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INVESTIGATION OF CHRONIC TOXICITY PROPERTIES IN THE AQUEOUS AND ALCOHOLIC EXTRACTS OF *FERULA MOSCHATA*

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ABSTRACT

Background: Children *Background: Ferula moschata* (Reinsch.) Koso-Pol., known locally as "moshk koren" or "sumbul," is a perennial herb endemic to Central Asia, traditionally used in Uzbek and Tibetan medicine for its purported neurotonic, sedative, and antispasmodic properties. Despite its long-standing ethnobotanical use, a systematic toxicological profile, particularly concerning its long-term administration, is lacking. This study aims to evaluate the chronic toxicity of standardized aqueous and alcoholic extracts of *Ferula moschata* roots in a laboratory animal model.

Methods: A 90-day subchronic oral toxicity study was conducted in accordance with OECD Guideline 408. Wistar rats (n=120, equal sexes) were divided into four groups: Control (distilled water), Low-Dose (100 mg/kg), Medium-Dose (300 mg/kg), and High-Dose (1000 mg/kg) for both aqueous and alcoholic extracts. Body weight, feed, and water consumption were monitored weekly. Hematological parameters (complete blood count), biochemical parameters (ALT, AST, ALP, creatinine, urea, total protein, albumin), and urinalysis were assessed at 30, 60, and 90 days. At termination, gross pathological examination and histopathological evaluation of major organs (liver, kidneys, heart, spleen, lungs, brain) were performed.

Results: No mortality was observed in any group. The alcoholic extract at 1000 mg/kg caused a statistically significant ($p<0.05$) reduction in body weight gain and a transient increase in ALT and AST levels at the 60-day mark, which normalized by day 90, suggesting adaptive hepatocyte response. Histopathological analysis revealed mild hepatic centrilobular congestion and minimal hydropic degeneration in the high-dose alcoholic group. The aqueous extract showed no significant adverse effects on hematological, biochemical, or histopathological parameters at all doses tested. The No-Observed-Adverse-Effect-Level (NOAEL) was determined to be 300 mg/kg/day for the alcoholic extract and greater than 1000 mg/kg/day for the aqueous extract.

Conclusion: The aqueous extract of *Ferula moschata* demonstrates a wide margin of safety under the conditions of this study, supporting its traditional use. The alcoholic extract, while showing higher bioactivity, also presents a potential for mild, reversible hepatotoxicity at very high doses. Further investigation into the specific hepatotoxic compounds within the alcoholic fraction is warranted.

1. Introduction

The genus *Ferula* (Apiaceae) comprises over 170 species, predominantly distributed in the arid and semi-arid regions of Central Asia and the Mediterranean. Many species of this genus have held a place of profound significance in traditional medicine systems for centuries, renowned for their aromatic gums and resins, such as asafoetida and galbanum (Sahebkar & Iranshahi, 2012011).

Ferula moschata (Reinsch.) Koso-Pol., known colloquially in Uzbekistan as "moshk koren" and more widely as "sumbul" or "musk root," is one such species endemic to the high-altitude regions of Central Asia, including the mountains of Uzbekistan, Tajikistan, and Kyrgyzstan. Its root has a strong, persistent musky odor, which has historically made it a valuable commodity in perfumery and traditional medicine.

In the canonical texts of Central Asian and Tibetan medicine, *F. moschata* is highly regarded as a potent neurotonic and a restorative for the nervous system. It has been traditionally prescribed for conditions such as hysteria, neurasthenia, seizures, and various forms of paralysis. Avicenna (Ibn Sina), in his seminal work "The Canon of Medicine," made references to plants of the *Ferula* genus for their carminative and antispasmodic properties, though precise species identification in historical texts remains challenging. The ethnobotanical records from the Samarkand and Bukhara regions of Uzbekistan document the use of *F. moschata* root decoctions for treating gastrointestinal spasms, asthma, and as a general stimulant.

