, 1941).

##### **Experimental design**

All biological experiments performed complied with the rulings of the Institute of Laboratory Animal Resources, Commission on life Sciences, National Research Council (NRC, 1996). Rats (n=42 rats), were

housed individually in wire cages in a room maintained at  $25 \pm 2$  °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 (36 rats) was injected subcutaneous by alloxan monohydrate to induce diabetic rats then classified into sex sub groups as follow:

- Group (2): Fed on standard diet only as a positive control (rats with diabetes).
- Group (3): Fed on standard diet containing 20% meatballs without plant parts extracts.
- Group (4): Fed on standard diet containing 20% beef meatballs formula with 0.1 % (w/w) PPME.
- Group (5): Fed on standard diet containing 20% meatballs with 0.1 % (w/w) ROSME.
- Group (6): Fed on standard diet containing 20% meatballs with 0.1 % (w/w) EPME.
- Group (7): Fed on standard diet containing 20% meatballs with 0.1 % (w/w) mixture, PPME+ ROSME+ EPME by equal parts.

#### **Induction of diabetes**

Diabetes was induced in sixty three normal healthy rats by injection into operationally with freshly prepared alloxan monohydrate in saline at a dose level of 150 mg/ kg body weight (Lazarow and Palay, 1954). Immediately after injection animals were received 5% glucose solution over night to overcome drug induced hypoglycemia (Wohaieb and Godin, 1987 and Kakkar *et al.*, 1998). After five days blood glucose was analyzed by a drop of blood was obtained from tail vein and subjected to a strip of haemogluco test. All rats with fasting blood sugar > 126 mg/dl were considered to be diabetics and included in the experiment.

#### **Blood sampling**

At the end of experiment period, 28 days, blood samples were collected after 12 hours fasting using the abdominal aorta and rats were scarified under ether anesthetized. Blood samples were received into glass centrifuge tubes, containing oxalate solution (1.34 %) as anticoagulant. After centrifugation at 3000 rpm for 10 min., plasma was with drown and used for the analysis of blood lipid parameters and vitamins. The erythrocyte residue was washed with three successive portions of sodium chloride solution (0.9 %) and then haemolysed with deionised water for

30 min. Haemolysate was then centrifuged at 30,000 rpm for 30 min. and the supernatant fractions was transferred to a clean test tube and analyzed of antioxidant enzymes (Stroev and Makarova, 1989). Liver organ was removed and used for GSH and MDA determination.

#### **Hematological analysis**

Different tested parameters in serum were determination using specific methods as follow: glutamic oxaloacetic transaminas (AST/GOT), glutamic pyruvic transaminas (ALT/GPT), urea and creatinine concentration according to Yound, (1975), Tietz, (1976), Fawcett and Soctt, (1960) and Bartles *et al.*, (1972), respectively. Enzymatic determination of plasma glucose was carried out colorimetrically according to Yound, (1975) and Tietz, (1976).

#### **Glutathione (GSH) determination in liver tissue**

GSH was determined by HPLC according to the method of Burhan *et al.*, (2008). Tissue liver samples, ranging from 0.3 to 0.5 g, were minced and homogenized in 1 mL serine borate buffer (SBB) (pH = 7.2). The buffer used contains L-serine and borate, which can inhibit  $\gamma$ -glutamyl transpeptidase (GGT), exists in liver and may hydrolyze GSH. SBB is therefore always used during homogenization of tissue samples to prevent loss of GSH. The homogenate was centrifuged for 5 min at 5000g. For GSH analysis, 20 $\mu$ L of supernatant and 230 $\mu$ L of SBB were added to 750 $\mu$ L of 1 mM N-1-(pyrenyl) maleimide (NPM) solution and incubated at room temperature for 5 min. A 10 $\mu$ L aliquot of 2M HCl was used to stop the reaction. Derivatized tissue samples were filtered through 0.45 $\mu$ m nylon filters and injected directly onto the HPLC system. When GSSG or total GSH was assayed, 20 $\mu$ L of supernatant and 105 $\mu$ L of SBB (pH = 8.3) were added to 125 $\mu$ L of dithiothreitol (DTT) (2 mM) and incubated at room temperature for 30 min. The mixture was then derivatized with *N*-nitrophenol which were taken overnight at 4 °C in the presence of 0.2 ml of 1% 1-fluoro-2,4-dinitrobenzene and injected onto the HPLC system.

#### **Malondialdehyde content (MDA)**

Lipid peroxide levels measured as malondialdehyde in liver were determined by as thiobarbituric acid reactive substances (TBARS) as described by Stroev and Makarova, (1989). Half milliliter of homogenate were added to 1.0 ml of thiobarbituric acid reagent, consisting of 15% TCA, 0.375% thiobarbituric acid (TBA) and 0.01% butylated hydroxytoluene in 0.25 N HCl. Twenty-five microliters of 0.1 M

FeSO<sub>4</sub>.7H<sub>2</sub>O was added and the mixture was heated for 20 min in boiling water. The samples were centrifuged at 1000 rpm for 10 min and the absorbance was read at 535 nm using Labo-med. Inc., spectrophotometer against a reagent blank. The absorbance of the samples was compared to a standard curve of known concentrations of malonaldehyde.

#### **Statistical Analysis**

All measurements were done in triplicate and recorded as mean±SD. Statistical analysis was performed with the Student *t*-test and MINITAB 12 computer program (Minitab Inc., State College, PA).

