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Research Article

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The lethal dose 50 (LD50) and weight effect of *Ageratum conyzoides* Methanol leaf extract on Aloxan-induced diabetic rats.

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Abstract

Weight management should be part and parcel of diabetes mellitus (DM) treatment strategy, especially T2DM, including selecting oral antidiabetes/hypoglycemic medications and insulin products that are weight beneficial. Weight gain and body mass are central to the formation and rising incidence of DM. In this study, the crude extract after maceration was subjected to solvent-solvent fractionation using chloroform, ethyl acetate and ethanol, in increasing order of polarity. **Findings:** The LD50 of the extract is above 5000mg/Kg body weight. Also, there is significant differences between the weight of rats in the control and treated groups in both the crude extract and the fractions as their respective p-values ($p=0.348$ and 0.91) was above the confidence level ($p<0.05$). Similarly, the average percentage weight (A%W) increase showed that all the methanol leaf extracts treated groups (both crude and fractions) including metformin group, had significant weight reduction (with their respective values far below 0.5) when compared to Groups 1 and 2 in which their average percentage weight increase were 11.55±4.50* and 9.08±0.94* respectively. **Conclusion**: The methanol leaf extract of *A. conyzoids* had a great weight loss effect on the diabetic rat even more than the metformin standard drug. Thus, the methanol leaf extracts *A. conyzoids* could be effectively used in the management of diabetic overweight or obese patients in ethnomedicinal practice.

Keywords: *Ageratum conyzoids*, weight effect, diabetes, methanol, maceration, fractionation, and LD50.

1. 0 Introduction

Weight management should be an integral part of diabetes mellitus (DM) treatment strategy, especially type 2 diabetes mellitus, which includes selecting oral antidiabetes or hypoglycemic medications and insulin products that are weight beneficial. Weight gain and body mass are central to the formation and rising incidences of type 1 and type 2 diabetes. Weight loss in individuals or patients at high risk of diabetes, especially overweight or obese individuals, is an effective prevention method and a major component of the currently prevailing diabetes prevention strategies. The connection or relationship between weight and type 2 diabetes mellitus (T2DM) is very strong, with studies confirming that the vast majority of patients with T2DM are overweight or obese, and are at very highest risk of developing T2DM (Wilding, 2014). Notwithstanding this strong relationship, not all individuals who are obese or overweight will develop diabetes, and not all individuals diagnosed with T2DM are overweight.

Generally, DM is a persistent chronic metabolic disorder characterized by hyperglycaemia and insulin resistance, and is associated with carbohydrate, lipid, and protein metabolisms that contribute to several kinds of complications, including diabetic cardiomyopathy and other microvascular complications such as retinopathy, neuropathy and nephropathy (Patel and Goyal 2011). Persistent hyperglycemia in the course of DM contributes to diabetic complications characterized by overproduction of reactive oxygen species (ROS) and buildup of lipid peroxidation byproducts (Yachamaneni and Dhanraj 2017). Experimental diabetes induced by alloxan (ALX) selectively disrupts the pancreatic β cells, which are known to be one of the most fragile structures to oxidative stress by generating excess ROS and produces heart lesions that are similar to human diabetic cardiomyopathy (Ojewale *et al*., 2020). Oxidative stress contributes to increased protein, lipid, and carbohydrate metabolisms, which precipitate increased free radical release accompanied by a decrease in antioxidants, thereby leading to diabetes.

Indeed, the association between excess weight, defined as overweight (BMI ≥25.0 kg/m^2) and obesity (BMI ≥30.0 kg/m^2), and increased incidence of diabetes risk is well documented (Abdullah *et al*., 2010). With regards to body weight and diabetes, studies should be focused on the potential impact on diabetes occurrence of eliminating excess weight in the population, knowing well that obesity is one of the major risk factor for type 2 diabetes mellitus (T2DM) (Abdullah *et al*., 2010). Consequently, weight loss or weight maintenance is important in the management of people with T2DM. Nevertheless, obesity and continuing increases in weight present formidable challenges to the management of T2DM. Not only does weight impact glycemic control, but weight gain resulting from diabetes therapy often creates a barrier to compliance with treatment. In prediabetes, weight loss has been shown to delay the onset or decrease the risk of T2DM, while in established T2DM weight loss has been shown to improve glycemic control, with severe calorie restriction even reversing the progression of T2DM (Wilding 2014). Some clinical trials have shown that weight reduction significantly improves glycemic control and blood pressure in T2DM patients and lowers the risk of progression of T2DM as well as CV diseases and cancer (Ross *et al*., 2011). Balancing adequate glycemic control and obesity risk is a challenge for clinicians when choosing an antidiabetic medication regimen, since several antidiabetic medications are associated with weight gain (Privolus *et al*., 2011)

