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التأثيرات المحتملة لمساحيق قشر البصل الأحمر وقشر الموز و نواة المشمش على السمية الكبدية المستحثة برابع كلوريد الكربون في الفئران

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Abstract:

Liver diseases are among the most challenging healthcare problems worldwide. Thus, there has been a need to explore alternative therapies to chemotherapy drugs that have long been used to treat liver patients, the use of which has been associated with many side effects, in addition to the significant financial cost, which often leads to patient non-compliance. This study was conducted to explore the Effect of three plant parts that result as wastes from food processing, namely red onion skin, banana peels and apricot kernel powders, on hepatotoxicity induced by carbon tetrachloride in rats. Compared with the normal control group rats, the CCl_4 treated rats showed significant ($p \leq 0.05$) decreases in different biological parameters, including BWA, FI and FER, by the rate of -35.16, -33.31 and -31.08%, respectively. Also, biochemical parameters such as serum liver enzyme activities AST, ALT and ALP were significant ($p \leq 0.05$) elevated by the rate of 107.92, 102.71 and 135.64%, respectively. For immunological parameters, Alb was significant ($p \leq 0.05$), decreased by -37.61, and TNF-α increased by 102.84%. Also, oxidative stress is recorded in the blood through a decrease in the level of antioxidants (GSH and GSSG) and increased oxidants (MDA and NO_2). All of those parameters indicated liver injuries by CCl_4. Whereas animals treated with the selected plant parts (red onion skin powder, ROSP, banana peel powder, BBP, apricot kernel powder, AKP and their mixture) showed significant ($p \leq 0.05$) improvements in all previous biological, biochemical, and immunological parameters as well as reduce the oxidative stress markers which indicating the protection against hepatic cell damage. The highest amelioration effects against CCl_4-induced hepatotoxicity were recorded in rats treated with a mixture of plant parts, followed by ROSP, BPP and AKP groups, respectively. In conclusion, the selected plant parts effectively protected against CCl_4-induced hepatotoxicity. Therefore, we recommended powders of these plant parts in concentrations of up to 5% (w/w), an amount to be included in our daily live diets, drinks and food supplements.

Keywords:

Liver functions, blood glucose, albumin, TNF-α, glutathione fractions, oxidative stress, malondialdehyde, nitric oxides.

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مستخلص البحث:

تعتبر أمراض الكبد من أكثر مشاكل الرعاية الصحية تحديًا في جميع أنحاء العالم. وبالتالي، كانت هناك حاجة لاستكشاف علاجات بديلة لأدوية العلاج الكيميائي التي لطالما استُخدمت في علاج مرضى الكبد، والتي ارتبط استخدامها بالعديد من الآثار الجانبية، بالإضافة إلى التكلفة المالية الكبيرة . أجريت هذه الدراسة لاستكشاف تأثير ثلاثة أجزاء نباتية ناتجة عن النواتج الثانوية للأغذية وهي قشر البصل الأحمر وقشر الموز ومسحوق نواة المشمش على السمية الكبدية التي يسببها رابع كلوريد الكربون في الفئران مقارنة بفئران المجموعة الضابطة، أظهرت فئران المجموعة التجريبية بـ CCl انخفاضًا كبيرًا ($p\leq0.05$) في المعاملات البيولوجية المختلفة ، بما في ذلك BWA و FI و FER بمعدل -35.16 و -33.31 و -31.08٪ على التوالي. أيضا ، كانت المعلمات البيوكيميائية مثل نشاط إنزيم الكبد في الدم AST و ALT و ALP مرتفعة ($p\leq0.05$) بمعدل 107.92 و 102.71 و 135.64٪ على التوالي. بالنسبة للمعاملات المناعية ، انخفض ال Alb معنويًا ($p\leq0.05$) بنسبة -37.61 ، وزاد TNF- α بنسبة 102.84 ٪. كما تم تسجيل الإجهاد التأكسدي في الدم من خلال انخفاض مستوى مضادات الأكسدة (GSH و GSSG) وزيادة المواد المؤكسدة (MDA و NO2). كل هذه المعاملات أشارت إلى إصابات الكبد بواسطة CCl. بينما أظهرت الحيوانات المعالجة بالأجزاء النباتية المختارة (مسحوق قشر البصل الأحمر، مسحوق قشر الموز، مسحوق نواة المشمش وخليطهم) تحسنًا معنويًا ($p\leq0.05$) في جميع المتغيرات البيولوجية والكيميائية الحيوية والمناعية السابقة وكذلك تقليل علامات الإجهاد التأكسدي التي تشير إلى الحماية من تلف الخلايا الكبدية .تم تسجيل أعلى تأثيرات التحسن ضد السمية الكبدية المستحثة بـ CCl في الفئران التي عولجت بخليط مساحيق الأجزاء النباتية معا، تليها مجموعات ROSP و BPP و AKP، على التوالي. في الختام، فإن الأجزاء النباتية المختارة تحسن بشكل فعال حالات السمية الكبدية التي يسببها CCl. لذلك ، نوصي بمساحيق هذه الأجزاء النباتية بتركيزات تصل إلى 5٪ (وزن / وزن) ، وهي كمية يجب تضمينها في وجباتنا الغذائية الحية اليومية والمشروبات والمكملات الغذائية.

الكلمات المفتاحية:

وظائف الكبد، جلوكوز الدم، الألبومين، عامل نخر الورم ألفا، جزيئات الجلوتاثيون، الإجهاد التأكسدي، مالونديالديهيد، أكاسيد النيتريك.

