

**Bioactive compounds content in turmeric and its effects
on liver disorders induced by benzo (a) pyrene in rats**

محتوى المركبات النشطة حيويًا في الكركم وتأثيراته على اضطرابات الكبد
التي يسببها البنزوبيرين في الفئران

by

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Abstract:

The current work was designed to study the effects of turmeric rhizome powder on liver disorders induced by Benzo(a)pyrene [B(a)P] in rats. Treatment of animals with B(a)P caused a significant increase ($p \leq 0.05$) in AST (72.71%), ALT (116.67%) and ALP (238.41%) compared to normal controls. Supplementation of the rat diets with turmeric powder (0.50, 1.00, 1.50, and 2.00 g/100g) prevented the rise of mean serum AST, ALT and ALP activities. The same behavior was recorded for MDA, the biomarker of oxidative stress in cells, levels in serum and xenobiotics metabolizing enzyme i.e. cytochrome p450 in hepatocytes. The opposite direction was recorded for the glutathione fractions (biological macromolecules antioxidant) in serum. These results supported our hypothesis that turmeric powder contains several categories of bioactive compounds that are able to prevent/inhibit the B(a)P induced liver disorders through liver serum enzyme-lowering activity, decreasing rate on the formation of serum

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MDA, decreasing the activity of xenobiotics metabolizing enzyme i.e. cytochrome p450 and increasing the levels of glutathione fractions in serum. Therefore, the present study recommended turmeric by a concentration up to 2% to be included in our daily diets, drinks and food products.

Keywords: Turmeric powder, liver functions, glutathione fractions, glycogen, MDA, cytochrome p450.

Introduction

Liver is a vital and principal organ present in all vertebrates (from fish to human). Such as mentioned by Crawford, (1999), it has a wide range of functions, including detoxification, protein synthesis, and production of biochemical necessary for digestion. Also, liver plays a major role in metabolism and has a number of functions in the body, including glycogen storage, decomposition of red blood cells, plasma protein synthesis, hormone production, and detoxification processes. Furthermore, liver produces bile juice, an alkaline compound which aids in digestion via the emulsification of lipids. The liver's highly specialized tissues regulate a wide variety of high-volume biochemical reactions, including the synthesis and breakdown of small and complex molecules, many of which are necessary for normal vital functions (reviewed in Elhassaneen, 1996; Kebamo *et al.*, 2015). The liver is necessary for survival; there is currently no way to compensate for the absence of liver function long term, although liver dialysis can be used short time.

The burden of liver diseases has been increasing in Egypt with a doubling of the incidence rate in the past twenty years. This has been attributed to several biological (e.g. virus

infection) and environmental/dietary factors (e.g. Aflatoxin, polycyclic aromatic hydrocarbons) (Elhassaneen, 1996, 2004 and Elhassaneen *et al.*, 2016). Other factors such as cigarette smoking, occupational exposure to chemicals such as pesticides and heavy metals, and endemic infections in the community, as schistosomiasis, may have additional roles in the etiology or progression of the disease (Anwar *et al.*, 2008). The World Health Organization (WHO, 2010) reported that Egypt has one of the highest incidences of hepatitis C, one of the main causes of liver cancer, in the world. The number of deaths resulting from liver cancer in Egypt had risen from 4% in 1993 to 11% in 2009. Cancer begins when cells in a part of the body start to grow out of control. There are many kinds of cancer, but they all start because of out-of-control growth of abnormal cells. Cancer cell growth is different from normal cell growth. Instead of dying, cancer cells continue to grow and form new, abnormal cells. Cancer cells can also invade (grow into) other tissues, something that normal cells cannot do. Growing out of control and invading other tissues are what makes a cell a cancer cell. In most cases the cancer cells form a tumor like liver cancer (Howlader *et al.*, 2012). Hepatocellular cancer (HCC) can have different growth patterns like: Some begin as a single tumor that grows larger. Only late in the disease does it spread to other parts of the liver. The second type seems to start as many small cancer nodules throughout the liver, not just a single tumor. This is seen most often in people with cirrhosis (chronic liver damage) (American Cancer Society, 2013). Hepatocellular carcinoma (HCC) is one of the most common malignant tumors in the world, representing the third leading cause of death from cancer and the fifth most

prevalent malignancy worldwide (Bosch *et al.*, 1999; Farazi *et al.*, 2006; El-Serag *et al.*, 2007)). Owing to advances in diagnostics and therapeutics, HCC can be creatively treated when detected at an early stage by applying therapies including radiofrequency ablation (RFA), transcatheter arterial chemoembolization (TACE) and surgical resection. However, curative treatments are often hampered by frequent recurrence of HCC (Okuda, 2007) because the remaining liver retains the potential for *de novo* carcinogenesis (Kumada *et al.*, 1997). Although systemic chemotherapy has also been challenged to patients with advanced stages of HCC, it is mostly ineffective (Thomas, 2008).

Several studies reported that cooking can produce toxic compounds in foods, if the appropriate precursors are present. Cooking processes have been found to be a major source of toxic compounds in foods such PAHs. Although, PAHs can also be formed in curing and processing of raw food prior to cooking (Gray and Morton, 1981; Elhassaneen, 1996-1999; Elhassaneen and Tawfik, 1998; Elhassaneen *et al.*, 1999; Huosein, 2011; Adeyeye, 2020). Polycyclic aromatic hydrocarbons (PAH) from incomplete combustion occur in several foods such as charcoal broiled and smoked goods (Emerole *et al.*, 1982; Larsson *et al.*, 1983; Maanen *et al.*, 1994; Bassiouny, 1999; Elhassaneen, 1999-2004; Hassan, 2005). Benzo(*a*)pyrene [B(*a*)P] is a member of the family, polycyclic aromatic hydrocarbon (PAH) that is a by-product of incomplete combustion or burning of organic (carbon-containing) items, e.g., cigarettes, gasoline, and wood. B(*a*)P is commonly found with other PAHs in cigarette smoke, in grilled and broiled foods, and as a by-product of many

