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THE POSSIBLE PROTECTIVE EFFECT OF NIGELLA SATIVA SEEDS OIL AGAINST PARACETAMOL-INDUCED HEPATIC DAMAGE IN MALE RATS.

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ABSTRACT

Nigella sativa (N. sativa), black cumin, known as Habit El-Barakah) is regarded as one of the greatest forms of healing medicine available. Liver is continuously exposed to a variety of toxic agents like drugs and chemicals that may interfere with hepatic function and may cause hepatic damage. Nigella sativa seeds oil is excellent as antioxidant and lowers cholesterol, thereby may be considered as a hepatoprotective agent. Paracetamol (also known as acetaminophen) overdose can cause severe hepatotoxicity and even liver failure and hepatic centrilobular necrosis in experimental animals and humans.

The aim of this work is to study the protective and therapeutic roles of N sativa seeds oil against paracetamol-induced hepatotoxicity in rats

Thirty adult male rats weighing 180-200 g were randomized into five groups. Group I (control group); group II; received N sativa seeds oil 100 µl /kg bw; group III was given toxic dose of paracetamol (500 mg/kg bw); group VI was given N sativa seeds oil (100 µl /kg bw); after one hour received paracetamol and group V received paracetamol (500 mg/kg bw) and after one hour given N sativa seeds oil. All treatments were given once daily for 5 consecutive days using stomach tube. Fresh blood and sera were collected 24 hours after the last dose. Complete blood picture and some biochemical parameters were assayed

Paracetamol treated group had elevated red blood cells count (RBCs), hemoglobin (Hb), hematocrit (Hct), platelets count (pl) and neutrophils as compared to control one .Decreased Red cell distribution width (RDW), lymphocytes and monocytes were recorded in paracetamol – intoxicated group compared to control group. Decreased serum glucose and increased activities of aspartate aminotransferase (ASAT), alanine aminotransferase (ALAT) and alkaline phosphstase

(ALP), total protein, total cholesterol and triglycerides were observed in paracetamol- intoxicated group. Insignificant increases of albumin, globulin,A/G ratio, creatinine and total bilirubin were seen in paracetamol-intoxicated rats when compared with control group. Calcium and phosphorus had insignificant increases in paracetamol-intoxicated group and those treated with N sativa pre- and post paracetamol compared to control group.

In group IV, N sativa seeds oil improved the altered previously mentioned parameters where N sativa seeds oil was given before paracetamol more than group V which received N sativa seeds oil after paracetamol

It was concluded that N sativa seeds oil hasprotective role on blood picture and blood biochemical parameters when given before paracetamol in rats more than if given after paracetamol.

Key words: Paracetamol – complete blood count-liver functions.

INTRODUCTION

Herbs play a major role in the management of various liver disorders along with other system associated diseases **(Rajasekaran & Periasamy, 2011)**. N sativa belonging to the buttercup family Ranunculaceae, is commonly known as black seeds.

N sativa seeds have many pharmaceutical uses. The seeds have occupied special place for their medicinal value for centuries in the Middle East and Southeast Asia (**Gilani, et al., 2004)**. They have been traditionally used in the treatment of a number of ailments including hypertension, respiratory health, stomach and intestinal health, kidney, bladder and liver function, circulatory and immune system support and for general overall wellbeing **(Deliorman, et al., 2002; Malhotra, 2006 and Tasawar, et al., 2011)**. Numerous traditional applications of Nigella seeds recorded as medicinal and pharmacological activities **(Gilani, et al., 2004).**

The role of black granules and its components against various maladies are multidimensional, owing to its rich nutritional profile. Black granules (seeds) contain substantial amounts of alkaloids like nigellicine, nigellidine and nigellimine; reported as cholesterol lowering agents

(Mehta, et al., 2009 and Sultan, 2009). Besides balanced fatty acid profile, it contains considerable quantities of tocopherols and allied bioactive compounds ;thymoquinone and ρ-cymene **(Wajs, et al., 2008, and Nagi, et al., 2010)**.

