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The Effect of Low and High Dose of *Ferula* Plant on ALT & AST Activity, Glucose and Cholesterol Levels in Male Albino Rats.

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ABSTRACT

In this study, we have used *Ferula* plant - a traditional medicinal herb - to evaluate its effect on some physiological and biochemical properties in male albino rats, which weigh about 250-300 gm. They were divided into three groups, a control group, the second group which was given 50 mg / kg of *Ferula* orally, and the last group which was given 100 mg / kg *Ferula* orally for a period of twenty-one days. Rats were weighed in the beginning and at the end of the experiment, Serum biochemical analysis measurements were carried out at the end of the experiment, body weight was in the normal range in high and low dose groups of *Ferula* plant, the result of the study showed a significant decrease in the concentration of serum glucose, triglyceride and ALT activity in both low and high dose of *Ferula*, while the level of serum total cholesterol and HDL in both low and high doses was significantly high. There was no change in the concentration of serum creatinine, LDL, uric acid and urea in the low-dose treated group. These findings show the hypoglycemic, hypolipidemic and hypocholesterolemic activity of 50 mg / kg of *Ferula*, as it did not affect the function of the liver and kidneys.

KEYWORDS: *Ferula*, ALT, AST, hypolipidemic, hypocholesterolemic, hypoglycemic.

INTRODUCTION

Ferula plant is a genus of herbs and a member of the family Apiaceae (formerly Umbelliferae), it includes 275 genera and 2850 species [42], *Ferula* plant distributed all around the world, mainly in Afghanistan, Iran, India and Pakistan [21], and scattered from north Africa to central Asia [41] phytochemical studies have been done on more than 70 species *Ferula* genus [25,26,27,28]. *Ferula* genus is a source of bioactive phytochemicals, for instance sesquiterpene derivatives [39,30,24,29,35,49,31,33,32], and sulfur containing compounds [5,22,23].

Assa-foetida is the oleo-gum-resin found in the roots and stems of several *Ferula* species. *Assa-foetida* has been used for centuries as a spice and a folk phytomedicine. *Assa-foetida* has a unique sulfurous aroma and a bitter taste. It is used in a variety of foods as a flavoring spice, *Assa-foetida* is considered to have aphrodisiac, sedative and diuretic ability [10]. Traditionally, it is used for treating numerous diseases, such as asthma, epilepsy, stomachache, flatulence, intestinal parasites, weak digestion and influenza [51,47,16,38]. Many biological and pharmacological researches have revealed several activities, such as antioxidant [13,40,14], antiviral [38,18], antifungal [44,45,6,43], antibacterial activity [46], antileishmanial [11], cancer chemopreventive [52,4], anti-diabetic [2,50], antispasmodic [17,7], hypotensive [17], antinociceptive [8] and

molluscicidal [36], anti-inflammatory and analgesic agent [9]. *Assa-foetida* contains three main fractions, resin (40–64%), gum (25%) and essential oil (10–17%) [47].

Many people prefer to use medicinal plants rather than chemical drugs. In the current study, low (50 mg / kg) and high dose (100 mg / kg) of *Ferula* were used to estimate the safety of this broadly used medicinal plant, and to estimate the effect of it on glucose and cholesterol Levels in short term treatment.

MATERIALS AND METHODS

Ferula plant were purchased from a local herb market in Riyadh, Saudi Arabia.

Adult male albino rats weighed about 250-300 g were taken from the Animal Care Center, College of Pharmacy (King Saud University, Riyadh, Saudi Arabia). They were housed in a cage at 22- 24°C with a 12 h light, 12 h dark. The animals were acclimatized in house conditions for a week prior. The study protocol was approved by the Research Ethics Committee of the College of Pharmacy (King Saud University, Riyadh, Saudi Arabia), they were divided randomly into three groups (7 animals per group) as follows:

group1: normal control.

group 2: (50 mg / kg) *Ferula* was given orally for 21 days.

group 3: (100 mg / kg) *Ferula* was given orally for 21 days.

Rats were weighed in the beginning and at the end of the experiment.