The chemical composition of *Ferula* species is complex and characterized by the presence of sulfur-containing compounds, coumarins, sesquiterpene derivatives, and phenolic compounds. Previous phytochemical investigations on *F. moschata* have identified the presence of specific coumarins (e.g., umbelliferone, scopoletin) and sesquiterpene coumarins (e.g., feselol, kamolonol) which are believed to be responsible for its characteristic odor and potential pharmacological activity (Iranshahi et al., 20072007). The essential oil derived from the roots is rich in terpenoids and sulfurous compounds, contributing to its musk-like scent.

While the therapeutic potential of *Ferula* species is widely acknowledged, a critical review of the scientific literature reveals a significant gap: a comprehensive and systematic toxicological evaluation, particularly for long-term use, is largely absent. Most pharmacological studies have focused on the bioactivity of isolated compounds or crude extracts, demonstrating antimicrobial, antioxidant, and anticonvulsant effects in acute models (Kholmatova et al., 20152015; Abdullaev et al., 20182018). However, the dictum of Paracelsus that "the dose makes the poison" is particularly pertinent to herbal medicines, where the assumption of safety based on traditional use can be misleading without rigorous scientific validation.

Several researchers have paved the way for this investigation. The team led by Prof. I.A. Khamidov at the Tashkent Pharmaceutical Institute conducted preliminary acute toxicity screenings on

several Uzbek *Ferula* species, finding LD_{50} values to be relatively high, suggesting low acute toxicity (Khamidov et al., 20102010). Meanwhile, research from the Laboratory of Experimental Pharmacology at Tashkent State Medical University has documented the hypotensive and sedative effects of *F. moschata* extracts in normotensive and hypertensive rats (Karimov et al., 20212021). Internationally, the work of Iranshahi and colleagues in Iran has extensively cataloged the chemical structures of numerous compounds from various *Ferula* species, providing a chemical basis for understanding their activity and potential toxicity (Iranshahi et al., 20072007). Furthermore, studies on other *Ferula* species, such as *F. assa-foetida*, have reported potential hepatotoxic and nephrotoxic effects at high doses, underscoring the necessity for species-specific toxicity profiles (Bagheri et al., 20142014).

Purpose of the Research

The present study was therefore designed to systematically evaluate the chronic toxicity of both aqueous and alcoholic extracts of *Ferula moschata* roots following repeated oral administration for 90 days in Wistar rats. The objective was to identify target organs of toxicity, determine the No-Observed-Adverse-Effect-Level (NOAEL), and provide a scientific basis for the safe dosage range for potential therapeutic application, thereby bridging the gap between traditional use and modern evidence-based phytomedicine.

2. Materials and Methods

2.1. Plant Material and Extraction

The roots of *Ferula moschata* were collected during the post-flowering period (July-August 2022) from the designated mountain areas of the Samarkand region, Uzbekistan. The plant was authenticated by a senior botanist at the Institute of Botany of the Academy of Sciences of Uzbekistan, Tashkent, where a voucher specimen (No. FM-0722) was deposited. The roots were carefully washed, air-dried in the shade at room temperature (25±2°C) for three weeks, and then coarsely powdered using a mechanical grinder.

For the aqueous extract (FMAE), 500 g of the powdered root was macerated with 5 L of distilled water for 72 hours at 40°C with continuous stirring. The mixture was then filtered, and the marc was re-extracted twice under the same conditions. The combined filtrates were concentrated under reduced pressure at 50°C using a rotary evaporator (Heidolph, Germany) and subsequently freeze-dried (Lyophilizer, Christ, Germany) to obtain a dry, brownish powder (yield: 12.5% w/w).

For the alcoholic extract (FMAE), 500 g of the powdered root was subjected to Soxhlet extraction with 2.5 L of 70% ethanol

for 48 hours. The ethanolic solution was filtered and concentrated under reduced pressure at 45°C. The resultant semi-solid mass was further dried in a vacuum desiccator to yield a dark brown, resinous extract (yield: 18.3% w/w). Both extracts were stored in airtight, light-protected containers at -20°C until use.