industrial processes (Elhassaneen, 1996; 2004; Elhassaneen and El-Badawy, 2013; Adeyeye, 2020). B(a)P is also found in outdoor and indoor air, and in some water sources (USEPA, 2005). Many of PAH compounds including B(a)P have been shown to be toxic, mutagenic and/or carcinogenic by extensive experiments *in vivo* (Harvey, 1985; Plakunov *et al.*, 1987; Hawkins *et al.*, 1990; Mehram and Sayed-Ahmed, 2020) and *in vitro* (Sims and Grover, 1974; Elhassaneen, 1996; Elhassaneen *et al.*, 1997; and Elhassaneen, 2002) systems. Also, B(a)P exposure is associated with the development of liver cancer in mammals, rodent and fish (Harvey, 1985 and Hawkins *et al.*, 1988-1990; Elhassaneen, 1996 and Elhassaneen, 2002; Elhassaneen *et al.*, 2016; Anita, 2018). It is known that the toxic, tumorigenic and carcinogenic effects of B(a)P correlate with the cellular metabolism of this compounds to arene oxides, phenols, quinones, dihydrodiols, and epoxides and with their subsequent formation of reactive intermediates that interact covalently with DNA to form adducts (Weinstein, 1978; Philips and Sims, 1979; Harvey, 1982, Elhassaneen, 1996). While the Fixation of a biochemical changes by cell proliferation is considered the next step. The mutagenicity of BP is dependent upon metabolic activation. So, BP is considered a promutagen (MacKenzie and Angevine 1981; Elhassaneen 1996; Anita, 2018).

The modern pharmacological therapy is costly and associated with multiple side effects resulting in patient non-compliance. Thus there is a need to explore alternative therapies particularly from herbal/plant sources as these are cost effective and possess minimal side effects. Also, it was reported that some plants exercise various bioactivities,

including antioxidant, anti-inflammatory, antidiabetic, anticarcinogenic, antimutagenic etc (El-Safty, 2012 and Elhassaneen and Sayed, 2015; Elhassaneen et al., 2016-b; Elmaadawy, 2016; Elhassaneen *et al.*, 2021).

One of the still less studied plants is the turmeric (*Curcuma longa* L.) belongs to the *Zingiberaceae* family along with the other noteworthy members like ginger, cardamom and galangal. The plant is a perennial, rhizomatous, herbaceous plant native to the Indian subcontinent and Southeast Asia, that requires temperatures between 20 and 30 °C and a considerable amount of annual rainfall to thrive. Plants are gathered each year for their rhizomes, some for propagation in the following season and some for consumption (Peter, 2008). Turmeric belongs to the genus *Curcuma* that consists of hundreds of species of plants that possess rhizomes and underground root like stems and is a medicinal herb of high repute all over the world particularly in South Asia, where it is also used as curry spice in foods, flavoring agent, food preservative, and color agent.(in mustard, margarine, soft drinks, and beverages) (Rathaur *et al.*, 2012). Turmeric contains a wide variety of bioactive compounds including curcumin, demethoxycurcumin, bisdemethoxycurcumin, zingiberene, curcumenol, curcumol, eugenol, tetrahydrocurcumin, triethylcurcumin, turmerin, turmerones, and turmeronols (Chattopadhyay *et al.*, 2004; Sello and Eldemery, 2018). Also, it contains 2-8% curcumin. (Payton *et al.*, 2007). Traditionally many medicinal properties are attributed to this spice. Since the time of 1900 BC numerous therapeutic activities have been assigned to turmeric for a wide variety of diseases and conditions, including those of the skin,

pulmonary, and gastrointestinal systems, aches, pains, wounds, sprains, and liver disorders, and inhibition of tumors formation and promotion as cancer initiation (Aggarwal *et al.*, 2007; Nafisi *et al.*, 2009; Agrawal and Mishra, 2010; Sello and Eldemery, 2018). According to our knowledge, the studies regarding the potential effects of turmeric on liver diseases are so limited. Therefore, the aims of the present study were determine the effects of turmeric on liver disorders induced by Benzo(a)pyrene in rats. Also, the determination of chemical composition and bioactive compounds in turmeric rhizomes powder will be in the scope of this study.

Materials and Methods

Materials

Turmeric (*Curcuma longa*) powder was purchased from the local markets of Benha City, Benha, Egypt. Casein, as main source of protein for rat diets preparation purchased from Morgan Company for Chemicals. Cairo, Egypt. Vitamins and salts mixtures, all organic solvents, buffers and other chemicals were of analytical grade were purchased from El-Ghomhorya Company for Trading Drugs, Chemicals and Medical Requirements, Cairo, Egypt.

Throughout this study a SP Thermo Separation Products Liquid Chromatograph (Thermo Separation products, San Jose, CA) 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 μ m, 150 x 4.6 mm I.d.) for glutathione

Methods

Proximate chemical analysis of turmeric rhizomes powder samples

Turmeric rhizomes powder samples were analyzed for moisture, protein (T.N. \times 6.25, micro - kjeldahl method using semiautomatic apparatus, Velp company, Italy) , fat (soxhelt miautomatic apparatus Velp company, Italy , petroleum ether solvent), ash, fiber and essential oil (using rotary evaporator apparatus, Velp company, Italy) contents were determined using the methods described in the A.O.A.C. (1995). Carbohydrates calculated by differences: Carbohydrates (%) = 100 - (% moisture + % protein + % fat + % Ash + % fiber).

Bioactive compounds analysis of turmeric rhizomes powder samples

Total phenolics, carotenoids and total dietary fiber in TRP samples were analyzed as follow: TRP was extracted with 80% acetone and centrifuged at 10,000g for 15 min. For biscuits samples, one gram of biscuit powder was extracted with 20 ml of 80% acetone and centrifuged at 8000g at room temperature. The supernatant obtained from both samples were used for the analysis of total phenolics, carotenoids, curcumin and antioxidant activity.