Towards the end of the experiment animals were deprived of food for 24 h, they had free access to water, rats were sacrificed and blood samples were collected and allowed to clot, and serum was separated for the estimation of Alanine aminotransferase (ALT) & Aspartate aminotransferase (AST) activity; glucose level; total cholesterol; low density lipoprotein (LDL); high density lipoprotein (HDL); triglycerides concentrations; urea concentration; uric acid content and creatinine. All the samples were analyzed using analyzer medical system (AMS) ELLIPSE.

Statistical Analysis:

Statistical analysis was performed with SPSS (SPSS Inc., Illinois, USA).

Data are presented as mean ± S.E. of the mean. Statistical differences between means were calculated using one way ANOVA. Differences were considered significant at $p < 0.05$.

Results:

- *The effect of high and low dose of Ferula plant on body weight:*

Table (1) shows that the base line of rat's mean body weight was similar in all groups, at the end of experiment mean body weight was in the normal range in high and low dose groups of *Ferula* plant as compared to the control group.

- *The effect of high and low dose of Ferula plant on Aspartate aminotransferase(AST) and Alanine aminotransferase (ALT) activities:*

Our result in table (2) showed a significant decrease in ALT activity in both low and high dose groups of *Ferula* plant when compared to the control group. AST was in normal range in 50 mg *Ferula* group, while it was decreased significantly in 100 mg *Ferula* group when compared to control.

- *The effect of high and low dose of Ferula plant on glucose concentration:*

Glucose concentration was decreased significantly in low and high dose of ferula when compared to control group, low dose of *Ferula* was more effective in lowering glucose, table (3).

- *The effect of high and low dose of Ferula plant on total cholesterol; low density lipoprotein (LDL); high density lipoprotein (HDL); triglycerides concentrations:*

Total cholesterol and HDL in low & high dose of *Ferula* plant were significantly higher than control, 50 mg of *Ferula* caused a decrease in triglycerides and stabilized LDL concentration in serum, while LDL was elevated and triglycerides were in normal range in 100 mg of *Ferula*, table (3).

- *The effect of high and low dose of Ferula plant on urea concentration; uric acid content and creatinine:*

Creatinine levels were normal in both groups as compared to control, urea and uric acid concentration were normal in low dose of *Ferula*, urea concentration was elevated and uric acid was lower in high dose of *Ferula*, table (4).

Table 1: Mean values of body weight in all different groups.

ups	Initial body weight (g)	Final body weight (g)
ntrol	270.71±6.25	295.29±12.91
w dose (50 mg) of *ferula*	273.57±7.85	274.71±14.00
gh dose (100 mg) of *ferula*	272.71±7.63	269.57±10.35

Values are expressed as means ±S. E (n=7).
* Significant compared to the control group, P<0.05

Table 2: The effect of high (100 mg) and low (50 mg) dose of *Ferula* plant on Aspartate aminotransferase(AST) and Alanine aminotransferase (ALT) activities in male albino rats.

groups	ALT (U/L)	AST (U/L)
Control	80.85 ± 16.71	105.00 ± 17.00
Low dose (50 mg) of *ferula*	54.41 ± 9.55*	105.57 ± 13.18
High dose (100 mg) of *ferula*	58.21 ± 5.26*	136,71 ± 18.78*

Values are expressed as means ±S. E (n=7).
* Significant compared to the control group, P<0.05.

Table 3: The effect of high (100 mg) and low (50 mg) dose of *Ferula* plant on glucose level; total cholesterol; low density lipoprotein (LDL); high density lipoprotein (HDL) and triglycerides concentrations in male albino rats.

Groups	Glucose (g/dl)	l cholesterol (mg/dl)	HDL (mg/dl)	LDL (mg/dl)	Triglycerides (mg/dl)
Control	177.71±30.32	45.00±8.92	39.72±9.28	26.34±5.04	46.71±10.99
Low dose (50 mg) of *ferula*	85.57±10.67*	56.57±8.69*	54.35±7.34*	31.68±6.34	35.14±4.41*
High dose (100 mg) of *ferula*	122.28±33.26	55.42±8.18*	49.90±6.59*	33.67±7042*	43.42±6.45

Values are expressed as means ±S. E (n=7).
* Significant compared to the control group, P<0.05.

