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STUDIES ON INFLUENCE OF SELECTED HERBAL EXTRACTS ON PIOGLITAZONE ACTIVITY IN NORMAL RATS

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ABSTRACT:

Diabetes, or type 2 diabetes, is a long-term metabolic disorder characterized by disturbances in the digestion of carbohydrates, proteins, and lipids as well as problems controlling blood sugar levels. In order to assess the safety and effectiveness of Momordica charantia, these plants were utilized both alone and in combination with the standard antidiabetic medication Pioglitazone. 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. Additionally, the study aimed to determine whether the drug interactions observed in rats (rodents) were pharmacokinetic, pharmacodynamic, or both in nature. Blood samples may be acquired by cutting a side ear vein many times in order to measure the levels of 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. The observed increase in serum pioglitazone levels and pharmacokinetic parameters suggest the presence of a pharmacokinetic interaction between AEMC and pioglitazone. Existing diabetic medications are associated with certain limitations, such as inconsistent drug responses among individuals, difficulty in maintaining glycemic control, and adverse side effects. Due to the fact that herbal medicines are composed of natural substances, they may be erroneously perceived as innocuous.

Keywords: Diabetes, Pioglitazone, blood glucose level, Momordica charantia

INTRODUCTION

Diabetes mellitus (DM), as defined by Li et al. (2017), is a long-lasting metabolic disorder that has the potential to give rise to various complications and grievous ailments. India has the highest prevalence of diabetics of any country worldwide. Moreover, India is the diabetes capital of the globe, according to the Indian Heart Association, with an estimated 109 million people diagnosed with diabetes by 2035 (Hemaiswarya et al., 2022).

Additionally, protracted elevation of blood glucose levels within the body gives rise to a range of complications, including microvascular complications such as “retinopathy, nephropathy, neuropathy, and cardiomyopathy”, as well as macrovascular complications including coronary artery disease. At present, sulfonylureas, biguanides, thiazolidinediones, α-glucosidase inhibitors, meglitanides, incretin mimetics, DPP4 inhibitors are all viable therapeutic options for type II diabetes (Hemaiswarya et al., 2022).

Certain herbal supplements, when combined with prescription medications, may induce potentially hazardous adverse effects. A patient's injury or a potentially fatal event may not be discovered until these interactions take place (Gupta et al., 2017). It is logical to suggest that concurrent administration of a substance and a drug should occur at least one to two hours apart, or several hours apart. It is recommended to completely refrain from combining the herb and drug, as such combinations have been frequently reported to cause interactions with the specific drug or are contraindicated (Hoda et al., 2019). Currently, herb-drug interactions are a stark reality despite their widespread application (Sharma and Patial, 2022).

Diverse bioactive constituents of M are responsible for these advantageous effects. M. Charantia, which have been utilized for the treatment of numerous diseases since antiquity, are significant sources of phytoconstituents. However, M. Charantia. Despite the fact that charantia exhibits a wide range of pharmacological activities, reported adverse effects in recent years have restricted its widespread use (Hauner, 2022).

In order to investigate DM, a network pharmacology approach is implemented, which

comprises drug-target-disease networks comprised of target proteins, drugs, and the disease Hu et al., 2024). As a result of their minimal adverse effects, multicomponents, and targets, network pharmacology has been extensively applied to the investigation of the action mechanisms and bioactive compounds of natural products intended for the treatment of DM (DSouza et al., 2021). The intention of the current investigation was to construct a rodent model that accurately reproduces the metabolic attributes and natural progression of "type 2 diabetes, while also meeting the criteria for pharmacological screening.

MATERIAL AND METHOD

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. For rapid evaluation of the selected herbal extracts in normal rats, only the pharmacodynamic response (blood glucose and insulin) was assessed in this portion of the study.

Pioglitazone was selected as standard. The results were compared using "two-way ANOVA, Bonferroni post-test to find statistical significance, *** Significant at P0.05 ns, **Significant at P<0.01; * Significant at P<0.05 compared to control".

RESULT AND DISCUSSION

Table 1: "Comparison of % blood glucose reduction of Pioglitazone 5mg/kg, 10mg/kg and 20mg/kg".

Time (h)	"Percent blood glucose reduction"		
	Pioglitazone (5mg/kg)	Pioglitazone (10mg/kg)	Pioglitazone (20mg/kg)
0	0.00±0.00	0.00±0.00	0.00±0.00
1	9.29±1.03	15.29±0.85	20.44±1.85
2	**16.22±0.64**	**25.75±1.09**	**33.92±1.45**
3	11.80±1.46	20.55±0.51	28.13±1.41
4	10.83±1.30	16.56±0.64	24.75±1.35
6	9.06±1.08	12.01±0.61	17.38±0.89
8	7.46±1.26	9.15±0.59	13.62±1.03
10	6.50±0.78	6.70±0.68	10.48±0.59
12	3.34±0.59	3.80±0.50	7.25±1.05

Graph 1: "Comparison of % blood glucose reduction of Pioglitazone 5mg/kg, 10mg/kg and 20mg/kg".