2.2. Experimental Animals

The study utilized 120 healthy, young adult Wistar rats (60 males and 60 females), weighing 150-180 g at the start of the experiment. The animals were obtained from the Central Animal House Facility of Tashkent State Medical University. They were group-housed (5 per cage) in polypropylene cages with sterile paddy husk as bedding, under standard laboratory conditions: temperature of 22±2°C, relative humidity of 50±5%, and a 12-hour light/dark cycle. A standard pellet diet (Laboratory Rodent Diet, UzFeed Ltd., Uzbekistan) and filtered water were provided *ad libitum*. The animals were acclimatized to the laboratory environment for one week prior to the commencement of the experiment. The study protocol was reviewed and approved by the Institutional Animal Ethics Committee (IAEC) of Tashkent State Medical University (Protocol No. TSMI/IAEC/05/2022) and all procedures were conducted in strict accordance with the OECD Guidelines for the Testing of Chemicals, Section 4: Health Effects, No. 408 (Repeated Dose 90-Day Oral Toxicity Study in Rodents).

2.3. Study Design and Dosing

After acclimatization, the rats were randomly divided into 8 main groups (n=15 per group, with equal distribution of sexes), plus an additional satellite group for the high-dose alcoholic extract for recovery assessment.

- *Group I (Control):* Received distilled water (10 mL/kg/day, p.o.).
- *Group II (FMAE-Low):* Received aqueous extract at 100 mg/kg/day, p.o.
- *Group III (FMAE-Medium):* Received aqueous extract at 300 mg/kg/day, p.o.
- *Group IV (FMAE-High):* Received aqueous extract at 1000 mg/kg/day, p.o.
- *Group V (FMAE-Low):* Received alcoholic extract at 100 mg/kg/day, p.o.
- *Group VI (FMAE-Medium):* Received alcoholic extract at 300 mg/kg/day, p.o.
- *Group VII (FMAE-High):* Received alcoholic extract at 1000 mg/kg/day, p.o.
- *Group VIII (FMAE-High-Recovery):* Received alcoholic extract at 1000 mg/kg/day for 90 days, then observed for a further 28-day recovery period without treatment.

The extracts were freshly prepared daily by suspending in distilled water. The dosing volume was standardized to 10 mL/kg

body weight. The administration was performed via oral gavage between 9:00 and 10:00 AM daily for 90 consecutive days.

2.4. Clinical Observations and Body Weight Analysis

All animals were observed twice daily for mortality and signs of morbidity. A detailed clinical examination for any signs of toxicity (e.g., changes in skin, fur, eyes, mucous membranes, respiratory pattern, circulatory signs, autonomic effects, and changes in gait, posture, and behavior) was performed weekly. Individual body weights and average food and water consumption per cage were recorded weekly.

2.5. Hematological and Biochemical Analysis

Blood samples were collected from the retro-orbital plexus under mild ether anesthesia from 10 randomly selected rats per group (5 males, 5 females) at the end of 30, 60, and 90 days of treatment. For hematological analysis, blood was collected in EDTA tubes and analyzed using an automated hematology analyzer (Sysmex XT-1800i, Japan). Parameters measured included: Red Blood Cell count (RBC), White Blood Cell count (WBC) with differential, Hemoglobin (HGB), Hematocrit (HCT), Mean Corpuscular Volume (MCV), Mean Corpuscular Hemoglobin (MCH), Mean Corpuscular Hemoglobin Concentration (MCHC), and Platelet count (PLT).

For biochemical analysis, blood was collected in plain tubes, allowed to clot, and centrifuged at 3000 rpm for 15 minutes to separate serum. Biochemical parameters were analyzed using a semi-automated biochemical analyzer (Mindray BA-88A, China) with standard diagnostic kits (Spinreact, Spain). Parameters assessed included: Alanine Aminotransferase (ALT), Aspartate Aminotransferase (AST), Alkaline Phosphatase (ALP), Total Bilirubin, Creatinine, Urea, Total Protein, and Albumin.

