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The pharmacological effects of ashwagandha root extract in rats induced with metabolic syndrome

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Abstract
Medicinal plants hold significant pharmaceutical and therapeutic potential, offering promising avenues for novel product development beneficial to human health. Herbs have played a vital role in healthcare systems globally, serving as effective remedies for preventing and managing various health conditions. In the present study, the pharmacological effects of the root extract of Withania somnifera (Ashwagandha) were evaluated, with a special focus on its role in managing metabolic syndrome using a rat model. The research emphasized assessing parameters such as antihyperglycemic, antihyperlipidemic, anti-inflammatory, and antioxidant effects to understand the therapeutic potential of the extract. The results suggest that Ashwagandha root extract exhibits considerable efficacy in ameliorating metabolic syndrome-related symptoms with minimal side effects. These findings highlight the plant's potential for incorporation into formulations aimed at addressing metabolic disorders. Further studies should aim to explore broader pharmacological activities, including cardiovascular and neuroprotective effects, to establish its utility in diverse clinical applications.

Keywords: Ashwagandha root, hyperglycemic, metabolic syndrome, dyslipidemia

Introduction
Metabolic syndrome is a multifactorial disorder characterized by the coexistence of central obesity, dyslipidemia, hypertension, insulin resistance, and hyperglycemia, all of which increase the risk of type 2 diabetes and cardiovascular diseases [1, 2]. Modern lifestyle factors such as high-calorie diets rich in fructose and fats, along with physical inactivity, contribute significantly to its rising prevalence worldwide [3]. Current therapeutic approaches mainly involve lifestyle modification and pharmacological agents that target individual components of the syndrome, such as antihypertensives, hypoglycemic drugs, and lipid-lowering agents [4]. However, these treatments often address only one aspect of the disorder, may require lifelong administration, and can cause adverse effects, thereby limiting patient compliance [5]. Medicinal plants with multiple pharmacological activities are gaining importance as potential therapeutic agents for metabolic syndrome. Ashwagandha (*Withania somnifera*), a well-known adaptogenic herb in Ayurveda, has demonstrated antioxidant, anti-inflammatory, antihyperglycemic, and hypolipidemic properties in various experimental and clinical studies [6-9]. Its bioactive constituents, particularly withanolides, have been shown to modulate insulin sensitivity, reduce oxidative stress, and regulate lipid metabolism, which are central pathological mechanisms in metabolic syndrome [10]. Considering the complexity of metabolic syndrome, where oxidative stress, inflammation, and insulin resistance interact to drive disease progression, Ashwagandha offers a promising holistic approach that may target multiple components simultaneously [11]. Therefore, evaluating the therapeutic potential of Ashwagandha in experimental models of metabolic syndrome could provide scientific evidence supporting its traditional use and highlight its role as a safer, multi-targeted intervention. This study is aimed at exploring its pharmacological effects, which may pave the way for developing Ashwagandha-based therapeutic strategies in the management of metabolic syndrome.

Materials and Methods
All the animals used in the experiment were approved by the Institutional Animal Ethics Committee (IAEC). The disease was induced by giving High fat diet to the Animals.

The composition of high fat diet was prepared using following ingredients: corn oil (400 g), Saccharose (150 g), total milk powder (80 g), Lard (100 g), egg yolk (200 g), sodium deoxycholate (10 g), tween 80 (36.4g), propylene glycol (31.1g), vitamin mixture (2.5g), cooking salt (10 g), mineral mixture (1.5g), distilled water (300ml).

Rats will be randomly assigned to the following groups:

- **Control Group (Placebo):** Rats will be fed a standard diet and given a vehicle (saline or a similar neutral substance) daily.
- **Disease group:** The high fat diet and fructose solution was given to the rats for the 35 days inducing the disease.
- **Standard group:** Atorvastatin 20mg/kg and metformin was used as standard.
- **Treatment-1:** Ashwagandha at a dose of 100mg/kg was given to the animals after 35 days of induction period.
- **Treatment-2:** Ashwagandha at a dose of 200mg/kg was given as high dose after the 35 days of induction period.

Sr. No.	Evaluation Parameter
1.	Weekly parameter-body weight, blood glucose level
2.	Biochemical parameter Lipid profile test-HDL, LDL, TGs, TC
3.	Anti-oxidant Assay-CAT, GSH

Results and Discussion

Effect of Ashwagandha on body weight of animals

The body weight of animals in all groups was monitored throughout the experimental period, and the results are expressed as mean ± SEM (N=6).

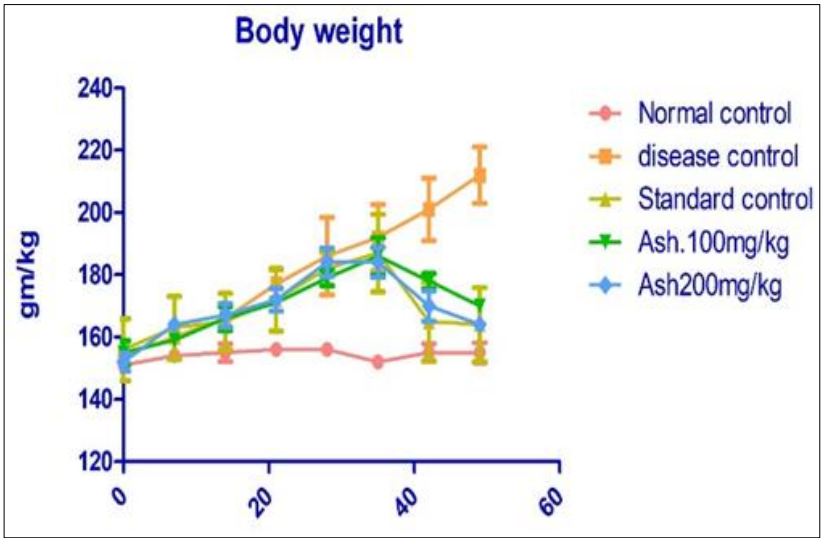

Fig 1: Body weight

By day 49, the standard control group recorded 164±11.87 g, while Ashwagandha 100 mg/kg and 200 mg/kg groups reached 170±2.09 g and 164±2.0 g, respectively, all showing significantly lower body weight gain compared to the disease control (p<0.05 to p<0.001). These findings suggest that Ashwagandha treatment helped to regulate body weight in a dose-dependent manner.