#### **Results and Discussion**

##### **Extractive value of selected plant parts using different organic solvents**

The extractive values in different organic solvents are based on the quantity, which are soluble in them. It makes a valuable test to check the quality of drug/additive/food supplement etc and any variation in the chemical constituents may cause a change in the extractive values. Thus, it helps in the determination of the adulteration and is an index of the purity of the material. The extractive value of selected plant parts therefore, were determined by successive extraction in different solvents using a Soxhlet's apparatus. The results are shown in Table (1). The extractive value for selected plant parts in water and hexane was low (2.31-3.42%) while relatively high in methanol and ethanol 2.65-7.91%). Similar data was recorded by Saleh (2016) for other plant parts including orange peel, sweet violet blossoms and marjoram leaves. All of those data confirmed that selected plant parts components were found in both lipohylic and hydrophilic phases i.e. accordance with the known rule "like dissolve like". The variation in the extractive values may be possible due to the presence of specific compound according to the solubility, soil condition, atmospheric condition and water content of the sample (Saleh, 2016). All of these data indicated that the methanol extracts of the selected plant parts were recommended for the further studies from the practical and economical point of view.

**Table 1.** Extractive value of selected phyto by-products using water and different organic solvents

Phyto by-products	Mean extract, yield (%) $\pm$ SD			
	Water	Methanol	Ethanol	Hexane
Pomegranate peel (PP)	2.19 $\pm$ 0.75	4.02 $\pm$ 0.99	2.65 $\pm$ 0.64	2.31 $\pm$ 0.69
Red onion skin (ROS)	3.01 $\pm$ 1.33	7.91 $\pm$ 1.76	5.88 $\pm$ 2.07	3.42 $\pm$ 1.10
Eggplant peel (EP)	2.52 $\pm$ 0.98	5.66 $\pm$ 0.88	3.71 $\pm$ 1.13	2.48 $\pm$ 0.60

Each value represents mean  $\pm$ SD.

**Antioxidant activity and total phenolics of selected plant parts methanolic extracts**

**Antioxidant activities**  
 The antioxidant activities and total phenolics of four selected plant parts methanolic extracts are shown in Table (2) and Figures (1-2). From such data it could be noticed that the selected plant parts methanolic extracts showed considerable differences in antioxidant activity (AA= 72.11 $\pm$ 3.03 to 91.55 $\pm$ 4.21%). Red onion skin methanolic extract (ROSME) and Eggplant peel methanolic extract (EPME) showed strong activity because of its high phenolics content (198.44  $\pm$  14.51 and 61.89  $\pm$ 13.32 mg GAE. g<sup>-1</sup>, respectively) while Pomegranate peel methanolic extract (PPME) showed relatively low content in both antioxidant activity and the total phenolics (72.11  $\pm$ 3.03% and 31.63 $\pm$ 7.45 mg GAE. g<sup>-1</sup>, respectively).

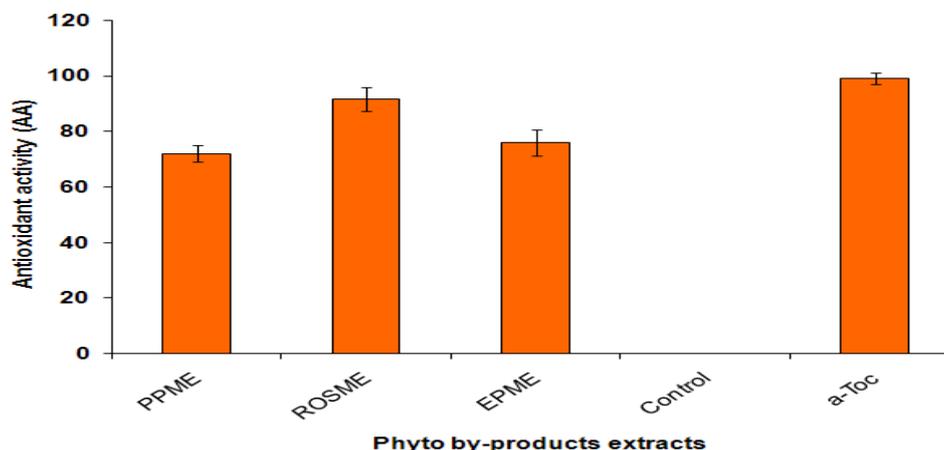
**Table 2.** Antioxidant activity and total phenolics of selected phyto by-products methanolic extracts

Selected plant parts	Antioxidant activity AA (%)	Total phenolics (mg GAE. g <sup>-1</sup> extract)
Pomegranate peel methanolic extract (PPME)	72.11 $\pm$ 3.03	31.63 $\pm$ 7.45
Red onion skin methanolic extract (ROSME)	91.55 $\pm$ 4.21	198.44 $\pm$ 14.51
Eggplant peel methanolic extract (EPME)	76.19 $\pm$ 4.65	61.89 $\pm$ 13.32
$\alpha$ -tocopherol, 50 mg/L	98.99 $\pm$ 2.11	-----

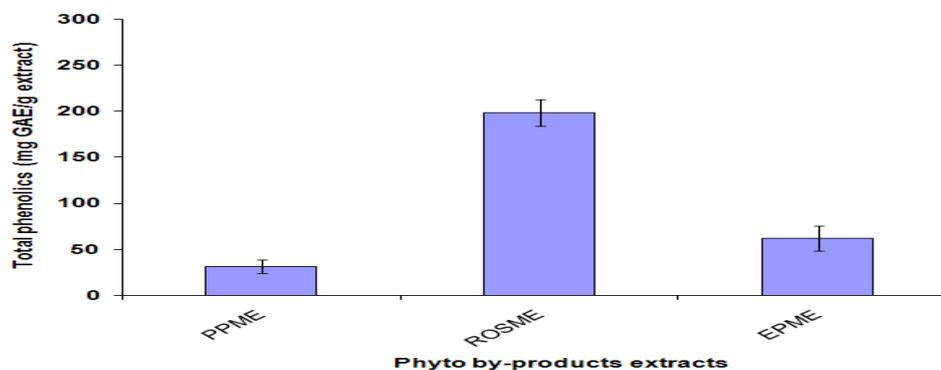
Each value represents mean  $\pm$ SD.

