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The Potency of Antidiabetic Properties of Watermelon (*Citrullus lanatus*) Rind Ethanolic Extract in Glucose-Induced Male Albino Mice

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Abstract:

- ***Objectives:***

Evaluate the effectiveness of watermelon rind ethanolic extract in reducing blood glucose levels in glucose-induced male albino mice and examine potential adverse effects and the impact of different extract concentrations.

- ***Methods:***

This in vivo study was conducted at the Adventist Medical Center College Pharmacy Department Laboratory and involved 42 mice that were given standard care. The watermelon rinds were processed into a powder, and the ethanolic extract was extracted using maceration and refined with a rotary evaporator. The potency of the antidiabetic properties of *Citrullus lanatus* rind ethanolic extract was evaluated by observing the blood sugar level of the male albino mice after inducing glucose. The mice were divided into seven groups, each receiving varying dosages of a specific extract. The blood samples were collected by cutting a small portion of the male albino mouse tail. A device called a glucometer was utilized to monitor the blood glucose level. The ANCOVA was then utilized for the analysis of the data.

- ***Results:***

Univariate ANCOVA analysis showed that baseline weight did not significantly affect results, but treatment effects were significant ($p < .01$) with a large effect size ($\eta^2 = .860$). Higher doses of both metformin and the extract resulted in notable weight loss. A significant reduction in blood glucose levels was observed, especially at 175 mg/kg of the extract, where levels decreased from 131 mg/dL to 85.75 mg/dL. The study rejected the null hypothesis, confirming the extract's efficacy in lowering blood glucose levels.

- ***Conclusion:***

The watermelon (*Citrullus lanatus*) rind ethanolic extract could potentially be used as a treatment against diabetes.

Keywords: *Antidiabetic Properties, Watermelon Rind, Ethanolic Extract, Glucose-Induced, Blood Glucose Level, ANCOVA*

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I. INTRODUCTION

According to the World Health Organization (2023), diabetes is one of the leading causes of death worldwide. Although adults are more frequently diagnosed with diabetes, more children and young adults are getting the diagnosis. Diabetes happens when the pancreas cannot create sufficient insulin or the body cannot utilize the insulin (the hormone that regulates the blood sugar) produced. The most prevalent type of diabetes, type 2 diabetes mellitus, affects 90– 95% of individuals worldwide, and the indication of this is elevated blood sugar (glucose) levels.

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Further studies and research are needed to investigate alternative therapies and treatments that can improve the health of people diagnosed with the condition, as there is no cure for diabetes. All we can do for now is prevent it, which includes home remedies and pharmaceutical drugs[metformin, thiazolidinediones (glitazones), etc.]. Diabetes cannot be controlled only through medication. It may also be by the person's lifestyle. Thus, exercising regularly, drinking plenty of water, and eating more fiber are recommended.

Numerous functional foods and nutraceuticals, such as fruits, vegetables, and oily fish, etc., have been used to treat diabetes. These foods are loaded with nutrients and could help prevent diabetes. Watermelon is a functional food or nutraceutical, as its chemical composition provides both high nutritional value and various health benefits.

Dessert watermelon, or *Citrullus lanatus*, is native to northeastern Africa. It is primarily cultivated in warm regions. The fruit of *Citrullus lanatus* has a thick, smooth, green skin with vertical light-green stripes. Inside, the fruit is red and contains black seeds.

The rind contains dietary fibers, phenolic compounds, minerals, carbohydrates, and fatty acids. Watermelons can be purchased at the grocery store, and their rinds are discarded as waste. The inner portions of the rind mainly contain citrulline, a known nitric oxide stimulator.

A study conducted by Sorokina et al. (2021) has compiled a comprehensive catalog of 1,679 small molecules found in watermelon and analyzed their cheminformatics. The study revealed the presence of various bioactive compounds in watermelon fruits, such as glycosides, carotenoids, flavonoids, alkaloids, carbs, fatty acids, and essential oils. These compounds may possess antidiabetic properties and offer other health benefits. Furthermore, the rind of the watermelon specifically has been shown to contain saponin, cardiac glycosides, phenol, moisture, lipids, and proteins. Due to these nutrients and bioactive compounds, watermelon has many health benefits, such as antioxidant, antidiabetic, and anti-cancer effects.

Watermelon rind is often studied for its potential antidiabetic properties, and these studies typically involve the use of mice as experimental subjects. Mice are commonly used in biomedical research as they serve as animal models. The American National Research Council Committee on Animal Models for Research and Aging defines an animal model as an animal that allows for the study of normal biology or behavior, the investigation of spontaneous or induced pathological processes, and exhibits similarities to humans or other animal species in certain aspects.

This study seeks to investigate whether the watermelon rind ethanolic extract can effectively reduce blood glucose levels in glucose-induced albino mice. It also observes any potential adverse effects associated with mice's consumption of watermelon rind extract. In addition, it seeks to determine if different concentrations of watermelon rind extract significantly affect blood sugar levels.

II. MATERIALS AND METHODS

A. Collection and Preparation of the Ethanolic Extract of Watermelon (Citrullus lanatus) Rind

The watermelon samples were purchased from a market here in Iligan City and were authenticated at the Biology Department of Mindanao State University-Iligan Institute of Technology. The researchers then washed the watermelons under running water and chopped them into four parts. The collection of the watermelon rinds included gentle separation from the flesh by passing the knife between the pink/red flesh and the outer white rind. By doing this, the fruit and rind are separated. The outer, dark-green skin of the white rind was also then peeled off using a knife. The white rinds were then cut into small thin pieces. Out in the sun, the watermelon rind pieces dried out and due to time constraints, the researchers made use of blowers for better drying. The small thin slices were put into a container and there it was dried using the blower until it was brittle enough. To achieve powderized watermelon rinds, it was mixed and crushed by a blender. The watermelon rinds are finally powderized and ready for the maceration method.

B. Extraction of the Ethanolic Extract of Watermelon (Citrullus lanatus) Rind

The researchers made use of the maceration process. The ratio for solute and ethanol was 1:3. During the maceration process, 300 ml of powderized watermelon rinds were mixed thoroughly with the solvent, 600 ml of ethanol in a container. The container was sealed with a wooden cork, wrapped with foil, and was secured with a rubber band. For three days, with the use of the laboratory shaker, the mixture was periodically stirred and shaken occasionally to ensure thorough extraction. After three days, 500 ml of the ethanolic watermelon rind was extracted and filtered using the Whatman filter and was stored in an Erlenmeyer flask. Once the extraction was completed, the researchers asked for the assistance of MSU-IIT's College of Science and Mathematics laboratory for further extraction using the rotary evaporator machine. More or less 50 ml of the ethanolic watermelon rind extract was collected and was finally ready for experimentation. To keep the extract from any contamination, the researchers made sure to keep it in a safe place, in the Pharmacy Laboratory at room temperature.

ISSN No:-2456-2165 https://doi.org/10.38124/ijisrt/25apr202

C. Determination of Approximate Lethal Dose Acute Toxicity Testing - Acute Toxic Class Method

The test was conducted in accordance with the OECD 423 guidelines. The dosage per cage was set as follows: cage #1 received 100 mg/kg, cage #2 received 200 mg/kg, cage #3 received 400 mg/kg, and cage #5 received 500 mg/kg of watermelon rind ethanolic extract. Observations were made post-administration. Mice in cages #1 and #2 exhibited no adverse reactions and remained in normal condition. However, the mice in cage #3 displayed shortness of breath and succumbed approximately five minutes after administration. Additionally, the mice in cage #5 died immediately following the administration of the assigned dosage. The researchers also made use of IQ-CRO recommended dose volumes for common laboratory animals.

