

## Therapeutic Effects of Powder and Alcoholic Aqueous Extract of *Vitellaria paradoxa* on Diabetic Rats

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**Abstract:** The objective of this work study the therapeutic effect of powder and alcoholic aqueous extract of *Vitellaria paradoxa* in blood glucose and lipid profile of diabetic rats. In the experiment thirty rats were divided into six groups (n=5). Streptozotocine was intraperitoneally given at dose 65 mg/kg body weight, animals showing fasting blood glucose higher than 300mg/dl were selected and used as diabetic rats. *Vitellaria Paradoxa* powder and alcoholic aqueous extracts were administered at dose levels (10,20g/kg/diet powder), (100,200 mg/kg body weight orally extract). Hypoglycemic and hypolipidemic effects of the *Vitellaria Paradoxa* were evaluated by the determination of blood glucose, plasma insulin, total cholesterol, triglyceride, LDL-cholesterol, ALT, AST, creatinine, uric acid and bilirubin. Also, evaluated some blood antioxidant parameters by the determination of MDA, SOD and GSH. The results showed high exhibited levels of insulin in *Vitellaria Paradoxa* powder and extract comparing with diabetic control. The results showed that the diabetic rats receiving *Vitellaria Paradoxa* powder and alcoholic aqueous extract had significantly lower levels of serum total cholesterol, triglyceride and LDL-cholesterol levels than those of diabetic control group. All treated groups showed significant increase in superoxide dismutase compared with diabetic control group.

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### 1. Introduction

Diabetic is considered as most serious diseases which that linked to hyperglycemia which occurs either when the pancreas cannot produce enough insulin, or when the body cannot effectively use the produced insulin (Ramachandran et al., 2010). Visceral obesity one of the main risks of metabolic disorders Dysregulated production of certain inflammatory cytokines that exceeding the anti-inflammatory adipose tissue-derived mediators (adipokines as adiponectin) is known to stimulate a state known as insulin resistance (Nishimura et al., 2009).

Diabetes mellitus is a serious health problem. DM results in hyperglycemia in comparison with absolute insulin deficiency which characterized as type I DM or type II in insulin resistance due to receptor insensitivity to endogenous insulin (EL-Hilaly et al., 2007, Aly, 2010).

Shea (*Vitellaria Paradoxa*) is an off-white or ivory-coloured fat extracted from the nut of African Shea tree (*Vitellaria paradoxa* formally *Butrysperrum paradoxum*) (Alfred 2016). Zhenwei et al. (2012) *Vitellaria Paradoxa* and oil is rich in the essential amino acids. It also contains vitamins C, A, K and E and minerals of elements Ca, K, Fe, Na and P (Kanwaljit et al., 2015 and Hanaa, 2017). Malachi et al., (2018) *Vitellaria Paradoxa* aqueous extract were illustrated in high fat diet-induced hyperlipemicrats, showed a decrease in (Tc and TG.

LDL-c and atherogenic index levels (Harnafi et al., 2009). Also their produce have been associated with reduced risk of disease cancer, inflammation, immunomodulating, antithrombotic, antimicrobial, lipid peroxidation and osteoporosis (Samuel, 2015).

Therefore, the current study assessed to investigate the possible impact of *Vitellaria Paradoxa* powder and extract alone to healthy rats and against streptozotocine induced toxicity on rats by changes in biochemical and hematological parameters.

### 2. Materials and Methods

#### Samples preparation:

**Shea (*Vitellaria Paradoxa*):** was obtained from Agriculture Research Center, Giza, Egypt.

**Extraction of the alcoholic aqueous extract:** The extraction according to (Charles et al., 1993).

#### Experimental, Biological Evaluation:

##### Animals:

Male rats weight (69-74) provided standard diet (Table1) and water according to (NRC, 1995). Rats were subjected to streptozotocine dissolved in cold 0.01M citrate buffer, intraperitoneally given at dose 65 mg/kg body weight to induce diabetes. After injection, rats supplied with 5% glucose solution for 48 hrs. (Broca et al. 1999), glucose more than 300mg/dl were selected as diabetic rats.

##### Experimental design:

Thirty rats divided into six groups (n=5), one of them **Group1:** Normal untreated rats, received distilled water (2.5ml/kg).