These phytochemicals are important to attenuating the overall antioxidant capability of the body and reducing low-density lipoproteins (LDL) which may be produced due to free radical production **(Butt & Sultan, 2010 and Dahri, et al., 2005)**. Several pharmacological investigations explored that thymoquinone is effective against oxidative stress, cancer, immune dysfunction and diabetic complications.

Furthermore, it also regulates several hematological & serological functions; maintains body homeostasis and bears hypocholesterolemic effect **(Mathur, 2011)**. Minerals such as calcium, phosphorus and iron were found to be in appreciable amounts in N sativa seeds oil, while zinc, magnesium, manganese and copper in meager quantities **(Ashraf, et al., 2006 and Cheikh-Rouhou, et al., 2007)**. Black granules has been also probed as a source of polyphenols and fat-soluble vitamins(comprised more than 0.2% of total oil content), unsaturated fatty acids (linoleic and oleic acids) ,selenium **(Ramadan & Mörsel, 2004; Ashraf, et al., 2006; Cheikh-Rouhou et al., 2007)** and sterols **(Cheikh-Rouhou, et al., 2008).**

Liver is the most important organ concerned with the biochemical activities in the human body. It has great capacity to detoxify toxic substances and synthesize useful products **(Ganong, 2005**). Drug-induced liver injury is increasingly being recognized as a significant cause of both acute and chronic liver disease; commonly seen in paracetamol toxicity **(Kumar, et al., 2006 ; Oyagbemi & Odetola, 2010 and Patel, et al., 2010).** Paracetamol is a widely used antipyretic and analgesic drug. When taken in overdose, it may develop hepatotoxicity by over production of N-acetyl p- benzoquinoneimine (NAPQI) by cytochrome p450, however, when the rate of formation of this toxic metabolite exceeds the rate of detoxification by intracellular GSH, it oxidizes tissue macromolecules such as lipid or SH group of protein and alters the homeostasis of calcium after depleting GSH **(Oyagbemi & Odetola, 2010)**. Additional mechanisms of paracetamol induced hepatotoxicity include nucleotide alterations and protein synthesis

disruption **(Hinson, et al., 2010)**. During the last few years there has been an increase in the number of reports of liver failure associated with prolonged paracetamol administration for therapeutic reasons.

The aim of this study was to test the protective effect of N sativa seeds oil against paracetamol overdosing induced hepatotoxicity.

MATERIAL AND METHODS

The study was carried out on adult male albino rats (Rattus rattus) weighing 180–200 g. Rats were housed in controlled environment of animal house with food and water ad libitum. They were randomly divided into five groups (animals in each group n = 6). Group I received distilled water by gastric tube and kept as control group. Group II received N sativa seeds oil (100 µl /kg bw). Group III was given overdose of paracetamol suspension, Amriya Pharm Ind. Alexandria, Egypt (500 mg/kg bw). Group VI was given N sativa seeds oil 100 µl /kg body weight once daily; one hour after receiving paracetamol (500 mg/kg bw). Group V received paracetamol (500 mg/kg bw) , one hour later given N sativa seeds oil (100 µl /kg bw). All treatments were once daily for 5 consecutive days.

Twenty four hours after the last dose of paracetamol, the animals were fasted for 12 hours, then, sacrificed by cervical decapitation. Blood samples were collected for hematological studies in clean vials containing EDTA as anticoagulant and another blood samples were collected for different biochemical studies in clean vials without any anticoagulants for separation of serum. Blood samples were allowed to coagulate for 30 min at 37º C.

Red blood cells (RBCs), white blood cells (WBCs), differential WBCs counts, Hemoglobin (Hb) concentration, packed cell volume (PCV), mean corpuscular volume (MCV) , mean corpuscular hemoglobin (MCH) and mean corpuscular hemoglobin concentration (MCHC) were evaluated. Red cell distribution width (RDW), is a calculation of the variation in the size of RBCs, was also measured. These parameters were analyzed using automatic hematological system (sysmex hematology-coagulation system, Model MO-1000 I, Trans Asia, Japan) according to the manufacturer instructions.