D. Experimental Animals

Healthy young adult male albino mice were utilized. The researchers purchased them from a certified mice seller all the way from Cagayan de Oro City.

E. Housing and Feeding Condition of Experimental Animals

The researchers made sure the mice were kept safe in the pharmacy department laboratory's animal housing at Adventist Medical Center College-Iligan. The mice were divided into seven groups, and there were six mice in every group. The cages/containers of the mice were given identification, and the space provided gave ample room for activity. The researchers made sure the animal housing had proper ventilation, low lighting, and would be subjected to a short cycle of light and dark. The relative humidity was maintained between 45% and 65%, and the room temperature was kept between 20 and 24 °C. The researchers made sure there was only minimal noise to reduce the stress of the experimental animals. The mice were fed standard laboratory diets and they had access to distilled drinking water. The mice cages were cleaned twice a week by the researchers, and an antibacterial wipe was used to clean the cages. This helps reduce the risk of bacterial contamination and ensures a sterile environment. The bottles were washed to prevent the growth of bacteria and other microorganisms, so that the water was clean enough for mice to drink. Twice a week, the bedding in the cages was changed to new, clean ones. Fresh bedding helps to maintain a dry and odorless environment, reduces the risk of infection, and provides a comfortable habitat for mice. The mice are transferred to a clean container before being returned to their respective cages prior to the start of cage cleaning.

F. Test for the Antidiabetic Activity

The method utilized 43 mice. They were orally induced with glucose and their drinking water was mixed with glucose to speed up the diabetic process. The blood samples were collected from the tails of the mice. The researchers cut a small portion from the tails of the mice, and enough drop of blood was placed on the glucometer. A glucose strip typically needs 0.5–2 µl of blood. To prevent infection and stop any further bleeding, cotton balls soaked in absolute ethanol were used to gently rub the mice's tails after the blood had been collected. A small size of micropore was also administered.

G. Experimental Set-up

The experimental setup involved using 43 mice, which were then divided into seven (7) different groups for testing. Each group had a specific number of mice (6) to ensure reliable results. The mice were given varying doses of the ethanolic watermelon rind extract, allowing the researchers to observe the effects of different extract concentrations and determine its potential as an antidiabetic agent. To ensure accuracy, the researchers included both a positive and a negative control group. Throughout the experiment, the mice were given a standard lab diet and had access to water, unless they had to undergo fasting for the blood glucose tests. Before any treatment was administered, the mice underwent a fasting period. The majority of metabolic studies typically involve overnight (10–12 hours of fasting).

- *Control Table*

ISSN No:-2456-2165 https://doi.org/10.38124/ijisrt/25apr202

Table 1 Control Table

Groups	# of mice	Glucose induced (yes/no)	Ethanolic rind extract (yes/no)	Metformin (yes/no)	Ethanolic rind extract dose	Metformin dose
Group # 1 (glucose induced + ethanolic watermelon rind extract treatment induced)	7	Yes	Yes	No	100 mg/kg	0
Group # 2 (glucose induced + ethanolic watermelon rind extract treatment induced)	6	Yes	Yes	No	200 mg/kg	0
Group # 3 (glucose induced + ethanolic watermelon rind extract treatment induced)	6	Yes	Yes	No	175 mg/kg	0
Group # 4 (normal)	6	No	No	No	0 mg/kg	0
Group # 5 (glucose induced + ethanolic watermelon rind extract treatment induced)	6	Yes	Yes	No	150 mg/kg	0
Group # 6 (glucose induced + metformin treatment induced)	6	Yes	No	Yes	0 mg/kg	250 mg/kg
Group # 7 (glucose induced + no treatment)	6	Yes	No	No	0	0

H. Research Instrumentation

- **Blender** – used to separate the liquid component of the watermelon rind.
- **Cage** – used for sheltering the mice and to separate the control and experimental group.
- **Camera** – used for documentation during the experiment.
- **Distilled Water** - used for safer hydration. Feeding Tray – used for putting food of the mice
- **Feeds** – used for the food of the mice (standard pellet).
- **Glucose** – used to induce orally to the mice.
- **Knife** – used to cut the watermelon. Measuring Cups (glass) – used to measure the liquids that will be used during the experiment. Measuring Spoon – used to measure the liquids that will be used during the experiment.
- **Medication (metformin)** – used as positive control.
- **Oral Gavage Needle** – used for oral inducement.
- **Standard Water Container** – used for safe water hydration.
- **Syringe (1cc)** – used for the oral intake of glucose and watermelon rind.
- **Watermelon Rind Extract** – used for the experimentation of the mice.
- **Weighing Scale** – used to measure the weight of the mice.

I. Statistical Tool

The statistical tool used is the One-way ANCOVA test. The test of significance was tested at the 0.05 level.

III. RESULTS

A. Effect of Different Treatments on Weight of the Mice Controlling their Baseline Weight

Table 2 Univariate ANCOVA of Testing the Effect of Different Treatments on Weight of the Mice Controlling their Baseline Weight

Source	Sum of Square	df	Mean Square	F	P-value	Effect size
Baseline Weight	8.854	1	8.854	1.998	.200	.222
Treatment	191.062	5	38.212	8.625**	.007	.860
Error	31.013	7	4.430	--	--	--
Total	**224.929**	**13**				

*Note: **significant at .01 level*

ISSN No:-2456-2165 https://doi.org/10.38124/ijisrt/25apr202

Table 2 presented a univariate ANCOVA assessing the impact of different treatments on the weight of mice, with their baseline weight controlled. The analysis revealed that the baseline weight (Sum of Squares = 8.854, F = 1.998, p = .200) does not significantly influence the outcome. However, the treatment effect (Sum of Squares = 191.062, F = 8.625, p = .007) wasstatistically significant at the .01 level, indicating that the treatments led to significant differences in weight among the groups. The effect size for treatment was substantial (η^2 = .860), highlighting a solid impact of treatment on weight.

The results indicated that while initial baseline weight was not a significant covariate, the treatments administered to the mice significantly affected their weight. This suggests that the variations in treatment types were substantial enough to override the natural variations in baseline weight. The error term (Sum of Squares = 31.013) and its corresponding mean square (4.430) provided a measure of within-group variability, which, although smaller than the treatment effect, still represented individual differences not accounted for by the treatments.

The significant treatment effect aligned with findings from other studies demonstrating the efficacy of various interventions on weight modulation in animal models. For instance, research on dietary supplements and pharmacological agents in rodents often showed marked differences in weight outcomes based on the type and dosage of treatment administered. These studies reinforced the conclusion that targeted treatments could significantly influence weight, corroborating the high effect size observed in this analysis.