Hence weight loss in all overweight patients with or at risk of T2DM should be encouraged by physicians, and should consider the impact on weight when choosing the most appropriate glucose-lowering therapies for these patients. Studies have shown that more than 80% of people with T2DM are overweight or obese (Kushner and Sujak, 2009). Besides the heightened risk for co-morbid conditions, (including cancer, gastrointestinal disease, osteoarthritis, liver and

kidney diseases, sleep apnea, respiratory disease, and major depression), an increase in weight can have a substantial or significant effect on glycemic control in people with T2DM (Ashley *et al*., 2017). In one prospective study, T2DM treatment resulted in an initial improvement at 3 months that was followed by deterioration in HbA1c levels during the next 9 months in 50 obese (BMI 42.81 kg/m^2) patients compared with 50 non-obese patients (Pani *et al*., 2008). The deterioration in glycemic control was attributed to greater insulin resistance in obese patients, and elevated BMI was the most significant factor contributing to the deterioration. In contrast, weight loss can improve glycemic control and reduce mortality. Results from studies have shown that as little as a 1 kg weight loss in patients with diabetes or impaired glucose tolerance can have a substantial benefit for glycemic control, morbidity, and mortality (Anderson and Konz, 2001).

Hypoglycemic agents, which improve insulin sensitivity and beta cell function, typically are associated with improvements in glycemic control (i.e., glycosylated hemoglobin) (DeFronzo, 2010). Treatment-related weight gain is also a side effect of many oral antidiabetes agents and insulin. For instance, thiazolidinediones (TZD), sulfonylureas, and glinides are associated with weight gain. In contrast, α-glucosidase inhibitors and dipeptidyl peptidase-4 inhibitors are weight neutral, whereas glucagon-like peptide-1(GLP-1) agonists and metformin are associated with weight loss (Phung *et al*., 2010; Zinman *et al*., 2007). Besides weight change, oral hypoglycemic drugs also have other side effects. Therefore, the need to look into phytomedicinal plants with high bioactive constituents. Thus, this research is focused on the weight effect of *Ageratum conyzoides* Methanol Leaf extract.

A. conyzoides is an annual herbaceous plant which belongs to the Asteraceae family. It is widely distributed tropically and commonly found in different parts of Nigeria as grass weed especially during wet season. It is located in the savannah regions and swampy areas of Nigeria. It is generally called goat weed in English, and different local names: Igbo – 'Imi-esu'; Hausa- 'Ahenhen'; and Yoruba- 'Ula or Ujula' in Nigeria. Both leaves and roots of *A. conyzoides* is used in folk medicine to treat fever and gastrointestinal diseases such as diarrhea, dysentery, rheumatism, ovarian inflammation, and intestinal colic with flatulence (de Fátima Agra *et al*., 2007). The leaves are also used in dressing wounds and burns, and it has been shown to exhibit antibacterial activity (Anisuzzaman *et al*. 2007). In Nigeria, the leaves and roots are useful in treating boils, leprosy, skin diseases, eye pains, and inflammation. It has also been shown to possess antidysenteric, analgesic, fertility, antispasmodic, and muscle relaxation properties (Achola *et al*., 2004; Silva *et al*., 2000; Abena *et al*., 1993). It also possess anti-inflammatory and antipyretic properties (Ogbalu and Williams 2014). The leaves and roots are also useful in treating hepatitis, breast myiasis sores, and arthritis (Ita *et al*., 2009) as well as a potential source of antidiabetic agents (Gnagne *et al*., 2018; Koto-te-Nyiwa *et al*., 2015; Singh *et al*., 2013; Ngunaï *et al*., 2009).

To the best of my knowledge, I have not come across any research publication on *A. conyzoides* including other medicinal plants with respect to its effect on the weight of diabetic animals despite myriad of works on its efficacy on the management of diabetes and other metabolic syndromes (Gnagne *et al*., 2018; Koto-te-Nyiwa *et al*., 2015; Singh *et al*., 2013). Thus, this research is focused on the LD50 and weight loss effect of methanol leaves extracts of *A. conyzoides* on alloxan-induced diabetic rats.

