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## Comparative Anti-Hyperglycemic Effects of Aqueous Extracts of Mistletoe and Pear Leaf on Alloxan Induced Diabetic Rats.

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### ABSTRACT

Historical records revealed that leaves of mistletoe plant as well as that of pear tree are used to treat varieties of disorders including diabetes. These leaves are being considered beneficial as dietary supplements because of their anti-diabetic potential. This study seeks to compare the efficacy of aqueous extracts of mistletoe and pear leaf to justify their use and to rationalize the choice of one over the other. The comparative hypoglycemic effects of mistletoe and pear leaf extracts were studied in albino rats fed with the extracts for 15 days after induction of diabetes. Glucose concentration, body weight and skin fold thickness were compared between the two groups and with the absolute and diabetic control groups. Aqueous extracts of both mistletoe and pear leaves significantly reduced blood glucose concentration and reversed significantly the weight loss and loss of subcutaneous fat associated with diabetes in the rats used. However, there was no significant comparative effect between the two leaf extracts on the parameters studied. Both the aqueous extracts of *V. album* and *P. Americana* possess anti-hyperglycemic activity but the aqueous extract of *V. album* is more potent as a hypoglycemic agent. The hypoglycemic potential of these herbal leaves could be utilized in the desire to reduce the financial burden imposed by diabetes globally.

**Key words:** diabetes, hypoglycemia, *Viscum album*, *Persea Americana*, comparative efficacy.

### INTRODUCTION

Diabetes mellitus (DM) is an endocrine disease characterized by metabolic abnormalities, and by long-term complications involving blood vessels, eyes and kidneys<sup>1</sup>. There are several distinct types, all of which are characterized by fasting and postprandial hyperglycemia.

Diabetes mellitus is an emerging pandemic with incremental trend in global burden. Four different research estimates projected a future burden of its incidence spanning between 2010 and 2030 at 439 million adults, an increment of more than 50%<sup>2</sup>. The number of adults with diabetes would predictably increase by 20% in developed countries, and by 69% in developing countries. Increment in the number was attributed to urbanization, diets that promote obesity, and decreased physical activity<sup>2</sup>.

Global management of diabetes and its sequelae are expected to cost a total of \$376bn in 2010 and a projected estimated cost for the year 2030 exceeds \$490bn. Besides high healthcare costs, DM also imposes huge economic burdens bordering on low productivity and economic growth<sup>3</sup>.

One of the challenges is to reduce the human and financial costs through provision of cost-effective management, especially in the developing world where poverty is rate is high. Mistletoe (*Viscum album*) is a parasitic evergreen plant that lives on trees such as oak, elm, fir and apple. Leaves and young twigs of this plant are popularly used by European herbalists, especially in Germany, for the treatment of varieties of disorders including DM and diseases of the circulatory and respiratory systems (Ernst et al, 2003). The hypoglycemic effects of the extracts of this plant have been documented by several authors<sup>4,5,6</sup>. Similarly, the hypoglycemic effects of the extracts of pear leaf (*Persea americana*) in experimental animals have been well documented by several investigators<sup>7,8,9</sup>.

In the choice of herbal plants for the treatment of DM play several factors including potency. This study seeks to compare the efficacy of the extracts of these two plants (*Viscum album* and *Persea americana*) in lowering blood glucose concentrations in alloxan-induced diabetic rats.

## MATERIALS AND METHODS

**Plant Materials and Extracts:** Fresh leaves of *Viscum album* and *Persea americana* were collected in the reserve Garden of Soun Model College, Ogbomoso, Oyo State, Nigeria. These were submitted for identification and authentication in the Herbarium of the Environmental Biology Department, Ladoké Akintola University of Technology (LAUTECH), Ogbomoso, Nigeria.

Air dried and powdered leaves of both plants (200g each) were subjected to similar process of aqueous extraction in the Food Science Department of the Faculty of Engineering, Ladoké Akintola University of Technology, Ogbomoso. They were first boiled in distilled water and then allowed to simmer for about one hour. The mixture was then evaporated under reduced pressure at 40°C until all the solvent had been removed to give a yield of 18.2% (36.4g) for *Viscum album* and 3.5% (7g) for *Persea Americana*. The dried extracts were then reconstituted as suspension in distilled water.

