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Psidium Guajava (Guava) Leaf Extract As An Antihyperglycemic Agent

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Background:
Diabetes is a chronic metabolic disease characterized by elevated levels of blood glucose, which leads over time to serious damage to the kidneys, heart, blood vessels, eyes, and nervous system. This study aimed to validate and assess the antihyperglycemic activity of Psidium guajava leaf extract because guava leaf was used to treat diabetes in folk medicine from ancient times in Asia, Africa, and other parts of the world.
Methods:
The crude extract of Psidium guajava leaf was dissolved in distilled water 1g/10ml and used to evaluate antihyperglycemic activity using an oral glucose tolerance test (OGTT) in albino mice. The study used male Albino mice weighing 20 g- 30 g with a mean weight of 25 g. The experimental protocols and procedures were followed as per the standard protocol. All albino mice were colored differently and divided into three groups: Normal /reference group (GROUP A), Negative control group (GROUP B), and Case group (GROUP C). All groups of albino mice were fasted for five hours, followed by fasting blood glucose level measurement through a tail vein using a glucose meter, and their initial body weight was measured. Groups A and B were fed groundnuts, and group C was fed groundnuts and hypercaloric pellets for 14 days. The final body weight of albino mice in all groups was measured after fasting for 5 hours, and their final blood glucose level was recorded. Groups B and C were provided a calculated dose volume of Psidium guajava crude extract, respectively, according to their body weight. The blood glucose of each group was measured at intervals of 30 minutes, 1 hour, 2 hours, and 3 hours after oral administration of the dose.
Result: The clinical observation data of the Case group(C) were body weight 23.73g, initial glucose level 7.9 mmol/L, glucose levels after 0.5,1,2,3,4 hours were 7.6,7.2,7.1, 6.8, mmol/ respectively.
Conclusion:
The clinical observation shows a steady decrease in blood glucose level with time, confirming that Psidium guajava leaf extract may be useful in controlling diabetes.

Keywords: antihyperglycemic, albino mice, Psidium guajava leaf extract, folk medicine, cytotoxicity.

1. Introduction

Diabetes is a chronic metabolic disease characterized by elevated levels of blood glucose, which lead over time to serious damage to the heart, blood vessels, eyes, kidneys, and nerves (1,2,3,4). There are two types, and the most common is type 2 diabetes (5), which occurs when the body becomes resistant to insulin. Type 1 diabetes is insulin-dependent diabetes in which the pancreas produces little or no insulin by itself. The risk factors are less defined for type 1 diabetes than for type 2 diabetes. But autoimmune, genetic, and environmental factors are involved in the development of this type of diabetes.

The level of hyperglycemia associated with diabetes increases the risk of microvascular damage (retinopathy, nephropathy, and neuropathy). It is associated with reduced life expectancy, significant morbidity due to the related microvascular complications, increased risk of macrovascular complications (ischaemic heart disease, stroke, and peripheral vascular disease), and diminished quality of life. In 2000, an estimated 171 million people in the world had diabetes, and this is projected to increase to 783 million by 2045(6,7,8). Due to the toxicity and side effects of oral antidiabetic agents available, the use of herbal medicines for the treatment of diabetes has gained importance throughout the world. The World Health Organization also recommended and encouraged the practice of herbal medicine, especially in countries where access to the conventional treatment of diabetes is not adequate (9). The available literature shows that more than 400 plant species have hypoglycemic activity. Though some of these plants have a great reputation in the indigenous systems of medicine for their antidiabetic activities, many remain to be scientifically established (10).

Phytochemical constituents of Psidium guajava, flavonoid glycosides, such as strictinin, isostrictinin, and pedunculagin, are the effective constituents of Psidium guajava which have been used in the clinical treatment of diabetes due to their ability to improve the sensitivity of insulin.

During our search for bioactive constituents, we tested a crude extract of P. guajava for antidiabetic effect. Based on the significant antidiabetic activity of the plant extract, we focused on Psidium guajava for its phytochemical and antidiabetic studies. The guava leaves have been reported to contain β-sitosterol, pentacyclic triterpenoids, quercetin, avicularin, its 3-L-4-pyranoside, resin, tannin, flavinone-2 2'-ene, prenol, dihydro-benzo-phenanthridine, and a volatile oil rich in cineole, eugenol, and cryptonine. Guavas yield alkaloids, terpenoids, saponins, flavonoids, and polyphenols (11).

Psidium guajava, commonly known as guava, belongs to the family Myrtaceae. Psidium guajava (Myrtaceae) is an evergreen shrub growing extensively throughout the tropical and subtropical areas. The fruits of this plant are delicious and rich in nutrition. The other parts of the plant, like the leaves, also have lots of value. Different parts of the plant are used in the indigenous system of medicine for the treatment of various human illnesses. The leaves of Psidium guajava are used in the treatment of diarrhea, gastroenteritis, dysentery, pulmonary diseases, cough, etc. Herein, investigated chemical composition of the leaves of Psidium guajava (12).