Regarding the selected extracts stability, the decrease in absorbance of  $\beta$ -carotene in the presence of different selected plant parts methanolic extracts (and well-known antioxidants used as standards) with the oxidation of  $\beta$ -carotene and linoleic acid is shown in Figure (3). Such data indicated that ROSME extract recorded the lowest decreasing followed by EPME and PPME extracts, respectively. The values of ROSME extract absorbance's through 120 min are coming well i.e. closing the line of 50 mg.L<sup>-1</sup> of  $\alpha$ -tocopherol followed by the EPME and PPME extracts. These data proved the very high stability of the ROSME extract and relatively high stability of the rest tested plant parts extracts i.e. EPME and PPME when comparing with that more common standard  $\alpha$ -tocopherol. The present data are similar to that obtained by many authors (Velioglu *et al.*, 1998; Ellassaneen *et al.*, 2016; Saleh, 2016 and Sayed Ahmed, 2016) who found that several food by-products/plant parts extracts including onion skin and eggplant powders recorded highly antioxidant activity and phenolics content as well as exhibited high antioxidant stability when comparing with the  $\alpha$ -tocopherol as the standard antioxidant.

On the other side, data in Figure (4) indicated that when all selected plant parts methanolic extracts were included in the statistical analysis, there was a positive and highly significant ( $p \leq 0.05$ ) relationship between total phenolics and antioxidant activity. The highest value was recorded for ROSME ( $r^2 = 0.926$ ,  $p \leq 0.05$ ) followed by EPME ( $r^2 = 0.918$ ,  $p < 0.05$ )

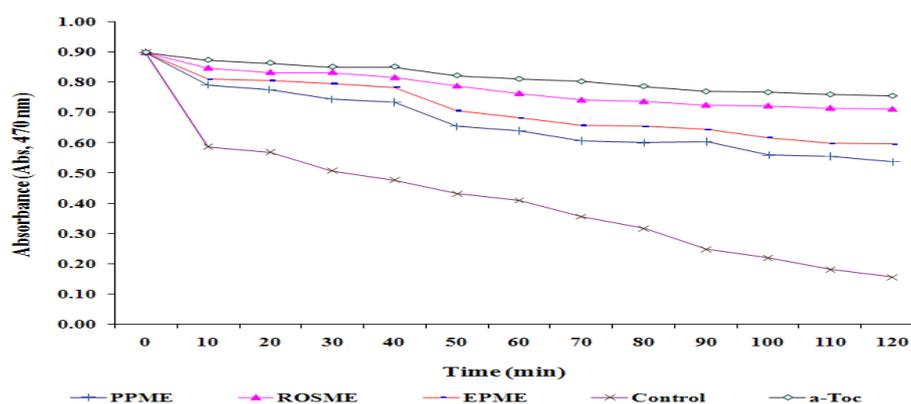


**Figure 1.** Antioxidant activity of selected phyto by-products methanolic extracts. PPME, pomegranate peel methanolic extract; ROSME, red onion skin methanolic extract; and EPME, eggplant peel methanolic extract.