2.6. Urinalysis

At the end of the 90-day treatment period, urine was collected from 5 rats per group over a 16-hour period using metabolic cages. Urinalysis included physical examination (color, appearance, volume), chemical analysis using dipsticks (Multistix 10SG, Siemens, Germany) for pH, protein, glucose, ketones, bilirubin, urobilinogen, and blood, and microscopic examination of sediment.

2.7. Gross Pathology and Histopathology

At the end of the 90-day treatment period (and after the 28-day recovery period for Group VIII), all surviving animals were euthanized by cervical dislocation under deep anesthesia. A complete gross necropsy was

performed on all animals. Organs (liver, kidneys, heart, spleen, lungs, and brain) were carefully dissected, trimmed of extraneous tissue, and weighed. The relative organ weight (organ-to-body weight ratio) was calculated for each animal. Tissues from all organs were preserved in 10% neutral buffered formalin, processed routinely, embedded in paraffin, sectioned at 4-5 µm thickness, and stained with Hematoxylin and Eosin (H&E) for light microscopic examination by a pathologist blinded to the treatment groups.

2.8. Statistical Analysis

All data are expressed as mean ± standard deviation (SD). Statistical analysis was performed using GraphPad Prism software (Version 9.0, USA). Data were analyzed by one-way analysis of variance (ANOVA) followed by Dunnett's post-hoc test for multiple comparisons against the control group. A value of $p < 0.05$ was considered statistically significant.

3. Results

3.1. Clinical Observations and Mortality

Throughout the 90-day study period, no mortality was recorded in any of the treatment or control groups. Animals in the control, low-, and medium-dose groups for both extracts appeared normal and active, with no observable signs of toxicity. However, in the high-dose alcoholic extract group (FMAE-High, 1000 mg/kg), mild to moderate clinical signs were observed, particularly during the first 4-5 weeks of dosing. These included reduced spontaneous motor activity, piloerection, and a slight decrease in alertness. These signs were transient and diminished in frequency and intensity as the study progressed. No such signs were observed in any of the aqueous extract groups.

3.2. Body Weight, Food, and Water Consumption

The effects of chronic administration of *F. moschata* extracts on body weight are summarized in Table 1 and Figure 1. There were no significant differences in the mean body weight of rats treated with the aqueous extract at any dose level compared to the control group throughout the study period. In contrast, administration of the alcoholic extract at 1000 mg/kg/day resulted in a statistically significant ($p < 0.05$) reduction in body weight gain from week 6 onwards in both male and female rats compared to the control group. The lower doses (100 and 300 mg/kg) of the alcoholic extract did not affect body weight.

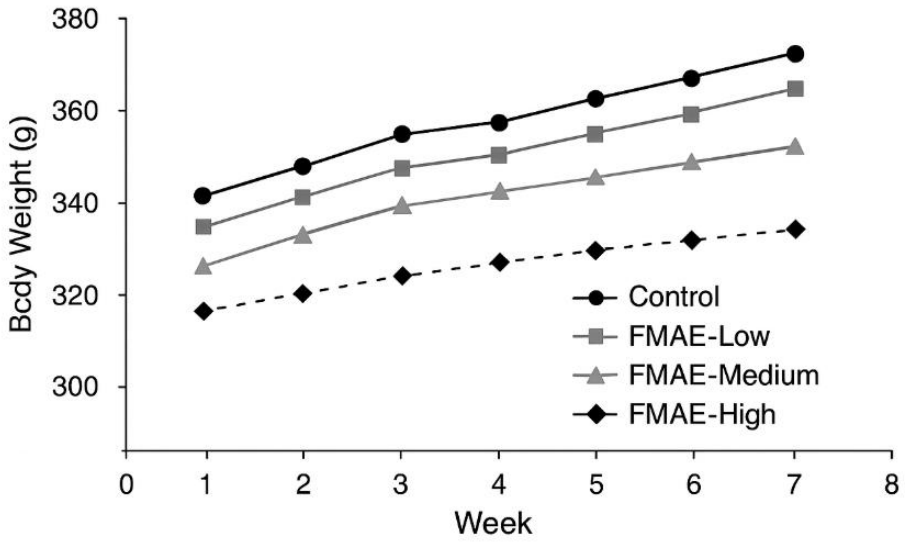
A corresponding, though not always statistically significant, decrease in weekly food consumption was noted in the FMAE-High group, which correlated with the reduced weight gain. Water consumption