In China, for example, the leaves have been used as folk medicine for the treatment of diarrhoea and hyperglycaemia for a long time.

Previous phytochemical studies on the leaves resulted in the isolation of various terpenoids, flavonoids, and tannins, and some of them showed a variety of bioactivities, especially antioxidant activities. To take full advantage of the whole part of Psidium guajava and find out more ingredients with potential antioxidant and antitumor activities. Hence, Psidium guajava L. (Myrtaceae) has been widely used as food and traditional medicine (13).

Guava leaves (Psidii guajavae folium) are dark green, elliptical, oval, and characterized by their obtuse apex. Guava leaves, along with the pulp and seeds, are used to treat certain respiratory and gastrointestinal disorders, and to increase platelets in patients suffering from dengue fever (14). Guava leaves are also widely used for their antispasmodic, cough sedative, anti-inflammatory, antidiarrheic, antihypertension, antiobesity, and antidiabetic properties (15). Studies on animal models have also established the role of guava leaves isolates as potent antitumor, anticancer, and cytotoxic agents (16). Guava leaves are widely employed for treating diarrhoea and digestive ailments, while the fruit pulp is utilized to enhance the platelet count for treating dengue fever. The potential of guava leaf extracts for diarrhoea treatment was also studied (17). The flavonoids present in guava leaf extract chiefly determine their antibacterial activity, while quercetin, which is the most predominant flavonoid of guava leaves, exhibits strong antidiarrheal activities. The antidiarrheal activity of quercetin is ascribed to its relaxing effect on the intestinal muscle lining, which prevents bowel contractions. Guava leaf polysaccharides (GLPs) can be utilized as an antioxidant additive in food and for diabetes treatment. The presence of a unique variety of bioactive polyphenolic compounds, like quercetin and other flavonoids, and ferulic, caffeic, and gallic acids, present in guava leaves primarily determines their bioactive and therapeutic properties (18).

Chemistry of the plant

Phytochemical constituents of Psidium guajava, flavonoid glycosides, such as strictinin, isostrictinin, and pedunculagin, are the effective constituents of Psidium guajava which have been used in clinical treatment of diabetes due to their ability to improve sensitivity of insulin(13).

Other components are phenolic compounds, carotenoids, and vitamins, mainly ascorbic acid (C) and tocopherol (E), which are effective free-radical scavengers. These substances tend to be effective in the reduction of stroke and cancer incidence, already attributed to the consumption of fruits and vegetables. They act mainly by preventing the oxidative cell damage caused by the inactivation of free radicals generated by the metabolism, inflammatory processes, environmental conditions, and UV radiation

Considering the importance of antioxidants in the human body, the regular consumption of significant amounts of fruits and vegetables has been promoted by specialists to prevent degenerative and chronic diseases.

2. Extraction

The solvent extraction technique was used, whereby the dried powdered sample was soaked and resoaked using methanol, filtered, concentrated, and stored in a petri dish for a while to evaporate the remaining solvents

Percentage yield of the Psidium guajava crude extracts.

The percentage yield of Psidium guajava crude extracts after concentration with the rotary evaporator machine was calculated.

The formula used is shown below.

$$\%\text{yield of crude extract} = \frac{M_1 - M_O}{M_O} \times 100\%$$

Where,
M_1- Mass of the plate dish and dried sample extract and
M_o- Mass the plate dish without the sample extract

Measured mass of crude extract
Mass of empty petri dish = 99.5g
Mass of petri-dish and crude extract 208g
Mass of dried Psidium guajava extract was =108.5g

$$\%\text{yield} = \frac{208g-99.5g \times 100\%}{208g}$$

%yield = 52.16%

3. Phytochemical screening

This test was conducted to identify bio-active compounds present in Psidium guajava leaf extract using laboratory reagents as shown below: (19)

3.1 Test for flavonoids

H_2SO_4 test: A Small amount of crude extracts in a test tube was treated with drops of concentrated. H_2SO_4 and observed for the formation of an orange color.

3.2. Test for saponins

1 mL of crude extract was diluted with 20 mL of distilled water, shaken well in a test tube, and observed for the formation of foam in the upper region of the test tube, which gives the information that saponins were present in the extracts.

3.3. Test for terpenoids

5 ml of crude extract was mixed with 2 ml of chloroform, and 3 ml of concentrated sulfuric acid (H_2SO_4) was added carefully to form a reddish-brown coloration at the interface, which indicates the presence of terpenoids.

3.4. Test for phenolic compounds

$FeCl_3$: crude extract treated with neutral ferric chloride solution and observed for the formation of violet color, which indicates the presence of phenolic compounds.