**Group2:** Diabetic rats control.

**Group3:** Diabetic rats received *Vitellaria Paradoxa* powder (PO) (10g/kg/diet).

**Group4:** Diabetic rats received *Vitellaria Paradoxa* powder (PO) (20g/kg/diet).

**Group5:** Diabetic rats received alcoholic aqueous extracts of *Vitellaria Paradoxa* (EX) (100mg/kg) dissolved in distilled water 1 ml/kg.

**Group6:** Diabetic rats received alcoholic aqueous extracts of *Vitellaria Paradoxa* (EX) (200mg/kg) dissolved in distilled water 1 ml/kg.

At the end of 4 weeks, animals were sacrificed. Body weights were measured three times a week. Daily changes in body weights were percentages. Food efficiency ratio (FER) was calculated at the end of experiment.

#### Biochemical Analysis:

Bood glucose by an enzymatic colorimetric method according to (Siest et al., 1981). Insulin by Enzymatic Linked Immuno sorbent Assay (ELISA) Kit as described by (Nakagawa et al., 1973). Total cholesterol, HDL-cholesterol and triglyceride according to (Allian et al., 1974; Richmond 1973 and Fossati and Principle 1982), respectively. LDL-cholesterol and VLDL-cholesterol were calculated by the Friedewald Formula according to (Friedewald 1972). Bilirubin, Plasma (ALT and AST) were according to (Reitman and Frankel 1957). Plasma total protein

was determined an enzymatic method according to (Henry, 1964). Plasma uric acid was estimated an enzymatic method according to (Trinder, 1969). Plasma creatinine was determined according to (Henry 1974). (SOD) activity by (Dechatelet et al., 1974). Determination of (MDA) in red blood cells RBCs by the method described by Stocks and Donnandy (1971). Glutathione (GSH) according to (Beutler, 1984). Liver for every rat were collected and immersed in 10% neutral buffered formalin as fixative and sent to Cancer Institute for histopathological examination according to (Bancroft et al. 1996).

**Statistical analysis:** The obtained data were statistically analyzed using computerized SPSS (Statistic Program Sigmastat, Statistical Soft-Ware, SAS Institute, Cary, NC). Effects of different treatments were analyzed by one way ANOVA (Analysis of variance) test using Duncan's multiple range test and  $p < 0.05$  was used to indicate significance between different groups (Snedecor and Cochran, 1967).

#### Results and Discussion

Data in table (1) showed the final weight was increased in all rats. Among the treated groups, the highest weight gain% in diabetic groups received *Vitellaria Paradoxa* powder (10g then 20g), followed by extract of *Vitellaria* (200 then 100mg) at percentage (89.9%), (89.8%), (83.5%) and (77.7%) respectively.

Table (1): Effect of powder and alcoholic aqueous extract of *Vitellaria Paradoxa* on body weight gain, food intake and food efficiency ratio of diabetic rats

Groups Parameters		Initial weight (g)	Final weight (g)	weight gain (g)	weight gain %	Daily food intake	food efficiency ratio
Control -ve		70.3± 2.7	149.40± 20.7	79.1.0± 8.27	112.53	13.66± 3.63	5.75± 1.81***
Diabetic control		72.1± 3.49	103.94± 15.3	31.8± 5.32*	44.14	10.28± 2.97	2.89± 0.80
Treated with <i>Vitellaria Paradoxa</i>	PO (10g/kg/diet)	71.5± 2.9	135.8± 18.2	64.3± 7.2***	89.9	12.0± 3.6	5.35± 1.3***
	PO (20g/kg/diet)	69.9± 3.5	132.7± 19.7	62.8± 6.1**	89.8	11.55± 2.3	5.43± 1.0***
	EX (100mg/kg)	70.4± 2.3	125.11± 17.7	54.7± 6.7	77.71	11.12± 3.39	4.9± 1.7**
	EX (200mg/kg)	71.8± 2.7	131.7± 21.7	59.99± 7.31*	83.55	12.0± 4.1	4.9± 1.8**

Each value is the mean+ SD of 5 rat. Significant with control group \* $p < 0.05$  \*\*  $P < 0.01$

Food efficiency ratio of (+ve) control was (2.89), the highest significant were *Vitellaria Paradoxa* powder at level (20g) and (10g) recorded (5.43 and 5.35) and alcoholic aqueous extract. These results approved with (Ozlem et al., 2005) who studied that, body weight was significant lower in groups with

streptozotocin while administration glibornuide increased body weights in the diabetic groups.