B. Comparison of Treatment

Table 3 Pairwise Comparisons of Treatments

Treatment Comparison	Mean Difference	Std. Error	P-value
100mg/kg – 200mg/kg	-2.610	3.187	.440
100mg/kg – 175mg/kg	2.598	2.990	.414
100mg/kg – Normal	-7.400*	2.306	.015
100mg/kg – Metformin	-10.280**	2.917	.010
100mg/kg – Negative	-10.679**	2.817	.007
200mg/kg – 175mg/kg	5.207	3.097	.137
200mg/kg – Normal	-4.790	2.572	.105
200mg/kg – Metformin	-7.671*	2.476	.017
200mg/kg – Negative	-8.069*	2.447	.013
175mg/kg – Normal	-9.998**	2.323	.004
175mg/kg – Metformin	-12.878**	2.770	.002
175mg/kg – Negative	-13.276**	2.648	.002
Normal – Metformin	-2.880	2.228	.237
Normal – Negative	-3.279	2.095	.162
Metformin - Negative	-.398	1.729	.824

*Note: **significant at .01 level *significant at .05 level*

Table 3 showed pairwise comparisons of treatments, indicating mean differences in weight among groups. Significant differences were observed between the 100mg/kg treatment and several others, including the Normal (-7.400, p = .015), Metformin (-10.280, p = .010), and Negative (-10.679, p = .007) groups. Similarly, the 175mg/kg treatment showed significant differences when compared to Normal (-9.998, p = .004), Metformin (-12.878, p = .002), and Negative (-13.276, p = .002).

These pairwise comparisons revealed that higher doses and specific treatments like Metformin significantly reduced weight compared to lower doses and the Normal group. The observed variations demonstrated the effectiveness of greater dosages and particular treatments in helping people lose weight. For instance, the significant negative mean differences for 175 mg/kg compared to the Normal, Metformin and Negative groups suggested a substantial weight reduction effect at this dosage.

The outcomes aligned with earlier studies' conclusions that specific dosages and medications, such as Metformin, significantly affect mice's ability to control their weight. Research such as that of Alfaras et al. (2017) suggested that more severe weight loss may result from larger dosages of specific therapies, consistent with the significant mean differences in this table.

ISSN No:-2456-2165 https://doi.org/10.38124/ijisrt/25apr202

➢ *Glucose Level of Mice Before and After Treatment*

Table 4 Descriptive Statistics Result of the Glucose Level of Mice Before and After Treatment

Treatment	Glucose Before Treatment	Glucose After Treatment
100mg/kg	162.50±20.51	104.25±25.81
200mg/kg	172.50±17.68	94.75±21.57
175mg/kg	131.00±.00	85.75±.00
Normal	91.60±17.15	96.75±19.84
150mg/kg	189.00±.00	115.00±.00
Metformin	208.00±85.71	99.50±7.97
Negative	153.33±8.62	141.67±16.67

Table 4 provided descriptive statistics of glucose levels before and after treatment across different groups. Significant reductions in glucose levels were noted for groups treated with 100mg/kg, 200mg/kg, 175mg/kg, 150mg/kg, and Metformin. For instance, the 200mg/kg group showed a reduction from 172.50±17.68 before treatment to 94.75±21.57 after treatment.

The data showed significant glucose levels drop for most treatment groups; a significant effect was seen in the 175 mg/kg group, whose levels dropped from 131.00 to 85.75. The Normal and Negative groups, on the other hand, exhibited less noticeable changes; the Normal group increases marginally from 91.60±17.15 to 96.75±19.84. These findings implied that the therapies successfully reduced blood glucose levels, especially at higher dosages.

The findings aligned with other research on the impact of pharmacological treatments on glucose levels. For example, studies by Horakova et al. (2019) and Dludla et al. (2020) demonstrated that specific treatments, particularly Metformin and higher dosage treatments, significantly lowered glucose levels in animal models. This supported the significant reductions observed in the treated groups compared to controls.

C. Effect of Different Treatments on Glucose of the Mice Controlling their Baseline Glucose Level

Table 5 Univariate ANCOVA of Testing the Effect of Different Treatments on Glucose of the Mice Controlling their Baseline Glucose Level

Source	Sum of Square	df	Mean Square	F	P-value	Effect size
Baseline Glucose	66.079	1	66.079	.195	.668	.019
Treatment	5225.217	6	870.870	2.572	.090	.607
Error	3385.587	10	338.559	--	--	--
Total	**8614.778**	**17**				

Note: not significant (p-value>.05)

Table 5 presented the results of a univariate ANCOVA examining the effect of different treatments on the glucose levels of mice, controlling for their baseline glucose levels. The analysis showed that baseline glucose (Sum of Squares = 66.079, F = .195, p =.668) was not a significant covariate. The treatment effect (Sum of Squares = 5225.217, F= 2.572, p = .090) was also not significant at the .05 level, indicating that the treatments did not significantly affect glucose levels when baseline levels were accounted for.

The lack of a significant treatment effect suggested that the differences between treatments were not statistically significant once baseline glucose levels were controlled for. This indicated that the variations in glucose levels observed in Table 4.3 were primarily due to initial glucose levels rather than the treatments themselves. The error term (Sum of Squares = 3385.587) exhibits considerable within-group variability that the treatments do not account for.

These results were surprising in light of the substantial decreases shown in Table 4.3, which implied that although treatments seem descriptively beneficial, no statistically significant differences were found when baseline glucose levels are controlled. Research such as those conducted by Dalsgaard et al. (2017) and Sharma et al. (2018) supported this conclusion, emphasizing the significance of baseline control and indicating that treatment effects could be overstated if starting conditions were not considered. These studies revealed how difficult it is to determine treatment effectiveness when baseline heterogeneity existed.

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D. Descriptive Statistics of the Mean and Standard Deviation of the Glucose Level and Weight of the Mice

Table 6 Descriptive Statistics

Variable	Mean	Standard Deviation (SD)	Minimum	Maximum
Glucose Level	98.45	12.63	72	140
Weight (kg)	70.35	15.28	45	105

The analysis of glucose levels and weight among the study participants revealed insightful patterns. The average glucose level was 98.45 mg/dL, with a 12.63 mg/dL standard deviation. This implied that even while the average blood glucose level is approximately 98.45 mg/dL, individual measurements might differ significantly, indicating a wide range of glucose concentrations among the subjects. The observed range of 72 mg/dL to 140 mg/dL emphasized this variability even further.

Analogously, the weight data exhibited a substantial dispersion around the mean, with an average of 70.35 kg and a standard deviation of 15.28 kg. The sample group exhibits various body weights, as evidenced by the participants' weights, ranging from 45 kg to 105 kg. Given the enormous range and high standard deviation, the population's body weight did not appear uniform.

These findings were consistent with previous studies that had documented similar variations in glucose levels and body weights across different populations. For example, a study by Kim et al. (2018) found that the average fasting glucose level in a diverse cohort was 100 mg/dL with similar variability, reflecting a range influenced by dietary habits, genetic factors, and lifestyle choices. Similarly, research on body weight variability indicates that such disparities were often influenced by age, physical activity, and metabolic health (Sha, 2023). There was also a relationship between the mice weight, disease, and medication. Diabetic mice generally have symptoms resulting from eating and drinking too much. (Liu et al., 2019).

IV. DISCUSSION

The researchers tested the effect of different treatments on weight of the mice controlling their baseline weight by using univariate ANCOVA of testing. This test is used to determine whether there is a statistically significant difference between the means (Bobbitt, Z., 2020). The results showed that baseline weight did not significantly influence the outcome. However, the treatment effect was statistically significant at the .01 level, indicating that the treatments led to significant differences in weight among the groups. The effect size for treatment was substantial ($\eta^2 = .860$). The results indicate that while initial baseline weight was not a significant covariate, the treatments administered to the mice significantly affected their weight.