3.5. Test for alkaloids

Wagner's reagent: 50ul of crude extract was treated with 1.27g of iodine and 2g of potassium iodide in 100 mL of distilled water.

4. Cytotoxicity testing

An in vivo single-dose toxicity test was carried out using two groups of albino mice, each with two mice: a control group and a treated group. Crude extracts were dissolved in distilled water to obtain a dose volume, and each mouse in the treated group was orally administered based on their weight after fasting for 5 hours, whereby 1000g of mice is equal to 5 mL of the acute dose of the solvent extract. The physiological changes of mice were observed and recorded during the testing for 7 days.

5. Anti-diabetic testing

5.1. Animal preparation

The study used male Albino mice weighing 20 g- 30 g with a mean weight of 25 g. These were bred in the Animal Laboratory at the Department of Veterinary Medicine, Sokoine University of Agriculture. The albino mice were housed in a biology laboratory at the College of Natural and Mathematical Sciences (CNMS) throughout the study, at a temperature of 25 °C and fed with rodent pellets and water. The experimental protocols and procedures in this study were approved by the Department of Veterinary Medicine, Sokoine University of Agriculture, and the biology department at the College of Natural and Mathematical Sciences. All albino mice were colored differently for easy identification during clinical analysis.

Induction of experimental animals

The 20 male albino mice of 20 g- 30 g body weight were grouped into three groups, each with three albino mice:

GROUP A: Normal group/reference group

GROUP B: Negative control group

GROUP C: Positive control group

Both groups of albino mice fasted for five hours. following the period of fasting, the fasting blood glucose level was recorded through the tail vein for each mouse using a glucose meter, and their initial body weight was measured, then placed in their respective cages, group A and B fed with groundnuts, group C fed with groundnuts and hypercaloric pellets for 14 days.

The final body weight of albino mice in all groups was measured after fasting for 5 hours, and their final blood glucose level was recorded. Groups B and C were administered a calculated dose volume of distilled water and Psidium guajava crude extract, respectively, according to their body weight.

Blood glucose of each group was measured at the intervals of time 30 minutes, 1 hour, 2 hours, and 3 hours after oral administration of the dose.

Preparation of dose solution

The dried crude extract of Psidium guajava, after being obtained, a dose solution was prepared using distilled water as the vehicle solvent in this study.

From Pharmaceutical calculation rules,

We used one gram of crude extract =10 ml of distilled water.
Also, the relationship that was used

We only used 1.9g of the crude extracts, and thus, dissolved them in 19 mL of vehicle solvents.

1g ≡10ml
1.9g ≡?
After the calculations, 19 mL was required to be used, and the extracts were ready for dosing. And the remaining dose of crude extract was stored.

6. Results.

6.1phytochemical screening.

The phytochemical constituents in Psidium guajava methanolic extract were determined using different tests and found to contain alkaloids, terpenoids, phenolics, flavonoids, and saponins, as shown in Table 1 below.

PHYTOCONSTITUENTS	TEST PERFORMED	RESULT
Alkaloids	Wagner's reagent	Present
Terpenoids	Salkowski test	Present
Phenolic	Ferric chloride test	Present
Flavonoids	Sulphuric acid test	Present
Saponins	Distilled water test	Present

Table 1: Phytochemical screening of Psidium guajava leaves

6.2. cytotoxicity testing.

The mouse's body weight was determined and the was used to determine the weight gain/loss by subtracting the initial body weight from that at the final of the test.

Results obtained were presented in a tabular form as:

Mice group	Color	Initial weight (g)	Calculate dose	Final weight (g)	Weight gain
1	Red painted mice	26.5	0.13	28	1.5

2	Green painted mice	29	0.16	31.5	2.5

Table 2: Results on cytotoxicity

Note. Weight gain = final weight – initial weight

6.3. Observation from experimental results.

In this study, there was no death recorded following by dose administration of Psidium guajava methanolic extract; the mice were healthy, and no signs of toxicity were observed because during clinical analysis, there were no physiological changes in their characters. Based on body weight change in red mice treated with 0.13mmol/l and green mice treated with 0.16mmol/l of dose extract, body weight slightly increased by 1.5g and 2.5g, respectively. This proved that Psidium guajava methanolic extract contained no significant toxic effect.

6.4. anti-diabetic testing

From anti-diabetic testing of methanolic Psidium guajava crude extract in albino mice, the following data were obtained as presented in the tables below:

Normal/reference group.

Anti-diabetic testing of Psidium guajava methanolic extract revealed that group A (normal/reference group) body weight and blood glucose level increased slightly upon feeding with groundnuts. This justified the direct relationship between body weight and blood glucose level in albino mice, as shown on the table above.