The clear serum obtained after centrifugation was used for the estimation of different biochemical analysis. The levels of serum glucose.

ASAT, ALAT, ALP, total protein, albumin, bilirubin, cholesterol, triglyceride, creatinine, calcium and phosphorus were determined using an auto-analyzer (Beckman, Calif, USA, or ADVIA, Tokyo, Japan) according to the manufacturer instructions.

Globulins were determined by subtracting value of serum albumin from the value of serum total proteins. A/G ratio was obtained by subdividing values of serum albumin by those of serum globulins.

Results of hematological and biochemical estimations were reported as mean ± SD of six animals in each group. The data were subjected to one way ANOVA using SPSS followed by Post Hoc Tests. The P value <0.05 was considered statistically significant.

RESULTS

Nigella sativa seeds oil alone did not alter the different measured parameters significantly except the increased level of platelets count.

Significant decline in serum fasted glucose level was recorded in paracetamol- intoxicated group when compared with control. N sativa seeds oil pre- and post- paracetamol improved these changes and turned back near to normal level (table 1)

The total serum protein and the concentrations of enzymes measured were observed to vary significantly ($p<0.05$) among the test groups and the control. From the results obtained, there was a significant increase ($p< 0.05$) in total serum protein of the paracetamol compared to the control group. There was a significant increase ($p < 0.05$) in ASAT, ALAT and ALP in paracetamol- intoxicated group when compared with control group. Co- administration of N sativa seeds oil pre- or post- paracetamol produced a significant reduction ($p < 0.05$) in ASAT, ALAT and ALP compared with the overdosed- paracetamol group (table 1).

Significant increase in serum triglycerides and serum total cholesterol of paracetamol treated group were noticed ($p < 0.05$) which have been ameliorated in N.sativa seeds oil pre- and post paracetamol groups were (table 1).

On the other hand, creatinine and total bilirubin didn't alter in different treated groups (table 1).

Table (1): Effect of pre- and post- N sativa seeds oil treatment on some biochemical parameters in paracetamol – overloaded rats.

groups / parameters	C	N	P	N+P	P+N
Glucose(mg/dl)	73.50±4.89	75.00±4.73	65.50±3.02a	73.00±2.97b	76.33±2.25b
ASAT(u/l)	48.00±8.39	42.33±4.89	120.50±9.40a	57.83±5.19ab	57.83±3.54ab
ALAT(u/l)	34.83±5.12	36.00±6.07	54.50±5.39a	47.67±3.39ab	49.33±6.89a
*ALP (u/L)	146.80±25.07	143.80±26.57	183.80±16.38a	148.20±21.71b	152.00±14.53b
TP(g/dl)	7.92±0.27	7.99±0.47	8.16±0. .40a	8.08±0. .27b	8.04±0. .39b
Albu.(g/dl)	3.02±0.09	3.23±0.34	3.33±0.23	3.11±0. .43	3.19±0.11
Globu.(g/dl)	4.90±0. .29	4.76±0.30	5.00±0.33	4.97±0.38	4.86±0. 14.53
A/G	o.60±.05	0.69±0.09	0.67±0.10	0.64±0.08	0.64±0.08
Tch.(mg/dl)	70.17±5.12	65.50±6.53	76.50±4.37a	64.17±4.31ab	75.17±4.26
Triglyc(mg/dl)	65.83±8.13	65.50±7.69	121.67±15.19a	64.00±6.78b	59.83±7.76b
Cr (mg/dl)	0.59±0.02	0.58±0.01	0.60±0.03	0.60±0.01	0.60±0.03
T bili.(mg/dl)	0.33±0.03	0.38±0.02	0.41±0.02	0.40±0.02	0.38±0.02

Results are expressed as M±SD of 6 animals except for ALP* only 5 animals.

a significant at $p \leq o.05$ when compared with control group.

b significant at $p \leq o.05$ when compared with paracetamol- overdose group.

Complete blood cells count and differential leucocytic count in different treated rats are shown in table 2. Increased RBCs count, Hb and HCt in paracetamol treated group when compared by control group. N. sativa seeds oil pre- and post- paracetamol returned these parameters to nearly normal level (table 2). Platelet count increased significantly in all treated groups (table 2).