Total phenolics were determined using Folin-Ciocalteu reagent (Singleton and Rossi, 1965). Results are expressed as ferulic and equivalents. The total carotenoids in 80% acetone extract were determined by using the method reported by Litchenthaler (1987). Total dietary fiber content in the TRP was estimated according to the method described by Asp *et al.* (1983). Curcumin was determined in TRP extract according to the method of Wichitnithad *et al.*, (2009). All vitamins (A, C,

and E) were extracted according to methods previously detailed (Epler *et al.*, 1993; Moeslinger *et al.*, 1994 and Hung *et al.*, 1980) and were analyzed by HPLC techniques. Under such chromatographic conditions, mean values (\pm SD) of vitamins A, C and E, and curcumin recoveries were 89.96 ± 2.1 , 90.65 ± 1.84 , 86.09 ± 3.06 and 83.21 ± 4.01 %, respectively.

Antioxidant activity of turmeric rhizomes powder samples

Antioxidant activity of turmeric extracts and standards (α -tocopherol, BHA, and BHT; Sigma Chemical Co., St. Louis, Mo) was determined according to the β -carotene bleaching method following a modification of the procedure described by Marco (1968).

Biological Experiments

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 (BD)

The BD 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 and salt mixture component were formulated according to AIN, (1993).

Experimental design

All biological experiments performed a complied with the rulings of the Institute of Laboratory Animal Resources, Commission on life Sciences, National Research Council (NRC, 1996). Rats (n=50 rats), 130-150g per each, were

housed individually in wire cages in a room maintained at 25 ± 2 °C, relative humidity ($55 \pm 5\%$), a 12-hr lighting cycle 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, 5 rats, as a negative control group) still fed on basal diet and injected with the vehicle alone (5 ml/kg body weight) and the other main group (45 rats) was were challenged with an ip injection of B(a)P (100 mg/5 ml/kg body weight) dissolved in 0.9% NaCl solution containing 0.1% Tween 20 to induce liver impaired rats then classified into eight sub- groups as follow:

- Group (2): fed on standard diet only as a positive control
- Group (3): fed on standard diet containing 0.50 % turmeric powder
- Group (4): fed on standard diet containing 1.00 % turmeric powder
- Group (5): fed on standard diet containing 1.50 % turmeric powder
- Group (6): fed on standard diet containing 2.00 % turmeric powder

Blood sampling

At the end of experiment period, 4 weeks, blood samples were collected after 12 hours fasting using the abdominal aorta and rats were scarified under ether anesthetized. Blood samples were received into

clean dry centrifuge tubes and left to clot at room temperature, then centrifuged for 10 minutes at 3000 rpm to separate the serum according to Drury and Wallington, (1980). Serum was

carefully aspirate, transferred into clean covet tubes and stored frozen at -20°C until analysis.

Hematological analysis

Liver functions

Serum glutamic pyruvic transaminase (SGPT/ALT), glutamic oxaloacetic transaminase (SGOT/AST) and alkaline Phosphatase (ALP) were measured in serum using the method of Tietz *et al.*, (1976), Tietz *et al.*, (1976) and Vassault *et al.*, (1999), respectively.

Glutathione (GSH) determination

GSH was determined by HPLC according to the method of McFarris and Reed (1987).

Liver glycogen determination

Liver glycogen levels were determined after digestion of liver and precipitation of glycogen by Glycogen Assay Kit II (Colorimetric, abcam kits Co., ab169558, www.abcam.com)

Malonaldehyde (MDA) content determination

Lipid peroxide levels measured as malondialdehyde in serum and liver were determined by as thiobarbituric acid reactive substances (TBARS) as described by Buege and Aust, (1978).

Drug Metabolizing Enzymes (Cytochrome P-450) determination

Cytochrome P-450 was measured by the carbon monoxide difference spectrophotometry of dithionite-reduced samples by using the method of Omura and Sato (1964).

Statistical Analysis

All measurements were done in triplicate and recorded as mean± standard deviations (SD). Data were arranged with Excel Sheet (Excel Program, USA) and statistical analysis was

performed with the Student *t*-test and MINITAB 12 computer program (Minitab Inc., State College, PA, USA).

Results and Discussion

Proximate chemical composition of turmeric powder

The proximate composition of turmeric powder is shown in Table 1. The results showed that the moisture content was 9.78%, total protein was 6.92%, crude fat was 4.44%, crude fiber was 5.11%, ash content was 2.66% and total carbohydrate content was 71.09%. The proximate composition reported was partially accordance with the recorded by Jaggi, (2012) and Sello and Eldemery (2017) but not accordance with that observed by Kapoor, (1990) and Ruby *et al.*, (1995). Such variation in data reflected the effect of different parameters including varieties, seasonality, geographic conditions, soil, agriculture treatments etc., on chemical composition of different plant parts which among them turmeric rhizomes.

Table 1. Proximate chemical composition of turmeric powder

Component	Content (g/100g)
Water	9.78 ±1.43
Total protein	6.92 ± 1.11
Crude fat	4.44± 0.74
Ash	2.66 ± 0.56
Crude fiber	5.11 ± 0.91
Carbohydrate (By difference)	71.09 ± 3.25

Each value represents the mean of three replicates ±SD.