TEST GROUP		Initial body weight(g)	Initial blood glucose level(mmol/l)	Final body weight (g)	Final blood glucose level(mmol/l)	Blood glucose level after dose administration (mmol/l)			
						0.5 hour	1hour	2hours	3hours
A	**A_R**	23.0	4.0	27.20	4.7	4.7	4.7	4.8	4.8
	A_G	25.0	5.2	29.43	5.6	5.7	5.6	5.5	5.6
	A_B	26.5	4.9	31.15	5.2	5.1	5.3	5.2	5.2

Table 3: Anti-diabetic testing for the reference group.

Negative control group.

In group B (negative control group) each mice administered a calculated dose volume of solvent vehicle (distilled water) to access its effect in blood glucose level of albino mice, the values of blood glucose level measured after time intervals found to remain fairly constant, thus solvent vehicle (distilled water) contained no effect on blood glucose level.

TEST GROUP		Initial body weight(g)	Initial blood glucose level(mmol/l)	Final body weight (g)	Final blood glucose level(mmol/l)	Dose distilled water (mg/kg/Bw)	Blood glucose level after dose administration (mmol/l)			
							0.5 hour	1hour	2hours	3hours
B	**B_R**	27.9	7.3	32.54	7.4	0.16	7.4	7.3	7.4	7.4
	B_G	26.4	4.8	31.10	5.6	0.16	5.5	5.5	5.6	5.6
	B_B	23.9	4.6	28.65	5.3	0.14	5.3	5.3	5.2	5.3

Table 4: anti-diabetic testing for the negative control group

Positive control group.

Group C (positive control), each mouse was administered a calculated liquid dose of Psidium guajava extract according to their body weight, and the blood glucose level was found to decrease steadily with time, which justified the anti-hyperglycemic activity of Psidium guajava methanolic extract. The bar chart below shows how blood glucose levels varied with time intervals.

TEST GROUP		Initial body weight (g)	Initial blood glucose level(mmol/l)	Final body weight (g)	Final blood glucose level(mmol/l)	Dose concentration (mg/kg Bw)	Blood glucose level after dose administration (mmol/l)			
							0.5 hour	1hour	2hours	3hours
C	**C_R**	20.3	5.1	23.73	7.9	0.16	7.6	7.2	7.1	6.8
	C_G	28.9	6.0	33.26	8.6	0.12	8.5	8.5	8.3	8.2
	C_B	23.7	4.6	31.29	8.2	0.17	8.1	7.8	7.8	7.4

Table 5: Anti-diabetic testing for the positive control group.

7. Discussion

7.1. Cytotoxicity testing

The cytotoxicity testing was part of this study, which was conducted to prevent human exposure to potential risks associated with the use of Psidium guajava extract. In this study of analysis of the acute oral toxicity, there was no mortality was observed in albino mice with their respective calculated administered dose of 1000 mg/kg body weight.; thus, the extract relatively non-toxic since substances with LD50 between 2000 mg/kg and 5000 mg/kg orally are considered to have low toxicity, in this case many researcher conducted the acute toxicity such as Sekhar et al(20). who showed that Psidium guajava extract has an LD50 greater than 5000mg/kg and mice remain healthy after 10 days of additional observation.

It should be noted that body weight is an important parameter that can control the health status of an animal; weight loss is frequently used as the first indicator of the harmful effects of drugs. A substance is considered toxic if it causes a mass reduction of more than 10%, and this condition may be considered a sign of toxicity even if other changes do not occur. Animals' weight loss during subacute toxicity can be attributed to antinutritional substances such as tannins and saponins present in this plant. substances have been reported to cause malabsorption of nutrients in the organism. Antinutrients would be responsible for the low intake of food and thus the reduction in body weight of animals treated at different doses of the extract compared to the control group. in this study, there was no weight loss, which proved this plant was not toxic.

7.2. Anti-diabetic testing

GROUP A (reference group)

From anti-diabetic testing of Psidium guajava methanolic extract, group A (normal/reference group) body weight and blood glucose level were found to increase slightly upon feeding with groundnuts. This justified the direct relationship between body weight and blood glucose level in albino mice.

By reference to the graphical interpretations of the results. Firstly, consider group A, which shows the relationship between body glucose with the change of time. The graph also gives the effect of body weight on the blood glucose of the body, similarly, the environmental effects since the group was used as the reference group.