**Animals:** 20 male albino rats (180-200g) were used. They were obtained from the animal house of the College of Health Sciences, LAUTECH, Ogbomoso. These were bred in well-ventilated room at room temperature and under controlled lighting of 12:12 hour light/dark cycle. They were allowed unrestricted access to pelletized rat feed and clean water. They were randomly divided into four groups of five rats (n=5).

**Induction of Diabetes:** Animals were fasted for 12 hours and baseline fasting blood glucose concentrations were measured. They were then given a single dose of intraperitoneal injection of alloxan monohydrate solution (150mg/kg) freshly dissolved in distilled water. Hyperglycemia was confirmed 72 hours after, in blood obtained from the tail vein. Blood glucose measurement was done using ACCUCHEK<sup>R</sup> Glucometer calibrated in mg/dl. Only animals with

venous blood glucose concentrations of 170mg/dl and above were selected as diabetic.

**Measurement of Blood Glucose Concentrations:** A single drop of fresh whole blood from the tail vein was allowed to drop on the ACCUCHECK strips provided with the glucose monitor. The results were then read off on the meter 45seconds after application of the blood sample to the strips. The ACCUCHECK meter measurements were expressed as mg/dl.

**Experimental Design:** Albino rats were divided into 4 groups (A, B, C, and D) each consisting of 5 rats (n=5). Group A consists of normal healthy (non diabetic or absolute control) rats while the remaining 3 groups consist of alloxan induced diabetic rats. Groups A and B (group B served as the diabetic control) received no extract while groups C and D received 300mg/kg oral daily dose of aqueous extracts of *Viscum album* and *Persea Americana* respectively for 13 days. Baseline body weights, thickness of skin fold and blood glucose concentrations were measured before administration of alloxan and extracts (day 0) and were subsequently measured on days 5, 9 and 13.

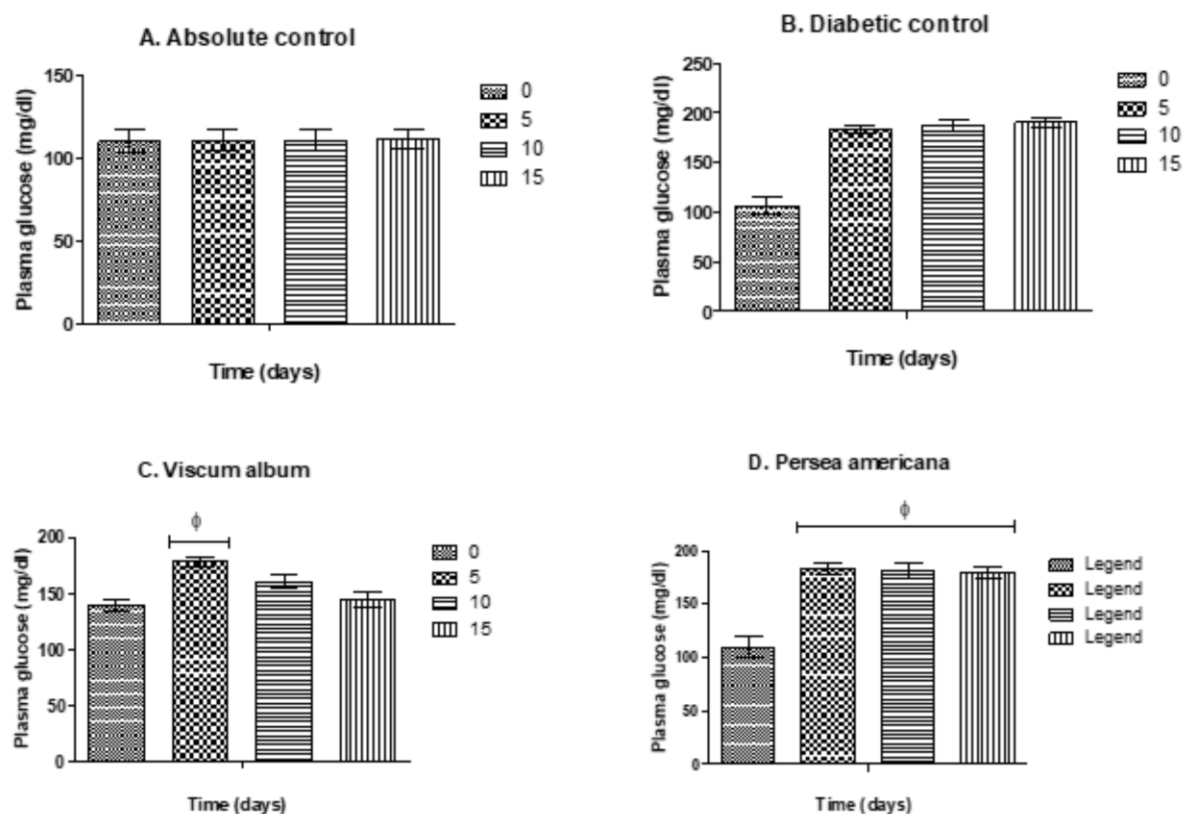
**Data and Statistical analysis:** Data were expressed as mean± S.E.M. One way analysis of variance (ANOVA) followed by Dunnet's test were used to identify data that are significantly different from the control groups. Differences were considered to be significant at  $P < 0.05$ .