Effect of ashwagandha on blood glucose level of animals

The levels of Blood glucose was significantly increased in the disease group showing in the compared to the normal group and it is increased in standard and test group compared to the disease group.

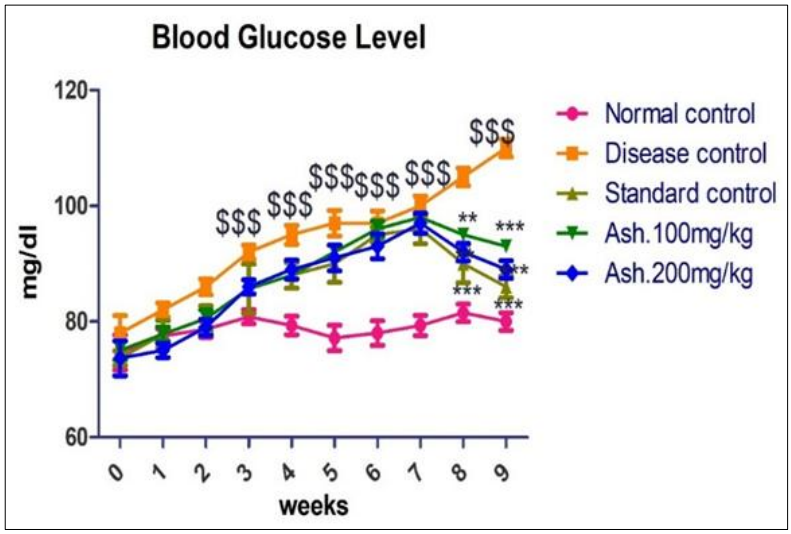

Fig 2: blood Glucose level

Effect of ashwagandha on lipid profile of animals

Sr. No.	Animal group	Serum HDL	Serum LDL	Serum TG	Serum TC
1.	Normal control	54±1.3	7.52±1.8	65±2.5	99±1
2.	Disease control	28±1.2$^{\$\$\$}$	32.67±4.02$^{\$\$\$}$	166±8$^{\$\$\$}$	155±7$^{\$\$\$}$
3.	Standard control	52±1.6***	11.37±1.48***	82±3***	106±1.5***
4.	Ashwagandha 100mg/kg	36±1.3*	19±2.10*	119±3***	124±2***
5.	Ashwagandha 200mg/kg	46±1.5***	14±1.19**	94±2.1***	115±1.3***

The levels of TC, LDL and TG was significantly increased in the disease group showing in the compared to the normal group and it is decreased in standard and test group compared to the disease group. While the levels of HDL was significantly decreased in the disease group showing in the compared to the normal group and it is increased in standard and test group compared to the disease group. Statistical significance denoted as (*-p<0.05, **,-p<0.01 and ***-p<0.001 compared to the disease control group.

Effect of ashwagandha on antioxidant enzymes of animals

Sr. No.	Animal group	Glutathione assay	Catalase assay
1.	Normal control	23.52±0.91	0.575±0.05
2.	Disease group	12.72±1.3$^{\$\$\$}$	0.226±0.040$^{\$\$\$}$
3.	Standard group	21.5±1.3***	0.554±0.010***
4.	Ashwagandha 100mg/kg	18 ±0.2**	0.416±0.033*
5.	Ashwagandha 200mg/kg	20±0.3***	0.495±0.031**

The levels of Catalase and Glutathione was significantly decreased in the disease group showing in the compared to the normal group and it is increased in standard and test group compared to the disease group.

Animals in the disease control group exhibited a steady and significant rise in body weight and food intake compared to the normal control group, reflecting obesity and altered feeding behavior due to high-fat and high-fructose consumption. In contrast, the Ashwagandha-treated groups showed regulated body weight and normalized food intake, comparable to the standard group. This suggests that Ashwagandha may play a role in appetite regulation and energy balance, possibly by influencing satiety signals and improving metabolic utilization of lipids and glucose [12]. These findings are consistent with previous studies reporting the anti-obesity and adaptogenic properties of Ashwagandha through modulation of the hypothalamic-pituitary-adrenal axis and adipokine secretion [13].

Ashwagandha restored the altered liver and kidney function markers toward normal values, confirming its hepatoprotective and Reno protective activity [14]. Antioxidant assays revealed that Ashwagandha significantly enhanced Catalase (CAT) and Reduced Glutathione (GSH) levels, indicating its free radical scavenging property and ability to strengthen the endogenous antioxidant defense system [15].

Conclusion

Ashwagandha root extract has shown promising pharmacological effects in experimental models of metabolic syndrome. Its ability to improve glucose and lipid metabolism, enhance antioxidant defense, and protect vital organs such as the liver, kidney, and pancreas demonstrates its therapeutic relevance. The outcomes of this study suggest that Ashwagandha may play a significant role in addressing the global burden of metabolic syndrome, either as a standalone natural therapy or in combination with conventional drugs.

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