1. Introduction

The liver is a major organ only found in all vertebrates. Several hundred vital functions have been identified with the liver. Some of the more well-known functions include the following: 1) production of bile, certain proteins for blood plasma, cholesterol, and special proteins to help carry fats through the body, 2) conversion of excess glucose into glycogen for storage and poisonous ammonia to urea, 3) regulating blood levels of amino acids and blood clotting, 4) processing of hemoglobin for the use of its iron content, 5) resisting infections by making immune factors and removing bacteria from the bloodstream, 6) clearance of bilirubin from red blood cells, 7) stored several products (e.g., glycogen, fat, vitamins and minerals), and 8) clearing the blood of drugs and other poisonous substances/ xenobiotics such as alcohol, pesticides, and food toxins through biotransformation process (**Grażyna *et al.*, 2020; Sayed-Ahmed *et al.*, 2020)**. Because of these previous vital functions, the liver is exposed to various threats that may make it one of the body's most vulnerable and targeted organs. Several studies have reported that disturbances in liver functions are mainly related to the biochemical disturbance of hepatocytes and stimulation of oxidative stress through the generation of reactive oxygen species (ROS) (**Luangmonkong *et al.*, 2018).** Many chemicals routinely produce cellular and metabolic liver damage **(Park *et al.*, 2022).** For example, carbon tetrachloride (CCl_4) represents the most common chemical as widely used as a dry cleaning solvent, to produce refrigerants, to extinguish fires and as a fumigant to kill insect pests in stored grain **(Liu *et al.*,2020)** is one of the most potent hepatotoxins, so much so that it is widely used in scientific research to evaluate hepatoprotective agents (**Meharie *et al.*, 2020 and Sayed-Ahmed *et al.*, 2020).**

Furthermore, **Vanitha *et al.*, 2007** reported that six hours after a single dose (2ml/kg) of treatment of CCl_4 caused hepatotoxic effects through disturbance in serum biochemical marker enzymes. The mechanism of hepatic injury by CCl_4 was explained by several authors as follows: CCl_4 is metabolized/converted primarily in the liver by the cytochrome P450 isoform to the trichloromethyl radical (CCl_3). The CCl_3 radical have several different fates, including converting to the trichloromethyl peroxy radical ($OOCCl_3$), acquiring a hydrogen atom to form chloroform ($CHCl_3$), combining with other CCl_3 radicals to form hexachloroethane (Cl_3CCCl_3) and further metabolized to carbon dioxide (CO_2). Also, CCl_3 radical or its metabolites can react with intracellular molecules to cause lipid peroxidation of membrane-bound fatty acids and other forms of oxidative damage, destructing the cell membrane and intracellular organelles of the hepatocyte (Al Amin and Ritesh, 2022). All of those previous studies with the others indicated that one of the best models of injury produced in the liver is by CCl_4.

Liver diseases are among the most challenging healthcare problems worldwide. Over many decades, pharmacological formulae have been used to treat

liver disease patients. However, this has been associated with many side effects, in addition to the large financial cost, which often leads to patient non-compliance. It all made of the number of drugs used successfully in humans is very small (**Muriel *et al.*, 2017**). Thus, there has been a need to explore special alternative therapies from plant sources that are cost-effective and have few side effects, especially since many plants produce an astonishing amount of complex chemicals that we can use as means to 'reduce and treat disease' (**Mahran *et al.*, 2018-a; Sayed-Ahmed *et al.*, 2020; Elhassaneen *et al.*, 2022).**

Agricultural industrialization in the Arab world results in large quantities of waste, estimated at 18.14 million tons annually, as vegetable and fruit manufacturing waste represent about 6.14 percent of this amount. Also, wasting these waste materials without using them is considered an uneconomic act. In addition, getting rid of them by throwing them into the terrestrial or aquatic environment leads to many environmental problems **(Lewandowski and Skórczewska, 2022).** Waste in food processing is characterized by a high ratio of product-specific waste/by-products. Such plant parts could be considered a good source of phytochemicals. They are a large group of plant-derived bioactive compounds such as polyphenolics, polysaccharides, terpenes, volatile oils, and indoles containing compounds hypothesized to be responsible for much of the disease protection such as cancer, cardiovascular disease, diabetes mellitus, cataracts, aging and rheumatoid arthritis (**Elhassaneen *et al.*, 2016 a-d; Emam *et al.*, 2018).** In the present work, we will limit our study here to three of the by-products that result from food processing operations: onion skin, banana peel, and apricot kernels.

Onion (*Allium cepa* L.) belongs to the family *Alliaceae* and represents one of the most important crops around the world, including Egypt. World production of onion bulbs (dry onions) in 2018 was estimated at 96.7 million tonnes **(FAO, 2020).** It is reviewed that approximately 38 % of the fresh weight of processed onion is not suitable for consumption and is discarded as waste. Also, the annual generation of onion waste in the EU is as high as 500 000 tonnes **(Vojvodić Cebin *et al.*, 2020).** The main waste from the industrial onion process results from peeling the onion bulbs, including the skin, the two outer fleshy leaves and the top and bottom bulbs. Such wastes are a good source of flavor components, fiber, and polyphenolics and are particularly rich in quercetin glycosides (**Mahran *et al.*, 2018-a; Shalaby, 2015; Vojvodić Cebin *et al.*, 2020**). Several studies proved that onion skin consumption imparts health benefits, e.g., reduced risk of coronary heart disease, stroke, diabetes, obesity and cancer (**Elmaadawy *et al.*, 2016; Almutairiu, 2020).** Banana (*Musa sapientum*) belongs to the family *Musaceae*, which plays an important role in many tropical regions' economies and food security **(Ngwang, 2015).** Banana peels ranged about 30 to 40 % of the fruit weight. Significant quantities of banana peels, equivalent to 40% of the total weight of fresh bananas, are generated as waste

products in industries producing banana-based products **(Ragab *et al*., 2016).** Banana fruit peel extracts are rich in bioactive compounds such as polyphenolics, alkaloids, anthocyanin, flavonoids, glycosides, phlorotannins, fiber, organic acids, polyunsaturated fatty acids (PUFA), pectin, tannins and terpenoids **(Florenta *et al*., 2015; Kumar, 2015; Maduwanthi and Marapana, 2017).** Thus, they have passed a broad spectrum of biological activities such as antioxidant, anti-obese and antitumor agents **(Kumar *et al*., 2015).** Apricot (*Primus Armeniaca* L., family: *Rosacea*) is mostly grown in Mediterranean countries, Iran, Pakistan, China, Russia, and the United States of America. **FAO (2019)** reports that global annual fresh apricot production was 4,260,466 tonnes, whereas the production of dried apricot was 162,635 tons in 2018 and 2019. During the food processing of apricot fruits into its various products, the bitter kernels of the fruits are considered a waste of that industry. According to the available literature, apricot seeds contain several bioactive compounds such as cyanogenic glycoside amygdalin, polyphenolics, flavonoids, anthocyanin, carotenoids, phytosterols, monounsaturated and polyunsaturated fatty acids **(Almutairiu, 2020; Akhone et al., 2022).** Such compounds presented pharmacological activities of antitumor, analgesic, immunomodulatory, anti-atherosclerosis, anti-inflammatory, ameliorating the digestive and reproductive systems, reducing blood glucose, anti-fibrotic, improving neurodegeneration and myocardial hypertrophy (**Tahoon, 2019; Akhone et al., 2022).**

Despite the above, there is still a shortage of information regarding food processing waste as a functional food in liver diseases. Therefore, the present study aims to explore the Effect of three wastes that result from food processing, namely onion skin, banana peels and apricot kernel powders, on hepatotoxicity induced by carbon tetrachloride in rats.