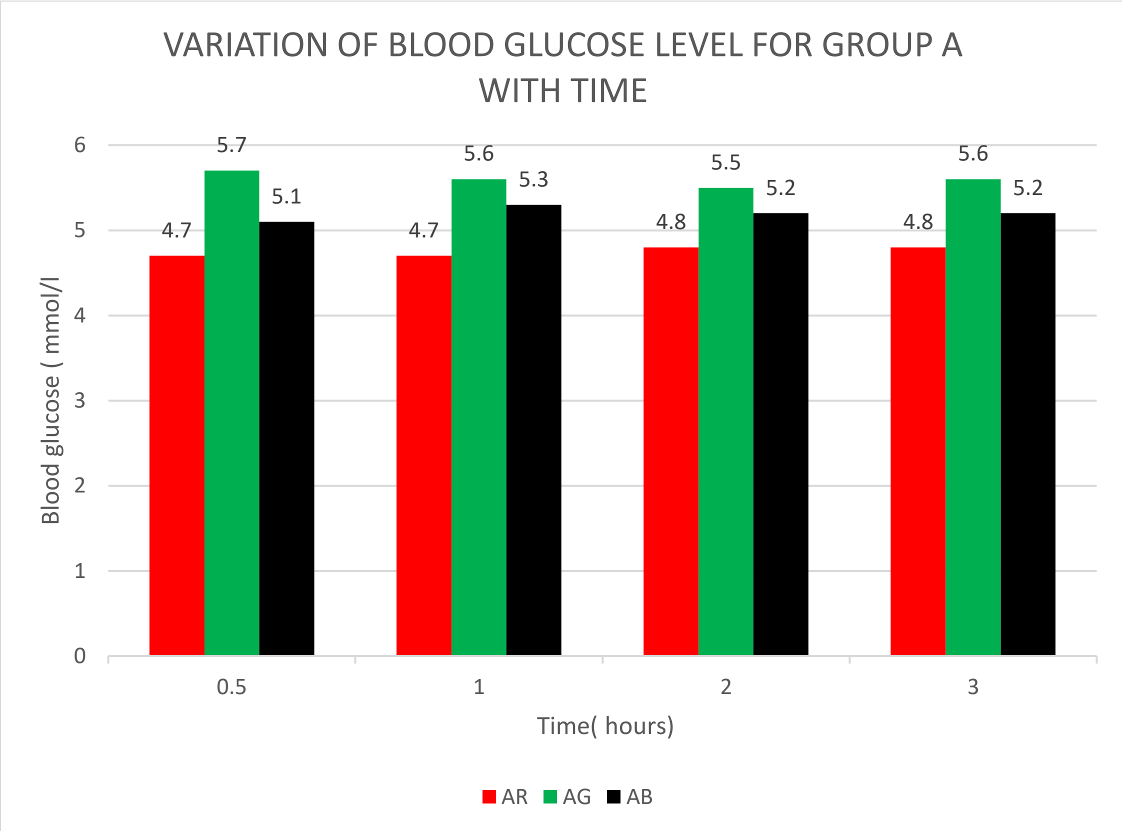

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Figure 1: Variation of blood glucose level for group A with time.

As shown above, the mice in this group were colored in red, green, and black colors on their necks, which aimed to differentiate them from one another, especially during the administration of doses based on their weight. When the mice were brought from Sokoine University of Agriculture, the initial weight was taken, in this group, 23g, 25g, and 26.5g weight for the mice colored red, green, and black, respectively and their respective initial blood glucose was measured to be 4.0mmol/l, 5.2mmol/l and 4.9 mmol/l. After feeding them for 14 days, their body weight as final was measured to be 27.2g, 29.43g, 31.15g, and their final blood glucose measured was 4.7mmol/l for red, 5.7mmol/l for green, and 5.1mmol/l for black. In that sense, the blood glucose level increased with the increase in body weight. Thus, it proves the fact that the blood glucose level is proportional to body weight because blood glucose level increases body mass index, causing an increase in lipid biosynthesis and hence body weight (21). The minute changes in blood glucose level that were seen were due to environmental changes. As for the 3 hours of dose administration.

GROUP B (negative group)

From anti-diabetic testing of Psidium guajava methanolic extract, group B (negative control group) body weight and blood glucose level were found to increase slightly upon feeding with groundnuts. This justified the direct relationship between body weight and blood glucose level in albino mice.

Consider group B, which shows the relationship between blood glucose with the change over time. The graph also shows the effect of body weight on the blood glucose of the body, the environmental effects. Group B was used to check the biological effects of vehicle solvent (distilled water) water which was used in the study.