2.0 Materials and Methods

Reagents: All reagents were of analytical grade.

2.1 Plant materials:

Collection: The plant (*Ageratum conyzoides*) was collected from Air Force Institute of Technology, Kaduna and identified by Dr Shehu Gallah Umar of Botany Department, Ahmadu Bello University Zaria, Kaduna Nigeria on 15th September, 2021. The plant leaves were then detached.

Drying: The detached leaf parts were shade dried under laboratory temperature for two weeks. The dried leaves were then pounded using Pestle and Mortar to obtain fine coarse particles to increase their surface area for extraction.

2.2 Extraction Procedure:

Maceration method was employed for this study.

Soaking: The pounded leaf parts were soaked in 5.5liter of 70% methanol. After adding the solvent, they were vigorously stirred using VTCL Excella Mixer for even percolation of the solvent. They were then allowed to stand for 72hours.

Filtration: After 72hours of soaking, they were filtered using Whatman No I filter paper in Filtration Funnel. The filtrates were collected and subsequently concentrated in an Electronic Thermostatic Water Bath (HH-W420) at 50.1^{o}C to obtain the desired extracts. The extract was then weighed, and the percentage yield determined.

2.3 Acute Toxicity (LD_{50}) Determination:

Acute toxicity study was carried out to determine the LD50 of the crude extract. It was carried out according to OECD (Organization for Economic Cooperation and Development), 2008 guidelines with little modification. Prior to the conduct of the experiment, the animals (rats) were randomly selected and placed into three groups (n=5) and acclimatized to laboratory condition for two weeks. All groups were fasted overnight prior to administration of extract. The 70% methanol extract was prepared in distilled water and administered orally.

Group one: Control (Given only water).
Group two: Received 2000mg extract per Kg body weight.
Group three: Received 5000mg extract per Kg body weight.

Procedure: Starting with group 2, on day 1, one rat was dosed and observed for 24hours followed by dosing of two rats on day 2. Finally on day 3, the remaining two rats were equally dosed. They were then observed for two weeks for any clinical changes while their respective weights were noted every 4 days interval. Group 3 were similarly administered orally with the extract according to the group's dosage. They were also observed for two weeks and weights taking as in group 2.

2.4 Fractionation of the Methanolic Crude Extract:

The crude extract was subjected to solvent-solvent fractionation using the following solvent system in the increasing order of polarity after n-Hexane had been used to defat the extract; Chloroform, Ethlyacetate and Ethanol. The extract was dissolved in small portion of distilled water and poured in a separating funnel. n-Hexane and distilled water were then added in the ratio of 60ml: 40ml. The separating funnel was then shaking properly and mounted on a retort stand. The n-hexane portion (upper layer) was collected in a petri-dish. The aqueous portion was reconstituted with another 100ml of n-hexane to collect any remnant of n-hexane soluble portion. Similar steps was equally followed for other solvents (chloroform, ethylacetate and ethanol) by adding 100ml of the respective solvents, in two stepwise circle, on aqueous portion in sequential other.

The respective solutions of each solvent were concentrated on a Water Bath to get a fine fraction of each solvent to be used for the study.

2.5. Weight effect study:

The weight effect of both crude extract and the fractions were determined after induction of diabetes in rats using Alloxan, $C_4H_2N_2O_6.H_2O$ (KEM LIGHT Laboratory Put Ltd, Mumbia, India. CAS No. 2244-11-3) as the diabetogenic agent.

Induction of Diabetes: Both male and female (non-pregnant) rats were selected randomly after two weeks of laboratory acclimatization. Prior to induction, the rats were starved for 24hours and 150mg of alloxan per kg body weight was given

intraperitonally. Food and water were reintroduced after 1hour of induction. After 48hours of induction of diabetes, the blood tested for glucosuria using Acuicheck Glucometer, and also after 72hours. Rats that showed blood glucose levels greater than 250mg/dl were selected and used for the study.

2.5.1 Effect of the Crude Methanol Leaf Extract on the Weights of Rats:

Experimental Design: Four groups (n=4) were created and treated accordingly once a day for 4 weeks except group one as follows.

Group1 (Normal Healthy Control): Given only vehicle (0.9% normal saline);
Group 2 (Negative Diabetic Control): Given only vehicle (0.9% normal saline);
Group 3 (Positive Diabetic Control): Given standard drug (metformin) only (125mg/kg body weight);
Group 4: Diabetic rats which received crude extract in three divided doses of 50mg, 100mg and 200mg per kg body weight.

