

Hypolipidemic and Hypoglycemic Activities of Asafoetida (*Ferula assafoetida* Linn.) Ultrasonically Extracted in Diabetes Mellitus

Meeram Chaudhary¹, Rabbiya Sarwar², Aneesa Mahreen^{2*}, Asma Kanwal², and Tehreem Farooq³

¹University of Lahore Teaching Hospital, Lahore, 54000, Pakistan.

²Department of Community Medicine and Public Health, Rashid Latif Medical College, Lahore, 54000, Pakistan.

³HITEC Institute of Medical Sciences Heavy Industries Taxila Cantt, Taxila, 47070, Pakistan.

*Corresponding Author: Aneesa Mahreen. Email: aneesa.mahreen@rlmc.edu.pk

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Abstract: Diabetes mellitus is a chronic metabolic disorder which is characterized by hyperglycemia, oxidative stress and lipid dysregulation. *Ferula assafoetida* Linn. (*asafoetida*) is a Phenolics, flavonoids, coumarins, ferulic acid, volatile oils and sulphur compounds which have antidiabetic activity. Ultrasound-assisted extraction (UAE) is a green technique that can improve recovery of heat-sensitive phytochemicals. Resin of *asafoetida* was extracted using UAE with 70% ethanol (30-40 Hz, 20-30 min) and compared with the conventional maceration. The total phenolic content (TPC), total flavonoid content (TFC) and antioxidant activity were measured. Thirty wistar rats were divided in to control, diabetic control, diabetic treated with UAE, conventionally extracted treated diabetic and diabetic treated with metformin groups. Glucose, glycated haemoglobin (HbA1c), insulin, lipid profile, alanin aminotransferase (ALT), aspartate aminotransferase (AST), creatinine and urea were determined. One-way ANOVA, followed by Tukey's test was used to analyze the data, with $p \leq 0.05$ being significant. UAE showed higher total phenolic and flavonoid content than conventional extraction. UAE showed 2,2-diphenyl-1-picrylhydrazyl (DPPH) inhibition levels of >80%, 2,2'-azino-bis(3-ethylbenzothiazoline-6-sulfonic acid) (ABTS) activity higher than 2-fold and ferric reducing antioxidant power (FRAP) reducing power nearly two folds higher. UAE treatment lowered glucose and HbA1c levels while insulin levels in diabetic rats. The levels of cholesterol, triglycerides, high-density lipoprotein (LDL) were reduced, high-density lipoprotein (HDL) were elevated, ALT, AST, creatinine and urea improved. UAE was effective in the recovery of *asafoetida* phytochemicals and exhibited significant antidiabetic, lipid-modulatory, hepatoprotective and nephroprotective potential in diabetic rats.

Keywords: Asafoetida; *Ferula Assafoetida*; Ultrasound-Assisted Extraction; Diabetes Mellitus

1. Introduction

Diabetes mellitus is a chronic metabolic disease characterized by impaired glucose homeostasis, oxidative stress and dysregulated lipid metabolism [1]. Natural products from plants have been proposed as complementary strategies for the diabetes management due to the potential effects of their bioactive compounds on glucose metabolism and oxidative stress [2]. There is evident that medicinal plants can improve glycaemic control through effects on insulin sensitivity, glucose metabolism, carbohydrate digestion and oxidative pathways [3].

Diabetic dyslipidaemia is a major metabolic abnormality and medicinal plants have shown potential in improving lipid profiles through multiple mechanisms [4]. Herbal medicines with phenolics, flavonoids and other bioactive compounds may contribute to hypolipidemic and associated oxidative effect [5]. The bioactivity of plant extracts is strongly influenced by the extraction methods which affects the recovery and composition of the bioactive compounds [6]. Ultrasound-assisted extraction (UAE) is an efficient and environmental friendly technique for recovering phenolics, flavonoids and other plant bioactives via