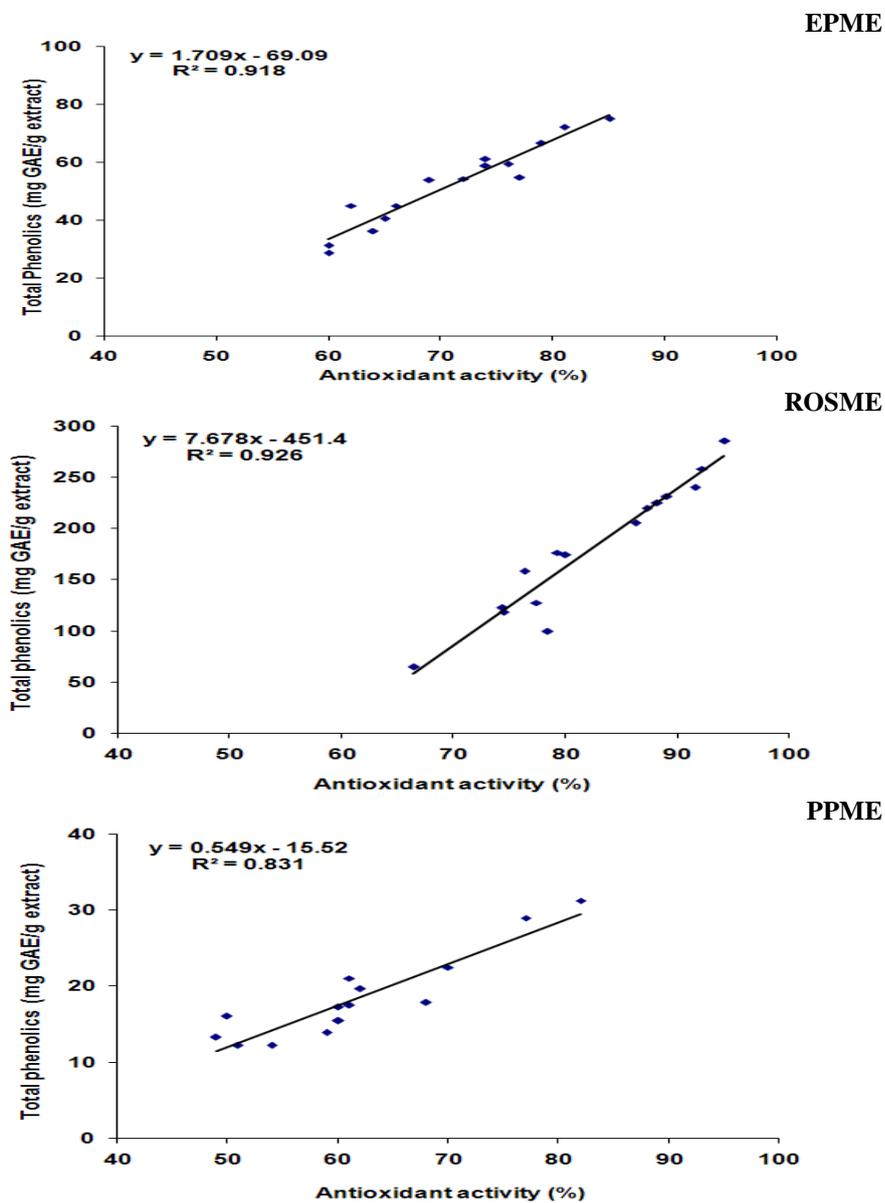


**Figure 2.** Total phenolics of selected phyto by-products methanolic extracts. PPME, pomegranate peel methanolic extract; ROSME, red onion skin methanolic extract; and EPME, eggplant peel methanolic extract.

and PPMER ( $r^2 = 0.831$ ,  $p < 0.05$ ), respectively. These relationships indicated that phenolic compounds probably play a major role in the antioxidant activity of the selected plant parts methanolic extracts and the rest/some roles were depended on the occurrence of other bioactive compounds beside the phenolics such vitamins (ascorbic acid and tocopherols), sterols, pigments and minerals (Mashal, 2016 and Sayed Ahmed, 2016). Data of the present study with the others proved the importance of using all selected plant parts methanolic extracts as natural antioxidants in different therapeutic applications.



**Figure 3.** Activity of selected phyto by-products methanolic extracts assayed by the  $\beta$ -carotene bleaching method ( $\alpha$ -tocopherol at 50 mg/L concentration was used as a reference). PPME, pomegranate peel methanolic extract; ROSME, red onion skin methanolic extract; and EPME, eggplant peel methanolic extract.



**Figure 4.** Relationship between total phenolic content and antioxidant activity (AA) of selected plant parts methanolic extracts. PPME, pomegranate peel methanolic extract; ROSME, red onion skin methanolic extract; and EPME, eggplant peel methanolic extract.

**The effect of phyto by-products methanolic extracts applied in beef meatballs on serum glucose of diabetic rats**

Data in Table (3) were shown the serum glucose concentration of alloxane-induced diabetic rats consumed the phyto by-products methanolic extracts applied in beef meatballs. From such data it could be noticed that treatment of animals with alloxan caused a significant increased ( $p \leq 0.05$ ) in serum glucose concentration by the ratio 85.59% compared to normal controls. Supplementation of the rat diets with meatballs (20%) decreased this value which recorded 63.64%. The decreasing rate was elevated with the blending of the meatballs with 0.1% w/w by PPME, ROSME, EPME and their mixture which recorded 40.87, 30.49, 34.83 and 21.64%, respectively. The mixture treatment gave maximum hypoglycemic yield when compared with the tested phyto by-products extracts separated. It could be mean that a combination of different phyto by-products extracts may be more efficient for reducing the serum glucose level because the interactive effects occurred by different categories of bioactive compounds of phyto by-products extracts used.

**Table 3.** The effect of phyto by-products methanolic extracts applied in beef meatballs on serum glucose concentration (mg/dL) of diabetic rats \*

Value	Control (ve-) Std diet	Control (ve+) Diabetic	Control (ve+) 20% meatballs	Meatballs + Phyto by-product methanolic extracts (0.1%, w/w)			
				PPME	ROSME	EPME	Mix
Mean	98.55	182.90	161.27	138.83	128.60	132.88	119.88
SD	8.43	13.56	14.92	4.76	5.98	13.82	5.93
% of Change	0.00	85.59	63.64	40.87	30.49	34.83	21.64

\*PPME, pomegranate peel methanolic extract; ROSME, red onion skin methanolic extract; EPME, eggplant peel methanolic extract and Mix, mixture of PPME+ ROSME+ EPME + MPP by equal parts. Means in the same row with different litters are significantly different at  $p < 0.05$ .