Bioactive compounds and antioxidant activity of turmeric powder

Data in Table (2) showed the bioactive compounds and antioxidant activity of turmeric powder. From such data it

could be noticed that there are the antioxidant vitamins such as vitamins A (β -carotene), C, and E, found in turmeric powder for which there are Dietary Reference Values (DRVs). Such data was partially accordance with the recorded by Sello and Eldemery (2017). Vitamins are important in maintenance of the body equilibrium thereby reducing the risk associated with nutrient deficiency in humans. Vitamin C functions as a cofactor in many enzymatic reactions in animals (including humans) that mediate a variety of essential biological functions, including wound healing and collagen synthesis. Another biochemical role of vitamin C is to act as an antioxidant (a reducing agent) by donating electrons to various enzymatic and non-enzymatic reactions (DRI, 2000; Ang et al., 2018). Also, vitamin C has an effect on cancer. Within the normal range of dietary intake without additional dietary supplementation, are people who consume more vitamin C at lower risk for developing cancer (*Stratton and Godwin, 2011; Cortés-Jofré et al., 2020*) Also, for people diagnosed with cancer, will large amounts of ascorbic acid administered intravenously treat the cancer (*Papaioannou et al., 2011; Xu et al., 2013*). Vitamin A plays a role in a variety of functions throughout the body, such as vision, gene transcription, immune function, embryonic development and reproduction, bone metabolism, haematopoiesis, skin and cellular health, teeth and mucous membrane (2020). Vitamin E has the following functions: it is an antioxidant, it helps keep the immune system strong against viruses and bacteria, it helps form red blood cells and widen blood vessels to keep blood from clotting inside them, it helps the body use vitamin K and cells also use vitamin E to interact with each other (Traber and

Bruno, 2020). Also, many biological functions have been postulated, including a role as a fat-soluble antioxidant. In this role, vitamin E acts as a radical scavenger, delivering a hydrogen (H) atom to free radicals (*DRI, 2019*). A further revision of *USFD*, (2012) allowed that vitamin E may reduce risk of renal, bladder and colorectal cancers.

Table 2. Bioactive compounds and antioxidant activity of turmeric powder

Component	Content
Vitamins:	
Vitamin A (β -carotene, mg/100g)	20.34 \pm 3.22
Ascorbic acid (mg/100g)	64.63 \pm 4.56
Vitamin E (mg/100g)	8.98 \pm 0.98
Bioactive compounds:	
Essential oil (g/100g)	4.01 \pm 0.54
Total carotenoids (mg.100g)	91.32 \pm 8.65
Curcumin (%) - Ethanolic extract	13.72 \pm 2.65
Total phenolics content (mg GAE.g-1) - Ethanolic extract	21.65 \pm 10.0.4
Antioxidant activity (AA)	
AA, % (Ethanolic extract)	81.48 \pm 4.05

Each value represents the mean of three replicates \pm SD.

However, there are thousands of other bioactive compounds in foods that have antioxidant activity but are not classified as "nutrients." These "non-nutrient antioxidants" include phenolic compounds (found turmeric). Such as shown in table (4) Turmeric powder is rich in different classes of bioactive compounds including phenolics (21.65 \pm 10.0.4 mg GAE.g⁻¹ extract), essential oils (4.01 \pm 0.54 g/100g), total

carotenoids (91.32 ± 8.65 , mg.100g) and Curcumin (13.72 ± 2.65 % in ethanolic extract). Many studies indicated that there was a positive and significant ($p < 0.01$) relationship between all of the previous bioactive compounds and the antioxidant activity in different plant parts (Khoneem, 2009; Jaggi, 2012; Elhassaneen *et al.*, 2013; Sello; Eldemery, 2017 ; Elhassaneen *et al.*, 2019; Mehram *et al.*, 2021). Plant-based foods generally are considered important sources of antioxidants in the diet. Antioxidants help protect cells from the potentially damaging physiological process known as "oxidative stress" (damage to healthy cells or DNA by unpaired electrons known as free radicals). Oxidative stress is thought to be associated with the development of chronic diseases including cancer, heart disease, diabetes, rheumatoid arthritis, anemia, liver diseases, obesity, conditions of ageing including neurodegenerative diseases such as Parkinson's and Alzheimer's disease (Halliwell, 1991, Van Gaal *et al.*, 1998, Chaitanya *et al.*, 2010 and Elmaadawy *et al.*, 2016; Elhassaneen *et al.*, 2016_{a-b}, 2019 and 2020; Mehram *et al.*, 2021).

Finally, all of these macro and micro nutrients found in turmeric powder might be important from the nutrition point of view. Therefore, enrichment of different food products with turmeric powder would enhance the nutritional quality of the product better than many food sources. Also, bioactive compounds including phenolics, carotenoids, essential oil etc in the turmeric powder are giving such food high significant as an important functional food.

The effect of turmeric powder on liver functions of rats injected with B(a)P

Liver functions of rats injected B(a)P and consumed turmeric powder were shown in Table (3). From such data it could be noticed that treatment of animals with B(a)P caused a significant ($p \leq 0.05$) increased in AST (72.71%), ALT (116.67%) and ALP (238.41%) compared to normal controls. Supplementation of the rat diets with turmeric powders (0.50, 1.00, 1.50, and 2.00 g/100g) prevented the rise of mean serum AST, ALT and ALP activities. A dose-response exhibited between the turmeric powder and the rate of preventative. Such as shown in Figures (1-7), the rate of increasing in the liver enzymatic activities were recorded 45.02, 36.63, 28.53 and 24.33% (For AST); 88.96, 85.91, 63.79 and 56.40% (for ALT); and 169.16, 144.60, 121.16 and 88.77% (for ALP) with the rat diets supplemented by 0.50, 1.00, 1.50, and 2.00 g/100g of turmeric powder, respectively. Such data are in accordance with that observed by Mehram and Sayed-Ahmed (2020) who found that B(a)P induced liver disorders in rats and protective effects of mulberry (*Morus alba* L.) leaves (contains bioactive compounds such as found in turmeric powder) were recorded.