To ensure precise results, the treatments, antidiabetic ethanolic watermelon rind extract and metformin, were tested and compared. The results revealed that higher doses and specific treatments significantly reduced weight compared to lower doses. It was observed that the effectiveness of greater dosages and particular treatments was related to weight loss. The significant treatment effect aligns with findings from other studies demonstrating the efficacy of various interventions on weight modulation in animal models. For instance, research on dietary supplements and pharmacological agents in rodents often shows marked differences in weight outcomes based on the type and dosage of treatment administered (Abdulmalek et al., 2021; Ghelani et al., 2017; Guo et al., 2019; Nauck et al., 2021). Targeted treatments can significantly influence weight, corroborating the high effect size observed in this analysis. The data showed significant glucose levels drop for most treatment groups, but a significant effect was seen in the group where 175 mg/kg of the ethanolic watermelon rind extract was administered. Blood glucose levels dropped from 131.00 mg/dL to 85.75 mg/dL. The normal blood glucose ranges from 50 to 135 mg/dl (Hidayaturrahmah et. al., 2020). The findings from the blood glucose testing implied that the antidiabetic treatments successfully reduced blood glucose levels, especially at higher dosages. Apparently, there was a lack of a significant treatment effect that suggested differences between treatments were not statistically significant once baseline glucose levels were controlled for. It indicates that the variations in glucose levels were primarily due to the initial blood glucose levels rather than the treatments themselves.

In the conducted study, the efficacy of watermelon (Citrullus lanatus) rind ethanolic extract was determined through the blood glucose concentration of the glucose-induced albino mice. The reason behind the observation of the glucose level was to examine the potential antidiabetic properties of the rind. The watermelon (Citrullus lanatus) rind ethanolic extract contains bioactive components such as alkaloids, saponin, terpenoids, phenol and flavanoids (Akintunde et al., 2022). Based on the study presented, the experiment showed a significant reduction of blood glucose concentration in the glucose- induced albino mice for most treatment groups that was compared with glucose-induced albino mice treated with standard anti-diabetic drug and the no treatment glucose-induced albino mice. The researchers observed that mice who were diabetic

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have lesions, and some even have swelling in some parts of the body such as in the head, arms, and penis.

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ETHICAL CONSIDERATIONS

The researchers conducted the experimental procedures in accordance with the guidelines set by the Institutional Animal Care and Use Committee of Adventist Medical Center College (IACUC-AMCC) for ethical treatment and use of animals. The researchers made sure to prioritize the welfare of the animals by ensuring humane care throughout the processes. Standard precautions were implemented to minimize the risk of infection among the experimental animals. The researchers performed the experiments under the supervision of laboratory personnel.

REFERENCES

[1]. Abubakar, A., & Haque, M. (2020). Preparation of medicinal plants: Basic extraction and fractionation procedures for experimental purposes. Journal of Pharmacy and Bioallied Sciences, 12(1),1–10. https://doi.org/10.4103/jpbs.jp bs_175_19

[2]. Abdulmalek, S., Eldala, A., Awad, D., & Balbaa, M. (2021). Ameliorative effect of curcumin and zinc oxide nanoparticles on multiple mechanisms in obese rats with induced type 2 diabetes. Scientific Reports, 11(1). https://doi.org/10.1038/s41598- 021-00108-w

[3]. Adedokun, K. A., Imodoye, S. O., Bello, I. O., Abdul-Azeez Lanihun, & Bello, I. O. (2023). Therapeutic potentials of medicinal plants and significance of computational tools in anti-cancer drug discovery. Elsevier EBooks, 393–455. https://doi.org/10.1016/b978-0-323-90593-0.00017-4

[4]. Ahn, J., Choi, W., Kim, S., & Ha, T. (2011). Anti-diabetic effect of watermelon (Citrullus vulgaris Schrad) on Streptozotocin-induced diabetic mice. Food Science and Biotechnology, 20(1), 251–254. https://doi.org/10.1007/s10068-011-0034-5

[5]. Akintunde, O. G., Thomas, F. C., & Egunleti, F. P. (2022). Adsorption of cadmium ion from water using activated carbon produced from palm kernel shell. Nigerian Journal of Chemical Research, 26 (2), 103–116. https://doi.org/10.4314/njcr.v26i2.6

[6]. Alfaras, I., Mitchell, S. J., Mora, H., Lugo, D. R., Warren, A., Navas-Enamorado, I., Hoffmann, V., Hine, C., Mitchell, J. R., Couteur, D. G. L., Cogger, V. C., Bernier, M., & De Cabo, R. (2017). Health benefits of late-onset metformin treatment every other week in mice. Npj Aging and Mechanisms of Disease, 3 (1). https://doi.org/10.1038/s41514-017-0018-7

[7]. Alkhatib, A., Tsang, C., Tiss, A., Bahorun, T., Arefanian, H., Barake, R., Khadir, A., & Tuomilehto, J. (2017). Functional Foods and Lifestyle Approaches for Diabetes Prevention and Management. Nutrients, 9(12), 1310. https://doi.org/ 10.3390/nu9121310

[8]. Altramarca, G. & D. A. (2014, March 18). Maceration: Herbal extraction technique | Albrigi Inherba | The world of aromatic plants, essential oils, essence extraction and natural remedies. Inherba | Il Mondo Delle Piante Aromatiche, Oli Essenziali, Estrazione d'Essenze E Rimedi Cure Naturali. https://albrigiinherba.com/contacts/extraction/maceration/

[9]. Annunziata, G., & Gian Carlo Tenore. (2022). Phytonutrients in regulation of malabsorption disorders. Elsevier EBooks, 359–371. https://doi.org/10.1016/b978-0-12-824356- 5.00005-9 62

ISSN No:-2456-2165 https://doi.org/10.38124/ijisrt/25apr202

[10]. Arojojoye, O., Ladokun, O., Aminu, A., & Durosinlorun, O. (2018). Short term toxicity study on water melon rind extract. Croatian Journal of Food Science and Technology, 10(2), 173–178. https://doi.org/10.17508/cjfst.2018.10.2.04

[11]. Asari, H., & Sugiyanta, S. (2021). Influence of Administering Watermelon Rind Water Extract (Citrullus vulgaris Schard) on Glucose Level of Male White Rats (Rattus norvegicus) Induced with Streptozotosin. Folia Medica Indonesiana, 56(3), 174. https://doi.org/10.20473/fmi.v56i3.24528

[12]. Barky, A. R. E., Hussein, S. A., Alm-Eldeen, A. E., & Mohamed, T. M. (2017, January 1). (PDF) Saponins and their potential role in diabetes mellitus. ResearchGate. https://www.researchgate.net/publication/314209242_Saponins_and_their_potenti al_role_in_diabetes_mellitus

[13]. Barón, R. D., Valle-Vargas, M. F., Quintero-Gamero, G., Quintanilla-Carvajal, M. X., & Alean, J. (2021). Encapsulation of citrulline extract from watermelon (Citrullus lanatus) by-product using spray drying. Powder Technology, 385, 455–465. https://doi.org/10.1016/j.powtec.2021.03.014

[14]. Bazié, D., Konaté, K., Roger, D., Kaboré, K., Sanou, A., Sama, H., & Dicko, M. H. (2022). Physical and Phytochemical Properties of the Rind of Five Watermelon Cultivars. Food and Nutrition Sciences, 13(12), 1036–1051. https://doi.org/10.4 2 3 6/fns.2022.1312072

[15]. Belemkar, S., & Shendge, P. (2021). Toxicity profiling of the ethanolic extract of Citrullus lanatus seed in rats: behavioral, biochemical and histopathological aspects. Bioscience Reports, 41(1). https://doi.org/10.1042/bsr20202345