In this direction, several researches have been done on the effect of onion consumption on diabetic conditions. The organosulfur compounds S-methylcysteine sulfoxide (SMCS) and S-allylcysteine sulfoxide (SACS) were linked to significant amelioration of weight loss, hyperglycemia, low liver protein and glycogen, and other characteristics of diabetes mellitus in rats (reviewed in Sheela *et al.*, 1995). They found

that the use of SMCS and SACS (200 mg.kg<sup>-1</sup>.day<sup>-1</sup>) gave results comparable to treatment with insulin or glibenclamide but without the negative side effect of cholesterol synthesis stimulation. Similarly, Baba Suresh and Srinivasan (1997) found that a 3% onion powder diet also reduced hyperglycemia, circulating lipid peroxides, and blood cholesterol (LDL-VLDL exclusively). *In vivo* analysis of the effects of quercetin on human diabetic lymphocytes showed a significant increase in the protection against DNA damage from hydrogen peroxide at the tissue level. Antioxidant activity was shown, but non-diabetic controls were not used and symptom relief was not mentioned. Jung *et al.*, (2011) reported that onion peel extract (OPE) might improve glucose response and insulin resistance associated with type 2 diabetes by alleviating metabolic dysregulation of free fatty acids, suppressing oxidative stress, up-regulating glucose uptake at peripheral tissues, and/or down-regulating inflammatory gene expression in liver. Moreover, in most cases, OPE showed greater potency than pure quercetin equivalent. These findings provide a basis for the use of onion peel to improve insulin insensitivity in type 2 diabetes. OPE might improve glucose response and insulin resistance associated with type 2 diabetic mellitus (T2DM) by alleviating metabolic dysregulation of free fatty acids, suppressing oxidative stress, up-regulating glucose uptake at peripheral tissues, and/or down-regulating inflammatory gene expression in liver. Moreover, in most cases, OPE showed greater potency than pure quercetin equivalent. These findings provide a basis for the use of onion peel to improve insulin insensitivity in type 2 diabetes.

Also, PPME and PGPP display potent hypoglycemic action in alloxane-induced diabetic rats. Such activity may be related to diverse phenolic compounds present in pomegranate and potato peel including punicalagin isomers, ellagic acid derivatives and anthocyanins (delphinidin, cyanidin and pelargonidin 3-glucosides and 3,5-diglucosides) chlorogenic, gallic, protocatechuic and caffeic acids (Onyeneho and Hettiarachchy, 1993 and Rodriguez *et al.*, 1994). These compounds are known for their properties in scavenging free radicals, inhibiting lipid oxidation *in vitro* and improve glucose response and insulin resistance associated with type 2 diabetes (Noda *et al.*, 2002 and Jung *et al.*, 2011).

**The effect of phyto by-products methanolic extracts applied in beef meatballs on malondialdehyde (MDA) concentration in liver tissue of alloxan-induced diabetic rats**

Data in Table (4) were shown the malondialdehyde (MDA) concentration a vital assay for the oxidative stress status, in liver tissue of alloxan-induced diabetic rats consumed the phyto by-products methanolic extracts applied in beef meatballs. From such data it could be noticed that treatment of animals with aloxan caused a significant increased ( $p \leq 0.05$ ) MDA concentration in liver tissue (46.49%) compared to normal controls. Supplementation of the rat diets with meatballs (20%) decreased this value which recorded 26.61%. Compared with diabetic control, MDA formation was suppressed by supplementation of the meatballs with 0.1% w/w/ by PPME, ROSME, EPME and their mixture which recorded 17.54, 14.33, 15.50 and 8.19 %, respectively. The highest suppression was recorded with the mixture treatment. It could be mean that a combination of different plant parts may be more efficient for reducing liver tissue MDA level, the biomarkers of oxidative stress and inflammation in liver, because the interactive effects occurred by different categories of bioactive compounds of plant parts used.

**Table 4.** The effect of phyto by-products methanolic extracts applied in beef meatballs on malondialdehyde concentration (MDA, nmol/mg tissue protein ) in liver tissue of diabetic rats\*

Value	Control (ve-) Std diet	Control (ve+) Diabetic	Control (ve+) 20% meatballs	Meatballs + Phyto by-product methanolic extracts (0.1%, w/w)			
				PPME	ROSME	EPME	Mix
Mean	3.42	5.01	4.33	4.02	3.91	3.95	3.70
SD	0.54	0.94	0.68	1.04	0.74	0.73	1.17
% of Change	0.00	46.49	26.61	17.54	14.33	15.50	8.19

\*PPME, pomegranate peel methanolic extract; ROSME, red onion skin methanolic extract; EPME, eggplant peel methanolic extract and Mix, mixture of PPME+ ROSME+ EPME + MPP by equal parts. Means in the same row with different litters are significantly different at  $p < 0.05$ .

Such data are in accordance with that observed by Jung *et al.*, (2011) who reported that oxidative stress and metabolic dysregulation of FFAs in diabetic condition were alleviated by onion peel extract (OPE) administration. Also, hepatic oxidant stress was reduced by 1% OPE, as assessed by increasing superoxide dismutase activity and blocking MDA formation. Moreover, hepatic expressions of TNF- $\alpha$  and IL-6 were suppressed by either 1% OPE or quercetin. Furthermore, Coskun *et al.*, (2005) reported that quercetin, dominant flavonoid in the selected phyto by-products extracts, had anti-oxidative and anti-inflammatory activities. Therefore, the present data proposed that the selected phyto by-products lead to improve insulin sensitivity, at least in part, through enhancing lipid metabolism, reducing oxidative stress in diabetic rats.