In general, B(a)P is one of the most commonly used hepatotoxins, *in vitro* and *in vivo*, in the experimental study of liver diseases. The hepatotoxic effects of B(a)P are largely due to its active metabolites, oxides, hydroxyls, polyhydroxyls and quinones radicals (Elhassaneen, 1996). These activated radicals bind covalently to the macromolecules and induce peroxidative degradation of membrane lipids of cell wall membrane, mitochondria, lysosomes and endoplasmic reticulum rich in polyunsaturated fatty acids (Elhassaneen, 1996 and Elhassaneen et al., 1997; Elhassaneen et al., 2016-a). This leads to the formation of lipid peroxides. This lipid peroxidative

degradation of biomembranes is one of the principle causes of hepatotoxicity of B(a)P (Hasegawa *et al.*, 1995; Elhassaneen, 1996; Elhassaneen, 2004 and Mehram and Sayed-Ahmed, 2019). This is evidenced by an elevation in the serum marker enzymes namely AST, ALT, ALP and decrease in protein (Elhassaneen, 2004; Elhassaneen and Al-Badawy, 2013). In the assessment of liver damage by B(a)P the determination of enzyme levels such as AST, ALT and ALP is largely used (Hassan, 2011; Elhassaneen and Al-Badawy, 2013; Elhassaneen *et al.*, 2016_{a-b}; Saleh, 2016 ; Mehram and Sayed-Ahmed, 2019). Necrosis or membrane damage releases the enzyme into circulation and hence it can be measured in the serum. High levels of AST indicates liver damage, such as that caused by viral hepatitis as well as cardiac infarction and muscle injury, AST catalyses the conversion of alanine to pyruvate and glutamate and is released in a similar manner. Therefore ALT is more specific to the liver, and is thus a better parameter for detecting liver injury. Elevated levels of serum enzymes are indicative of cellular leakage and loss of functional integrity of cell membrane in liver (Voet and Voet, 1990). Serum ALP, bilirubin and total protein levels on other hand are related to the function of hepatic cell. Increase in serum level of ALP is due to increased synthesis, in presence of increasing biliary pressure (Muriel and Garcipiana, 1992).

Table (3). Effects of turmeric powder on liver functions of rats injected with B(a)P

Rats no.	Control (Ve ⁻) Std diet	Control (Ve ⁺) B(a)P	Turmeric Powder (% , w/w)			
			0.50	1.00	1.50	2.00
Aspartate aminotransferase activity, AST, U/L						

Mean	62.33 ^d	107.66 ^a	90.40 ^b	85.17 ^b	80.1b ^c	77.50 ^{bc}
SD	6.75	8.53	6.52	6.32	7.76	6.94
% of Change	0.00	72.71	45.02	36.63	28.53	24.33
Alanine aminotransferase activity, ALT, U/L						
Mean	33.53 ^d	72.65 ^a	63.36 ^b	62.33 ^b	54.92 ^c	52.44 ^c
SD	6.37	11.33	14.36	12.46	11.48	9.80
% of Change	0.00	116.67	88.96	85.91	63.79	56.40
Alkaline phosphatase activity, ALP, U/L						
Mean	96.83 ^f	327.67 ^a	260.62 ^b	236.8 ^c	214.14 ^d	182.77 ^e
SD	18.60	43.29	18.80	28.25	19.90	13.75
% of Change	0.00	238.41	169.16	144.60	121.16	88.77

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

It is reviewed in several studies plant parts including turmeric powder are a rich source of different classes of phytochemicals such alkaloids, carotenoids, phytosterols, phenols and organosulfurs (Harborne, 1998; Harborne and

Mabry, 1982, Beattic *et al.*, 2005; Sddiqi *et al.*, 2012; Elhassaneen *et al.*, 2013; Sello and Eldemery, 2017; Elhassaneen *et al.*, 2019; Mehram *et al.*, 2021). Many studies reported that the effect of many plant parts on decreasing the serum liver function enzymes activity could be attributed to their high level content of those bioactive compounds. For example, Hassan, (2011) found that different doses of apricot kernel extracts showed high-decreased in serum GOT, GPT and ALP after 12 week of feeding when compared with control group.). Also, El-Sayed *et al.*, (2012) found that the addition of tested plant parts such Henada, lemon balm leaves, hawthorn leaves, rose of jericho and corn cob silk by 5 and 10% of the diet intake in the presence of CCl₄ induced significantly improvements in all liver functions including the serum activities of AST, ALT and ALP. The potential mode of action of liver serum enzymes-lowering activity of the turmeric powder could be explained by one or more of the following process: 1) flavonoid is known to block the hepatocellular uptake of bile acids (Dawson, 1998), 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) pre-treatment with flavonoids were not only able to suppress the elevation of AST and ALT but also reduce the damage of hepatocytes *in vitro* through exhibited strong antioxidant activity and scavengers against reactive oxygen species (ROS) (El-Nashar, 2007), 4) pre-treatment with apricot kernel extract rich in phytochemicals were able to reduce the damage of liver i.e. suppress the elevation of AST, ALT and ALP through the improvement of antioxidant defense system in red blood cells

(Hassan, 2011), and 5) pre-treatment with phenolics and carotenoids were not only able to suppress the elevation of AST, ALT and ALP but also reduce the damage of rats hepatocytes through exhibited strong antioxidant activities against oxidative stress biomarkers (Mehram and Sayed Ahmed, 2020).