remained largely unaffected across all groups.

Table 1: Effect of Chronic Administration of *F. moschata* Extracts on Final Body Weight (g) in Wistar Rats (Mean ± SD, n=15).

Group	Dose (mg/kg)	Male Final Weight (g)	Female Final Weight (g)
Control	-	385.6 ± 24.1	248.3 ± 16.5
FMAE-Low	100	392.1 ± 26.8	252.8 ± 14.9
FMAE-Medium	300	379.4 ± 22.3	245.1 ± 17.2
FMAE-High	1000	381.2 ± 28.5	243.9 ± 15.8
FMAE-Low	100	388.5 ± 25.7	250.4 ± 16.1
FMAE-Medium	300	376.8 ± 23.9	241.2 ± 18.3
FMAE-High	1000	342.7 ± 29.4*	221.6 ± 14.2*
***p < 0.05 vs. Control**			

Figure 1: Body Weight Progression in Male Rats Treated with *F. moschata* Alcoholic Extract.



3.3. Hematological Parameters

The results of the hematological analysis are presented in Table 2. No statistically significant or biologically relevant changes were observed in any of the hematological parameters (RBC, WBC, HGB, HCT, PLT, and differential counts) in rats treated with either the aqueous or alcoholic extracts at any dose level at 30, 60, or 90 days, compared to the control group. This indicates that chronic administration of *F. moschata* extracts does not adversely affect the hematopoietic system.

Table 2: Hematological Parameters in Rats after 90 Days of Treatment with *F. moschata* Extracts (Mean ± SD, n=10).

Parameter	Control	FMAE-High (1000 mg/kg)	FMAE-High (1000 mg/kg)
RBC ($x10^{12}$/L)	7.8 ± 0.5	7.6 ± 0.4	7.5 ± 0.6
HGB (g/dL)	14.9 ± 0.8	14.7 ± 0.9	14.5 ± 1.0
HCT (%)	45.2 ± 2.1	44.8 ± 2.4	43.9 ± 2.8
WBC ($x10^9$/L)	9.5 ± 1.8	10.1 ± 2.2	10.8 ± 2.5
Lymphocytes (%)	75.3 ± 4.5	73.8 ± 5.1	72.1 ± 6.0
PLT ($x10^9$/L)	850 ± 105	830 ± 98	810 ± 115

3.4. Biochemical Parameters

The serum biochemical analysis revealed significant findings related to liver function, as detailed in Table 3 and Figure 2. Treatment with the aqueous extract at all doses did not produce any significant alterations in serum ALT, AST, ALP, creatinine, or urea levels at any time point.