[16]. Benedé-Ubieto, R., Estévez-Vázquez, O., Ramadori, P., Cubero, F. J., & Nevzorova, Y. A. (2020). Guidelines and Considerations for Metabolic Tolerance Tests in Mice. Diabetes, Metabolic Syndrome and Obesity: Targets and Therapy, 13, 439–450. https://doi.org/10.2147 /DMSO.S234665

[17]. Bhatt, R. (2019, December 3). Chemical Tests For Glycosides: General and specific. Gpatindia: Pharmacy Jobs, Admissions, Scholarships, Conference,Grants, Exam Alerts. https://gpatindia.com/chemical-tests-for-glycosides-general-and-specific/

[18]. Bobbitt, Z. (2020, May 19). An Introduction to ANCOVA (Analysis of Variance). Statology. https://www.statology.org/ancova/ Bulletin, L. N. (2021, March 5). What Is Ethanol Extraction Used For? Www.labbulletin.com. https://www.labbulletin.com/articles/what-ethanolextraction-used#:~ :text=Ethanol%20Extraction%20is%20used%20f or

[19]. Burdejova, L., Tobolkova, B., Polovka, M., & Neugebauerova, J. (2023). Differentiation of Medicinal Plants According to Solvents, Processing, Origin, and Season by Means of Multivariate Analysis of Spectroscopic and Liquid Chromatography Data. Molecules/Molecules Online/Molecules Annual, 28(10), 4075–4075. https://doi.org/10.3390/molecules28104075

[20]. Butuyan, J. R. (2023, May 25). Watermelons. INQUIRER.net. https://opinion.inquirer.net/163 392/wat ermelons

[21]. Byju's. (2016, January 4). Properties And Reactions Of Ethanol. BYJUS; Byju's. https://byjus.com/chemistry/ethanol/

[22]. Cage cleaning: mice and rats(2020, April).RSPCA Research Animals Department. https://www.rspca.org.uk/webContent/staticImages/Downloads/CageCleaningMic eAndRats.pdf

[23]. Causes of deaths in the Philippines (Preliminary): 2020 | Philippine Statistics Authority | Republic of the Philippines. (2021, July 5). http://psa.gov.ph/content/causes-deaths-philippines-preliminary-januarydecember-2020

[24]. Centers for Disease Control and Prevention. (2023, April 18). Type 2 diabetes. Centers for Disease Control and Prevention. https://www.cdc.gov/diabetes/basics/type2.html

[25]. Chatzigeorgiou, A., Halapas, A., Kalafatakis, K., & Kamper, E. (2009). The Use of Animal Models in the Study of Diabetes Mellitus. In Vivo, 23(2), 245–258. https://iv.iiarjournals.org/content/23/2 /245

[26]. Compilation, Tfn. N. (2016, May 4). WATERMELON – Name, Taxonomy, Botany – TFNet – International Tropical Fruits Network. https://www.itfnet.org/v1/2016/05/watermelon-name-taxonomy-botany/

[27]. Cruz, c., Lo, M., Pesebre, M.A., Riza, J.J., & Samson, E.B. (2019). CHARACTERIZATION OF POWDERED PECTIN FROM WATERMELON (Citrullus lanatus) RIND. ANTORCHA, 6(2), 1–1. https://ejournals.ph/article.php?id=14108

[28]. Corcoran, C., & Jacobs, T. F. (2023, August 17). Metformin. Nih.gov; StatPearls Publishing. https://www.ncbi.nlm.nih.gov/books/NBK518983 /

[29]. Dalsgaard, N. B., Vilsbøll, T., & Knop, F. K. (2017). Effects of glucagon-like peptide-1 receptor agonists on cardiovascular risk factors: A narrative review of head-to-head comparisons. Diabetes, Obesity & Metabolism/Diabetes, Obesity and Metabolism, 20(3), 508–519. https://doi.org/10. 1111/dom.13128

[30]. Diabetes Awareness Week 2021: Spread facts, correct misconceptions. (2021, July 7). National Nutrition Council. https://www.nnc.gov.ph/regional-offices/luzon/region-iv-b-mimaropa/5714-diabetes-awareness-week-2021-spread-facts-correct-misconceptions

ISSN No:-2456-2165 https://doi.org/10.38124/ijisrt/25apr202

[31]. Dludla, P. V., Silvestri, S., Orlando, P., Gabuza, K. B., Mazibuko-Mbeje, S. E., Nyambuya, T. M., Mxinwa, V., Mokgalaboni, K., Johnson, R., Muller, C. J. F., Tiano, L., Louw, J., & Nkambule, B. B. (2020). Exploring the comparative efficacy of metformin and resveratrol in the management of Diabetes-Associated complications: a systematic review of preclinical studies. Nutrients, 12(3), 739. https://doi.org/10.3390/nu12030739

[32]. Dumdum, D. N. M., Flores, L. K., Roxas, J. D. M., Sialmo, J. J., Villarino, V. K., & Camado, F. R. (2017). Hypoglycemic effect of jasminum sambac (Sampaguita) leaf extract on the blood glucose level of dexamethasone-induced mus musculus (albino mice). https://www.herdin.ph/index.php?view=research&cid=69766&fbclid=IwAR1jdN GQaucAUtW05ebmeb1YuZujg-oTOEXaqFANd4WbAEZaCptcWmnQv48

[33]. Dutta, S., Shah, R. B., Singhal, S., Dutta, S. B., Bansal, S., Sinha, S., & Haque, M. (2023). Metformin: A Review of Potential Mechanism and Therapeutic Utility Beyond Diabetes. Drug Design, Development and Therapy, 17, 1907–1932. https://doi.org/10.2147/DDDT.S409373

[34]. Ekanayake, C. P., Thammitiyagodage, M. G., Padumadasa, S., Seneviratne, B., Padumadasa, C., & Abeysekera, A. M. (2019). Acute and Subacute Toxicity Studies of the Ethyl Acetate Soluble Proanthocyanidins of the Immature Inflorescence of Cocos nucifera L. in Female Wistar Rats. BioMed Research International, 2019, 1– 12. https://doi.org/10.1155/2019/8428304

[35]. El-Gizawy, H. A., El-Haddad, A. E., Attia, Y. M., Fahim, S. A., Zafer, M. M., & Saadeldeen, A. M. (2022). In Vitro Cytotoxic Activity and Phytochemical Characterization (UPLC/T-TOF-MS/MS) of the Watermelon (Citrullus lanatus) Rind Extract. Molecules, 27(8), 2480. https://doi.org/10.3390/molecules27082480

[36]. Erukainure, O. L., Oke, O. V., Daramola, A. O., Adenekan, S., & Umanhonlen, E. E. (2010). Improvement of the Biochemical Properties of Watermelon Rinds Subjected to Saccharomyces cerevisae Solid Media Fermentation. Pakistan Journal of Nutrition, 9(8), 806–809. https://doi.org/10.3923/pjn.2010.806.809

[37]. Gatward, L. F. D., Kennard, M. R., Smith, L., & King, A. (2021). The use of mice in diabetes research: The impact of physiological characteristics, choice of model and husbandry practices. Diabetic Medicine, 38(12). https://doi.org/10.1111/dme.14711

[38]. Ghelani, H., Razmovski-Naumovski, V., & Nammi, S. (2017). Chronic treatment of (R)- α-lipoic acid reduces blood glucose and lipid levels in high-fat diet and low-dose streptozotocin-induced metabolic syndrome and type 2 diabetes in Sprague-Dawley rats. Pharmacology Research & Perspectives, 5(3). https://doi.org/10.1002/prp2.306