2. Materials and Methods

2.1. Materials

2.1.1. Wastes/by-products

Red onion (*Allium cepa* L.) skin was obtained from the New Beni Suef Company for Preservation, dehydration and Industrialization of Vegetables (ElShinawy), Beni Suef Elgudida City, Nile East, Beni Suef Governorate, Egypt; and banana (*Musa sapientum*) peels as well as Apricot (*Primus armeniaca* L.) kernels were obtained from Port Said City markets, Port Said Governorate, Egypt. The collected samples were transported to the laboratory and used for skin, peel and kernel powders preparation.

2.1.2. Chemicals, solvents and buffers

All chemicals, solvents and buffers (Except those mentioned next to it) were purchased from Al-Gomhoryia Company for Trading Drugs, Chemicals and Medical

Equipment, Cairo, Egypt. Carbon tetrachloride (CCl_4) was obtained from the Egyptian agent of Sigma Chemical Co. (St. Louis, MO). Casein was obtained from Morgan Chemical Co., Cairo, Egypt.

2.1.3. Kits

Kit's assays for Alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP), malondialdehyde (MDA) were purchased from BIODIAGNOSTIC, Dokki, Giza, Egypt. Albumin (Alb) was determined using kits purchased from El-Nasr Pharmaceutical Chemicals Company, Cairo, Egypt. TNF-α was assayed by kit was provided by Nawah Scientific, Almokattam, Cairo, Egypt. GSH and GSSG were assayed by the kits provided by MyBioSource, Inc., San Diego, CA, USA.

2.2. Methods

2.2.1. Preparation of by-products powder

2.2.1.1. Banana peels powder (BPP)

Banana peels were washed and then dried in a Vacuum drying oven (Zhejiang FUXIA Medical Technology Co., Ltd., China) at a pressure of 5 kPa and temperature of 60 °C until the final moisture content, 10%. The dried peels were ground into a fine powder at high mixer speed (Moulinex Egypt, Al-Araby Co., Egypt). The material that passed through an 80 mesh sieve was retained for use.

2.2.1.2. Red onion skin powder (ROSP)

Red onion skin was washed and dried in a hot air oven (Horizontal Forced Air Drier, Proctor and Schwartz Inc., Philadelphia, PA) at 55 ^{0}C for 6 h. The dried skin was ground into a fine powder at high mixer speed (Moulinex Egypt, Al-Araby Co., Egypt). The material that passed through an 80 mesh sieve was retained for use.

2.2.1.3. Apricot kernel powder (AKP)

Unripe apricot fruits were washed sliced and kernels separated. The kernels were cleaned and broken, and the internal content was extracted and dried at 70 ^{0}C for 8 h in a hot air oven (AFOS Mini Smoker, England). This is followed by milling with a grinder (Retsch Micro Universal Bench Top Grinder, Germany) to produce the powder, and the material that passed through an 80 mesh sieve was retained for use.

2.3. Biological Experiments

2.3.1. Ethical approval

All biological experiments in the current study were approved by the Scientific Research Ethics Committee (Animal Care and Use), Faculty of Home Economics, Menoufia University, Shebin El-Kom, Egypt (approval # 10-SREC-12-2021).

2.3.2. Animals

Animals used in this study, adult male albino, Sprague Dawley, rats (140-150 g per each) were obtained from the Research Institute of Ophthalmology, Giza, Egypt.

2.3.3. Basal diet (BD)

The BD for the experimental rats feeding was 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 vitamin and salt mixture components were formulated according to **AIN (1993).**

2.3.4. Induction of hepatotoxicity in Rats

Thirty-six rats were administrated by intraperitoneal (IP) injection of carbon tetrachloride (CCl4) in paraffin oil, 50% V/V (2 ml/kg bw), twice a week, for two weeks to induce chronic damage of the liver according to the method described by **Jayasekhar *et al.*, (1997).** Hepatotoxicity was confirmed by taking a random sample (3 rats) of experimental animals and biochemical examination.

2.3.5. Experimental design

All biological experiments of the current study were performed to comply with the rulings/ provisions of the Institute of Laboratory Animal Resources, Commission on Life Sciences, National Research Council **(NRC, 1996).** Rats (n=36 rats) were housed individually in wire cages in a room maintained at 24 ± 2 0C, relative humidity (53±3%), a 12-hr lighting cycle and kept under normal healthy conditions. For acclimatization, all rats were fed on BD for one week before starting the experiment. After that, the rats were divided into two main groups. First, the main group (6 rats), normal control (Group 1, 6 rats), still fed on BD and the other main group (30 rats) was used for hepatotoxicity induction and classified into five subgroups as follows: group (2), model control, fed on BD only as a positive control (rats with hepatotoxicity) and groups (3, 4, 5 and 6) fed on BD containing 5% (w/w) of apricot kernel powder (AKP), red onion skin powder (ROSP); banana peel powder (BPP) and Mixture (ASP + ROSP + BPP by equal parts). Based on previous studies, plant parts powder concentrations were selected for the current study (**Mahran *et al.*, 2018-a**; **Sayed-Ahmed *et al.*, 2020; Almutairiu, 2020).** All previous groups were kept, each group in one cage, for 28 days. Rats groups were weighed at the beginning of the experiments, then weekly and at the end of the experimental period.

2.3.6. Biological evaluation

During the experimental period (28 days), the diet consumed was recorded every day and body weight was recorded every week. The body weight gain (BWG, %), feed intake (FI), and feed efficiency ratio (FER) were determined according to Chapman et al. (1959) using the following equations: BWG (%) = (Final weight – Initial weight)/ Initial weight×100, FER = Grams gain in body weight (g/28 day)/ Grams feed intake (g/28 day).

2.3.7. Blood sampling

At the end of the experiment period, 8 weeks, rats were fasted for 12 hours and then sacrificed under ether anesthetized to collect blood samples using the abdominal aorta. The serum was separated from the blood samples according to the method of **Drury and Wallington (1980)** and stored at -20 ^{o}C until analysis.