2.5.2 Effect of the Fractions of Methanol Leaf Extract on the Weights of Rats:

Experimental Design: Six groups (n=4) were created and treated accordingly once a day for 4 weeks except group one as follows.

Group1 (Normal Healthy Control): Given only vehicle (0.9% normal saline);

Group 2 (Negative Diabetic Control): Given only vehicle (0.9% normal saline);
Group 3 (Positive Diabetic Control): Given standard drug (metformin) only (125mg/kg body weight);

Group 4 Diabetic rats which receives Chloroform fraction in three divided doses of 50mg, 100mg and 200mg/kg body weight respectively;

Group 5 Diabetic rats which receives Ethylacetate fraction in three divided doses of 50mg, 100mg and 200mg/kg body weight respectively;

Group 6 Diabetic rats which receives Ethanol fraction in three divided doses of 50mg, 100mg and 200mg/kg body weight respectively.

Statistical analysis:

Data were reported as the mean ± SEM for triplicate determinations of each sample. Different samples were analyzed with analysis of variance, followed by the Post Hoc Turky test to identify differences between values. A p-value of <0.05 was considered to be statistically different. All statistical analyses were performed using the SPSS statistical package, Version 16.0 (SPSS Inc., Chicago, IL).

3.0 Results

3.1 Acute Toxicity Study (LD50 Determination)

In this study both groups 2 and 3 did not show any physical clinical changes such as their feeding habit and behaviour just like group 1 (control) and no mortality was recorded. However, rats' body weights relatively increased in both control and dosage administered groups (Figure 1). Therefore the LD50 of the extract is above 5000mg/Kg body weight. Hence, the extract will be safe for consumption.

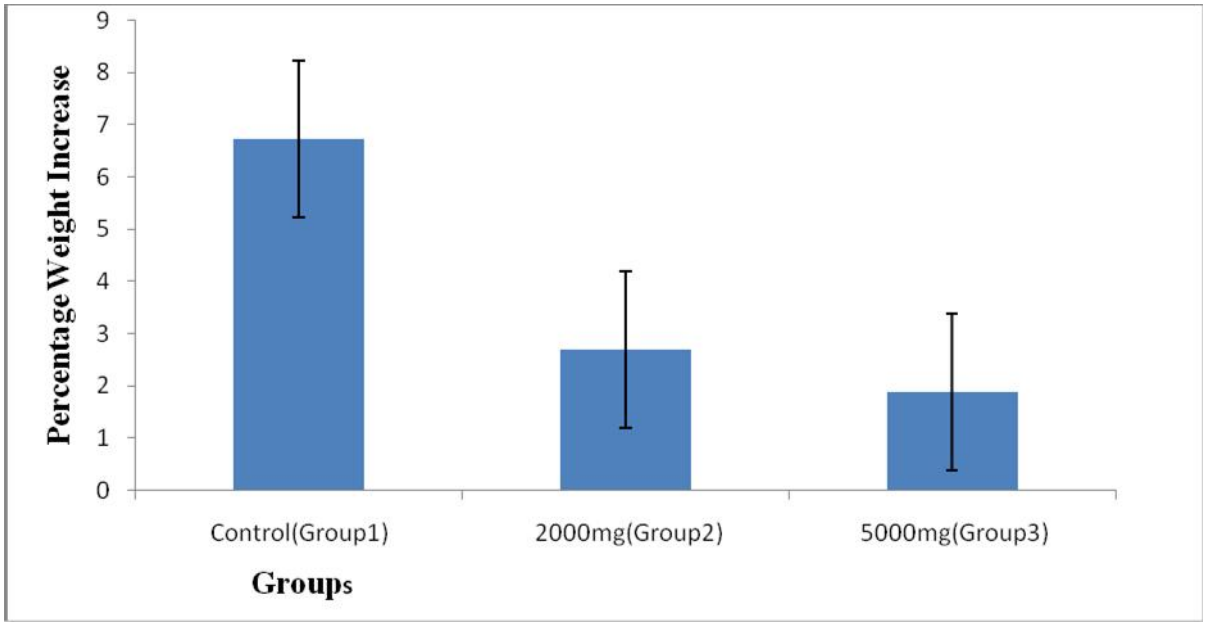

Figure 1: Percentage Weight Change after LD50 Study

3.2 Effect of the Methanol Leaf Extracts on the Weight of Rats:

Table 1: The ANOVA for Effects of Crude Methanol Leaf Extract on the Weight of Rats

ANOVA					
Average wieght (g)					
	Sum of Squares	df	Mean Square	F	Sig.
Between Groups	4194.438	5	838.888	1.206	.348
Within Groups	11822.658	17	695.450		
Total	16017.096	22			

The analysis of variance (Table 1) for the effect of the crude extract on the weight of the rats at 95% confidence level ($p<0.05$) showed that there is significant differences between the controls and the different dosages of the crude extract with values ($F=1.21$, $p=0.348$). Thus, the extract affected the weights of the rat when compared to the controls.