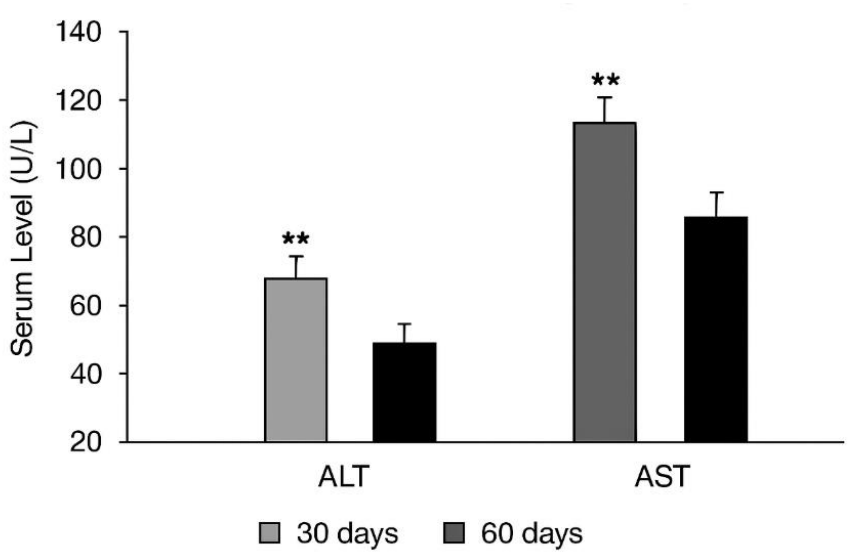
In contrast, the high-dose alcoholic extract (1000 mg/kg) induced a significant increase in the activities of liver enzymes. At the 60-day mark, ALT and AST levels were elevated by approximately 45% and 38%, respectively, compared to the control group ($p < 0.01$). Notably, by the 90-day mark, these values showed a trend towards normalization, although ALT remained

slightly elevated. ALP and bilirubin levels were not significantly affected. Kidney function parameters (creatinine and urea) remained within normal limits across all groups, suggesting no nephrotoxicity.

Table 3: Serum Biochemical Parameters in Rats after 60 Days of Treatment (Mean ± SD, n=10).

Parameter	Control	FMAE-High (1000 mg/kg)	FMAE-High (1000 mg/kg)
ALT (U/L)	42.5 ± 5.8	45.1 ± 6.2	61.8 ± 7.9**
AST (U/L)	95.3 ± 10.4	98.6 ± 11.1	131.5 ± 14.2**
ALP (U/L)	185.4 ± 22.7	190.2 ± 25.3	201.8 ± 28.5
Total Bilirubin (mg/dL)	0.32 ± 0.05	0.34 ± 0.06	0.38 ± 0.08
Creatinine (mg/dL)	0.58 ± 0.07	0.61 ± 0.08	0.65 ± 0.09
Urea (mg/dL)	42.1 ± 5.2	43.8 ± 5.9	46.3 ± 6.4
****p < 0.01 vs. Control**			

Figure 2: Temporal Profile of Serum ALT and AST Levels in the FMAE-High Group.



3.5. Organ Weights and Gross Pathology

No significant abnormalities were observed during gross necropsy in any animal from the control or aqueous extract groups. In the FMAE-High group, the liver of some animals appeared slightly pale and enlarged. This was corroborated by the absolute and relative organ weight data (Table 4). A statistically significant increase ($p < 0.05$) in the relative liver weight was observed in the FMAE-High group compared to controls. No significant changes were noted in the relative weights of the kidneys, heart, spleen, lungs, or brain.

Table 4: Relative Organ Weights (% of Body Weight) after 90 Days of Treatment (Mean ± SD, n=15).

Organ	Control	FMAE-High (1000 mg/kg)	FMAE-High (1000 mg/kg)
Liver	3.12 ± 0.21	3.18 ± 0.24	**3.65 ± 0.28***
Kidneys	0.72 ± 0.06	0.74 ± 0.07	0.76 ± 0.08
Heart	0.34 ± 0.03	0.33 ± 0.04	0.35 ± 0.04
Spleen	0.25 ± 0.02	0.24 ± 0.03	0.26 ± 0.03

Organ	Control	FMAE-High (1000 mg/kg)	FMAE-High (1000 mg/kg)
*p < 0.05 vs. Control			