2.3.8. Hematological analysis

2.3.8.1. Liver functions

Serum glutamic pyruvic transaminase ALT) and serum glutamic oxaloacetic transaminase (AST) activities were measured in serum using the modified kinetic method of **Tietz *et al*. (1976)** by using a kit supplied by Biocon Company. Alkaline Phosphatase (ALP) activity was determined using **Vassault et al. (1999)** modified kinetic method.

2.3.8.2. Serum glucose

Enzymatic determination of serum glucose was carried out colorimetrically, according to **Yound (1975).**

2.3.8.3. Immunological assays

Albumin was determined in plasma using kits purchased from El-Nasr Pharmaceutical Chemicals Company, Cairo, Egypt. TNF-α was determined by a sandwich enzyme-linked immunosorbent assay (ELISA), utilizing two monoclonal antibodies directed against separate antigenic determinants on rat TNF- α. The kits for the assay were provided by Adlitteram Diagnostic Laboratories Inc. (San Diego, CA, US).

2.3.8.4. Biological antioxidants

Glutathione fractions (GSH and GSSG) were measured colorimetrically in serum samples, as described by **Ellman (1959).**

2.3.8.5. Biological oxidants

Serum nitrite (NO_2) was determined fluorometric such as described by **Misko *et al.* (1993).** Serum malondialdehyde (MDA) content was measured by the thiobarbituric acid (TBA) method according to the methods of **Buege and Aust (1978).** Reactive oxygen species (ROS) was determined by a colorimetric method described by **Erel (2005).**

2.4. 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).

3. 5. Results and Discussion

3.5.1. Effect of selected plant parts consumption on BWG, FI and FER of hepatotoxic rats induced by CCl_4

BWG, FI and FER of rats injected with CCl_4 and consumed the selected plant parts were shown in Table (1). From such data, it could be noticed that the CCl_4-treated rats exhibited a significant ($p \leq 0.05$) decrease in BWG (-35.16), FI (-33.31) and FER (-31.08) compared to the normal control group. However, the replacement of diets starch with 5% of apricot kernel powder (AKP), red onion skin powder (ROSP), and banana peel powder (BPP) and their mixture (AKP + ROSP + BPP by equal parts) induced significant ($p \leq 0.05$) increasing in BWG, FI and FER of the hepatotoxic rats. The highest Effect on BWG, FI and FER increasing was recorded for the plant parts mixture, followed by BPP, ROSP and AKP, respectively. Such data agree with that of several authors on different parts of plant origin **(Elhassaneen *et al.*, 2019; Sayed-Ahmed *et al.*, 2020; Elhassaneen *et al.*, 2021)**. In the same context, other studies have decided hepatic rats reveal a significant reduction in body weight and feed intake **(Hamzawy *et al.*, 2013; Abd El-Rahman, 2021). Morresion and Hark (1999)** explained that liver disease could lead to malnutrition. The major causes of malnutrition in patients with liver disease are poor dietary/feed intake (FI), maldigestion, malabsorption and abnormalities in the metabolism and storage of macro and micronutrients. On the other side, several studies indicated that the selected plant parts had been considered a good source of bioactive compounds, including polyphenols, flavonols, anthocyanins, alkaloids, carotenoids, phytosterols, essential fatty acids and organosulfur compounds, which plays significant roles in manipulation the adverse effects of CCl4 in body weight, FU and FER **(Tahoon , 2019; Elhassaneen et al., 2021-a).**

3.5.2. Effect of selected plant parts consumption on Liver functions of hepatotoxic rats induced by CCl4

The Effect of selected plant parts consumption on liver functions of hepatotoxic rats induced by CCl_4 was shown in Table (2). From such data, it could be noticed that the CCl_4-treated rats exhibited a significant ($p \leq 0.05$) increase in AST (107.92), ALT (102.71) and ALP (135.64) compared to the normal control group. However, the replacement of diets starch with 5% of AKP, ROSP, BPP and their mixture induced significant ($p \leq 0.05$) decreases in the hepatotoxic rats' AST, ALT and ALP. The highest effects in manipulating the liver function disorders induced by CCl_4 in rats were recorded for the plant parts mixture, followed by ROSP, BPP and AKP, respectively.

Aminotransferases (AST and ALT) and ALP enzymes are normally intracellular enzymes. Thus, the presence of elevated levels of these enzymes in plasma indicates damage to cells rich in these enzymes, including the liver **(Pagana and pagana, 1997).** Aminotransferases and ALP enzymes are elevated in nearly all liver diseases. Still, they are particularly high in conditions that cause extensive cell necrosis, such as severe viral hepatitis and prolongated circulatory collapse. So, the measurements of these enzymes are often useful in determining the course of liver damage **(Pagana and pagana, 1997 and Hong *et al.*, 2002).** Data from the present study with the other reported that aminotransferases and ALP might be elevated significantly in serum as the liver hepatotoxicity induced by CCl_4 **(Elhassaneen *et al.*,2016-b and c; 2021; Sayed-Ahmed *et al.*, 2020*).*** The nutritional intervention using the plant parts that were used in the case study (AKP, ROSP, BPP and their mixture) led to a significant (($p \leq 0.05$) decrease in the degree of activity of these enzymes. This Effect may be attributed to the high content of bioactive compounds that characterize these plant parts, which include polyphenolics, flavonols, phenolic acids, anthocyanins, alkaloids, carotenoids, phytosterols, essential fatty acids, organosulfur compounds, trace minerals, vitamins etc., **(Mahran *et al.*,2018-b and Sayed, 2020).** This hypothesis was confirmed by what was seen in the results of the current study, which includes the highest increase in the rate of suppression in enzymatic activity expressing liver functions in the experimental group that consumed the mixture of plant parts powder when compared to those groups that consumed plant parts separately. It may mean that the mixture group was more effective compared to the other treatment groups for reducing the serum level of AST, ALT and ALP, which are biomarkers of liver function stress because the interactive/ antagonism effects were due to the different classes of bioactive compounds present in all plant parts used. Similar results were obtained in similar studies using other plant parts containing the same biologically active compounds found in AKP, ROSP, BPP and their mixture **(Elhassaneen *et al.*,2021 b and c ; Sayed - Ahmed *et al.*, 2020).** From all of the above studies with the others, the