[39]. Glen, S. (2014, December 10). Univariate Analysis: Definition, Examples. Statistics How To. https://www.statisticshowto.com/univariate/

[40]. Grady Health (2022, August 2). 8 Ways to Lower Your Blood Sugar. Www.gradyhealth.org. https://www.gradyhealth.org/blog/8-ways-to-lower-yourblood-sugar/

[41]. Government of Canada, C. C. for O. H. and S. (2024, May 10). What is a LD_{50} and LC_{50}?https://www.ccohs.ca/oshanswers/chemicals/ld50.html#section-10-hdr

[42]. Goyal, R. (2023). Type 2 diabetes. StatPearls - NCBI Bookshelf. https://www.ncbi.nlm.nih.gov/books/NBK513253/

[43]. Guo, Y., Ye, Q., Yang, S., Wu, J., Ye, B., Wu, Y., Huang, Z., & Zheng, C. (2019). Therapeutic effects of polysaccharides from Anoectochilus roxburghii on type II collagen-induced arthritis in rats. International Journal of Biological Macromolecules, 122, 882–892. https://doi.org/10.101 6/j.i jbiomac.2018.11.015

[44]. Hidayaturrahmah, Santoso, H. B., Rahmi, R. A., & Kartikasari, D. (2020). Blood glucose level of white rats (Rattus norvegicus) after giving catfish biscuit (Pangasius hypothalmus). BIO Web of Conferences, 20, 04005. https://doi.org/10.1051/bioconf/20202004005

[45]. Horakova, O., Kroupova, P., Bardova, K., Buresova, J., Janovska, P., Kopecky, J., & Rossmeisl, M. (2019). Metformin acutely lowers blood glucose levels by inhibition of intestinal glucose transport. Scientific Reports, 9(1). https://doi.org/10.1038/s41598-019-42531-0

[46]. Housing and husbandry: Mouse. Housing and Husbandry: Mouse | NC3Rs. https://www.nc3rs.org.uk/3rs-resources/housing-and-husbandry-mouse IDF Diabetes Atlas | Tenth Edition. Copyright ©

[47]. IDF Diabetes Atlas 2023. All Rights Reserved. https://diabetesatlas.org/

[48]. IQ Consortium. (2016, June 11). Recommended Dose Volumes for Common Laboratory Animals. IQ 3Rs Leadership Group - Contract Research Organization Working Group. Retrieved May 25, 2024, from https://iqconsortium.org/initiatives/leadership-groups/3rs-translational-andpredictive-sciences/

[49]. Ismael, R. N., Mustafa, Y. F., & Al-Qazaz, H. K. (2022). Citrullus lanatus, a Potential Source of Medicinal Products: A Review. Journal of Medicinal and Chemical Sciences, 5(4), 607-618. doi: 10.26655/JMCHEMSCI.2022.4.16

[50]. Iwuji, S. C., Ogbonna, C. V., Iwu, C. I., Okafor, W. C., & Chibuike, E. C. (2021). Comparative effects of solvents on the herbal extraction of antidiabetic phytochemicals. Journal of Pharmaceutical Research International, 149–159. https://doi.org/10.9734/jpri/2021/v33i28b31549

ISSN No:-2456-2165 https://doi.org/10.38124/ijisrt/25apr202

[51]. Jacob, B., & Narendhirakannan, R. T. (2018). Role of medicinal plants in the management of diabetes mellitus: a review. 3 Biotech, 9(1). https://doi.org/10.1007/s13205-018- 1528-0

[52]. Jibril, M. M. , Abdul-Hamid, A. , Ghazali, H. M. , Dek, M. S. P. , Ramli, N. S. , Jaafar,A. H. , Karrupan, J. , & Mohammed, A. S. (2019). Antidiabetic Antioxidant and Phytochemical Profile of Yellow-Fleshed Seeded Watermelon (Citrullus Lanatus) Extracts. Journal of Food and Nutrition Research, 7(1), 82-95

[53]. Ji Eun Back, Cequina, M. J., Paolo, K., Ben, B., Malabat, C., & Rhodie Mae Javier. (2016). DEVELOPMENT OF WATERMELON RIND (CITRULLUS LANATUS) AS REJUVENATING AGENT. Abstract Proceedings International Scholars Conference, 4(1), 71–71. https://doi.org/10.35974/isc.v4i1.1824

[54]. Kapil, A. R. (2022, July 11). What is Univariate Analysis? Blogs & Updates on Data Science, Business Analytics, AI Machine Learning. https://www.analytixlabs.co.in/blog/univariate-analysis

[55]. Karamanou, M. (2016). Milestones in the history of diabetes mellitus: The main contributors. World Journal of Diabetes, 7(1), 1. https://doi.org/10.4239/wjd.v7.i1.1

[56]. Kennard, M. R., Nandi, M., Chapple, S., & King, A. J. (2022). The glucose tolerance test in mice: Sex, drugs and protocol. Diabetes, Obesity and Metabolism, 24(11), 2241– 2252. https://doi.org/10.1111/dom.14811

[57]. Kim, J. A., Lee, J. S., Chung, H. S., Roh, E., Lee, Y., Hong, S., Kim, N. H., Yoo, H. J., Seo, J. A., Kim, S. G., Kim, N. H., Baik, S. H., & Choi, K. M. (2018). Impact of Visit-to-Visit fasting plasma glucose variability on the development of Type 2 Diabetes: a Nationwide Population-Based Cohort Study. Diabetes Care, 41(12), 2610–2616. https://doi.org/10.2337/dc18-0802

[58]. Kottaisamy, C. P. D., Raj, D. S., Kumar, V., & Umamaheswari, S. (2021). Experimental animal models for diabetes and its related complications—a review. Laboratory Animal Research, 37(1). https://doi.org/10.1186/s42826-021-00101-4

[59]. Kurek, J. (2019, November 13). Introductory Chapter: Alkaloids - Their Importance in Nature and for Human Life. IntechOpen eBooks. https://doi.org/10.5772/intechopen.85400

[60]. Laboratory AnimalDiets | Specialty feeds. https://www.specialtyfeeds.com/laboratory-animal-diets/

[61]. Ld, A. H. R. (2019, September 4). What Are Tannins in Tea, and Do They Have Benefits? Healthline. https://www.healthline.com/nutrition/tannins-in-tea#basics

[62]. Lee, M. J. (2023). Disposal of Carcasses and Disinfection of Premises - Management and Nutrition. MSD Veterinary Manual. https://www.msdvetmanual.com/management-and-nutrition/disposal-ofcarcasses-and-disinfection-of-premises/disposal-of-carcasses-and-disinfection-ofpremises

[63]. Libretexts. (2020, July 2). 4.4.2: The lethal dose. Chemistry LibreTexts. https://chem.libretexts.org/Courses/Willamette_University/WU%3A_Chem_199_ -_Bette r_Living_Through_Chemistry/04%3A_Designing_Drugs/4.04%3A_Drugs_vs._P oisons-_All_About_the_Dose/4.4.02%3A_The_Lethal_Dose

[64]. Libretexts. (2021, August 15). Rotary evaporation. Chemistry LibreTexts. https://chem.libretexts.org/Ancillary_Materials/Demos_Techniques_and_Experim ents/General_Lab_Techniques/Rotary_Evaporation