## RESULTS

Values of the weight, skin fold thickness and blood glucose concentrations were not significantly different between the two groups that receive the extracts (at  $P < 0.05$ ). There were significant differences between these two groups and the control groups which show that the two leaves extracts have significant anti-hyperglycemic actions but their efficacy in lowering blood glucose were similar.

**Table 1:** Effect of aqueous extracts of *Viscum album* and *Persea americana* on blood glucose concentration in diabetic rats. Values are expressed as mean ± S.E.M; n=5 for each treatments.

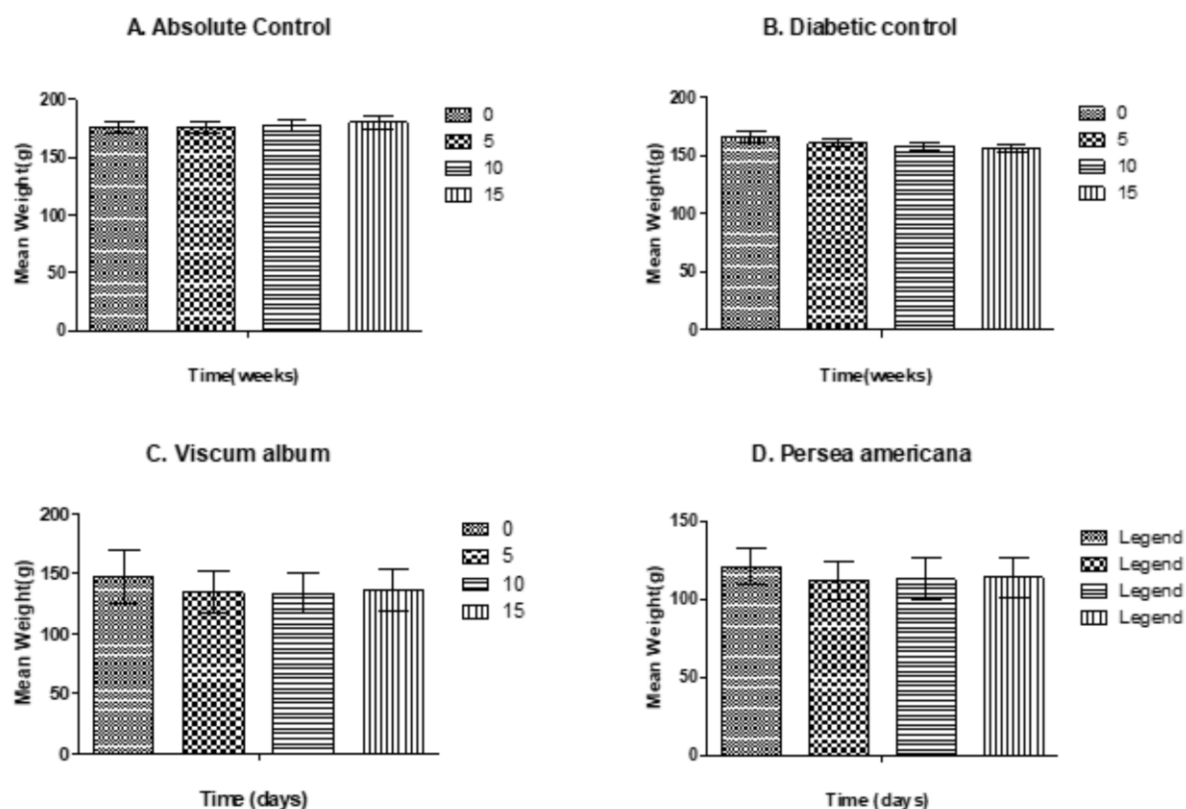
Days	Control	Group A	Group B	Group C
		<i>Diabetic control</i>	<i>300mg/kg Viscum album</i>	<i>300mg/kg P.americana</i>
0	110±7	106±9	139±6	
5	111±6	184±4	178±2	
10	111±6	187±5	160±1	
15	112±6	190±4	151±2	