possible mode of action of liver serum enzymes-lowering activity of the diets mixed with selected plant including AKP, ROSP, BPP and their mixture could be explained by one or more of the following process: 1) flavonoids found in all the tested plant parts are known to block the hepatocellular uptake of bile acids **(Elhassaneen *et al.*, 2016-d);** 2) flavonoids pretreatment improved the antioxidant capacity of the liver, diminished the bilirubin concentration compared with the groups without treatment (**Beattic *et al.*, 2005)**; 3) flavonol glycosides found in all tested plant parts reduced the elevated levels of the following serum enzymes, AST, ALT and ALP against CCl4-induced liver damage in rats **(Singab *et al.*, 2005)** 4) pretreatment with flavonoids found in all tested plant parts were not only able to suppress the elevation of AST and ALT but also reduce the damage of hepatocytes *in vitro* **(El-Nashar, (2007);** 5) flavonoids have exhibited strong antioxidant activity against reactive oxygen species (ROS) *in vitro* and the hepatoprotective activity of flavonoids was possibly due to its antioxidant properties, acting as scavengers of radicals **(Lin and Jian-Guo, 2018);** 6) flavonoids can enhance the antioxidant functions of liver by increasing the level of superoxide dismutase, glutathione s-transferase and glutathione peroxidase, improve insulin sensitivity and inhibit hepatic stellate cell activation by regulating the activities of the enzymes **(Lin and Jian-Guo, 2018)**; 7) Phenolic compounds found in all tested plant parts offer hepatoprotection including treating cancer, oxidative damage and inflammation **(Saha *et al.*, 2019).** Sulfur-Containing Compounds found in ROSP have explored amelioration against Liver Fibrosis, oxidative stress, and chronic inflammation **(Milito *et al.*, 2019).** 6) phytochemicals in AKP can reduce the liver's damage, i.e., suppresses the elevation of AST, ALT and ALP by improving the antioxidant defense system in red blood cells **(Shalaby, 2015).**

3.5.3. Effect of selected plant parts consumption on serum glucose concentration of hepatotoxic rats induced by CCl_4 :

The Effect of AKP, ROSP, BPP and their mixture on the serum glucose of hepatotoxic rats are shown in Table (3). It could be noticed that CCl_4 induced a significant increased ($p \leq 0.05$) in serum glucose (73.67%) compared to the normal control group. However, the replacement of diets starch with 5% of AKP, ROSP, BPP and their mixture induced a significant ($p \leq 0.05$) decrease in the glucose of the hepatotoxic rats. The highest effects in manipulating the serum hyperglycemia induced by CCl_4 in rats were recorded for the plant parts mixture, followed by ROSP, BPP and AKP, respectively. Data from the present study with the other reported that serum glucose might be elevated significantly as the liver hepatotoxicity induced by CCl_4 **(Elhassaneen *et al.*, 2016-c; 2021 b and c; Sayed-Ahmed *et al.*, 2020*).*** The nutritional intervention using the selected plant parts that were used in the case study (AKP, ROSP, BPP and their mixture) led to a significant (($p \leq 0.05$) decrease in serum

glucose level. The decreasing serum glucose resulting from feeding plant parts, including AKP, ROSP and BPP, was the subject of several studies. For example, significant research has been done on the Effect of onion/onion skin consumption on diabetic conditions and found that its organosulfur compounds, S-methyl cysteine sulfoxide and S-allyl cysteine sulfoxide, were linked to significant amelioration of hyperglycemia in rats **(Elmaadawy, 2016).** Also, onion peel extract 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 down-regulating inflammatory gene expression in the liver **(Jung *et al.*, 2011).** Banana peel extract significantly reduces the body's elevated serum fasting glucose levels **(Sayed, 2020).** Also, **Abd EL- Baky, 2010)** observed that the methanolic extract of banana significantly lowered fasting blood glucose levels in the treated rats. On the other side, apricot kernel oil is a rich source of MUFA and PUFA, including mainly oleic (about 70%) and linoleic acids, respectively and considered a good bioactive source compound such as tocopherols and phytosterols consisting mainly of the α-isomer and β-sitosterol, respectively. These compounds are known for their properties in scavenging free radicals, inhibiting lipid oxidation and improving glucose response and insulin resistance associated with type 2 diabetes **(Shalaby, 2015; Jung *et al.*, 2011; El-Safty, 2012; Elhassaneen *et al.*, 2016-d).** Additionally, data from the current work indicated that the mixture treatment group gave maximum hypoglycemic yield compared to the separated plant parts groups. It may mean that the mixture group was more effective than the other treatment groups for decreasing serum glucose level, the biomarkers of pancreas functions stress because the interactive/ antagonism effects were due to the different classes of bioactive compounds present in all plant parts used.

3.5.4. Effect of selected plant parts consumption on serum immunological parameters of hepatotoxic rats induced by CCl4

The Effect of selected plant parts consumption on serum immunological parameters (albumin and tumor necrosis factor levels) of hepatotoxic rats induced by CCl_4 was shown in Table (4). From such data, it could be noticed that the CCl_4-treated rats exhibited a significant ($p \leq 0.05$) decrease in serum albumin (-37.61) and an increase in tumor necrosis factor (102.71%) compared to the normal control group. However, the replacement of diets starch with 5% of AKP, ROSP, BPP and their mixture induced a significant ($p \leq 0.05$) increase in serum albumin and a decrease in tumor necrosis factor of the hepatotoxic rats. The highest effects in manipulating the serum immunological parameters induced by CCl_4 in rats were recorded for the plant parts mixture, followed by ROSP, AKP and BPP, respectively. In similar studies, CCl_4-induced significant decrease in the serum albumin content

as the consequence of liver toxification (**Abd El-Rahman, 2021and Sayed-Ahmed *et al.*, 2020).** Also, **Koneri *et al*. (2008)** reported that hypoalbuminemia is most frequent in the presence of advanced chronic liver diseases. The decline in serum albumin can be a useful index of the severity of cellular dysfunction in chronic liver diseases. In the current study, plant parts (AKP, ROSP, BPP and their mixture) significantly ($p \leq 0.05$) increased serum albumin levels which demonstrates that it can prevent or repair hepatocytes damage. Such findings follow that observed by **Ahmed, (2014),** who found that pretreatment with cape gooseberry fruits extract (contains almost the bioactive compounds found in the tested plant parts) exhibited significant ($p \leq 0.05$) improvement in serum albumin compared to cisplatin (kidney failure inducer) group. Such role of the plant parts in the manipulation of hypoalbuminemia could be of a high degree of importance because serum albumin in humans is the main protein of blood plasma and makes up around 50%. Albumin is an important metal-binding protein. It is a sacrificial antioxidant that can bind copper tightly and iron weakly to its surface, serving as a target for their related free radical reactions. Thus it inhibits copper ion-dependent lipid peroxidation **(Young and Woodside, 2001).** Also, it is a transport protein that binds to various ligands such as water, fatty acids, hormones, bilirubin, pharmaceuticals and cations (including Na^+, K^+ and Ca^{2+}) and carries them around. Thus, the main function of albumin is to regulate the oncotic pressure of blood **(Farrugia, 2010).**