Administration of streptozotocin to normal rats resulted in a significant increase in serum total cholesterol, triglyceride and LDL-cholesterol levels as shown in diabetic control Table (2), the results showed

that diabetic groups receiving powder and alcoholic aqueous extract of *Vitellaria Paradoxa* had significantly lower levels of serum total cholesterol, triglyceride and LDL-cholesterol levels than those of diabetic control group.

Concerning total cholesterol, data revealed that the groups treated with powder and alcoholic aqueous extract of *Vitellaria Paradoxa* decrease significantly of total cholesterol levels in comparing with diabetic control (110.0mg/dl). The highest significant  $P < 0.01$  in rats treated with *Vitellaria Paradoxa* PO at levels (20 & 10g), extract (200 & 100 mg), were (68.4, 76.8, 77.0 and 80.8mg/dl) respectively. Results in Table (2), indicated that all the test groups diabetic receiving powder and alcoholic aqueous extract of *Vitellaria Paradoxa* revealed significant decreases in triglyceride

and LDL-cholesterol levels in comparing with diabetic control.

**Harnafi et al., (2009)** found that *Vitellaria Paradoxa* caused a significant decrease on total cholesterol, triglyceride, LDL-c, significant increase in HDL-c for diabetic rats receiving *Vitellaria Paradoxa* (compared with diabetic control (23.0mg/dl). It was no significant differences in VLDL-c of the diabetic groups. Results indicated that *Vitellaria Paradoxa* showed decrease in atherogenic indexes (CHO / HDLc and LDLc / HDLc) than those of diabetic control group. These results are in accordance with those found by (**Harnafi et al., 2018**).

*Vitellaria Paradoxa* aqueous extract displayed a very high antioxidant power and hypolipidaemic (**Amrani et al., 2016 and Bravo et al., 2008**).

Table (2): Effect of powder and alcoholic aqueous extract of *Vitellaria Paradoxa* on serum lipids pattern of diabetic rats

Groups Parameters	T.C (mg/dl)	TG (mg/dl)	HDL-c (mg/dl)	LDL-c (mg/dl)	VLDL-c (mg/dl)	Cholesterol /HDLc	LDL/ HDLc
Control - ve	77.0± 9.08	90.6± 9.8	38.0± 1.5	23.6± 5.7	18.12	2.02	0.62
Diabetic control	110.0± 9.82	175.6± 13.76	23.0± 4.69	40.8± 17.97	35.12	4.78	1.77
Treated with <i>Vitellaria Paradoxa</i>	PO (10g/kg/diet)	76.80± 5.63**	100.6± 8.2**	33.3± 2.1**	28.20± 4.81**	20.12	0.76
	PO (20g/kg/diet)	68.4± 14.7**	94.3± 7.1**	34.0± 2.34**	26.7± 5.9***	18.86	2.01
	EX (100mg/kg)	80.8± 5.33*	115.0± 11.78*	31.3± 4.0**	36.60± 2.96	23.0	2.58
	EX (200mg/kg)	77.0± 11.4**	96.8± 9.8**	32.0± 2.34**	30.9± 7.6	19.36	2.4

Each value is the mean+ SD of 5 rats. Significant with control group \* $p < 0.05$  \*\*  $P < 0.01$

Data in table (3) revealed a significant decrease ( $P < 0.01$ ) and ( $p < 0.05$ ) in ALT level for diabetic rats receiving *Vitellaria Paradoxa* compared with diabetic rats, and significant decrease in AST. Therefore, it is possible to suggest that powder and extract protect against diabetic which improve AST and ALT levels in treated diabetic groups. Concerning urea and creatinine, were significantly decreased. It was noticed that a significant decrease ( $P < 0.01$ ) and ( $p < 0.05$ ) in uric acid levels of diabetic groups treated with powder and alcoholic aqueous extract of *Vitellaria Paradoxa* when compared with diabetic control. On the other hand, it was found that significant increase in bilirubin for control diabetic rats caused this ratio, by about 2 folds than that the group treated with powder and aqueous extract of *Vitellaria Paradoxa*. It was suggested that antioxidant activity of the extract better compared to (non-diabetic) (**Sushruta et al., 2006**). These results of treatment effects of *Vitellaria Paradoxa* leaves or alcoholic aqueous extracts on some renal function represented in creatinine, uric

acid, bilirubin. Extract improve the structural and function alintegrities of blood cells, liver and kidney.