#### **The effect of phyto by-products methanolic extracts applied in beef meatballs on reduced glutathione (GSH) concentration in liver tissue of alloxan-induced diabetic rats**

Data in Table (5) were shown the reduced glutathion (GSH) concentration in liver tissue of alloxan-induced diabetic rats consumed the tested phyt by-product extracts applied in beef meatballs. From such data it could be noticed that treatment of animals with aloxan caused a significant decreased ( $p \leq 0.05$ ) in liver GSH content (20.17%) compared to normal controls. Compared to the diabetic control, biological antioxidant activity enhancement of beef meatballs supplemented with 0.1% phyto by-products methanolic extracts was demonstrated by significant ( $p \leq 0.05$ ) increasing of GSH content in liver. The rate of increasing was elevated to 17.52, 13.48, 9.66, 12.00 and 8.81 % for meatballs supplemented with PPME, ROSME, EPME and their mixture , respectively. So, the increasing in liver GSH content was depending on the type of the phyto by-products extracts applied in beef meatballs. The highest biological antioxidant activity enhancement was recorded for applying the mixture of the selected plant parts extracts followed by ROSE, EPME and PPME, respectively.

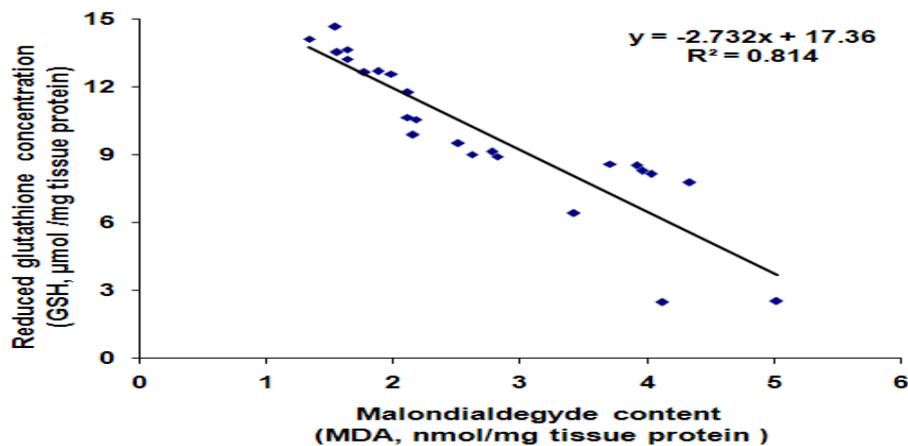
GSH is an important biological antioxidant. It is normally play the role of an intracellular radical scavenger and is the substrate of many xenobiotic elimination reactions. A marked decreased level of GSH is reported in the plasma of diabetic patients (Seghrouchni *et al.*, 2002). GSH systems may have the ability to manage oxidative

**Table 5.** The effect of phyto by-products methanolic extracts applied in beef meatballs on reduced glutathione concentration (GSH,  $\mu\text{mol} / \text{mg}$  tissue protein) in liver tissue of diabetic rats\*

Value	Control (ve-) Std diet	Control (ve+) Diabetic	Control (ve+) 20% meatballs	Meatballs + Phyto by-product methanolic extracts (0.1%, w/w)			
				PPME	ROSME	EPME	Mix
Mean	9.42	7.52	7.77	8.15	8.51	8.29	8.59
SD	1.13	0.87	2.32	1.24	0.76	1.43	0.87
% of Change	0.00	-20.17	-17.52	-13.48	-9.66	-12.00	-8.81

\*PPME, pomegranate peel methanolic extract; ROSME, red onion skin methanolic extract; EPME, eggplant peel methanolic extract and Mix, mixture of PPME+ ROSME+ EPME + MPP by equal parts. Means in the same row with different litters are significantly different at  $p < 0.05$ .

stress with adaptational changes in enzymes regulating GSH metabolism i.e link between hyperglycemia and GSH depletion. It could be interpreted by Lee *et al.*, (1995) who reported that, in hyperglycemia conditions, glucose is preferentially used in polyol pathway that consumes NADPH necessary for GSH regeneration by the GSH-reductase enzyme. Hyperglycemia is therefore indirectly the cause of GSH depletion. In the present study, it was reported that feeding the diabetics rats with beef meatballs supplemented with phyto by-products methanolic extracts significantly removed some of the metabolic disorders induced by T2DM in liver cells through increasing the GSH synthesis. Many studies reported the potent antioxidant capacity of those plant parts extracts (PPME, ROSME and EPME) in both *in vitro* and *in vivo* studies (Saleh, 2016). Such effect leads to increase GSH and stimulate its related antioxidant enzymes activity i.e. GSH-peroxidase and GSH-reductase (Fayez, 2016). The present data are confirmed by the correlation analysis showed in Figure (5) which indicated that GSH depletion in liver cells is negatively correlated ( $r^2=814$ ,  $p \leq 0.05$ ) with the increasing MDA concentration as the feeding of some selected phyto by-products applied in beef meatballs.



**Figure 5.** Correlation between MDA content and GSH detected in diabetic rats feeding selected phyto by-products applied in beef meatballs.

### **The effect of phyto by-products methanolic extracts applied in beef meatballs on liver functions of alloxan-induced diabetic rats**

Liver function enzymes activities (aspartate aminotransferase, AST and alanine aminotransferase, ALT) in serum of alloxan-induced diabetic rats consumed the selected phyto by-product extracts were shown in Table (6). From such data it could be noticed that treatment of rats with aloxane caused a significant increased ( $p \leq 0.05$ ) in AST and ALT (17.27 and 14.43%) compared to normal control group. Supplementation of the rat diets with meatballs (20%) decreased the rise of serum AST and ALT compared to the diabetic group by the ratio of 11.69 and 11.74%, respectively. The rate of decreasing was elevated with the supplementation of the meatballs with 0.1% w/w/ by PPME, ROSME, EPME and their mixture which recorded 6.07, 2.98, 4.10 and 2.30; and 6.49, 3.87, 4.94 and 2.05% for AST and ALT, respectively. The rate of suppression was increased with the the mixture treatment gave maximum reduction yield of liver functions enzymes activities when compared with the phyto by-products extracts separated. It could be mean that a combination of different plant parts may be more efficient for reducing serum level of AST and ALT, the biomarkers of liver functions stress, because the interactive effects occurred by different catagories of bioactive compounds of plant parts used.

