RESEARCH PAPER

An Assessment of Influence of Selected Herbal Extracts on Pioglitazone Activity in Rabbits

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Received: 28th Feb, 2026; Revised: 6th March 2026; Accepted: 7th April, 2026; Available Online: 20th April, 2026

ABSTRACT
Type 2 diabetes mellitus is the most prevalent form of the disease, distinguished by chronic hyperglycemia, resistance to insulin, and impaired secretion and function of insulin. The research was carried out on normal albino rats in order to rapidly determine the impact of aqueous extracts of Momordica charantia on the pharmacodynamic activity (specifically, blood glucose level) and Pioglitazone activity, with the intention of establishing the safety of their combined clinical administration. Blood samples may be acquired by cutting a side ear vein many times in order to measure the levels of insulin, blood sugar, and the regular medication. Pioglitazone, at dosages of 5, 10, and 20 mg/1.5 kg bd.wt, reduced the levels of glucose in the blood in a dosage-dependent way. When administered alone, AEMC significantly and dose-dependently decreased the blood glucose level of normal rodents. The pharmacodynamic interaction between Momordica charantia and Pioglitazone could potentially be attributed to their synergistic hypoglycemic effect.
Keywords: Diabetes, Pioglitazone, blood glucose level, Momordica charantia
How to cite this article: Tiwari S, Dhongade HKJ. An Assessment of Influence of Selected Herbal Extracts on Pioglitazone Activity in Rabbits. Int J Drug Deliv Technol. 2026;16(54s): 702-704. DOI: 10.25258/ijddt.16.54s.60
Source of support: Nil.
Conflict of interest: None

1. INTRODUCTION

Diabetes mellitus is a persistent metabolic disorder distinguished by hyperglycemia, which is an elevation in blood glucose levels. This is one of the key causes of mortality worldwide, per the WHO. Over time, chronic diabetes mellitus serves as a precursor to various disorders, ultimately resulting in the coexistence of multiple disorders (Yadav et al., 2024). Therefore, caution must be exercised to prevent the potential for adverse effects, such as overmedication, undermedication, or medication combinations used specifically to treat clinical disorders (Hu et al., 2024). Further investigation into the safety of such drug combinations would be preferable in order to generate more information in this regard (Hemaiswarya et al., 2022).

Consequently, herbal remedies entered the realm of "antiquated wisdom" and fraudulent medicine. Unfortunately, herbal medicines continued to lack adequate clinical efficacy and material quality control in some instances (Sharma and Patial., 2022). Thoroughly reviewing the topic is strongly recommended, as it allows for separating valuable information from unimportant details and paves the way for developing several superior native medicines (Gupta et al., 2017). Numerous unidentified plant compounds exist, and novel pharmaceuticals are developed daily. Sadly, the interaction between herbs and drugs continues to be contradictory. Presently, it is understood that millions of patients concurrently use conventional and herbal medications, frequently without their physicians' knowledge (Xu et al., 2020).

Multiple therapeutic attributes of M. Anaerobic, anti-ulcerogenic, anti-oxidative, anti-diabetes, anthelmintic, anti-mutagenic, anti-lipolytic, "antifertility, hepatoprotective, and anti-inflammatory activities, in addition to hypoglycemic, anti-bacterial, anti-viral, anti-tumor, immunomodulatory, and anti-oxidant properties", have been investigated in relation to M. charantia (Hoda et al., 2019).

Insulin resistance causes the "chronic, progressive nature of type 2 diabetes mellitus (T2DM)" (Hauner, 2022). The etiology of T2DM is prolonged due to oxidative stress. Pioglitazone is a thiazolidinedione insulin sensitizer (Qu et al., 2024). The purpose of this research was to determine whether biochemical and biological parameters of diabetic rodents responded differently to monotherapy and combination therapy with Pioglitazone.

2. MATERIAL AND METHOD

This section examined the effects of specific antipsychotic medications on the pharmacokinetics and pharmacodynamics of a chosen dose of Pioglitazone (10 mg/1.5 kg bd.wt) in healthy rabbits. Additionally, the study provides confirmation for the presence of interaction among dissimilar species; further information is provided below.

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Materials consisting of: The experimental protocols and conditions were consistent across all sets of selected drugs, including the standard drug, Pioglitazone, which was extracted. The research utilized Albino rodents (Wistar strain) of both sexes, which were obtained from Mahaveer Enterprises in Hyderabad, India. Standard laboratory conditions were adhered to, including "an ambient temperature of 25±2°C and a relative humidity of 50±15%. A light cycle of 12" hours was followed by a dark cycle of 12 hours. "Ad libitum water and commercial pellet diets (Rayan's Biotechnologies Pvt.Ltd, Hyderabad, India)" were provided to the rats. The experimental protocol has obtained approval from both the government regulatory body and the Institutional Animal Ethics Committee. (516/01/A/CPCSEA Reg. No. Rats were famished for 18 hours prior to the experiment, with access to water, and were deprived of food and water throughout the experiment. Six Wistar rabbits, of either sex, that were in good health and weighed between 1.35 kg and 1.75 kg were utilized for the research. A standard diet was used to maintain the health of robust rabbits at room temperature on a 12-hour light & 12-hour dark cycle. When inserting a feeding tube into the oral cavity, care must be taken to prevent the tube from entering the trachea.