acoustic cavitation, which would potentially reducing the extraction time and solvent consumption [7]. Optimizing of the UAE conditions can improve phenolic recovery and biological properties of plant extracts [8]. It also increased anti-oxidant and anti diabetic activities compasred with conventional technique [9]. *Ferula assa-foetida* Linn. (asafoetida) is a medicinal plant containing bioactive phytochemicals with potential antioxidant and metabolic activities [10]. Ethanolic *F. assa-foetida* oleo-gum-resin extract has demonstrated hypoglycemic and hypolipidemic effects in Streptozotocin (STZ)-induced diabetic rats [11]. The extract also improved antioxidant status, attenuated biochemical and structural changes in pancreas of diabetic rats [12]. However, there is limited evidence on the hypoglycemic and hypolipidemic effects of ultrasonically extracted asafoetida, despite UAE can improve bioactive compounds recovery [7, 13]. Asafoetida (*Ferula assafoetida* Linn.) is an oleo-gum-resin traditionally used as a culinary spice and medicinal material. Its resin and volatile fractions contain ferulic acid, coumarins, sesquiterpene derivatives, and sulfur-containing compounds. Contemporary reviews describe antioxidant and other pharmacological properties of *F. assafoetida* and highlight the need for better phytochemical standardization and modern pharmacological validation [14-15]. Recent experimental evidence is particularly relevant to the present study. Latifi et al. reported that ethanolic *F. assafoetida* oleo-gum-resin extract improved serum glucose, insulin, antioxidant status, pancreatic morphology, and beta-cell characteristics in Streptozotocin (STZ) induced diabetic rats [16]. Another recent animal study reported antidiabetic effects of *F. assafoetida*-derived preparations, further supporting investigation of the plant in experimental diabetes [17]. In silico work has also identified *F. assafoetida* phytoconstituents as potential inhibitors of α -amylase and α -glucosidase, although such computational findings require experimental validation [18].

Extraction technique is an important determinant of phytochemical yield and biological activity. Conventional maceration can require relatively long processing times and greater solvent use, whereas UAE uses acoustic cavitation to improve solvent penetration and release intracellular or bound compounds. Recent reviews describe UAE as a green extraction technology with advantages including shorter processing time, lower solvent requirements, and improved recovery of phenolics and flavonoids when process variables are optimized [19-22]. Therefore, the present study evaluated whether UAE of asafoetida could enhance phytochemical recovery and biological effects in an experimental diabetes model.

2. Materials and Methods

2.1. Study design and plant material

The current experiment involved asafoetida resin which was subjected to ultrasound-assisted extraction method and compared to the conventional extraction process. The asafoetida resin was obtained from reputable suppliers and prepared according to original experiment protocol.

2.2. Extraction procedures

In case of UAE, the asafoetida resin powder was extracted with 70% ethanol using ultrasound at a frequency range of 30-40 Hz for 20-30 minutes. In the case of the conventional method, the extraction was conducted using maceration at similar solvent conditions.

2.3. Phytochemical and antioxidant analyses

Total phenolic content (TPC) was assessed via the Folin-Ciocalteu procedure and was expressed in mg gallic acid equivalents (GAE)/g of the extracts. The total flavonoid content (TFC) content was quantified through the aluminum chloride procedure and was expressed in mg quercetin equivalents (QE)/g of the extracts. Antioxidant activity was assessed by 2,2-diphenyl-1-picrylhydrazyl (DPPH) scavenging test, 2,2'-azino-bis(3-ethylbenzothiazoline-6-sulfonic acid) (ABTS) radical-cation decolorization test, and ferric reducing antioxidant power (FRAP) assays.

2.4. Experimental animals and diabetes induction

Thirty adult rats of the Wistar strain were allowed to acclimate to the laboratory environment. Diabetes was induced using streptozotocin injected intraperitoneally at 45 mg/kg. The rats were categorized into five groups: normal control group, diabetic control group, UAE-treated diabetic group, onventional extraction-treated diabetic group, and standard drug-treated group (metformin). Ethical approval for this study was taken from Rashid Latif Medical College with Ref No. IRB/2025/12.