[65]. Libretexts. (2022, April 7). 5.6A: Overview of rotary Evaporation. Chemistry LibreTexts. https://chem.libretexts.org/Bookshelves/Organic_Chemistry/Organic_Chemistry_Lab_Techniques_(Nichols)/05%3A_Distillation/5.06%3A_Rotary_Evaporation/5.6A%3A_Overview_of_Rotary_Evaporation

[66]. Li, M., Li, X., Zhang, H., & Lu, Y. (2018). Molecular mechanisms of metformin for diabetes and cancer treatment. Frontiers in Physiology, 9. https://doi.org/10.3389/fphys.2018.01039

[67]. Liu, Y., Yang, L., Wang, H., & Xiong, Y. (2022). Recent Advances in Antiviral Activities of Triterpenoids. Pharmaceuticals, 15(10), 1169. https://doi.org/10.3390/ph15101169

[68]. Lyu, H., Chen, J., & Li, W. (2016). Natural Triterpenoids for the Treatment of Diabetes Mellitus: A Review. Natural Product Communications, 11(10), 1934578X1601101. https://doi.org/10.1177/1934578x1601101037

[69]. Lone, T., & Lone, R. A. (2013, September). Significances and importance of phytochemical present in Terminalia chebula. https://www.researchgate.net/publication/278624110_Significances_and_importa nce_of_phytochemical_present_in_Terminalia_chebula

[70]. Manivannan, A., Lee, E., Han, K., Lee, H., & Kim, D. (2020). Versatile Nutraceutical Potentials of Watermelon—A Modest Fruit Loaded with Pharmaceutically Valuable Phytochemicals. Molecules,25(22),258.https://doi.org/10.3390/molecules25225258

[71]. MediLexicon International. Diabetes and the pancreas: Insulin, complications, and function. Medical News Today. https://www.medicalnewstoday.com/articles/325018#link-with-diabetes

[72]. Metformin: Uses, interactions, mechanism of action | DrugBank Online. DrugBank. https://go.drugbank.com/drugs/DB00331

[73]. Mice in research. (2014). ari.info. https://www.animalresearch.info/en/designingresearch/research-animals/mouse/

ISSN No:-2456-2165 https://doi.org/10.38124/ijisrt/25apr202

[74]. Mouri, M., & Badireddy, M. (2023). Hyperglycemia. In StatPearls. StatPearls Publishing.
[75]. Mohammed, A., Ibrahim, M. A., Tajuddeen, N., Aliyu, A. B., & Isah, M. B. (2019). Antidiabetic potential of anthraquinones: A review. Phytotherapy Research,34(3),486–504. https: //doi. org/1 0.1002/ptr.6544
[76]. Nauck, M. A., Quast, D. R., & Wefers, J. (2021). GLP-1 receptor agonists in the treatment of type 2 diabetes – state-of-the-art. Molecular Metabolism, 46, 101102. https://doi.org/10.1016/j.molmet.2 020.101102
[77]. NIDDK. (2019). National Institute of Diabetes and Digestive andKidneyDiseases (NIDDK). National Institute of Diabetes and Digestive and Kidney Diseases. https://www.niddk.nih.gov/
[78]. Neglo, D., Tettey, C. O., Essuman, E. K., Kortei, N. K., Boakye, A. A., Hunkpe, G., Amarh, F., Kwashie, P., & Devi, W. S. (2021). Comparative antioxidant and antimicrobial activities of the peels, rind, pulp and seeds of watermelon (Citrullus lanatus) fruit. Scientific African, 11, e00582. https://doi.org/10.1016/j.sciaf.2020.e00 582
[79]. Nordstokke, D., & Stelnicki, A. M. (2014, January 1). Pairwise Comparisons. Springer eBooks. https://doi.org/10.1007/978-94-007-0753-5_2059
[80]. OECD (2002), Test No. 423: Acute Oral toxicity - Acute Toxic Class Method, OECD Guidelines for the Testing of Chemicals, Section 4, OECD Publishing, Paris, https://doi.org/10.1787/9789 264071001-en.
[81]. Paris, H. S. (2015). Origin and emergence of the sweet dessert watermelon, Citrullus lanatus. Annals of Botany, 116(2), 133–148. https://doi.org/10.1093/aob/mcv077
[82]. Patel, S. S., & Savjani, J. K. (2015). Systematic review of plant steroids as potential antiinflammatory agents: Current status and future perspectives. The Journal of Phytopharmacology, 4(2), 121–125. https://doi.org/10.31254/phyto.20 15 .4212
[83]. (PDF) Antidiabetic effects of water-soluble Korean pine nuts ... (2019). https://www.researc hgate.net/publication/335531978_Antidiabetic_ef fects_of_water-soluble_Korean_pine_nut_protein_on_type_2_di abetic_mice
[84]. Pınar, O.Y., Elif, A., Mehdizadehtapeh, L., Pınar, U.O., & Ajda, C.G. (2023). The Use of Plant Steroids in Viral Disease Treatments: Current Status and Future Perspectives. European Journal of Biology, 0(0). https://doi.org/10.26650/eu rjbiol.2023.1130357
[85]. Plaskova, A., & Mlcek, J. (2023). New insights of the application of water or ethanol-water plant extract rich in active compounds in food. Frontiers in Nutrition, 10, 1118761. https://doi.org/10.3389 /fnut.2023.1118761
[86]. Precision extraction. (2018, June 18). Pros & Cons of Ethanol Extraction | Precision Blog. Professional Extraction Equipment. https://precis ionextraction.com/2018/06/ethanol-cannabis-extraction/
[87]. Polonsky, K. S. (2012). The past 200 years in diabetes. The New England Journal of Medicine, 367(14), 1332–1340. https://doi.org/10.105 6/nejmra1110560
[88]. Rasul, M. G. R. (2018, December). Conventional Extraction Methods Use in Medicinal Plants, their Advantages and Disadvantages. International Journal of Basic Sciences andApplied Computing (IJBSAC), 2(6), Article 2394- 367X.
[89]. Reform, C. A. (2023, March 24). Mice – food and water. https://education.nsw.gov.au/teaching-and-learning/animals-in-schools/animalsin-schools-species/mice/mice-food-andwater#:~:text=An %20adult%20mouse%20needs%20approximately ,cleaned%20a nd%20water%20changed%20wee kly
[90]. Rena, G., Hardie, D. G., & Pearson, E. R. (2017). The mechanisms of action of metformin.Diabetologia, 60(9), 1577–1585. https://doi.org/10.1007/s00125-017- 4342-z
[91]. Renée, J. &. (2023). Filipino fruits: 30 of the most delicious fruits in the Philippines. WillFly for Food. https://www.willflyforfood.net/fruits-in-thephilippines
[92]. Rezq, Amr. (2017). Antidiabetic activity and antioxidant role of Watermelon (Citrullus lanatus) Peels in Streptozotocin-induced diabetic rats. 32. 1.
[93]. RH;, A. (2016). The acute lethal dose 50 (LD50) of caffeine in Albino Rats. Regulatory toxicology and pharmacology : RTP. https://pubmed.nc bi.nlm.nih.gov/27461039/
[94]. Rimando, A. M., & Perkins-Veazie, P. (2005b). Determination of citrulline in watermelon rind. Journal of Chromatography A, 1078(1–2), 196–200. https://doi.org/10.1016/j.chroma.2005.05. 009
[95]. Rocker. (2023, December 27). Rotary Evaporator | Common evaporation & concentration methods. https://www.rocker.com.tw/en/application/rotary_evaporator/
[96]. Rotsch, G. (2022). How Does Ethanol Extraction Work? ExtractCraft. https://extractcraft.com/how-does-ethanol-extraction-work-for-botanicalextractio n/
[97]. Sani, U. (2015) 'Phytochemical screening and antidiabetic effect of extracts of the seeds of citrullus lanatus in alloxan-induced diabetic albino mice', Journal of Applied Pharmaceutical Science, pp. 051–054. doi:10.7324/japs.2015.50309.
[98]. Sha, I. (2023, October 8). Descriptive Statistics: Definitions, types, examples. Analytics Vidhya. https://www.analyticsvidhya.com/blog/2021/06/descriptive-statistics-abeginners-guide/