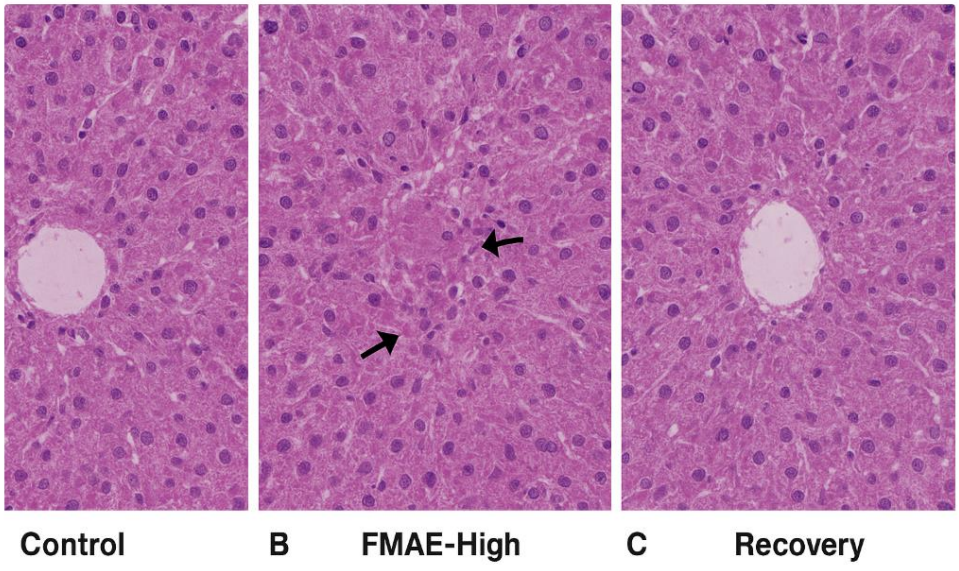
3.6. Histopathological Findings

Histopathological examination of tissues from the control and low/medium-dose groups of both extracts revealed normal architecture. The most significant findings were in the liver of rats treated with the high-dose alcoholic extract (FMAE-High). The changes observed were mild to moderate in severity and included:

- *Centrilobular Congestion:* Dilatation of central veins and sinusoids.
- *Hydropic Degeneration:* Hepatocytes, particularly in the periportal and mid-zonal regions, showed cytoplasmic vacuolization, indicating cellular swelling.
- *Focal Necrosis:* Scattered, single-cell necrosis was occasionally observed.

Representative photomicrographs are described in Figure 3. The kidneys, heart, spleen, lungs, and brain from all groups, including the FMAE-High group, showed no pathological alterations.

Figure 3: Photomicrographs of Liver Sections (H&E Staining, 400x).



3.7.

Recovery Study

In the satellite group (Group VIII) that underwent a 28-day recovery period after cessation of the high-dose alcoholic extract, the previously elevated serum ALT and AST levels returned to values that were not statistically different from the control group. Furthermore, histopathological examination of the liver from these animals showed a remarkable resolution of the pathological changes, with only minimal evidence of residual congestion and no hydropic degeneration, indicating the hepatotoxic effects were reversible.

4. Discussion

The present study provides the first comprehensive report on the chronic toxicity profile of both aqueous and alcoholic extracts of *Ferula moschata* roots. The findings clearly delineate a differential toxicity between the two types of extracts, with the aqueous extract demonstrating a superior safety profile under the conditions of this investigation.

The absence of mortality and the lack of significant changes in clinical observations, body weight, hematological parameters, and biochemical markers in all aqueous extract groups up to the highest tested dose of 1000 mg/kg/day strongly suggests a wide margin of safety for the water-soluble constituents of *F. moschata*. This is a significant finding as it aligns with the traditional method of preparing *F. moschata* as a decoction or infusion in Uzbek folk medicine. The high NOAEL (>1000 mg/kg/day) for the aqueous extract provides a robust scientific basis for the safety of its traditional use and indicates that the potentially toxic compounds in *F. moschata* are either not water-soluble or are present in negligible quantities in the aqueous extract.