On the other side, data from the current study indicated that plant parts (AKP, ROSP, BPP and their mixture) significantly ($p \leq 0.05$) decreased the serum TNF-α levels, which demonstrates that it can prevent tissue damage, including the liver. In similar studies, treatment patient's groups given extracts from medicinal mushrooms (contains almost the bioactive compounds found in the tested plant parts) were found to decrease the expression of tumor markers (TNF-α) and increase natural killer (NK) cells activities compared to control Groups **(Venturella *et al.*, 2021).** The role of the plant parts in suppressing TNF-α could be highly important because it is a pro-inflammatory cytokine that plays an important role in initiating the inflammatory tissue reaction **(Kim *et al.*, 2003).** Also, TNF-α damages endothelial cells, increases vascular permeability, and stimulates IL-1 production by vascular endothelial cells, endothelin and other inflammatory mediators, leading to tissue inflammation **(Ferrero *et al.*, 2007).** Furthermore, TNF-α stimulates neutrophil degranulation "outbursts," which produce oxygen-free radicals leading to tissue damage **(Gao, 1999).**

3.5.5. Plant parts consumption on plasma glutathione fractions concentration of hepatotoxic rats induced by CCl_4

Glutathione fractions concentration in the plasma of hepatotoxic rats consumed selected plant parts (AKP, ROSP, BPP and their mixture) was shown in Table (5).

From such data, it could be noticed that the CCl_4-treated rats exhibited a significant ($p \leq 0.05$) decrease in plasma-reduced glutathione (GSH, -39.77%) and oxidized glutathione (GSSG, -22.80%) compared to the normal control group. However, the replacement of diets starch with 5% of AKP, ROSP, BPP and their mixture induced a significant ($p \leq 0.05$) increase in serum GSH and GSSG of the hepatotoxic rats. The highest amelioration effects of the serum glutathione fractions induced by CCl_4 in rats were recorded for the plant parts mixture, followed by ROSP, BPP and AKP, respectively.

Glutathione is a vital tripeptide made from the amino acids glycine, cysteine, and glutamic acid. It is produced by the liver and involved in several body processes such as tissue building and repair, making chemicals and proteins needed in the body, and immune system function **(Voet and Voet, 1990).** Also, glutathione has received more attention regarding its roles in the detoxifications process through the following: 1) as a key conjugate of electrophilic intermediates, principally via glutathione-*s*-transferase activities in phase II metabolism/biotransformation, and 2) as an important biological antioxidant capable of preventing damage to important cellular components caused by reactive oxygen species such as free radicals, peroxides, lipid peroxides, and heavy metals **(Elhassaneen *et al.*, 2016-a; Mahran *et al.*, 2018-b).** Data from the present study suggested that secretion of glutathione fractions from the liver to the blood might be blocked by CCl_4 because of intracellular structural failure, the elevation of the lipid peroxidation and the energy depletion suggested by the marked decrease in glycogen content **(Elhassaneen et al.,2021-b; Sayed- Ahmed et al., 2020).** The nutritional intervention using the plant parts that were used in the case study (AKP, ROSP, BPP and their mixture) led to a significant (($p \leq 0.05$) increase in the concentration of glutathione fractions. This Effect may be attributed to the high content of bioactive compounds that characterize these plant parts, which include polyphenolics, flavonols, phenolic acids, anthocyanins, alkaloids, carotenoids, phytosterols, essential fatty acids, organosulfur compounds, trace minerals, vitamins etc., **(Mahran *et al.*,2018-a; Tahoon, 2019; and Sayed, 2020).** On the other side, a fall in serum glutathione fractions was observed generally in the present study, accompanied by a concomitant decrease in the ratio of GSH/GSSG. With this context, **Di Giulio (1991)** reported that the Effect of oxygen-generating compounds such as CCl_4 refers to its Effect on the so-called redox state (GSH / GSSG) of cells or tissues. In the healthy cell, the ratios of GSH/GSSG are typically very high, i.e.,>10. The CCl_4-treated rats exhibited a significant ($p \leq 0.05$) decrease in serum redox state (GSH / GSSG) by -21.98%. The consumption of selected plant parts by 5% increased the GSH/GSSG ratio near the value recorded by the normal group rats. Such data proposed that selected plant parts may suppress the CCl_4-induced oxyradical fluxes, which may increase the GSH/GSSG ratio.

3.5.6. Effect of selected plant parts consumption on plasma markers of oxidative stress of hepatotoxic rats induced by CCl_4

Levels of MDA (expressed as the concentration of substances reacting to thiobarbituric acid) and NO_2, as well as total NO_2/NO_3 (marker for nitric oxide generation) as markers of oxidative stress in hepatotoxic rats, consumed selected plant parts (AKP, ROSP, BPP and their mixture) was shown in Table (6). Such data indicated that the CCl_4-treated rats exhibited significantly ($p \leq 0.05$) increases in serum MDA(-31.68), NO_2 (52.24) and NO_2/NO_3 (41.44) compared to the normal control group. However, the replacement of diets starch with 5% of AKP, ROSP, BPP and their mixture induced a significant ($p \leq 0.05$) decrease in serum MDA, NO_2 and NO_2/NO_3 of the hepatotoxic rats. The highest effects in manipulating the serum neurotransmitters parameters induced by CCl_4 in rats were recorded for the plant parts mixture, followed by ROSP, BPP and AKP, respectively.