Although white blood cells didn't alter in paracetamol treated group, neutrophils percent increased and lymphocytes percent decreased in paracetamol treated group when compared with control group. Other differential leucocytes picture showed more or less similar per cent in different groups in relation to control group (table 2).

Table (2): Complete blood cells count and differential leucocytic count in pre- and post- N sativa seeds oil treatment rats toxicated with overdose of paracetamol.

groups / parameters	C	N	P	N+P	P+N
Hb (g/dl)	14.66±0.61	±0.48 14.97	15.40±0.63a	14.44±0.61	15.08±0.41
RBCs(million cells/mL)	7.58±0.68	7.92±0.22	8.53±0.07 a	7.88±0.66	8.46±0.28a
HCt (%)	45.74±5.23	48.37±1.82	51.14±1.56a	46.96±3.57	47.92± 1.71
MCV (fl)	59.55±1.05	59.63±2.07	58.89±1.94	57.56±3.50	57.78±2.67
MCH (pg/cell)	18.95±1.10	18.52±0.30	18.24±0.56	18.10±1.06	18.04±0.56
MCHC (gm/dL)	32.18±2.11	31.13±0.79	30.94±0.40	30.32±1.13 a	31.32±0.62
RDW	14.46±0.33	14.45±0.80	13.41±0.25a	14.49±0.79	14.08±0.65
Platelet count (x1000)	422.47±56.30	557.83±118.21a	562.83±89.83a	531.17±105.34	575.00±76.55a
WBCs(x1000)	10.99±1.07	9.70±0.86 a	10.82±0.96	10.77±1.48	9.85±0.84
Neutrophil (%)	24	25	31a	36 a	33 a
Basophila (%)	0	0	0	0	0
Eosinophils (%)	6	6	6	5a	5 a
Monocytes (%)	7	6	6	7	7
Lymphocytes (%)	63	61	57a	52 a	55 a

Results are expressed as M±SD of 6 animals.
a significant at $p \leq o.05$ when compared with control group.
b significant at $p \leq o.05$ when compared with paracetamol- overdose group.

Serum calcium and phosphorus had insignificant increases in paracetamol- intoxicated group and those treated with N sativa pre- and post paracetamol compared to control group (table 3).

Table (3): Effect of pre- and post- N sativa seeds oil treatment on calcium and phosphorus in paracetamol – overloaded rats.

groups / parameters	C	N	P	N+P	P+N
Ca (mg/dl)	13.28±0.21	13.16±0.13	13.39±0.13	13.39±0.24	13.21±0.30
P (mg/dl)	11.08±0.48	10.78±0.35	11.54±0.42	11.48±0.18	11.09±0.90

Results are expressed as M±SD of 6 animals.
a significant at $p \leq o.05$ when compared with control group.
b significant at $p \leq o.05$ when compared with paracetamol- overdose group.

DISCUSSION

Paracetamol is commonly and widely used analgesic- antipyretic agent. It is metabolized in the liver to an active metabolite, N-acetyl-p-benzoquinone imine (NAPQI), by the cytochrome-P-450 microsomal enzyme system with resultant oxidative stress, liver glutathione and glycogen depletion and hepatic necrosis **(Mitra, et al., 2000; Oyagbemi & Odetola, 2010)**. Paracetamol is relatively safe when taken at prescribed therapeutic doses. Paracetamol-induced liver injury is commonly used as models for investigation into the efficacy of hepatoprotective drugs **(Kumar, et al., 2006)**. In massive doses, it is known to produce hepatic necrosis, extra hepatic lesions and even fatality both in experimental animals and in human beings **(Fontana, 2008)**.