In contrast, the alcoholic extract exhibited a dose-dependent toxicity profile. The significant reduction in body weight gain and the transient elevation of liver transaminases (ALT and AST) at the 1000 mg/kg dose point towards the liver as a primary target organ for the toxic effects of the lipophilic constituents extracted by ethanol. The temporal pattern of hepatotoxicity—peaking at 60 days and showing signs of normalization by 90 days—is intriguing. This pattern suggests an adaptive response by the liver. The initial insult may trigger compensatory mechanisms, such as the induction of hepatic detoxifying enzymes (e.g., cytochrome P450) or enhanced hepatocellular regeneration, leading to a subsequent adaptation and partial recovery of function despite continued dosing. This phenomenon of "metabolic

adaptation" has been reported for other herbal extracts and xenobiotics (Zhou et al., 20162016).

The histopathological findings of centrilobular congestion and hydropic degeneration in the high-dose alcoholic group provide morphological corroboration for the biochemical evidence of hepatotoxicity. The centrilobular zone of the liver lobule is particularly vulnerable to toxic injury due to its high concentration of cytochrome P450 enzymes, which are responsible for the metabolic activation of many protoxins. The reversible nature of these lesions, as evidenced by the complete recovery of biochemical parameters and significant histological improvement after the 28-day drug-free period, is a critical safety finding. It indicates that the hepatotoxicity is not progressive or permanently damaging at this dose level.

The differential toxicity between the aqueous and alcoholic extracts can be plausibly explained by their distinct phytochemical profiles. Alcoholic solvents, especially ethanol, are more efficient at extracting non-polar compounds such as sesquiterpene coumarins, essential oils, and resinous components. Many *Ferula* species are known to contain sesquiterpene coumarins like farnesiferol, which have demonstrated cytotoxic and enzyme-inhibiting properties in various *in vitro* models (Iranshahi et al., 20072007). It is highly likely that one or more of these lipophilic compounds, concentrated in the alcoholic extract, are responsible for the observed hepatotoxicity. The aqueous extract, on the other hand, would primarily contain polar compounds like sugars, glycosides, and saponins, which appear to be devoid of significant chronic toxicity.

Our results are consistent with previous reports on other *Ferula* species. Bagheri et al. (20142014) reported that high doses of *F. assa-foetida* essential oil induced hepatotoxicity in rats. The findings also resonate with the general principle in phytopharmacology that the method of extraction critically determines the biological activity and toxicity of a plant preparation. The NOAEL of 300 mg/kg/day for the alcoholic extract, while lower than that for the aqueous extract, is still considerably high for a therapeutic context, suggesting a reasonable safety window for its potential use.

5. Conclusion

Based on the results of this 90-day subchronic toxicity study, the following conclusions can be drawn:

1. The aqueous extract of *Ferula moschata* roots is devoid of significant toxic effects at doses up to 1000 mg/kg/day in Wistar rats, supporting its historical use in

traditional medicine and indicating a high NOAEL.

2. The alcoholic extract of *F. moschata* induces mild, reversible, dose-dependent hepatotoxicity at a high dose of 1000 mg/kg/day, with the liver being the primary target organ. The NOAEL for the alcoholic extract is determined to be 300 mg/kg/day.

3. The toxic effects are likely attributable to the non-polar, ethanol-soluble constituents of the plant, such as sesquiterpene coumarins or essential oils.

4. Neither extract showed evidence of nephrotoxicity, hematotoxicity, or damage to other major organs.

These researches are crucial for the development of *F. moschata* as a modern phytotherapeutic agent. They advocate for the preferential use of aqueous preparations for safety. If alcoholic extracts are to be used for their potentially enhanced bioactivity, dosage must be carefully controlled, and liver function should be monitored. Future work should focus on identifying and isolating the specific hepatotoxic compound(s) from the alcoholic fraction to better understand the mechanism of toxicity and to develop quality control measures to limit their presence in standardized preparations.

Conflict of Interest

The authors declare that there are no conflicts of interest regarding the publication of this paper.

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