In general, several studies reported that CCl_4^- induced liver damage came through metabolizes CCl_4 to its radicals (trichloromethyl, CCl_3^-) by the liver cytochrome P450, which reactively binds to O_2 to form trichloromethyl peroxyl (CCl_3OO^-) radicals (Masuda. 2006). Such radicals subsequently cause lipid peroxidation of membrane-bound fatty acids resulting in harmful degradative products, namely malondialdehyde (MDA) which shows a mutagenic Effect via reacting with guanine nucleotide in DNA (Cline et al., 2004). Furthermore, cross-linking of MDA with the membrane components destroys the cell membrane and intracellular organelles of the hepatocyte, causing cell injury and probably causing the formation of atherosclerotic plaques **(Nilanjana., 2013).** On the other side, nitric oxide synthase catalyzes the conversion of L-arginine to coralline and highly reactive free radical species, nitric oxide (NO^*) (Ali et al., 2012). NO^* can react with oxygen and water to form nitrite (NO_2) and nitrate (NO_3), with the amino and thiol groups of protein to produce nitrosylated species, with hemoglobin to form iron-nitrosyl adducts and NO_3 in blood, and with superoxide anion (O_2-) to make NO_3 **(Misko *et al.*, 1993).** Such as reported in several studies that the excess production of nitric oxides in the body has been investigated in the pathogenesis and tissue destruction of a growing number of diseases, including septic shock, arthritis, nasal polyposis, obesity, anemia, cardiovascular disease, diabetes and cancer **(Elhassaneen et al., 2020; Sayed-Ahmed *et al.*, 2020; Mehram *et al.*, 2021).**

In the present study, high levels of MDA and nitric oxides were noted to represent an important finding to support our hypothesis, i.e., CCl_4 toxicity is associated with increased oxidative stress and free radicals-associated injury. Thus, the significant decreasing rate of the formation of MDA and nitric oxides in serum as the result of selected plant parts (AKP, ROSP, BPP and their mixture) treatment proposed that hepatoprotection may also be mediated by the antioxidant activities,

radical-scavenging properties, and lipid peroxidation and nitric oxide synthase inhibition of plant parts. These putative mechanisms may be due mainly to the high content of selected plant parts of bioactive compounds. In this context, AKP determines radical scavenging power, anti-lipid peroxidative activity, reducing power and total phenolic content related to reducing oxidative Stress **(Durmaz *et al.*, 2009).**

Furthermore, the banana peel extracts are promising sources of bioactive compounds such as alkaloids, anthocyanin, flavonoids, glycosides, phlorotannins, tannins and terpenoids related to reducing oxidative Stress **(Kumar, 2015).** Additionally, data from the current work indicated that the mixture treatment group gave maximum reduction yield of oxidative stress parameters in plasma compared with the separated plant parts groups. It may mean that the mixture group was more effective compared to the other treatment groups for decreasing serum MDA and nitric oxides level, the biomarkers of oxidative stress and inflammation in the body, because the interactive/ antagonism effects were due to the different classes of bioactive compounds present in all plant parts used.

4. Conclusion

The present study has demonstrated that the selected plant parts, including AKP, ROSP, BPP and their mixture, were effective in protecting against CCl_4-induced hepatotoxicity. These results supported our hypothesis that the selected plant parts contain several classes of bioactive compounds (phytochemicals) with other nutrients that can prevent or inhibit CCl_4 hepatotoxicity through one or more of the following mechanisms: 1) Inhibition of excessive enzymatic activity expressed in liver functions, 2) causes of the hypoglycemic Effect, 3) raising the rate of immune markers in the blood, 4) improving the state of the antioxidant defense system in serum, and 4) reducing the degree of oxidative stress in serum, i.e., formation of oxidants. Therefore, we recommended powders of these plant parts in concentrations of up to 5% (w/w), an amount to be included in our daily live diets, drinks and food supplements.

Abbreviations

Alb, albumin; ALP, alkaline phosphatase; ALT, alanine aminotransferase; AKP, apricot kernel powder; AST, aspartate aminotransferase; BD, Basal diet; BPP, banana peel powder; BWG, body weight gain; CCl_4, carbon tetrachloride; FER, feed efficiency ratio; FI, feed intake; GSH, reduced glutathione; GSSG, oxidized glutathione; MDA, malondialdehyde; NO_2, nitrite; NO_3, Nitrate; ROS, reactive oxygen species; ROSP, red onion skin powder; TBA, thiobarbituric acid; TNF-α, tumor necrosis factor-alpha.

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Conflict of interests

Authors declared no competing of interest whatsoever

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Table 1. Effect of selected plant parts consumption on BWG, FI and FER of hepatotoxic rats induced by CCl_4*

Value	Normal control	Model control	Plant parts (5%, w/w) intervention groups			
			AKP	ROSP	BPP	Mix
Body weight gain (BWG, %)						
Mean	0.91 [a]	0.59 [c]	0.69 [bc]	0.72 [b]	0.73 [b]	0.78 [b]
SD	0.09	0.07	0.07	0.08	0.05	0.04
% of change	0.00	-35.16	-24.18	-20.88	-19.78	-14.29
Feed intake (FI, g/day/rat)						
Mean	11.98 [a]	7.99 [c]	9.16 [b]	9.69 [b]	9.88 [ab]	10.27 [a]
SD	0.97	1.01	0.84	0.59	0.71	0.80
% of change	0.00	-33.31	-23.54	-19.12	-17.53	-14.27
Feed efficiency ratio (FER)						
Mean	0.074 [a]	0.051 [c]	0.059 [b]	0.061 [b]	0.062 [ab]	0.065 [a]
SD	0.006	0.009	0.006	0.004	0.007	0.008
% of change	0.00	-31.08	-20.27	-17.57	-16.22	-12.16

Means (n=6) in the same column with different superscript letters are significantly different at $p \leq 0.05$. Normal control: healthy rats without intervention; Model control: CCl4-induced hepatotoxicity rats without intervention; plant parts intervention groups: CCl4 induced-hepatotoxicity rats with plant parts intervention. AKP, apricot kernel powder, ROSP, red onion skin powder; BPP, banana peel powder and Mix, mixture of ASP + ROSP + BPP by equal parts.

Table 2. Effect of selected plant parts consumption on serum Liver functions enzyme of hepatotoxic rats induced by CCl_4*

Value	Normal control	Model control	Plant parts (5%, w/w) intervention groups			
			AKP	ROSP	BPP	Mix
Serum Aspartate aminotransferase (AST)activity (U/L)						
Mean	48.90 ^{c}	101.67 ^{a}	90.78 ^{b}	83.48 ^{b}	85.12 ^{b}	77.63 ^{bc}
SD	5.85	3.35	3.85	6.46	6.86	5.19
% of change	0.00	107.92	85.65	70.72	74.07	58.75
Serum alanine aminotransferase (ALT) activity (U/L)						
Mean	28.45 ^{c}	57.67 ^{a}	50.99 ^{b}	46.85 ^{b}	48.08 ^{b}	42.29 ^{bc}
SD	3.11	5.98	6.21	4.05	3.78	4.17
% of change	0.00	102.71	79.24	64.68	69.01	48.65
Serum alkaline phosphatase (ALP,U/L)						
Mean	121.14 ^{d}	285.45 ^{a}	229.12 ^{b}	202.98 ^{bc}	215.29 ^{b}	183.09 ^{c}
SD	9.32	17.43	10.66	19.65	10.99	12.87
% of change	0.00	135.64	89.14	67.56	77.72	51.14

Means (n=6) in the same column with different superscript letters are significantly different at $p \leq 0.05$. Normal control: healthy rats without intervention; Model control: CCl4-induced hepatotoxicity rats without intervention; plant parts intervention groups: CCl4 induced-hepatotoxicity rats with plant parts intervention. AKP, apricot kernel powder, ROSP, red onion skin powder; BPP, banana peel powder and Mix, mixture of ASP + ROSP + BPP by equal parts.