Data in table (4) revealed a significant elevation in fasting blood glucose and significant decrease in plasma insulin level of diabetic control when compared with all the rats, plasma insulin in groups treated with powder and alcoholic aqueous extract of *Vitellaria Paradoxa* exhibited high levels of insulin in comparing with diabetic control (4.8Uu/ml). The groups treated with *Vitellaria Paradoxa* powder had (9.01 and 9.51Uu/ml) *Vitellaria Paradoxa* extract had significant increase ( 7.3 and 7.2 Uu/ml) respectively.

As evident from Table (4) significant decrease in fasting blood glucose was observed in the diabetic groups treated with powder and alcoholic aqueous extract of *Vitellaria Paradoxa* when compared with diabetic control. Rats with diabetes induced by streptozotocin (**Heibashy, 2005**) or alloxan (**Ye et al., 2002**), reduced fasting blood glucose and HbA1C when rats fed on the tested therapeutic plant origins (**Lima et al., 2006 and Eidi and Eidi, 2009**). Free

radicals and the associated oxidative stress play an important role in the cause and subsequent complication of diabetes mellitus.

Table (3): Effect of powder and alcoholic aqueous extract of *Vitellaria Paradoxa* on serum ALT, AST, urea, creatinine, uric acid and bilirubin of diabetic rats

Groups Parameters	ALT (Iu/ml)	AST (Iu/ml)	Urea (mg/dl)	Creatinine (mg/dl)	Uric Acid (mg/dl)	Bilirubin (mg/dl)	
Control -ve	12.6 ± 5.85	28.40 ± 4.8	12.2 ± 2.9	0.8 ± 0.10	2.8 ± 0.38	0.45 ± 0.03	
Diabetic control	30.8 ± 4.29	45.4 ± 3.50	29.70 ± 3.2	2.64 ± 0.15	4.04 ± 0.58	1.0 ± 0.03	
Treated with <i>Vitellaria Paradoxa</i>	PO (10g/kg/diet)	26.2 ± 7.2	29.4 ± 2.96*	24.2 ± 3.32*	1.86 ± 0.43**	2.8 ± 0.5**	0.55 ± 0.09**
	PO (20g/kg/diet)	21.4 ± 7.4**	26.0 ± 3.93**	23.7 ± 2.6**	1.7 ± 0.11**	2.54 ± 0.6**	0.44 ± 0.06**
	EX (100mg/kg)	25.1 ± 6.2	38.9 ± 6.1	25.1 ± 3.7	2.1 ± 0.18	2.94 ± 0.35*	0.53 ± 0.08**
	EX (200mg/kg)	24.8 ± 3.1*	34.7 ± 8.2	23.25 ± 2.4**	1.9 ± 0.08	2.7 ± 0.7**	0.47 ± 0.07**

Each value is the mean+ SD of 5 rats. Significant with control group \*p< 0.05\*\* P< 0.01

Table (4): Effect of powder and alcoholic aqueous extract of *Vitellaria Paradoxa* on blood glucose, plasma insulin of diabetic rats

Groups Parameters	Insulin (u\l)	Fasting blood glucose (mg/dl)	
Control -ve	12.6 ± 1.85	113.40 ± 15.8	
Diabetic control	4.8 ± 0.99	329.4 ± 63.50	
Treated with <i>Vitellaria Paradoxa</i>	PO (10g/kg/diet)	9.01 ± 1.2**	228.14 ± 35.7*
	PO (20g/kg/diet)	9.51 ± 1.1**	209.4 ± 42.96**
	EX (100mg/kg)	7.33 ± 2.2*	268.9 ± 46.1
	EX (200mg/kg)	7.22 ± 2.4*	255.7 ± 48.2

Each value is the mean+ SD of 5 rats. Significant with control group \*p< 0.05 \*\* P< 0.01

Data in table (5) revealed decrease significantly in malondialdehyde (MDA) and a significant elevation in (SOD) and glutathione (GSH) levels were observed in the diabetic groups treated with *Vitellaria Paradoxa* powder and alcoholic aqueous extract when compared with diabetic control.