Table 2: Post Hoc Test for Effect of Crude Extract on the Weight of the Rats

Multiple Comparisons						
Average wieght (g) Tukey HSD						
(I) Different groups	(J) Different groups	Mean Difference (I-J)	Std. Error	Sig.	95% Confidence Interval	
					Lower Bound	Upper Bound
1	2	-2.69417	20.14149	1.000	-67.1208	61.7325
	3	21.45333	20.14149	.888	-42.9733	85.8800
	43	33.99083	20.14149	.557	-30.4358	98.4175
	5	20.64333	20.14149	.903	-43.7833	85.0700
	6	28.16833	20.14149	.727	-36.2583	92.5950
2	1	2.69417	20.14149	1.000	-61.7325	67.1208
	3	24.14750	18.64739	.784	-35.5000	83.7950
	4	36.68500	18.64739	.399	-22.9625	96.3325
	5	23.33750	18.64739	.806	-36.3100	82.9850
	6	30.86250	18.64739	.576	-28.7850	90.5100
3	1	-21.45333	20.14149	.888	-85.8800	42.9733
	2	-24.14750	18.64739	.784	-83.7950	35.5000
	4	12.53750	18.64739	.983	-47.1100	72.1850
	5	-.81000	18.64739	1.000	-60.4575	58.8375
	6	6.71500	18.64739	.999	-52.9325	66.3625
4	1	-33.99083	20.14149	.557	-98.4175	30.4358
	2	-36.68500	18.64739	.399	-96.3325	22.9625
	3	-12.53750	18.64739	.983	-72.1850	47.1100
	5	-13.34750	18.64739	.977	-72.9950	46.3000
	6	-5.82250	18.64739	1.000	-65.4700	53.8250
5	1	-20.64333	20.14149	.903	-85.0700	43.7833
	2	-23.33750	18.64739	.806	-82.9850	36.3100
	3	.81000	18.64739	1.000	-58.8375	60.4575
	4	13.34750	18.64739	.977	-46.3000	72.9950
	6	7.52500	18.64739	.998	-52.1225	67.1725
6	1	-28.16833	20.14149	.727	-92.5950	36.2583
	2	-30.86250	18.64739	.576	-90.5100	28.7850
	3	-6.71500	18.64739	.999	-66.3625	52.9325
	4	5.82250	18.64739	1.000	-53.8250	65.4700
	5	-7.52500	18.64739	.998	-67.1725	52.1225

Key: 1=Group1; 2=Group2; 3=Group3; 4=Group4 50mg; 5=Group4 100mg; 6=Group4 200mg

The Post Hoc Turky test is a multiple comparison test used to compare the mean difference between groups independently. From this test (Table 2), there are significant differences between any of the group (1 to 6) as all their respective p-values were above 0.05.

Table 3: The ANOVA for Effects of Extract Fractions on the Weight of Rats

ANOVA					
Average Weight (g)					
	Sum of Squares	df	Mean Square	F	Sig.
Between Groups	5275.746	11	479.613	.468	.910
Within Groups	35849.660	35	1024.276		
Total	41125.406	46			

Similar to that of crude extract (Table 1), the analysis of variance for the effect of the extract fractions on the weight of the rats (Table 3) at 95% confidence level ($p<0.05$) showed that there is significant differences between the controls and the different dosages of the fractions with values ($F=0.47$, $p=0.91$). Thus, the extract affected the weights of the rat when compared to the controls. Also, the Post Hoc multiple comparison test showed that there is significant difference between any groups (1 to 12) as all their respective p-values were above 0.05.

Table 4: Effect of the Crude Extract on the Weight of Rats.