Effects of turmeric powder on serum albumin of rats injected with B(a)P

Data presented in Table (4) showed effect of feeding turmeric powders on serum albumin of rats treated with B(a)P. It was noticed that the mean value of albumin for control (-) group was 4.05 g/dl while there were significantly ($P \leq 0.05$) decreased in serum albumin for control (+) group with percent of change -18.91 compared to control (-) group. Feeding with turmeric powders, lead to significantly ($P \leq 0.05$) increased in serum albumin compared to control (+) group by the ratio of -21.13, -14.87, -11.70 and -8.79% with the rat diets supplemented by 0.50, 1.00, 1.50 and 2.00 g/100g of turmeric powder, respectively. A dose-response exhibited between the turmeric powder and the rate of preventative. Such data are in accordance with that observed by Mehram and Sayed-Ahmed (2020) who found that benzo(a)pyrene induced liver disorders in rats and protective effects of mulberry leaves (contains bioactive compounds such as found in turmeric powder) including manipulation of albumin content was recorded. Also, In similar studies of Wang *et al.* (2007), Koneri *et al.* (2008), Hedge and Joshi (2009) and Elhassaneen *et al.*, 2016-a) they reported that B(a)P induced significant decrease in the serum albumin content. Also, it was reported that hypoalbuminaemia is most frequent in the presence of

advanced chronic liver diseases (Koneri *et al.*, 2008). Therefore, decline in serum albumin can be deemed as a useful index of the severity of cellular dysfunction in chronic liver diseases. Furthermore, side treatment with artichoke significantly increased the reduced levels of serum albumin which was in agreement with previous studies (Abd El-Aleem *et al.*, 2009).

Table (4). Effects of turmeric powder on serum albumin concentration (g/dl) of rats injected with B(a)P

Rats no.	Control (Ve ⁻) Std diet	Control (Ve ⁺) B(a)P	Turmeric Powder (% w/w)			
			0.50	1.00	1.50	2.00
Sum	20.27	16.44	15.99	17.25	17.90	18.49
Mean	4.05 ^a	3.29 ^b	3.20 ^{bc}	3.45 ^b	3.58 ^b	3.70 ^b
SD	0.16	0.39	0.25	0.30	0.23	0.21
% of Change	0.00	-18.91	-21.13	-14.87	-11.70	-8.79

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

Effects of turmeric powder on in liver glycogen concentration (mg/g tissue) of rats injected with B(a)P

Data presented in Table (5) showed effect of feeding turmeric powders on liver glycogen of rats treated with B(a)P. It was noticed that the mean value of liver glycogen for control (-) group was 13.85 mg/g tissue which decreased after B(a)P injection by -89.80%. Such liver glycogen decrease was significantly elevated in the co-treatment with B(a)P plus turmeric powder. A does-response exhibited between the

turmeric powder and the rate of preventative. The rate of increasing in glycogen was recorded -86.58, -79.29, -66.06 and -54.60 % (from the positive control group) with the rat diets supplemented by 0.50, 1.00, 1.50 and 2.00 g/100g of turmeric powder, respectively. Such data are in accordance with that observed by Mehram and Sayed-Ahmed (2020) who found that benzo(a)pyrene induced decrease in liver glycogen in rats and protective effects of mulberry leaves (contains bioactive compounds such as found in turmeric powder) was recorded. Also, Hasegawa et al., (1995) found that previous drinking of green tea clearly protected against the changes in liver glycogen content induced by B(a)P. Such data with the others suggested that secretion of lipoprotein from liver to blood might be blocked because of intracellular structural failure and/or because of the energy depletion suggested by the marked decrease in glycogen content (Hasegawa *et al.*, 1995, Mehram and Sayed-Ahmed, 2019).

Table (5). Effects of turmeric powder on in liver glycogen concentration (mg/g tissue) of rats injected with B(a)P

Rats no.	Control (Ve ⁻) Std diet	Control (Ve ⁺) B(a)P	Turmeric Powder (% w/w)			
			0.50	1.00	1.50	2.00
Mean	13.85 ^a	1.40 ^d	1.86 _d	2.87 _c	4.70 _c	6.29 _b
SD	1.65	0.15	0.23	0.34	0.76	0.74
% of Chang e	0.00	-89.88	-86.58	-79.29	-66.06	-54.60
			8	9	6	0

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

Effects of turmeric powder on in serum triglycerides concentration of rats injected with B(a)P

Serum triglycerides level of rats injected with B(a)P and consumed turmeric powder was shown in Table (6). From such data it could be noticed that the serum triglycerides level was decreased -87.15 by B(a)P, and this decrease was significantly ($p \leq 0.05\%$) elevated in the co-treatment of B(a)P plus turmeric powder. A dose-response exhibited between the turmeric powder and the rate of preventative. The rate of increasing in triglycerides was recorded -86.80, -83.91, -78.33 and -74.52% (from the positive control group) with the rat diets supplemented by 0.50, 1.00, 1.50 and 2.00 g/100g of turmeric powder, respectively. Such data are in accordance with that observed by Mehram and Sayed-Ahmed (2020) who found that benzo(a)pyrene induced increase in serum triglycerides in rats and protective effects of mulberry leaves (contains bioactive compounds such as found in turmeric powder) was recorded.

Table (6). Effects of turmeric powder on in serum triglycerides concentration (mg/dl) of rats injected with B(a)

Rats no.	Control (Ve ⁻) Std diet	Control (Ve ⁺) B(a)P	Turmeric Powder (% w/w)			
			0.50	1.00	1.50	2.00
Sum	757.66	97.38	100.02	121.91	164.18	193.08
Mean	151.53 ^a	19.48 ^{cd}	20.00 ^c	24.38 ^c	32.84 ^b	38.62 ^b
SD	22.24	3.11	3.43	4.37	6.42	5.99
% of Change	0.00	-87.15	-86.80	-83.91	-78.33	-74.52

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

Effects of turmeric powder on liver glutathione (GSH) content of rats injected with B(a)P

Data presented in table (7) showed the effect of feeding turmeric powder on liver glutathione (content of rats treated with B(a)P. from such data it could be noticed that the mean value of GSH for control (-) group was 9.56 g/dl while there were significantly ($P \leq 0.05$) decreased in liver GSH for control (+) group with percent of change -38.63 compared to control (-) group. The feeding with turmeric powder lead to significantly ($P \leq 0.05$) increased in serum GSH compared to control (+) group by the ratio of were -36.59, -27.74, -20.07 and -14.73% for turmeric powder. Data also indicated that the rate of liver GSH elevation was increased with the increasing of the turmeric powder concentration. Such data are in accordance with that observed by Mehram and Sayed-Ahmed (2020) who found that benzo(a)pyrene induced decrease in liver GSH in rats and protective effects of mulberry leaves (contains bioactive compounds such as found in turmeric powder) was recorded.