**Table 6.** The effect of phyto by-products methanolic extracts applied in beef meatballs on liver functions (AST and ALT activities) activities of diabetic rats\*

Value	Control (ve-) Std diet	Control (ve+) Diabetic	Control (ve+) 20% meatballs	Meatballs + Phyto by-product methanolic extracts (0.1%, w/w)			
				PPME	ROSME	EPME	Mix
Serum aspartate aminotransferase (AST, IU/L)							
Mean	46.6	54.65	52.05	49.72	47.99	48.51	47.67
SD	4.21	5.88	11.21	6.09	4.87	4.25	5.57
% of Change	0.00	17.27	11.69	6.70	2.98	4.10	2.30
Serum alanine aminotransferase (ALT, IU/L)							
Mean	29.74	34.03	33.23	31.67	30.89	31.21	30.35
SD	2.98	1.04	6.32	1.54	6.21	5.33	2.77
% of Change	0.00	14.43	11.74	6.49	3.87	4.94	2.05

\*PPME, pomegranate peel methanolic extract; ROSME, red onion skin methanolic extract; EPME, eggplant peel methanolic extract and Mix, mixture of PPME+ ROSME+ EPME + MPP by equal parts. Means in the same row with different litters are significantly different at  $p < 0.05$ .

The effect of plant parts extracts on decreasing the serum liver function enzymes activity have been reported by many studies (El-Nashar, 2007; Elhassaneen *et al.*, 2013 and Sayed Ahmed, 2016). Such effects could be attributed to their high level content of phytochemicals. Our present data with the others reported that PPME, ROSME and EPME are a rich source of different classes of phytochemicals such flavonols, phenolic acids, anthocyanins, alkaloids, carotenoids, phytosterols and organosulfur compounds (Onyeneho and Hettiarachchy, 1993; Rodriguez *et al.*, 1994; Velioglu *et al.*, 1998; Singh *et al.*, 2002; Beattic *et al.*, 2005 and Mohamed, 2012). In general, aminotransferases are normally intracellular enzymes. Thus, the presence of elevated levels of aminotransferase in the plasma indicates damage to cells rich in these

enzymes. For example, physical trauma or a disease process can cause cell lysis, resulting release of intracellular enzymes into the blood. Two amino transferases were found in plasma are of particular diagnostic value AST and ALT. AST enzyme is one of the enzymes tested in the cardiac enzyme series. This enzyme is found in very high concentration within the heart muscles, skeletal muscle cells, and to a lesser degree in the kidney and pancreas. ALT is found predominately in the liver lesser quantities are found in the kidneys, heart and skeletal muscles (Pagana and pagana, 1997).

### **The effect of phyto by-products methanolic extracts applied in beef meatballs on kidney functions of alloxan-induced diabetic rats**

Data in Table (7) illustrated the kidney functions (urea and creatinine concentrations) in serum of alloxane-induced diabetic rats consumed the phyto by-product extracts. From such data it could be noticed that treatment of animals with alloxan caused a significant increased ( $p \leq 0.05$ ) in serum urea concentration (13.57 and 12.00%) compared to normal control group. Supplementation of the rat diets with meatballs (20%) decreased the rise of serum urea and creatinine and recorded 10.66 and 10.00%, respectively. Compared with diabetic control, urea and creatinine were suppressed by supplementation of the meatballs with 0.1% w/w by PPME, ROSME, EPME and their mixture which recorded 2.88, 3.98, 2.08 and 3.17; and 6.00, 4.00, 6.00 and 2.00% for urea and creatinine concentrations, respectively. The rate of suppression was increased with the the mixture treatment gave maximum reduction yield of kidney functions enzymes activities when compared with the phyto by-products separated. It could be mean that a combination of different plant parts may be more efficient for reducing serum level of urea and creatine, the biomarkers of kidney functions stress, because the interactive effects occurred by different categories of bioactive compounds of plant parts used.

The effect of plant parts extracts on decreasing the serum kidney function parameters have been reported by many studies (Rodriguez *et al.*, 1994; El-Nashar, 2007; Mohamed, 2012; Elhassaneen *et al.*, 2013; Elhassaneen *et al.*, 2016 and Sayed Ahmed, 2016). Such as reviewed in

**Table 7.** The effect of phyto by-products methanolic extracts applied in beef meatballs on kidney functions (serum urea and creatinine concentrations) of diabetic rats\*

Value	Control (ve-) Std diet	Control (ve+) Diabetic	Control (ve+) 20% meatballs	Meatballs + Phyto by-product methanolic extracts (0.1%, w/w)			
				PPME	ROSME	EPME	Mix
Urea concentration (mg/dL)							
Mean	49.89	56.66	55.21	53.46	52.53	53.07	52.12
SD	4.32	6.29	4.55	2.88	3.98	2.08	3.17
% of Change	0.00	13.57	10.66	7.16	5.29	6.37	4.47
Creatinine concentration (g/dL)							
Mean	0.50	0.56	0.55	0.53	0.52	0.53	0.51
SD	0.03	0.05	0.02	0.03	0.11	0.12	0.04
% of Change	0.00	12.00	10.00	6.00	4.00	6.00	2.00