In spite of significant advances in medicinal plant research and rapid strides in modern medicine, there continues to be a need for more precise, safe and effective treatment for liver disorders **(Oliveria, et al., 2005).**

It is estimated that 30-40% of all kinds of diseases can be prevented with a healthy lifestyle and dietary measures **(Farah, 2005 and Butt, & Sultan, 2010)**. Various plants rich in phytochemicals

possess the ability to quench free radicals and ameliorate oxidative stress **(El-Missiry & El-Gindy, 2000 and Butt & Sultan, 2010).**

Black cumin is rich in bioactive molecules. It can play important role in diet-based strategies against various physiological threats including oxidative stress, diabetes mellitus and elevated cholesterol level **(Ramadan & Mörsel, 2004 and Kanter, et al., 2005)**.

Elevated levels of serum enzymes are indicative of cellular leakage and loss of functional integrity of cell membrane in liver **(Larrey, 2003)**.Hepatocellular necrosis leads to high level of serum markers in the blood, among these, aspartate transminase, alanine transaminase represents 90% of total enzyme **(Nelson & Brusche, 2003)** and have been reported to be a marker for severe liver injury **(Lee, 2003 and Jaeschke & Bajt, 2006)**, but the elevated levels of enzymes are decreased to near normal levels after five days treatment of N. sativa seeds oil indicating that it offered protection by returning the elevated enzymes to normal against the damage effect of paracetamol.

Blood glucose concentration is known to depend on the ability of the liver to absorb or produce glucose. The liver performs its glucostatic function owing to its ability to synthesize or degrade glycogen according to the needs of the organism, as well as via gluconeogenesis **(Ahmed, et al., 2006). (Kruszynska & McIntyre, 1991)** reported that the blood sugar level after overnight fasting in cirrhotic patients is believed to decrease only in severe hepatic failure. In this study, decreased serum glucose level was recorded in paracetamol – intoxicated group.

Hypoglycemic effect of paracetamol may be attributed to decreased hepatic glucose production and / or lower supply of gluconeogenic precursors (alanine, glycerol and lactate) to liver results in decreased hepatic gluconeogenesis. Decreased blood glucose level has been observed by **(Bhaumik & sharma, 2002)** in rabbits following a single IV injection of 400 mg paracetamol /kg body weight. They suggested that this reduction might be due to failure of the damaged hepatic parenchyma to perform their normal mechanism of glucose production. The blood glucose levels returned to normal levels in rats treated with N sativa seed oil pre- and post paracetamol.This improvement may be attributed to the hepatoprotective role of N sativa

seeds oil against the paracetamol toxicity due to presence of many antioxidants polyphenols and fat-soluble vitamins(comprised more than 0.2% of total oil content), unsaturated fatty acids (linoleic and oleic acids) and selenium **(Ramadan & Mörsel, 2004; Ashraf et al., 2006 and Cheikh-Rouhou, et al., 2007)** .

Hemopoietic and leukocytic are two dynamic systems which react quickly to chemical intoxications, and condition the maintenance of homeostasis by an organism. Increased RBC is seen in dehydration (i.e. reticulocyte count). Elevated reticulocytes imply a normo-regenerative anemia. Thrombocytosis is seen in many inflammatory disorders.

Neutrophilia and lymphocytopenia were prominent in differential leukocyte count in all the animals subjected to paracetamol induced hepatotoxicity. This might be due to stress coupled with inflammatory changes in body tissue, which is responsible for phagocytosis of toxic substances since neutrophilia was induced by tissue demand for phagocytic function **(Bhaumik & Sharma, 2002).** In the present study, increased neutrophils were observed .Since neutrophils has been investigated in acetaminophen toxicity is neutrophil-induced oxidant stress **(Hinson, et al., 2010).**The increased neutrophils may explain the hepatic damage to liver cells. Nonetheless, **(Liu & coworkers, 2006)** reported that depletion of neutrophils in mice by treatment with anti-Gr-1 antibody (RB6-8C5) significantly protected mice against acetaminophen-induced liver injury, as evidenced by markedly reduced serum ALT levels, centrilobular hepatic necrosis, and improved mouse survival.

However, the role of neutrophils in the development of acetaminophen toxicity has been questioned because substantial recruitment does not occur until after acetaminophen-induced liver injury in the mouse **(Jaeschke & Hasegawa, 2006)**

All these value reversed back towards normal levels in the animals of group IV indicating the efficacy of the pre- treatment with N sativa seed oil in paracetamol treated rats.