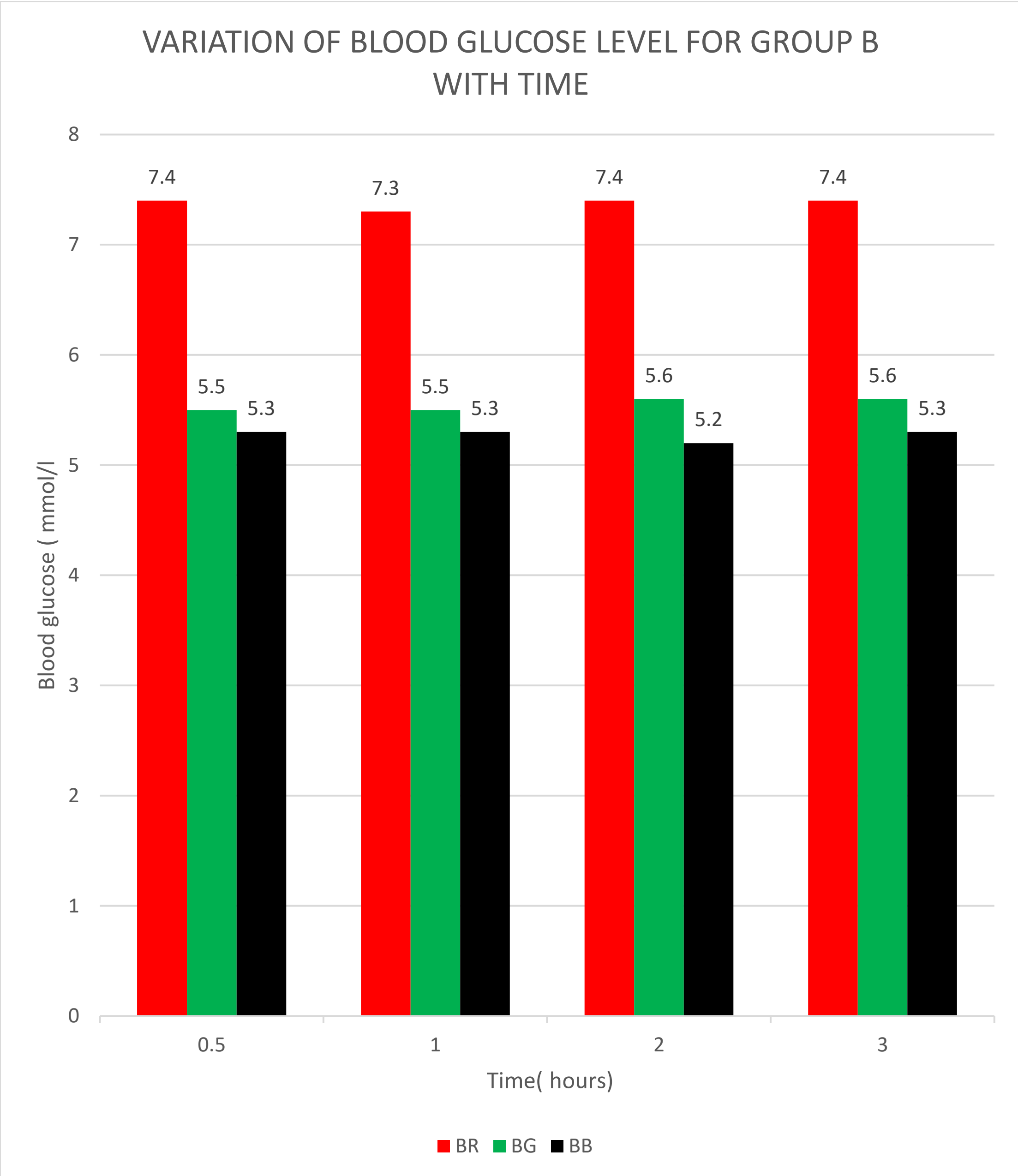

Figure 2: Variation of blood glucose level for group B with time

As shown above, the mice in this group were also colored in red, green, and black colors on their tails, which aimed to differentiate them from one another, especially during the administration of doses based on their weight. Initial weight was taken, in this group 27.9g, 26.4g,23.5g weight for the mice colored red, green, and black, respectively, and their respective initial blood glucose was measured to be 7.3mmol/l, 4.8mmol/l, and 4.6 mmol/l. After feeding them for 14 days, their body weight as final was measured to be 32.54g, 31.10g, 28.65g, respectively, and their final blood glucose measured was 7.4mmol/l for red, 5.6mmol/l for green, and 5.3 mmol/l for black. In that sense, the blood glucose level increased with the increase in body weight. Thus, it proves the fact that the blood glucose level is proportional to body weight because blood glucose level increases body mass index, causing an increase in lipid biosynthesis and hence body weight. The minute changes in blood glucose level that were seen were due to environmental changes. As for 3 hours of dose administration. The mice in this group (negative control group) were administered the vehicle solvent (distilled water) to investigate the possible alteration of distilled water on blood glucose level, but it was observed that the solvent that was used did not affect the blood glucose level (21).

GROUP C (positive group)

By reference to the graphical interpretations of the results of group C, which shows the relationship between body glucose with the change of time. The graph also gives the effect of body weight on the blood glucose of a body, similarly, the environmental effects, and in addition, the group helps us to relate how the sample used was able to lower the blood glucose level in relation to the effect of solvents as how was done in group B.