2.5. Biochemical assessments

Glucose, HbA1C, and insulin levels were determined in blood samples. Lipid profile tests included total cholesterol (TC), triglycerides (TG), low-density lipoprotein (LDL), and high-density lipoprotein (HDL). Liver function tests included alanin aminotransferase (ALT) and aspartate aminotransferase (AST). Kidney function tests included creatinine and urea.

2.6. Statistical analysis

Results were presented as mean $\pm$ standard deviation (SD). All statistical analysis were performed using IBM SPSS version 26.0. Differences among groups were analyzed by using one-way analysis of variance (ANOVA), followed by Tukey's test where $p < 0.05$ was statistically significant. The same statistical approach was used to the phytochemical, antioxidant, glucose, HbA1c, insulin, lipid profile, liver function and kidney function parameters.

3. Results

3.1. Phytochemical composition and antioxidant activity

The UAE extracts showed a considerably higher phytochemical yield when compared to the conventional extracts. The TPC in UAE was more than 35 mg GAE/g while that in conventional extraction was about 22 mg GAE/g. For the TFC, UAE produced more than 28 mg QE/g while in conventional extraction, it was only 16 mg QE/g (Table 1). The UAE extracts were seen to have a higher antioxidant activity in all the assays performed. The DPPH scavenging activity for UAE was more than 80%, compared to about 60% for conventional extraction. ABTS activity was increased too, whereas FRAP reducing power almost doubled after treatment with UAE.

Table 1. Phytochemical composition and antioxidant activity

Parameter	UAE extract	Conventional extraction	Effect of UAE
Total phenolic content (TPC)	>35 mg GAE/g	~22 mg GAE/g	Higher phytochemical yield
Total flavonoid content (TFC)	>28 mg QE/g	~16 mg QE/g	Higher phytochemical yield
DPPH scavenging activity	>80%	~60%	Increased antioxidant activity
ABTS activity	Increased	Lower	Increased with UAE
FRAP reducing power	Almost doubled	Baseline	Markedly increased with UAE

3.2. Glycemic control

In diabetic rats, an increase in blood glucose was found to be >200 mg/dL, while that of HbA1c was ~9.4%, along with low levels of insulin (~4 μ U/mL). In UAE-treated groups, there was a significant decrease in blood glucose to ~130 mg/dL, HbA1c to ~6.2%, and increased level of insulin to ~11 μ U/mL. While conventional extractions had little effect, metformin almost normalized levels as described in Table 2.

Table 2. Glycemic control in diabetic rats

Parameter	Diabetic control	UAE-treated rats	Conventional extraction	Metformin
Blood glucose	>200 mg/dL	~130 mg/dL	Little effect	Almost normalized
HbA1c	~9.4%	~6.2%	Little effect	Almost normalized
Insulin	~4 μ U/mL	~11 μ U/mL	Little effect	Almost normalized

3.3. Lipid profile

The diabetic controls had high levels of dyslipidemia, which were evidenced by the high levels of TC, TG, and LDL and low levels of HDL. In the UAE-treated rats, there was an improvement by lowering the levels of TC, TG, and LDL by 30% (Table 3) and raising HDL levels by 25%. Conventional mining resulted in slight improvement.

Table 3. Lipid profile in diabetic rats

Parameter	Diabetic control	UAE-treated rats	Effect of UAE	Conventional extraction
Total cholesterol (TC)	Increased	Decreased	↓ ~30%	Slight improvement
Triglycerides (TG)	Increased	Decreased	↓ ~30%	Slight improvement
Low-density lipoprotein (LDL)	Increased	Decreased	↓ ~30%	Slight improvement
High-density lipoprotein (HDL)	Decreased	Increased	↑ ~25%	Slight improvement

3.4. Liver and kidney function

Diabetes mellitus resulting from Streptozotocin raised the values of ALT to about 85 U/L, AST to about 56 U/L, creatinine to about 1.6 mg/dL, and urea to about 44 mg/dL. On administration of UAE, these values were lowered to about 52 U/L, 30 U/L, 1.0 mg/dL, and 21 mg/dL, respectively as summarized in Table 4.