\*PPME, pomegranate peel methanolic extract; ROSME, red onion skin methanolic extract; EPME, eggplant peel methanolic extract and Mix, mixture of PPME+ ROSME+ EPME + MPP by equal parts. Means in the same row with different litters are significantly different at  $p < 0.05$ .

these studies the decreasing in serum uric acid and creatinine as the result of feeding phyto by-products including PPME, ROSME, EPME could be attributed to their higher content of phytochemicals such flavonols, phenolic acids, anthocyanins, alkaloids, carotenoids, phytosterols and organosulfur compounds. The possible mode of action of kidney serum parameters-lowering level of the phyto by-product extracts could be explained by one or more of the following process. Polyphenols found in such plant parts improved the kidney weight and serum levels of urea nitrogen, creatinine and creatinine clearance as well as increased the activity of superoxide dismutase in the kidney (reviewed in El-Nashar, 2007). While, many authors such Badary *et al.*, (2005) and Mohamed *et al.*, (2005) found that flavanone produced significant protection of renal function by significant reduction in serum urea and creatinine concentrations, decreased polyuria and reduction in body weight loss, marked reduction in urinary fractional sodium excretion as well as protected kidney tissues. Finally, Van Hoorn *et al.*, (2006) noticed that flavonoids lowered plasma creatinine and urea concentration, both indicating a better postoperative kidney functions.

In conclusion, the present study has demonstrated the potency of PPME, ROSME, EPME and their mixture to ameliorate hyperglycemia and its complications in diabetic rats. The complications include elevated the GSH and decreased the MDA (suppressed oxidative stress) in liver cells and improve the liver and kidney functions. All of these effects could be attributed to their strong antioxidant activity as the result of high phenolics content. These findings provide a basis for the use of phyto by-products extracts for the prevention and early treatment of T2DM.

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## إضافة المستخلصات النباتية الى كرات اللحم البقرى لمعالجة ارتفاع سكر الدم ومضاعفاته فى الفئران المصابة بالسكري المستحث بالألوكسان

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### الملخص العربي :

ينتشر مرض السكري فى شتى أنحاء العالم بما فى ذلك مصر، حيث تسجل الإحصاءات أن هناك فرد من بين كل عشرة أشخاص مصاب بهذا المرض. وتشكل خطورة هذا المرض فى المضاعفات العديدة التى يحدثها ومنها الإجهاد التأكسدى وفساد الدهون والالتهابات وغيرها. لذلك وضعت العديد من الإستراتيجيات لتحسين تلك المضاعفات، حيث أن المعالجات المبكرة والوقاية تلعب دورا حيويا فى إختزال عدد السكان المصابين بهذا المرض. لذلك أجريت الدراسة الحالية بهدف إستبيان مدى فعالية ثلاثة من المستحضرات الميثانولية للنواتج الثانوية النباتية لبعض مصانع الأغذية وهى قشور الرمان والبصل الأحمر والباذنجان المضافة الى كرات اللحم البقرى لمعالجة ارتفاع سكر الدم ومضاعفاته فى الفئران المصابة بالسكري المستحث بالألوكسان. ولقد أوضحت النتائج أن معاملة الفئران بالألوكسان قد تسبب فى زيادة معنوية ( $p \leq 0.05$ ) فى جلوكوز الدم وذلك بنسبة 85,09% مقارنة بالمجموعة الضابطة الطبيعية. كما أدى تدعيم الوجبات الخاصة بالفئران بكرات اللحم بنسبة 20% الى حدوث إنخفاض فى تلك النسبة من سكر الدم لتسجل 63,64%. وعند خلط كرات اللحم بالمستحضرات الميثانولية لقشور الرمان والبصل الأحمر والباذنجان بنسبة 0,1% (وزن/وزن) ومخلوط منها بنسب متساوية قد أحدث إنخاضا معنويا ( $p \leq 0.05$ ) فى نسبة سكر الدم لتسجل معدل إنخفاض 40,87، 30,49، 34,83، 21,64% للمستخلصات السابقة على الوالى. ولقد سجل نفس السلوك لمستوى مركب المالونالدهيد فى أنسجة الكبد الذى يعد مؤشرا حيويا على الجهد التأكسدى والالتهابات فى الكبد. كما حدث تحسن فى وظائف الكبد والكلى فى الفئران المصابة بالسكر وبمعدلات مختلفة نتيجة لخلط كرات اللحم بالمستحضرات الميثانولية لقشور الرمان والبصل الأحمر والباذنجان المختبرة ومخلوطها. ولقد أوضحت النتائج أن تلك التأثيرات تعزى الى النشاط العالى المضاد للأكسدة للمستخلصات النباتية لغناها بالمركبات الفينولية النشطة حيويا. ولعل هذه الإستشكافات تشكل القاعدة الأساسية لإستخدام المستخلصات النباتية لتلك النواتج الثانوية فى الوقاية والعلاج المبكر لمرض السكري من النوع الثانى.

**الكلمات المفتاحية:** قشر الرمان، قشر البصل، قشر الباذنجان، النشاط المضاد للأكسدة، الفينولات الكلية، المالونالدهيد، الجلوتاثيون، وظائف الكبد