Groups	AW of rats at day 0 (g)	AW after 4 Weeks(g)	A%W Increase
1	123±9.39	136.38±6.27	11.55±4.50*
2	152.75±12.51	139.07±12.15	9.08±0.94*
3	114.5±17.59	115.43±19.23	0.05±1.71
4 (50mg)	108.5±14.59	102.39±10.62	-4.46±3,58
4 (100mg)	118.25±17.36	115.74±15.33	-1.7±1.85
4 (200mg)	115.25±11.78	108.21±10.01	-2.79±1.59

Keys: AW= average weight; A%W= average percentage weight increase.

The values in Table 4 are given as Mean±SEM. The values in superscript (*) indicate groups with relatively significant average percentage weight increase.

Table 5: Effect of the Extract Fractions on the Weight of the Rats

Groups	AW of rats at day 0 (g)	AW after 4 Weeks (g)	A%W Increase
1	123±9.39	136.38±6.27	11.55±4.50*
2	152.75±12.51	139.07±12.15	9.08±0.94*
3	114.5±17.59	115.43±19.23	0.05±1.71
4 (50mg)	133.5±12.76	133.43±16.46	-0.88±3.07
4 (100mg)	130.25±15.81	126.11±12.87	-2.46±1.89
4 (200mg)	127.75±9.82	124.54±9.15	-2.42±2.34
5 (50mg)	105±13.58	108.64±23.16	0.19±9.49
5 (100mg)	131.5±20.67	125.64±9.21	2.43±9.96**
5 (200mg)	131.5±17.28	125.64±21.23	-5.7±3.99
6(50mg)	143.75±30.37	136.64±23.91	-3.09±3.69
6 (100mg)	141.25±16.25	138.07±13.36	-1.59±2.48
6 (200mg)	115.5±7.98	107.74±10.18	-7.03±4.65

The values in Table 5 are given as Mean±SEM. The values in superscript (*) indicate groups with relatively significant average percentage weight increase. All the fraction treated groups with the exception of Group 5 (100mg dose**) had their A%W Increase below 0.5.

3.3 Effect of Dosages Administered on the Weight of the Rats:

The effect of the extract administered doses on the weight of the rats (Figures 2and 3) indicated that the average percentage weight (A%W) increase in both crude methanol leaf extract (Figure 2) and extract fractions (Figure 3) tilt towards negative value.