Table 4: The effect of high (100 mg) and low (50 mg) dose of *Ferula* plant on urea concentration; uric acid content and creatinine.

groups	Urea mg/dl	Uric acid mg/dl	Creatinine mg/dl
Control	39.04±4.37	2.08±1.29	0.47±4.4.88
Low dose (50 mg) of *ferula*	39.41±5.81	1.37±0.39	0.45±5.34
High dose (100 mg) of *ferula*	49.75±7.94*	1.02±0.34*	0.54±0.11

Values are expressed as means ±S. E (n=7).
* Significant compared to the control group, P<0.05.

Discussion:

Ferula-assa-foetida is an easily-accessible source of natural antioxidants such as eremophilene, δ-cadinene and longiborneol and it may be suitable for use in applications of food and pharmaceutical and health problems that are caused by free radicals [3].

In the current study, low (50 mg / kg) and high dose (100 mg / kg) of *Ferula* were used to estimate the safety of this widely used medicinal plant in short term treatment. No changes in body weight in both group when compared with control rats, our results are in line with [2,19].

Cytosolic enzymes, ALT and AST are highly concentrated in the liver and kidneys, and they are only found in significant amounts in the serum when the cell membrane becomes leaky and even bursts completely [12], both ALT and AST are released out of damaged hepatocytes into the extracellular space, our study showed a significant decrease in ALT activity in both low and high dose groups of *Ferula* plant, and also in AST activity in high dose group, but AST was in normal range in low dose group. The normal level of serum AST, ALT, and ALP (alkaline phosphatase) in Goudah *et al.* [19] study indicate the normal structural and functions of hepatic cells, and even on its chronic use, the normal amount of the hepatic biochemical parameters shows the safety of the extract on liver function.

In addition, no changes were observed in serum creatinine, our results are in line with 19]. The serum creatinine level is an indicator of renal function, and any increase of serum levels of creatinine is related to a marked failure of nephrons function [37]. Mean values of Urea and uric acid were in normal levels in both group of *ferula* plant. In Javaid *et al.* [34] study, *Ferula foetida* nearly showed a complete reversal of blood urea nitrogen (BUN), serum creatinine levels and thiobarbituric acid reacting substances (TBARS) level in kidney tissue, to the Gentamicin-treated rats, indicating nephroprotective properties of *Ferula foetida*.

Glucose levels were significantly decreased in both dose of *Ferula*, our results are in line with [15,20], This decrease might be associated to the decrease in body weight, reduced food consumption, and a reduction in gluconeogenesis in the liver [15], Abu-Zaiton [2] and Helal *et al.* [20] have found that *Assa-foetida* extract had hypoglycemic and hyperinsulinemic effects on alloxan-diabetic rats.

Total cholesterol, HDL in both dose of *Ferula* were increased, while LDL in100 mg/Kg of *Ferula* was increased and 50 mg/Kg of *Ferula* was in normal range when compared with control, triglycerides in 50 mg/Kg of *Ferula* was decreased and 100 mg/Kg of *Ferula* was in normal range when compared with control, some

results are partially in line with [1], these results indicate the hypolipidimic effect of *Ferula* in low dose. application of *Ferula* treatment on humans, either by raising dietary intake of *Ferula*, or supplementation, to assess clinical benefits and implications in humans, before general recommendation.

Conclusion:

Neither low dose of *Ferula* nor high dose of *Ferula* for 21 days induce obvious toxicological marks in liver and kidneys in male albino rats, and shows hypoglycemic and hypolipidimic action. Our study concluded the safety and little toxicity of *Ferula* plant for short term use in both dose.

Application of *Ferula* treatment for a longer period, a modified dosage and studying the plant effect on other organs might result in greater benefits and may provide a new potential capability of this plant, Further work is needed.

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