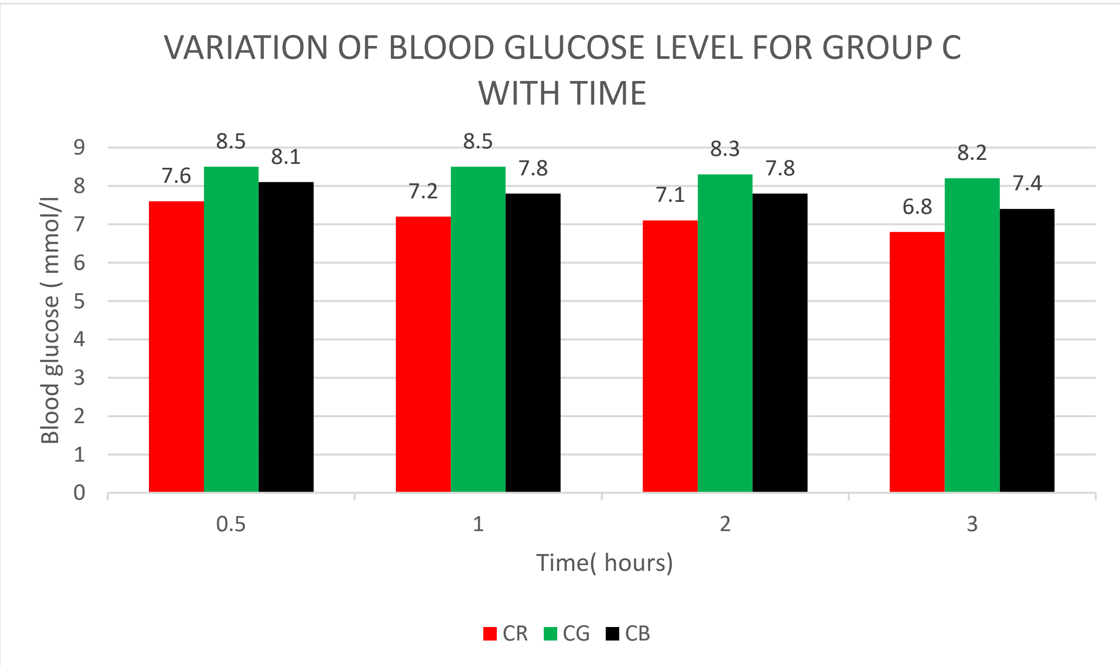

Figure 3: Variation of blood glucose level of group C with time

As shown above, the mice in this group were also colored in red, green, and black colors on their necks, which aimed to differentiate them from one another, especially during the administration of doses based on their weight. When the mice were brought from Sokoine University of Agriculture, the initial weight was taken, in this group, 20.3g, 28.9g,23.7g weight for the mice colored red, green, and black, respectively, and their respective initial blood glucose was measured to be 5.1mmol/l, 6.0mmol/l, and 4.6mmol/l. After feeding them for 14 days with food as how was stated in the methodology, their final body weight as final was measured to be 23.73g, 33.26g, 31.29g, and their final blood glucose level was measured to be 7.9mmol/l for red, 8.6mmol/l for green, and 8.2mmol/l for black. The blood glucose level, when it was measured, seemed to increase at a higher rate than the other groups. This was because in this group, there were hypercaloric pellets, which have a large value of glucose and are associated with an increase in body weight. Thus, it proves the fact that the blood glucose level is proportional to body weight because blood glucose level increases body mass index, causing an increase in lipid biosynthesis and hence body weight (21).

The experimental procedures were successfully followed and during an induction of dose the mice were grouped in three groups aiming on comparison of the effects of solvents and the crude extracts of Psidium guajava leaves if any, also a study was conducted to confirm the traditional use of Psidium guajava leaves for the treatment of diabetes as reported in documentation. The study was carried out to investigate the acute toxicity and anti-diabetic activity of methanolic Psidium guajava extract using albino mice. Since the mice were grouped three times with group A, group B, and group C., the aim was to compare the effects of vehicle solvent and the crude sample as how was used in group B and C, respectively, by referring to the normal group A that was not dosed with anything.

During the study, it was observed that the solvent used (distilled water) did not affect the blood glucose level of the mice, as was done in group B. On the other hand, the study showed that there was a decrease in the blood glucose when the mice were dosed with the crude sample, and this provides detailed evidence that it's possible for Psidium guajava leaves can lower the glucose level of the blood. In the study also there was a direct relationship between glucose and body weight, and this was observed in all groups in the manner that the increase in body weight was proportional to the increased blood glucose level.

8. Conclusion and recommendation.

This study justified traditional healers' claims, anti-hyperglycemic activity of Psidium guajava methanolic leave extract as the blood glucose level in positive control group found to decrease steadily with time interval 0.5, 1, 2 and 3hours after dose administration, however to improve the use of this herbal medicine pharmaceutical industries must relies on modern extraction and processing of active compounds from medicinal plants.