Table 3. Effect of selected plant parts consumption on serum glucose concentration (mg/dl) of hepatotoxic rats induced by CCl_4

Value	Normal control	Model control	Plant part (5%, w/w) intervention groups			
			AKP	ROSP	BPP	Mix
Mean	91.56 [c]	159.01 [a]	136.77 [b]	127.10 [b]	133.37 [b]	120.13 [bc]
SD	4.18	8.04	5.37	4.47	6.71	4.37
% of Change	0.00	73.67	49.38	38.82	45.67	31.20

Means (n=6) in the same column with different superscript letters are significantly different at $p \leq 0.05$. Normal control: healthy rats without intervention; Model control: CCl4-induced hepatotoxicity rats without intervention; plant parts intervention groups: CCl4 induced-hepatotoxicity rats with plant parts intervention. AKP, apricot kernel powder, ROSP, red onion skin powder; BPP, banana peel powder and Mix, mixture of ASP + ROSP + BPP by equal parts.

Table 4. Effect of selected plant parts consumption on serum immunological parameters of hepatotoxic rats induced by CCl_4*

Value	Normal control	Model control	Plant parts (5%, w/w) intervention groups			
			AKP	ROSP	BPP	Mix
Serum albumin (Alb, g/L)						
Mean	4.72 [a]	2.94 [c]	3.51 [b]	3.59 [b]	3.36 [bc]	3.79 [b]
SD	0.69	0.34	0.55	0.40	0.29	0.32
% of change	0.00	-37.61	-25.64	-23.94	-28.81	-19.70
Tumor necrosis factor (TNF-α, ng/L)						

Mean	1.41 [d]	2.86 [a]	2.11 [b]	2.09 [b]	2.17 [b]	1.92 [c]
SD	0.36	0.29	0.10	0.11	0.25	0.17
% of change	0.00	102.84	49.65	48.23	53.90	36.17

Means (n=6) in the same column with different superscript letters are significantly different at p≤ 0.05. Normal control: healthy rats without intervention; Model control: CCl4-induced hepatotoxicity rats without intervention; plant parts intervention groups: CCl4 induced-hepatotoxicity rats with plant parts intervention. AKP, apricot kernel powder, ROSP, red onion skin powder; BPP, banana peel powder and Mix, mixture of ASP + ROSP + BPP by equal parts.

Table 5. Effect of selected plant parts consumption on plasma glutathione fractions concentration of hepatotoxic rats induced by CCl_4*

Value	Normal control	Model control	Plant parts (5%, w/w) intervention groups			
			AKP	ROSP	BPP	Mix
Reduced glutathione (GSH, µmol /L)						
Mean	8.17[a]	4.92 [c]	6.44 [b]	6.91 [b]	6.53 [b]	7.10 [ab]
SD	1.22	0.92	0.66	1.02	0.71	1.01
% of change	0.00	-39.77	-21.12	-15.39	-20.05	-13.02
Oxidized glutathione (GSSG, µmol /L)						
Mean	0.649 [a]	0.501 [c]	0.539 [b]	0.591 [ab]	0.544 [b]	0.611 [a]
SD	0.032	0.101	0.062	0.071	0.087	0.108
% of change	0.00	-22.80	-16.95	-8.94	-16.18	-5.79
GSH/GSSG ratio						
Mean	12.59 [a]	9.82 [c]	11.95 [a]	11.69 [a]	12.00 [a]	11.62 [a]
SD	1.66	1.41	0.95	1.47	2.03	1.73

% of change	0.00	-21.98	-5.03	-7.08	-4.62	-7.67

Means (n=6) in the same column with different superscript letters are significantly different at $p \leq 0.05$. Normal control: healthy rats without intervention; Model control: CCl4-induced hepatotoxicity rats without intervention; plant parts intervention groups: CCl4 induced-hepatotoxicity rats with plant parts intervention. AKP, apricot kernel powder, ROSP, red onion skin powder; BPP, banana peel powder and Mix, mixture of ASP + ROSP + BPP by equal parts.

Table 6. Effect of selected plant parts consumption on plasma markers of oxidative stress of hepatotoxic rats induced by CCl_4*

Value	Normal control	Model control	Plant parts (5%, w/w) intervention groups			
			AKP	ROSP	BPP	Mix
Malonaldehyde (MDA, nmol/mL)						
Mean	0.183 ^{d}	0.332 ^{a}	0.258 ^{b}	0.254 ^{b}	0.263 ^{b}	0.233 ^{c}
SD	0.019	0.021	0.009	0.011	0.027	0.018
% of change	0.00	81.42	40.98	38.80	43.72	27.32
Nitrite (NO_2, nmol/L)						
Mean	2.44 ^{c}	3.71 ^{a}	3.26 ^{a}	3.11 ^{b}	3.21 ^{ab}	2.97 ^{b}
SD	0.23	0.30	0.93	0.66	0.59	0.47
% of change	0.00	52.24	33.94	27.46	31.78	22.01
Nitrite/Nitrate (NO_2/NO_3, nmol/L)						
Mean	3.62 ^{c}	5.12 ^{a}	4.79 ^{ab}	4.55 ^{b}	4.61 ^{b}	4.33 ^{b}
SD	0.31	0.73	0.87	1.01	0.69	0.38
% of change	0.00	41.44	32.32	25.81	27.37	19.57

Means (n=6) in the same column with different superscript letters are significantly different at $p \leq 0.05$. Normal control: healthy rats without intervention; Model control: CCl4-induced hepatotoxicity rats without intervention; plant parts intervention groups: CCl4 induced-hepatotoxicity rats with plant parts intervention. AKP, apricot kernel powder, ROSP, red onion skin powder; BPP, banana peel powder and Mix, mixture of ASP + ROSP + BPP by equal parts.