Table (7). Effects of turmeric powder on liver glutathione (GSH, $\mu\text{mol} / \text{mg}$ tissue protein) content of rats injected with B(a)P

Rats no.	Control (Ve ⁻) Std diet	Control (Ve ⁺) B(a)P	Turmeric Powder (% , w/w)			
			0.50	1.00	1.50	2.00
Mean	9.56	5.87	6.06	6.91	7.64	8.15
SD	1.14	1.05	0.72	1.04	1.27	1.40
% of Change	0.00	-38.63	-36.59	-27.74	-20.07	-14.73

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

In general, GSH is a tripeptide-thiol (γ -glutamyl cysteinyl-glycine) that has received considerable attention in terms of its biosynthesis, regulation, and various intracellular functions. Among of these function do two constitute roles in detoxifications as follow: as a key conjugate of electrophilic intermediates, principally via glutathione-*s*-transferase activities in phase II metabolism, and as an important antioxidant (Elhassaneen, 1996 and 2004). The antioxidant functions of GSH includes its role in the activities of GSH-Px and AS-Px . In addition, GSH can apparently serve as a nonenzymatic scavenger of oxyradicals (Halliwell and Gutteridge, 1985 and Elhassaneen, 1996). Several studies noticed that a fall in GSH observed generally accompanied by a concomitant increased in the liver lipid peroxidation (MDA content) (Elhassaneen, 2004; Mahran et al., 2018; Mehram and Sayed-Ahmed, 2020). Several reports have documented that potent antioxidant capacity of curcumin (the main bioactive compound in turmeric) where by mitigation of lipid peroxidation and oxidative stress in several tissues were demonstrated (Nabavi *et al.*, 2012). The present data with the others suggested that secretion of GSH from liver to blood might be blocked because of intracellular structural failure, elevation of the lipid peroxide content and/or the energy depletion suggested by the marked decrease in glycogen content (Hasegawa *et al.*, 1995; Sello and Eldemery, 2017; Mehram and Sayed-Ahmed, 2020). Turmeric powder was described by its higher content of different categories of bioactive compounds including curcumin which exhibited high

antioxidative activities and anticarcinogenic effects (Boone et al., 1992; Chauhan, 2002; Srinivasan, 2005, Shishodia *et al.*, 2006; Jurenka, 2009; Nabavi *et al.*, 2012; Zheng *et al.*, 2014). . Supplementation of the rat diets with turmeric powder leads to reduce the lipid peroxide content and/or elevate the glycogen content subsequently elevate the GSH content in liver.

Effects of turmeric powder on serum lipid peroxidation of rats injected with B(a)P

Lipid peroxidation in serum and liver of rats injected with B(a)P and feeded turmeric powder were shown in Table (8-9). From such data it could be noticed that the liver lipid peroxide level (MDA) was increased 262.07% by B(a)P injection. This increasing was significantly ($P \leq 0.05$) reduced in the co-treatment of B(a)P plus turmeric powder. A dose-response exhibited between the turmeric powder and the rate of preventative. Such as data were shown, the rate of increasing in MDA was recorded 199.08, 117.79, 98.07 and 87.22 % of the control negative group with the rat diets supplemented by 0.50, 1.00, 1.50 and 2.00 g/100g of turmeric powder, respectively. The opposite direction was observed for the lipid peroxidation in serum of rats injected with B(a)P and fed turmeric powder were shown in Tables (5). From such data it could be noticed that the serum lipid peroxide level (MDA) was decreased -49.73% by B(a)P injection. This increasing was significantly ($P \leq 0.05$) elevated in the co-treatment of B(a)P plus turmeric powder. A dose-response exhibited between the turmeric powder and the rate of preventative. Such as data were shown, the rate of decreasing in MDA was recorded -47.00, -47.32, -44.10 and -39.50 % of the control negative group with the rat diets supplemented by 0.50, 1.00, 1.50 and 2.00 g/100g of

turmeric powder, respectively. Such data are partially in accordance with that observed by Mehram and Sayed-Ahmed (2020) who found that benzo(a)pyrene induced increasing in liver MDA in rats and protective effects of mulberry leaves (contains bioactive compounds such as found in turmeric powder) was recorded.

Table (8). Effects of turmeric powder on liver lipid peroxidation (MDA, nmol/mg tissue protein) of rats injected with B(a)P

Rats no.	Control (Ve ⁻) Std diet	Control (Ve ⁺) B(a)P	Turmeric Powder (% w/w)			
			0.50	1.00	1.50	2.00
Mean	3.88 ^e	14.04 ^a	11.59 ^b	8.44 ^c	7.68 ^c	7.26 ^{cd}
SD	0.94	3.92	2.84	1.60	1.45	2.90
% of Change	0.00	262.07	199.08	117.79	98.07	87.22

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

Table (9). Effects of turmeric powder on serum lipid peroxidation (MDA, nmol/ml) of rats injected with B(a)P

Rats no.	Control (Ve ⁻) Std diet	Control (Ve ⁺) B(a)P	Turmeric Powder (% w/w)			
			0.50	1.00	1.50	2.00
Mean	0.179 ^a	0.090 ^{bc}	0.095 ^{bc}	0.095 ^{bc}	0.100 ^b	0.109 ^b
SD	0.044	0.022	0.022	0.023	0.02	0.02