**Figure 1:** Graphs A-D show changes in the plasma blood glucose in alloxan-induced diabetic Wistar rats treated with oral aqueous extract of *V. album* and *P. americana*. Plasma glucose was estimated on days 0, 5, 10 and 15 of alloxan induction. Plasma glucose was significantly higher than for the control groups only on day 5 ( $p < 0.05$ ) in rats treated with *V. album*.

**Table 2:** Effect of diabetes and aqueous extracts of *Viscum album* and *Persea americana* on body weight. Values are expressed as mean  $\pm$  S.E.M;  $n=5$  for each treatments.

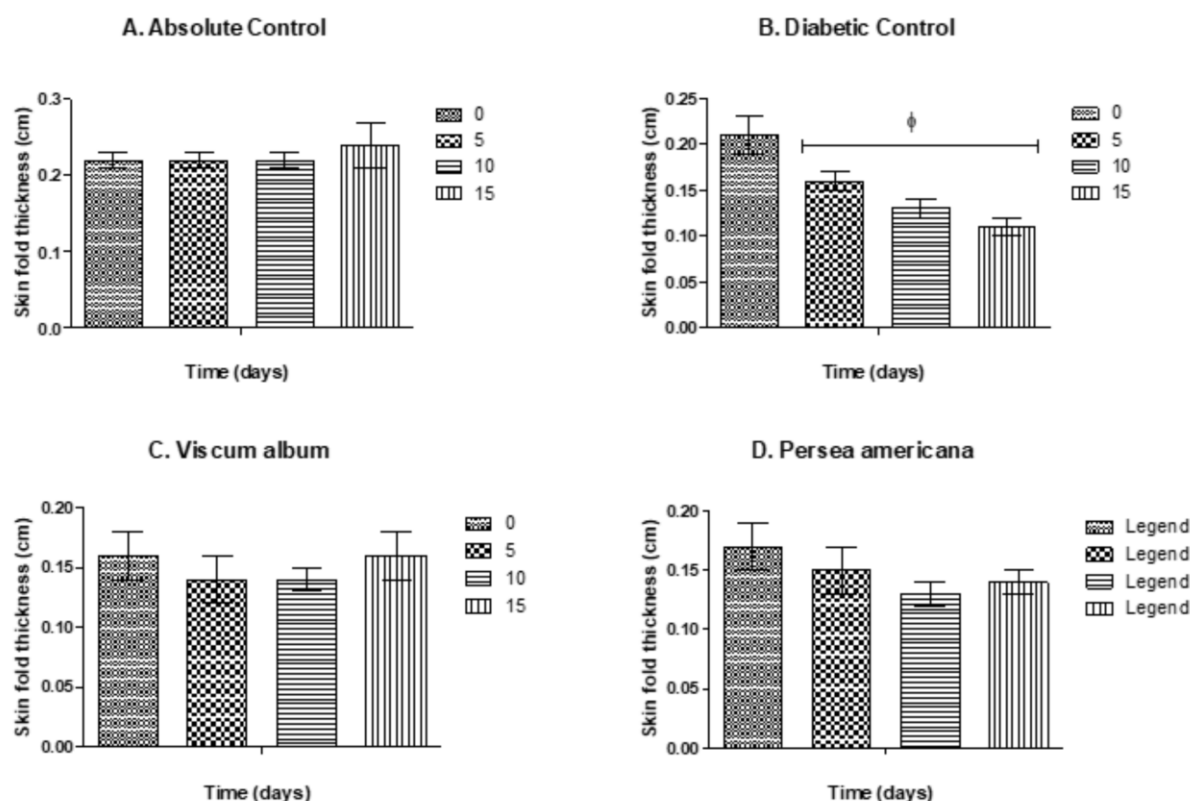
Days	Control	Group A	Group B	Group C
		<i>Diabetic control</i>	<i>300mg/kg Viscum album</i>	<i>300mg/kg</i>
<i>P.americana</i>				
0	176 $\pm$ 5	166 $\pm$ 5	147 $\pm$ 22	
121 $\pm$ 12				
5	176 $\pm$ 5	161 $\pm$ 3	134 $\pm$ 18	
112 $\pm$ 12				
10	177 $\pm$ 5	158 $\pm$ 3	133 $\pm$ 17	
113 $\pm$ 13				
15	180 $\pm$ 5	156 $\pm$ 3	136 $\pm$ 17	
114 $\pm$ 13				