Table 4. Liver and kidney function markers

Parameter	Diabetic control	UAE-treated rats	Change following UAE
ALT	~85 U/L	~52 U/L	Decreased
AST	~56 U/L	~30 U/L	Decreased
Creatinine	~1.6 mg/dL	~1.0 mg/dL	Decreased
Urea	~44 mg/dL	~21 mg/dL	Decreased

4. Discussion

The current finding demonstrate that UAE increased the extraction efficiency of phenolic and flavonoid compounds from asafoetida. The UAE extract that showed higher phytochemical content also exhibited greater antioxidant properties indicating positive association between phytochemical concentration and antioxidant properties. This findings are consistent with the evidence that ultrasound increased phenolic and flavonoid extraction via acoustic cavitation [19-22].

The performance of UAE depends on parameters such as solvent composition, extraction time, temperature, frequency, amplitude and solid to solvent ratio therefore optimization is essential for reproducibility [19, 20]. The observed improvement in glycaemic status may reflect due to antidiabetic potential of plant phenolics and asafoetida that may modulate glucose homeostasis through enhancing insulin action, inhibition of carbohydrate-digesting enzymes, decreased oxidative stress and inflammation and pancreatic β -cell protection [4-7, 10, 11]. In the present study, UAE-treated diabetic rats had lower glucose and HbA1c and higher insulin than diabetic controls and support a beneficial effect in the experimental model. The results are also in agreement with direct experimental evidence on *F. assafoetida*. Latifi et al. demonstrated that treatment of Streptozotocin-induced diabetic rats with an ethanolic extract of *F. assafoetida* improved serum glucose, insulin, antioxidant enzymes, pancreatic morphology and beta-cell features [16]. In 2024, a study using preparations from *F. assafoetida* also reported decrease in blood glucose in diabetic rats [17].

These independent observations further justify future studies into asafoetida, but results should not be considered as equivalent due to variations in extraction procedures, dosage, formulation, animal model and measurement of outcomes. The observed improvement in TC, TG, LDL and HDL in the present study indicates a hypolipidemic effect. Dyslipidaemia is one of the major metabolic components of diabetes and is strongly correlated with cardiovascular risk. The possible mechanisms of lipid lowering of medicinal and edible plants have been reviewed for modulation of lipid synthesis, fatty-acid oxidation, cholesterol transport and oxidative modification of lipoproteins [12, 13]. Thus, the ~30% reductions in TC, TG and LDL and ~25% increase in HDL observed here should be interpreted as promising preclinical findings, rather than evidence of clinical efficacy. The decreases in ALT, AST, creatinine and urea suggest amelioration of biochemical markers of hepatic and renal insult in treated animals. Oxidative stress and metabolic derangements are involved in diabetic tissue injury and phenolic-rich plant extracts can exert protective effects through antioxidant and anti-inflammatory pathways [8, 23, 24]. However, in this study,

biochemical improvement alone does not prove histological protection, since no new histopathological results were added during revision.

A major advantage of study was the direct comparison with conventional extraction utilizing the same solvent system as well as assessment of the phytochemical contents, antioxidant activity, glycemic markers, lipid parameters, and liver and kidney biochemical markers. But the study is still in the lab stage. The reported data are not sufficient to identify individual asafoetida components or their concentration, the optimum therapeutic dosage, long-term toxicity, pharmacokinetics or efficacy of the use. Thus, standardisation of the composition of extracts of asafoetida and well-designed clinical trials are necessary to consider asafoetida extracts for therapeutic or nutraceutical applications [6, 7, 25, 26].

5. Conclusions

UAE improved the phytochemical recovery and antioxidant activity of *Ferula assafoetida*. In diabetic rats induced by Streptozotocin, the UAE extract was observed to increase glycemic control, lipid profile and liver and renal function. These results suggest that the extract has potential as an antidiabetic agent and should be studied for safety, mechanism of action and clinical application.

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