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Reference

1. "Diabetes". World Health Organization. Archived from the original on 29 January 2023. Retrieved 29 January 2023.
2. "Diabetes Mellitus (DM) – Hormonal and Metabolic Disorders". MSD Manual Consumer Version. Archived from the original on 1 October 2022. Retrieved 1 October 2022.
3. Shoback DG, Gardner D, eds. (2011). "Chapter 17". Greenspan's basic & clinical endocrinology (9th ed.). New York: McGraw-Hill Medical. ISBN 978-0-07-162243-1.
4. Kitabchi AE, Umpierrez GE, Miles JM, Fisher JN (July 2009). "Hyperglycemic crises in adult patients with diabetes". Diabetes Care. **32** (7): 13351343. doi:10.2337/dc099032. PMC 2699725. PMID 19564476. Archived from the original on 2016-06-25.
5. "Symptoms and Causes of Diabetes". National Institute of Diabetes and Digestive and Kidney Diseases, US National Institutes of Health. 2024. Retrieved 16 May 2024.
6. www.who.int. Retrieved 2024-12-17.
7. "The top 10 causes of death". www.who.int. Retrieved 2024-08-12.
8. International Diabetes Federation. Archived from the original on 2023-08-10. Retrieved 2023-08-10.
9. Traditional medicine. Archived from the original on 27 July 2008.
10. WHO (2006) Definition and Diagnosis of Diabetes Mellitus and Intermediate Hyperglycemia. WHO, Geneva
11. Begum S, Hassan SI, Ali SN, Siddiqui BS. Chemical constituents from the leaves of Psidium guajava.Nat Prod Res 2004;18:135-40.
12. Eziuche Amadike Ugbogu, Okezie Emmanuel, Miracle Ebubechi Uche, Emmanuel Dike Dike, Benedict Chukwuebuka Okoro, Chibuike Ibe, Victor Chibueze Ude, Celestine Nwabu Ekweogu, Ositadinma Chinyere Ugbogu,The ethnobotanical, phytochemistry and pharmacological activities of Psidium guajava L.,Arabian Journal of Chemistry, Volume 15, Issue 5, 2022,103759, ISSN 1878-5352,https://doi.org/10.1016/j.arabjc.2022.103759.
13. Chaturvedi, T., Singh, S., Nishad, I., Kumar, A., Tiwari, N., Tandon, S., Saikia, D., Verma, R.S., 2021. Chemical composition and antimicrobial activity of the essential oil of senescent leaves of guava (Psidium guajava L.). Nat. Prod. Res. 35 (8), 1393–1397. https://doi.org/10.1080/14786419.2019.1648462.
14. Laily, N.; Kusumaningtyas, R.W.; Sukarti, I.; Rini, M.R.D.K. The potency of guava Psidium guajava (L.) leaves as a functional immunostimulatory ingredient. Procedia Chem. 2015, 14, 301–307. [CrossRef]
15. Chen, H.Y.; Yen, G.C. Antioxidant activity and free radical-scavenging capacity of extracts from guava (Psidium guajava L.) leaves. Food Chem. 2007, 101, 686–694. [CrossRef]
16. Ashraf, A.; Sarfraz, R.A.; Rashid, M.A.; Mahmood, A.; Shahid, M.; Noor, N. Chemical composition, antioxidant, antitumor, anticancer and cytotoxic effects of Psidium guajava leaf extracts. Pharm. Biol. 2016, 54, 1971–1981. [CrossRef] [PubMed]
17. Dewi, P.S.; Sutjiatmo, A.B.; Nurdiansyah, A. Antidiarrheal activity of water extracts of guava leaves (Psidium guajava L.) and water extracts of green tea leaves (Camellia sinensis L.) combination in Swiss Webster mice. Acta Pharm. Indones. 2013, 38, 67–70.
18. Farag, R.S.; Abdel-Latif, M.S.; Abd El Baky, H.H.; Tawfeek, L.S. Phytochemical screening and antioxidant activity of some medicinal plants' crude juices. Biotechnol. Rep. 2020, 28, e00536. [CrossRef]
19. Kancherla N, Dhakshinamoothi A, Chitra K, Komaram RB. Preliminary Analysis of Phytoconstituents and Evaluation of Anthelminthic Property of Cayratia auriculata (In Vitro). Maedica (Bucur). 2019 Dec;14(4):350-356. doi: 10.26574/maedica.2019.14.4.350. PMID: 32153665; PMCID: PMC7035446.
20. Dinesh Kumar, Sekar, Gaurav Kumar,L Karthik,K V Bhaskara Rao, Asian Journal of Plant Science and Research,2011.
21. Janghorbain M, Hedley AJ, and Jones RB: Is the association between glucose levels and "all causes" and cardiovascular mortality risk, dependent on body mass index? Met J. IR. I. 1991;6:205-212 10.