**Figure 2:** Graphs A-D show changes in the body weights of alloxan-induced diabetic Wistar rats treated with oral aqueous extract of *V. album* and *P.americana*. Body weight was estimated on days 0, 5, 10 and 15 of alloxan induction. Average body weights were not significantly different from the control in all the treatment groups throughout the study.

**Table 3:** Effect of diabetes and aqueous extracts of *Viscum album* and *Persea americana* on skin fold thickness. Values are expressed as mean  $\pm$  S.E.M; n=5 for each treatments

Days	Control	Group A	Group B	Group C
		<i>Diabetic control</i>	<i>300mg/kg Viscum album</i>	<i>300mg/kg P.americana</i>
0	0.22 $\pm$ 0.01	0.21 $\pm$ 0.02	0.16 $\pm$ 0.02	0.17 $\pm$ 0.02
5	0.22 $\pm$ 0.01	0.16 $\pm$ 0.01	0.14 $\pm$ 0.02	0.13 $\pm$ 0.01
10	0.22 $\pm$ 0.01	0.13 $\pm$ 0.01	0.14 $\pm$ 0.01	0.15 $\pm$ 0.02
15	0.24 $\pm$ 0.17	0.11 $\pm$ 0.01	0.16 $\pm$ 0.02	0.14 $\pm$ 0.01



**Figure 3:** Graphs A-D show changes in the subcutaneous fat (estimated by thickness of skin fold, TSF) of alloxan-induced diabetic Wistar rats treated with oral aqueous extract of *V. album* and *P. americana*. TSF measurements were taken on days 0, 5, 10 and 15 of alloxan induction. Average TSF values were significantly decreased in time-dependent trend in the absolute control group when compared with the control group ( $P < 0.05$ ). No significant decrease was observed in TSF in the groups treated with both *V. album* and *P. americana* compared with the control.

## DISCUSSION.

In this study we found that both aqueous extracts of Mistletoe and Pear leaves possess anti-hyperglycemic effects but the extract of *V. album* showed significantly more potency than the aqueous extract of *P. americana*. The individual hypoglycemic effects of different extracts of these leaves have been established by several investigators. Glucose is known to enter cells via several mechanisms<sup>10</sup>. Because glucose cannot easily diffuse through cell membranes, glucose entry into many cells, excluding the gastrointestinal membrane and the epithelium of the renal tubules, occurs with the aid of facilitated glucose transporter molecules<sup>11,12</sup>. The mechanisms for the reduction of blood glucose concentration by these leaves are yet to be fully established. The hypoglycemic effects of the two leaves must have been based on similar mechanism. This mechanism has to do with interference with glucose transporter molecules on cell surface. It follows that the active factors in the herbs in consideration share certain similarities with insulin molecule. It calls for further studies to elucidate the nature of the active factors in these herbs in order to maximize its gains. Herbal remedies are being used in several parts of the world for its minimal side effects and affordability<sup>13</sup>. It must be, especially in developing

world, where the financial cost of management of diabetes is not quite affordable. We conclude that in the quest to reduce the financial burdens of diabetes worldwide, it becomes important to explore scientifically the active agents in herbal formulations that showed great potentials in combating this problem. In this study, we conclude that neither mistletoe nor pear leaves extract has more efficacy in lowering blood glucose in diabetes mellitus.

## CONCLUSION

We conclude from this study that in the choice of dietary herbal remedies for the amelioration of the hyperglycemic state and its sequelae in diabetes type I patients, *Viscum album* is preferred to *Persea Americana* due to its significantly higher potency in reducing plasma glucose while in aqueous media. However, further research is needed to evaluate the two plants extracts in different solvents.

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