Gathering Blood Samples: A standard (Pioglitazone 10 mg/1.5 kg bd.wt) was given to the rodents, and samples of their blood were taken for blood glucose measurement at different intervals.

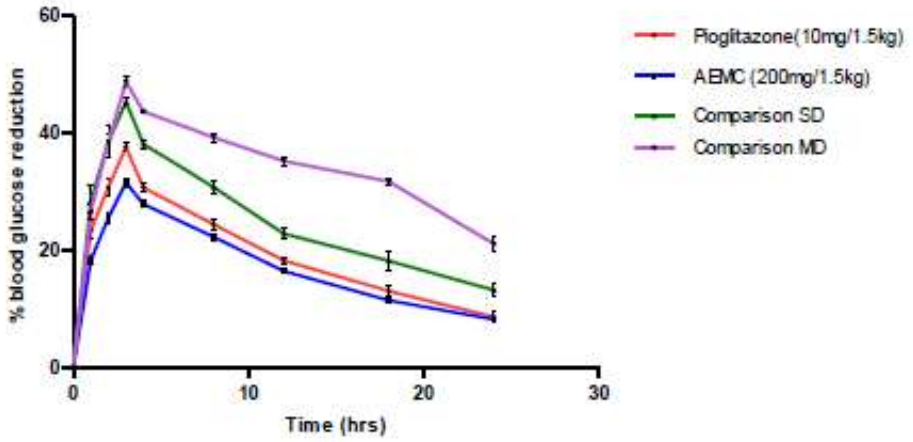
3. RESULT AND DISCUSSION

Table 1: "Percentage of blood glucose reduction of Pioglitazone 10mg/1.5kg, AEMC (200mg/1.5kg) and single and multiple dose Combinations".

Time (h)	Percent blood glucose reduction			
	Pioglitazone (5mg/1.5kg)	AEMC (200mg/1.5kg)	Single Dose	Combination (AEMC+ Pioglitazone)
0	0.00±0.00	0.00±0.00	0.00±0.00	0.00±0.00 ns
1	23.43±1.43	18.32±0.78	28.62±2.34**	26.61±1.43
2	30.79±1.42	25.56±0.96	38.54±1.32***	38.47±2.76***
3	37.67±0.80	31.58±0.73	45.39±0.81***	48.85±0.78***
4	30.72±0.81	27.93±0.52	38.16±0.64***	43.73±0.33***
8	24.46±0.95	22.32±0.52	30.85±1.09***	39.32±0.72***
12	18.28±0.54	16.49±0.33	22.86±0.88*	35.27±0.68***
18	13.06±0.86	11.48±0.42	18.20±1.69**	31.76±0.50***
24	8.63±0.91	8.23±0.35	13.24±1.20*	21.14±1.24***

"p>0.05 ns Significance followed by two-way ANOVA followed by Bonferroni post-test when compared with Pioglitazone (10mg/kg) group".

Graph 1: "The pharmacokinetic profile of Pioglitazone concentration Vs time with Pioglitazone in normal rabbits."



A specific dosage of AEMC (Aqeous extracts of M. charantia) lead to a notable decrease in blood glucose levels in rabbits. The combination of the chosen dose of AEMC with pioglitazone resulted in a substantial increase in its hypoglycemic activity, lasting from 1 to 24 hours, when compared to both single and multiple dose interventions. On Normal Rabbits, it was observed that specific doses of AEMC resulted in an rise in serum insulin levels, while single dose treatments of AEMC only marginally increased insulin levels. Significant increases in serum pioglitazone levels were observed in response to both single and multiple doses of AEMC.

"Pharmacokinetic parameters of pioglitazone, increase significantly with AEMC treatment at single and multiple doses." The observed increase in serum pioglitazone levels and pharmacokinetic parameters suggest the presence of a pharmacokinetic interaction between AEMC and pioglitazone. This interaction may be attributed to AEMC's ability to inhibit the pioglitazone metabolism, similar to how Momordica charantia has been documented to inhibit the CYP 3A4 isozyme (Deeba et al., 2020).

Pioglitazone, at dosages of 5, 10, and 20 mg/1.5 kg bd.wt, reduced the blood sugar level in a dosage-dependent way. Since 10 mg/1.5 kg bd.wt of this medication reduced blood glucose levels by 30–40% in normal rabbits, that dose was used for the association study. Serum insulin levels amplified and the amount of glucose in the blood significantly decreased at the pioglitazone dose (10 mg/1.5 kg bd.wt), with the greatest action occurring after 4 hours. Furthermore, it was shown that the highest level of it in the blood sample occurred after 4 hours. Because pioglitazone has a wide range of therapeutic applications, it was selected as the working prototype for a substance called in this study.

CONCLUSION

The determination of the rabbit study was to verify the occurrence or absenteeism of drug interactions with pioglitazone in a non-rodent model using specific drugs. Due to the fact that rabbits are one of the formal models for insulin bioassay [Goodman LS Gilman A., 2001], they were chosen for the investigation. can be conveniently managed within the laboratory setting, and adequate volumes of Blood samples may be taken to measure the levels of insulin, blood sugar, and the usual medication by cutting the outside of the ear vein many times.

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