The cumulative oxidative damage is likely one of the mechanisms producing the hepatotoxic effects of paracetamol administration in this study. The observed increase in the activities of ALAT, ASAT and ALP may be due to uncontrolled production of free radicals which release the

hepatic enzymes **(Ekam & Ebong, 2007).** The abnormal high level of serum ALAT, ASAT, ALP and bilirubin observed in our study **(Table 1)** are the consequences of paracetamol induced liver dysfunction and denoted the damage to the hepatic cells. In accordance with our study, **Oyagbemi & Odetola, 2010**) recorded that acute administration of paracetamol (3g/kg, 2 doses) produced a marked elevation of the serum levels of SGOT, SGPT, ALP, total proteins and significant reduction in serum albumin in treated animals when compared with control group.

Treatment with N sativa seeds oil reduced the enhanced level of serum ALAT, ASAT, ALP and bilirubin, which seem to offer the protection and maintain the functional integrity of hepatic cells. The present study reveals that N sativa seeds oil has protective effects against the hepatic injury induced by paracetamol. The protective effects were evidenced by a complete blockage of the acetaminophen-induced increase in serum ASAT, ALAT and ALP activities . These results were agreed with (**Meral & Kanter, 2003 and Kanter, et al., 2005)** who found that black cumin essential oil helped in restoring balance in the activities of liver enzymes which may be due to normalization of the level of lipid peroxidation and the stabilization of plasma membrane as well as repair of hepatic tissue.

Present results using the model of paracetamol-induced hepatotoxicity in rats demonstrated that N sativa seeds oil pre- and post-paracetamol caused significant inhibition of serum ALP and bilirubin levels. Effective control of bilirubin level and alkaline phosphatase activity has been described to point towards an early improvement in the secretory mechanism of the hepatic cell **(Oyagbemi & Odetola, 2010).**

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Paracetamol seems to cause impairment in lipoprotein metabolism **(Kanchana, et al., 2011).** High serum total cholesterol and triglyceride levels were recorded in paracetamol- toxicated group. The alteration in lipid profile might result from accumulation of triglycerides, inhibition of bile acid synthesis from cholesterol which is synthesized in

liver or derived from plasma lipids, leading to increase in cholesterol level.They were normalized in paracetamol- intoxicated groups given N sativa which could have favorable impact on serum lipid profile by decreasing total cholesterol, low density lipoprotein and triglycerides, while elevating the high density lipoproteins **(El-Dakhakhny, et al., 2000).** The oil is also rich in sitosterol that inhibits the absorption of dietary cholesterol **(Atta, 2003)**. Afterwards, (**Sultan, 2009)** reported that another component, Nigellamines lowered triglyceride levels in primary cultured mouse hepatocytes and its activity was equivalent to cholesterol lowering agent clofibrate. This effect may be minimized lipids by reducing the synthesis of cholesterol by hepatocytes or decreasing its fractional re-absorption from the small intestine thus lowering serum cholesterol level **(Lee, et al., 2003 and Cheikh-Rouhou, et al., 2008).**

No any much variations were noticed in serum calcium and phosphorus levels of all treated rats comparison to control group **(table 3**). Although some authors reported calcium homeostasis disturbance. When the rate of formation of toxic metabolite NAPQI exceeds the rate of detoxification by intracellular GSH, it oxidizes tissue macromolecules such as lipid or SH group of protein and alters the homeostasis of calcium after depleting GSH **(Oyagbemi & Odetola, 2010).**

CONCLUSION

All these results suggest that, paracetamol is a safe drug at low doses; apart from this it has some side effects also when administered at high doses. At high doses it impairs serum glucose level and modulating certain enzymes metabolism in albino rats. N sativa seeds oil may have a good hepatoprotective role on blood picture and blood biochemical parameters when given before paracetamol to prevent hepatotoxicity in rats more than if given after paracetamol.