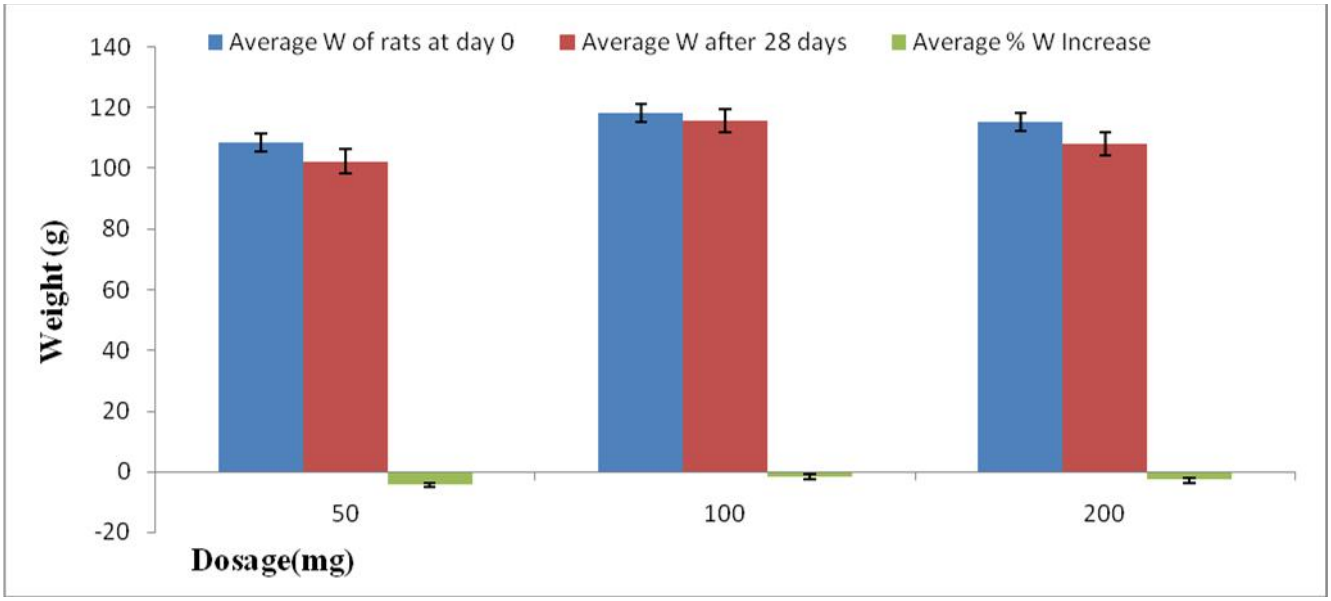

Figure 2: Effect of Crude Extract Dose on the Weight of Rats

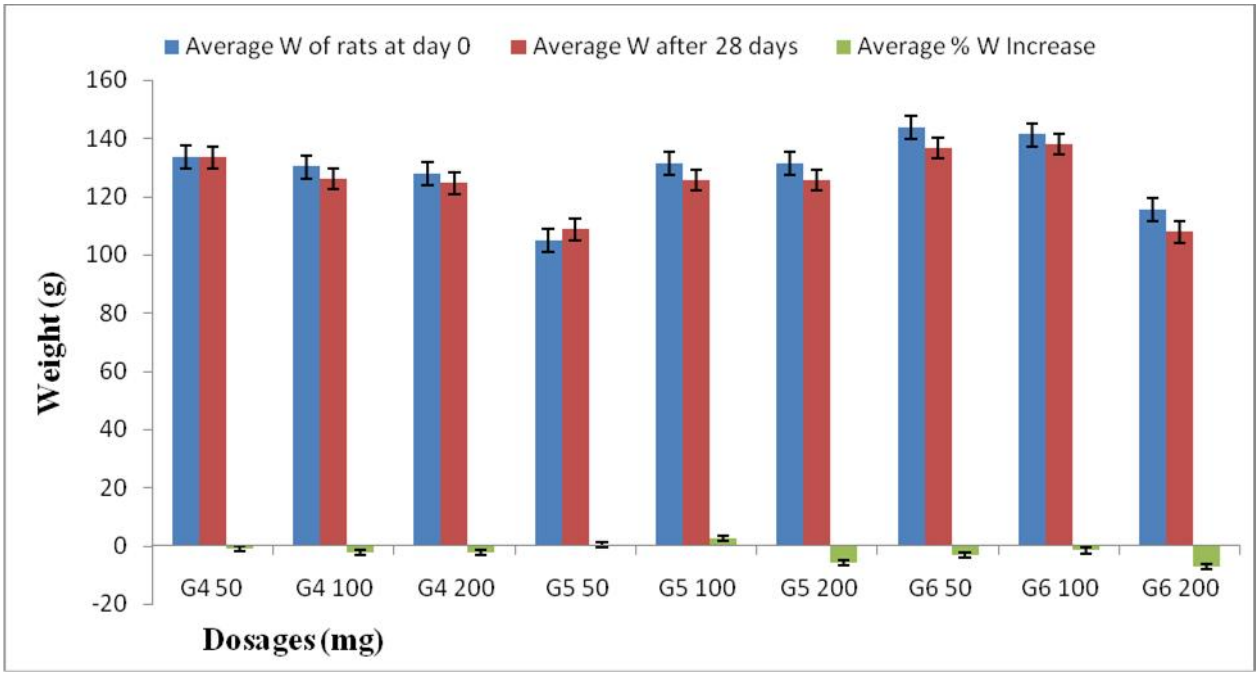

Figure 3: Effect of Extract Fraction Doses on the weight of Rats

Key: G4 50=Group4 50mg; G4 100=Group4 100mg; G4 200=Group4 200mg; G5 50=Group5 50mg; G5 100=Group5 100mg; G5 200=Group5 200mg; G6 50=Group6 50mg; G6 510=Group6 100mg; G6 200=Group4 200mg.

4.0 Discussion

This research was focused on the LD50 and effect of *A. conyzoids* methanol leaves extracts on the weight of alloxan-induced diabetic rats. Since weight gain is one of the predisposing factors of T2DM, any phytomedicinal plant(s) that have a weight reduction effect could have high potential hypoglycemic effect without weight gain as side effect (which is common for most oral hypoglycemic drugs in market today), and so could be a good source of oral hypoglycemic compounds in lead drug discovery and development. From this study, *A. conyzoids* has LD50 above 5000mg per Kg body weight with a strong weight reduction effect on the rats relative to the control (Figure 1). In separate research, Ojewale *et al*. (2019) stated that the LD50 of *A. conyzoides* was 5000 mg/kg body weight administered intraperitoneally. So the plant is safe for animal consumption since there were no acute toxicity effect on the experimental animals at 5000mg/Kg BW.