As evident from Table (5) significant decrease p< 0.05 in malondialdehyde (MDA) were observed in *Vitellaria Paradoxa* powder (20g) when compared with diabetic control was 19.2±0.8 increase significantly P< 0.001 in superoxide dismutase (SOD) in all treated groups when compared with diabetic control was 0.26.

Concerning glutathione (GSH), revealed increase significantly in all treated groups in comparing with diabetic control 4.22. These results are in agreement

with (El-Sheikh 2008; Rana and Soni 2008 and Dasgupta et al., 2014). Rats fed with *Vitellaria Paradoxa* powder improve activities of liver enzymes, such as (SOD) and (GSH-Px), (Vitaglione et al., 2014).

Level of MDA increased in diabetic non treated group when compared to groups treated with extract and with normal control group ( Wilson et al., 2001 and Ugwu et al., 2013) studied the lipid peroxides concentration which increased in diabetic rats kidney.

The results of SOD and CAT activities clearly showed that *Vitellaria Paradoxa* powder and extract contain a free radical scavenging activity, caused by the presence of •O<sub>2</sub>-and OH\*. This action, predominantly due to the extract, could involve



mechanism related to scavenging activity (**Roberto et al., 2003**).

Pathological examination of rats liver showed that diabetic control induced focal hepatic necrosis associated with inflammatory cells infiltration Pic. (2). The liver of the (normal control group) rats showing the normal histological structure of hepatic lobule. The liver of the diabetic rat treated with *Vitellaria Paradoxa* (10g/kg) powder showing few leucocytes in hepatic sinusoids Pic. (3). The liver of, diabetic rat treated with *Vitellaria Paradoxa* (20g/kg) showing slight activation of kupffer cells Pic. (4). The liver of the diabetic rat treated of *Vitellaria Paradoxa* extract

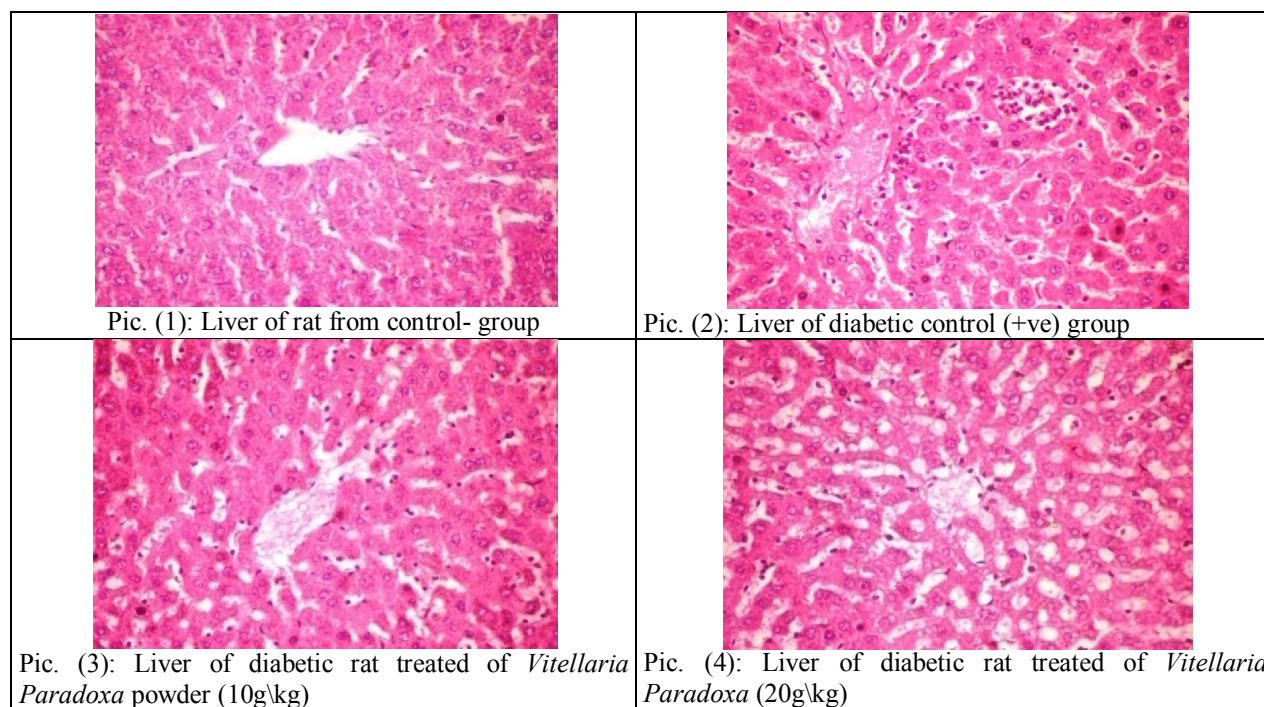
(100mg/kg) showing no histopathological changes Pic. (5). The liver of the, diabetic rat treated with *Vitellaria Paradoxa* (200mg/kg) showing cytoplasmic vacuolization of hepatocytes, hepatoportal blood vessel Pic. (6).