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التأثير الوقائي المحتمل لزيت بذورحبة البركة ضد الحث المدمر للباراسيتامول لكبد ذكور الجرذان

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الكبد من أهم أعضاء الجسم وأكبرها من حيث الحجم وعدد الوظائف، ويتأثر بكل ما يدخل الجسم من أدوية وسموم وغيرها. والباراسيتامول من أشهر أدوية المسكنات وأكثرها أمانا إذا استخدم بالجرعات العلاجية المحددة، لكن كثيرا ما تتجاوز الجرعة المستعملة حدود الجرعة العلاجية بسبب سوء الاستخدام أو الخطا أو للتخلص من الحياة ، وأحيانا بسبب وجوده في أكثر من دواء يتناولهم المريض في وقت واحد دون علمه.

ويهدف هذا البحث لدراسة التاثير الوقائي المحتمل لتناول زيت حبة البركة قبل وبعد الجرعات الزائدة من الباراسيتامول على كبد ذكور الجرذان وكذلك قياسات الدم المختلفة.

أوضحت الدراسة أن :

١– زيت حبة البركة وحده لم يغير في نتائج وظائف الكبد في الجرذان ، وكذلك قياسات الدم فيما عدا الزيادة المعنوية في عدد الصفائح الدموية.

٢– انخفاض مستوى سكر الدم في الحيوانات المعطاة جرعات زائدة من الباراسيتامول ، وتحسن مستواه في الحيوانات المعاملة بزيت حبة البركة قبل أو بعد الباراسيتامول.

٣– ارتفاع انزيمات وظائف الكبد في الحيوانات المعطاة (ASAT, ALAT and ALP) جرعات زائدة من الباراسيتامول بالمقارنة بالمجموعة الضابطة ، وتحسن مستواها في الحيوانات المعاملة بزيت حبة البركة قبل أو بعد الباراسيتامول.

٤– ارتفاع في مستوى الكوليستيرول والدهون ثلاثية الجليسرول في مصل الحيوانات المعطاة جرعات زائدة من الباراسيتامول بالمقارنة بالمجموعة الضابطة، وتحسن مستواهما في الحيوانات المعاملة بزيت حبة البركة قبل أو بعد الباراسيتامول.

٥- زيادة معنوية في بروتين مصل الدم الكلي ، وغير معنوية في الألبيومين والجلوبيولين في الحيوانات المعطاة جرعات زائدة من الباراسيتامول بالمقارنة بالمجموعة الضابطة ، وتحسن مستواه في الحيوانات المعاملة بزيت حبة البركة قبل أو بعد الباراسيتامول.

٦- أوضحت صورة الدم زيادة في عدد خلايا الدم الحمراء وعدد الصفائح الدموية ، والهيموجلوبين، (حجم خلية الدم الحمراء) RDW، ونقص (حجم خلايا لدم المضغوط) HCtوفي الحيوانات المعطاة جرعات زائدة من الباراسيتامول بالمقارنة بالمجموعة الضابطة ، وتحسن مستواه في الحيوانات المعاملة بزيت حبة البركة قبل أو بعد الباراسيتامول.

٧- رغم عدم تغير العدد الكلي لخلايا الدم البيضاء في الجرذان المعاملة بالباراسيتامول إلا أن عد الدم التفريقي لخلايا الدم البيضاء أوضح خللا واضحا في نسب توزيع أنواع خلايا الدم البيضاء فزادت نسبة الكريات المتعادلة ونقصت نسبة الخلايا الليمفاوية في الحيوانات المعطاة جرعات زائدة من الباراسيتامول بالمقارنة بالمجموعة الضابطة ، وتحسن مستواه في الحيوانات المعاملة بزيت حبة البركة قبل أو بعد الباراسيتامول.

٨- لم يتغير مستوى الكالسيوم والفوسفور في مصل جميع الحيوانات المختبرة.

وقد استخلص من البحث أن زيت حبة البركة له تأثير وقائي للكبد ولصورة الدم في الحيوانات المعطاة جرعات زائدة من الباراسيتامول خصوصا إذا استعمل زيت حبة البركة قبل الباراسيتامول.