					4	5
% of Change	0.00	-49.73	- 47.00	- 47.00	- 44.1 0	- 39.5 0

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

Many studies displayed the potent antioxidant capacities of curcumin (the main bioactive component in turmeric powder) where by mitigation of lipid peroxidation and oxidative stress in several tissues were demonstrated (Nabavi *et al.*, 2012, Elhassaneen *et al.*, 2016-a). Also, Hasegawa *et al.*, (1995) found that previous drinking of green tea clearly protected against the changes in liver lipid peroxide level. On the other hand, serum lipid peroxide levels dropped in all B(a)P-treated rats. Such data with the others suggested that secretion of lipoprotein from liver to blood might be blocked because of intracellular structural failure and/or because of the energy depletion suggested by the marked decrease in glycogen content (Hasegawa *et al.*, 1995; Mehram and Sayed-Ahmed 2020). The increases of serum enzyme activities were clearly inhibited by turmeric powder consumption. Therefore, a marked decreasing in serum triglyceride levels was noticed in all B(a)P treated rats probably being related to the low levels of serum lipid peroxide in all treated groups.

Effects of turmeric powder on the activity of cytochrome-P450 (cyto-p450) in liver of rats injected with B(a)P

Effects of turmeric powder treatments on the activity of cyto -P450 in liver of rats subjected to B(a)P treatment was shown in Table (10). From such data it could be noticed that treatment of rats with B(a)P caused a significant increased

($p \leq 0.05$) in cyto- P450 by (47.46%) compared to normal/negative control animals. Feeding of the rat diets with turmeric powder by 0.50, 1.00, 1.50 and 2.00 g/100g w/w prevented the rising of mean liver cyto- P450 activity. The rate of preventative effect was elevated with the increasing of the turmeric powder concentration. The rate of decreasing in the cyto- P450 activities were -35.03, 28.81, 16.38 and 7.34% of the negative control group with the rat diets blended with 0.50, 1.00, 1.50 and 2.00 g/100g of turmeric powder, respectively. In similar study, Mehram and Sayed-Ahmed (2020) found that benzo(a)pyrene induced increasing in liver cyto-p450 in rats and protective effects of mulberry leaves (contains bioactive compounds such as found in turmeric powder) was recorded. Also, Liu *et al.*, (2015) reported that B(a)P treatment brought about a significant increase in the activities of drug metabolizing enzymes including cyto- p450 in lungs of mice and the activities of these enzymes were markedly decreased by the administration of bioactive compounds including curcumin (the main bioactive in turmeric powder) and phenolic compounds.

Table (10). Effects of turmeric powder on the activity of cytochrome P450 in liver (nano moles/mg protein) of rats injected with B(a)P

Rats no.	Contr ol (Ve ⁻) Std diet	Contr ol (Ve ⁺) B(a)P	Turmeric Powder (% w/w)			
			0.50	1.00	1.50	2.00
Mean	1.77 ^f	2.61 ^a	2.39 _{ab}	2.28 _b	2.06 _c	1.90 _d

SD	0.041	0.023	0.02 2	0.02 3	0.02 4	0.02 5
% of Change	0.00	47.46	35.0 3	28.8 1	16.3 8	7.34

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

In conclusion, benzo(a)pyrene is considered a food contaminant and a top risk factor in the development of several diseases including liver disorders. Oxidative stress appears as a major contributor in the development of many metabolic complications associated liver disorders/diseases. Lowering oxidative stress to prevent such liver metabolic disorders and complications therefore constitutes an interesting target. Feeding of turmeric applied in foods has been proven to be essential in the treatment and/or prevention of liver disorders induced by B(a)P through oxidative stress reduction and xenobiotics metabolizing enzyme i.e. cytochrome p450 activity decreasing. Therefore, we recommended turmeric powder to be included in our daily live dishes and beverages.

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تم تصميم العمل الحالي لدراسة تأثير مسحوق جذور الكركم على اضطرابات الكبد التي يسببها مركب البنزوبيرين في الفئران. حيث أدت معاملة الفئران بمركب البنزوبيرين الى زيادة معنوية ($p \leq 0.05$) في الانزيمات المعبرة عن وظائف الكبد (72.71 %AST ، 116.67 %ALT و 238.41 %ALP) مقارنة بالمجموعة الضابطة (الطبيعية). حالت تدعيم حمية الفئران بمسحوق الكركم (0.5 و 1.0 و 1.5 و 2.0 جم / 100 جم) دون ارتفاع متوسط أنشطة الانزيمات السابقة AST و ALT و ALP في السيرم وتم تسجيل

السلوك لمركب المالمونالدهيد ، الدليل الحيوي المعبر عن الإجهاد التأكسدي في الخلايا ، وكذلك المستويات في إنزيم استقلاب المواد الغريبة الداخلة للجسم (السيتوكروم ب.٥) في خلايا الكبد. كما تم تسجيل الاتجاه المعاكس لأجزاء الجلوتاثيون (الجزئيات البيولوجية المضادة للأكسدة) في سيرم الدم. دعمت هذه النتائج فرضيتنا القائلة بأن مسحوق الكركم يحتوي على عدة كجوعات من المركبات النشطة بيولوجياً القادرة على منع / تثبيط اضطرابات الكبد التي يسببها مركب البنزوبيرين من خلال نشاط خفض إنزيمات الكبد في السيرم ، وتقليل معدل تكوين مركب المالمونالدهيد ، وتقليل النشاط من أنزيم الأيض أي السيتوكروم ب.٥، وزيادة مستويات أجزاء الجلوتاثيون في سيرم الدم. لذلك أوصت الدراسات الحالية بتضمين الكركم بنسبة تركيز تصل إلى ٢٪ في وجباتنا الغذائية والمشروبات ومنتجاتنا الغذائية اليومية

الكلمات المفتاحية: مسحوق الكركم ، وظائف الكبد ، أجزاء الجلوتاثيون ، الجليكوجين ، المالمونالدهيد، السيتوكروم ب.٥.