From the results of the effect of this methanol leaves extracts on the weight of rats, there is significant differences between the control and the treated groups in both the crude extract (Table 1) and the fractions (Table 3) as their respective p-values ($p=0.348$ and 0.91) was above the confidence level ($p<0.05$). Similarly, comparing the effect of the extracts on the average percentage weight increase showed that all the methanol leaf extracts treated groups (both crude and fractions) including metformin (standard drug) treated group, had significant weight reduction (with their respective values far below 0.5) when compared to Groups 1 (Normal Healthy Control) and 2 (Negative Diabetic Control) in which their A%W increase were 11.55±4.50* and 9.08±0.94* respectively (Tables 4 and 5). This is an indication that the methanol leaf extract of *A. conyzoids* had a great weight loss effect on the diabetic rat even more than the metformin standard hypoglycemic drug.

This weight lowering effect of the extract was equally significant across all the administered dosages (Figures 2 and 3) with 100mg ethylacetate fraction having the least effect. Hence, methanol leaf extract could be applied in ethnomedicine in the management of diabetic individuals even if the individual is either overweight (BMI≥25.0 kg/m^2) or obese (BMI≥30.0 kg/m^2).

By and large, weight reduction improves insulin sensitivity and preserves beta-cell function, leading to decreased fasting and postprandial glucose levels, and improved glycosylated hemoglobin (HbA1c) results(Choy *et al*., 2016).The more excess weight one has, the more resistant ones muscle and tissue cells become to ones own insulin hormone. As most of the patients are treated with oral antidiabetics it would be desirable for these drugs to promote weight loss so as to improve insulin sensitivity and preserves beta-cell function. Thereby preventing the accumulations of blood glucose levels which can lead to insulin resistance and trigger other metabolic consequences. However, a common side effect of most antidiabetics is weight gain, which in turn causes therapy adherence (García-Pérez *et al*., 2013; Grandy *et al*., 2013) to deteriorate. So far, metformin as well as glucagon-like peptide-1(GLP-1) receptor agonists and sodium glucose co-transporter 2 (SGT2) inhibitors is the only antidiabetic which leads to weight loss (Ashley *et al*., 2017; McDonagh *et al*., 2014; Wang *et al*., 2013), but can also cause serious side effects such as lactic acidosis and may not be used in patients with impaired kidney function (which is relatively often the case in diabetics) or heart insufficiency. Also, treatment-related weight gain is a side effect of many oral antidiabetes agents and insulin. For instance, the thiazolidinediones (TZD), sulfonylureas, and glinides are associated with weight gain. And excess weight is a well-known cardiovascular risk factor and is commonly encountered in T2DM patients, placing them at even higher risk of adverse events [2]. Most diabetics are already overweight at the time of diagnosis, and treatment with oral antidiabetics often leads to further weight gain. Nonetheless, clinical trials have shown that weight reduction significantly improves glycemic control and blood pressure in T2DM patients and lowers the risk of progression of T2DM as well as CV disease and cancer (Ross *et al*., 2011). Since, *A. conyzoids* methanol leaves extracts showed significant weight loss in this study as well as no or low toxicity (high LD50), it could be a good low cost alternative in the treatment and management of prediabetics and diabetics irrespective of their BMI in folk medicine. More so, the research can be taking to next level to probably identify and isolate the possible bioactive compound(s) which exhibit this weight reduction/loss effect for eventual development of the lead molecule; and subsequently discovery of new oral antidiabetic drug from this grass weed (*A. conyzoids*).

4.1 Conclusion

A. conyzoids methanol leaves extracts showed significant weight loss in this study as well as no or low toxicity (high LD50), so it could be a good low cost alternative in the treatment and management of prediabetics and diabetics irrespective of their BMI in folk medicine. Also, since most known oral antidiabetic drugs have other side effects besides weight gain, the bioactive compound(s) of this plant methanol leaf extract can be identified and isolated for possible lead compound development of eventual cheap and low cost hypoglycemic molecule(s).

Author Contributions

All authors made a significant contribution to this work, from the conception, through the study design, execution, acquisition of data, analysis and interpretation of results. They equally took part in drafting, revising and critically reviewing the manuscript, and gave final approval of the version to be published.

Conflict of Interest: There is no conflict of interest between and among authors in any aspect either financially or otherwise.

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