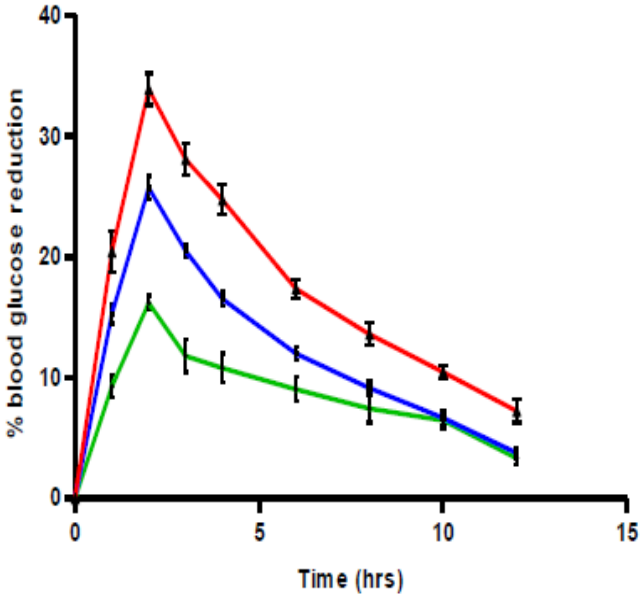
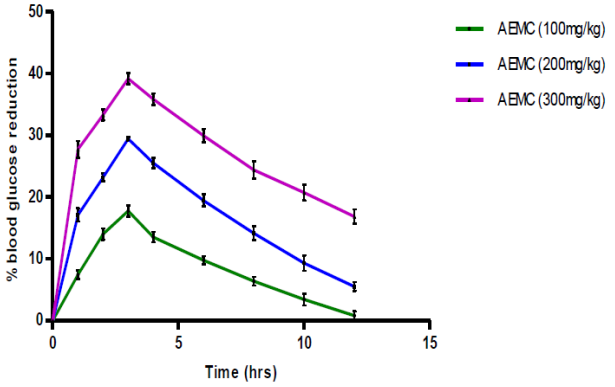


Table 2: "Comparison of % blood glucose reduction of AEMC(100mg/kg, 200mg/kg and 300mg/kg)."

Time (h)	"Percent blood glucose reduction"		
	AEMC (100mg/kg)	AEMC (200mg/kg)	AEMC (300mg/kg)
0	0.00±0.00	0.00±0.00	0.00±0.00
1	7.44±0.74	17.13±1.15	27.73±1.52
2	14.02±1.02	23.20±0.67	33.32±0.96
3	**17.76±1.00**	**29.43±0.32**	**39.18±0.98**

4	13.54±0.94	25.51±0.94	35.84±1.03
6	9.77±0.72	19.45±1.06	29.95±1.19
8	6.39±0.77	14.14±1.25	24.39±1.51
10	3.42±1.02	9.31±1.38	20.72±1.42
12	0.81±0.76	5.54±0.81	16.85±1.26

Graph 2: "Comparison of % blood glucose reduction of AEMC (100mg/kg, 200mg/kg and 300mg/kg)".



Diabetes requires food restriction, physical exercise, and medicine for the remainder of one's life. Addressing tendon and adipose tissue's sensitivity to insulin may help control type 2 diabetes, which increases insulin sensitivity (Choi et al., 2024). Additionally, they decrease the amount of glucose generated by the liver. Typically, thiazolidinediones are prescribed when alternative medications have proven ineffective in reducing blood sugar levels to the desired range. On occasion, these medications increase HDL cholesterol levels while decreasing triglyceride levels (Choi et al., 2024).

When administered alone, AEMC (Aqeous extracts of M. charantia) significantly and dose-dependently decreased the blood glucose level of normal rodents (Table1, Graph 1). It was discovered that a dose of 200 mg/kg bd.wt maximally reduced blood glucose levels by 30% (Table 2, Graph 2). It was observed that insulin levels increased during the optimum reduction of blood glucose with AEMC at 3 hours as opposed to 0 hours. In both single-dose and multiple-dose regimens, the hypoglycemic effects induced by Pioglitazone were enhanced by the specified dose of AEMC when provided jointly. With both single and multiple dose regimens, insulin levels were also observed to be altered during the maximal reduction in blood glucose levels. This suggests that a pharmacodynamic interaction can occur between AEMC and Pioglitazone in unintended rodents. Pharmacodynamic interactions can occur as a result of synergistic hypoglycemic effects or metabolic inhibition.

CONCLUSION

It has been demonstrated that pioglitazone has a significant impact on glucose management, or the proportionate decrease in blood glucose levels in healthy rodents; in healthy rats, the ideal proportionate decline in glucose levels was achieved after two hours of treatment.

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