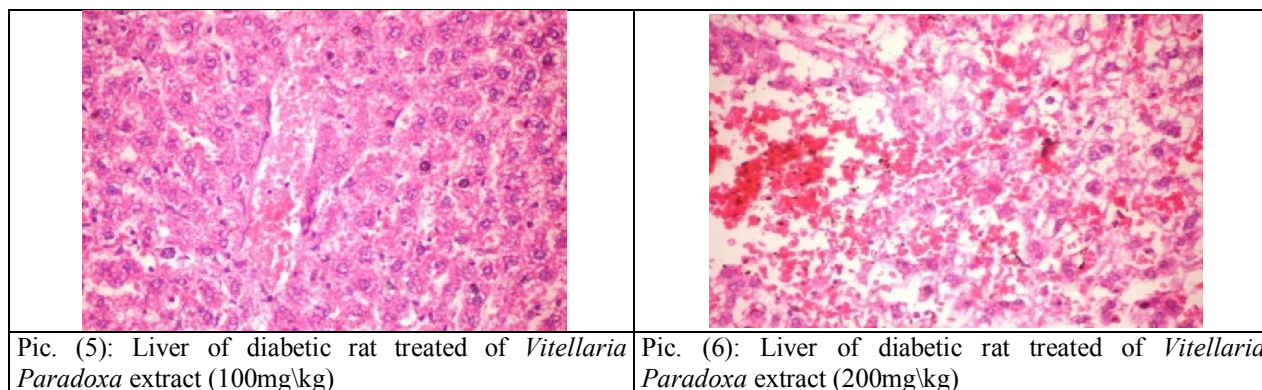
Indicating the induction was successful and there were no reversions. Lipid peroxide-mediated tissue damage has been observed in the development of both types 1 and 2 Diabetes (**Stanely et al., 2017**). In conclusion, the study showed that treatment with powder and alcoholic aqueous extract of *Vitellaria Paradoxa*, can traditional use in the management of diabetes and cardiovascular diseases.

Table (5): Effect of powder and alcoholic aqueous extract of *Vitellaria Paradoxa* on some blood antioxidant levels

Groups Parameters	MDA (U/mL)	SOD (mg/L)	GSH (U/mL)
Control -ve	11.26± 1.4	0.54± 0.12	9.27± 0.6
Diabetic control	19.2± 0.8	0.26± 0.09	4.22± 1.54
Treated with <i>Vitellaria Paradoxa</i>	PO (10g/kg/diet)	14.0± 1.2	6.25± 0.03*
	PO (20g/kg/diet)	12.5± 1.7*	7.7± 0.88**
	EX (100mg/kg)	15.6± 0.9	0.63± 0.08***
	EX (200mg/kg)	14.5± 1.2	0.66± 0.12***

Each value is the mean+ SD of 5 rats. Significant with control group \*p<0.05 \*\* P<0.01 \*\*\*P<0.001. MDA: malondialdehyde SOD: superoxide dismutase GSH: glutathione





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