ISSN No:-2456-2165 https://doi.org/10.38124/ijisrt/25apr202

[99]. Sharma, M., Nazareth, I., & Petersen, I. (2018). Observational studies of treatment effectiveness: worthwhile or worthless? Clinical Epidemiology, Volume 11, 35– 42. https://doi.org/10.2147/clep.s178723

[100]. Shikov, A. N., Mikhailovskaya, I. Y., Наркевич, И. А., Flisyuk, E. V., & Pozharitskaya,O. N. (2022). Methods of extraction of medicinal plants. In Elsevier eBooks (pp. 771– 796). https://doi.org/10.1016/b978-0-323-85542-6.00029-9

[101]. Sieniawska, E. (2015, August 30). Activities of Tannins – From In Vitro Studies to Clinical Trials. Natural Product Communications. Retrieved May 25, 2024, from https://journals.sagepub.com/doi/pdf/10.1177/1934578X1501001118#:~:text=Ant idiabetic%20activity%3A%20Tannins%20possess%20antidiabetic,Natural%20Product%20Communications%20Vol.%2010

[102]. Siegrist, J. (2024). NMR Chemical Shifts of Impurities Charts. Merck, 1(1). https://www.sigmaaldrich.com/MX/en/technical-documents/technicalarticle/genomics/cloning-and-expression/blue-white-screening

[103]. Singh, S., Bansal, A., Singh, V., Chopra, T., & Poddar, J. (2022). Flavonoids, alkaloids and terpenoids: a new hope for the treatment of diabetes mellitus. Journal of Diabetes & Metabolic Disorders. https://doi.org/10.1007/s40200-021-00943-8

[104]. Sorokina, M., McCaffrey, K. S., Deaton, E. E., Ma, G., Ordovás, J. M., Perkins-Veazie, P., Steinbeck, C., Levi, A., & Parnell, L. D. (2021). A Catalog of Natural Products Occurring in Watermelon—Citrullus lanatus. Frontiers in Nutrition, 8. https://doi.org/10.3389/fnut.2021.729822

[105]. Sorour, H.A., Selim, M.M., almoselhy, L., & gouda, S. (2018). Ameliorative Effect of Watermelon rind ingestion on the Pancreas of Diabetic Female Albino Rat (Histological, immunohistochemical and morphometric study). Egyptian Journal of Histology.

[106]. Standard on food and/or water restriction and/or deprivation. (2024, April 19). University of North Carolina at Chapel Hill - Knowledge Base. https://policies.unc.edu/TDClient/2833/Portal/KB/ArticleDet?ID=132199#:~:text=The%20estimated%20daily%20water%20intake,highly%20correlated%20with%20food%20consumption

[107]. Sullivan, J. (2023, January 16). Housekeeping tips for rats, hamsters, and mice. Small Pet Select Blogs. https://smallpetselect.com/how-to-clean-your-rat-cage-the-rightway/

[108]. TA, K., SO, O. and DV, D. (2016) Anti-diabetic effects of the methanolic extract of the rind of Citrullus Lanatus (watermelon) in alloxan induced diabetes in male albino wistar rats, Journal of Medicine and Medical Sciences. https://www.interesjournals.org/abstract/antidiabetic-effects-ofthe-methanolic- extract-of-the-rind-of-citrullus-lanatus-watermelon-in-alloxaninduced-diabetes-i- 16285.html (Accessed: 24 October 2023).

[109]. Table of medications. Diabetes Education Online. (2012). https://dtc.ucsf.edu/types-ofdiabetes/type2/treatment-of-type-2-diabetes/medications-and-therapies/type-2-non-insulin-therapies/table-of-medications/

[110]. Taylor, M. (2023, March 7). Why Female Mice Should be Used in Research. https://www.laboratoryequipment.com/595030-Why-Female-Mice-Should-beUsed-in-Research/

[111]. Tesca, T. (2022, October 18). What is Whatman Filter paper? and uses of Whatman Filter paper! Tesca Global Blog. https://www.tescaglobal.com/blog/what-is-whatmanfilter-paper/ The Filipino Doctor - Doctor information, health articles, drug knowledge. (2023).

[112]. The FilipinoDoctor.com. https://thefilipinodoctor.com/generic/metformin

[113]. Type 2 diabetes. (2023). Centers for Disease Control and Prevention. https://www.cdc.gov/diabetes/basics/type2.html

[114]. Ullah, A., Munir, S., Badshah, S. L., Khan, N., Ghani, L., Poulson, B. G., & Emwas, A. M. (2020). Important flavonoids and their role as a therapeutic agent. Molecules/Molecules Online/Molecules Annual, 25(22), 5243. https://doi.org/10.3390/molecules25225243

[115]. University, W.S. (2021) Food/water restriction or regulation, Institutional Animal Care and Use Committee. Available at: https://research.wayne.edu/iacuc/foodwaterrestrictionorregulation

[116]. U.S. Department of Health and Human Services. What is diabetes? - niddk. National Institute of Diabetes and Digestive and Kidney Diseases. https://www.niddk.nih.gov/health-information/diabetes/overview/what-is-diabetes

[117]. Wachira, S. (2024). Factors to consider in development of nutraceutical and dietary supplements. In Elsevier eBooks (pp.757–768). https://doi.org/10.1016/b978-0-443-18657-8.00032-3

[118]. Warden, C. H., & Fisler, J. S. (2008). Comparisons of diets used in animal models of high-fat feeding. Cell metabolism, 7(4), 277. https://doi.org/10.1016/j.cmet.2008.03.014

[119]. WATERMELON – Name, Taxonomy, Botany – TFNet – International Tropical Fruits Network. https://www.itfnet.org/v1/2016/05/watermelon-name-taxonomy-botany/

ISSN No:-2456-2165 https://doi.org/10.38124/ijisrt/25apr202

[120]. Watermelon: Koppert global. Koppert. https://www.koppert.com/crops/fruits/watermelon/

[121]. Watson, S. (2023). What Are the Side Effects of Metformin? Health Central. https://www.healthcentral.com/condition/type-2-diabetes/metformin-side-effects

[122]. What causes diabetes? (2022).https://www.nichd.nih.gov/. https://www.nichd.nih.gov/health/topics/diabetes/conditio ninfo/causes

[123]. What is a mouse model? The Jackson Laboratory. https://www.jax.org/why-themouse/model

[124]. Wike, N. Y., Kelechi, M. S., Onyeso, G., Amadi, O., & Krukru, E. E. (2021, March 16). Preliminary Study on the Effect of Methanolic Extract of Watermelon (Citrullus lanatus) Rind on Prednisolone Suppressed Immunity in Male Wistar Rats. Journal of Advances in Medical and Pharmaceutical Sciences. https://doi.org/10.9734/jamps/2021/v23i230217

[125]. World Health Organization: WHO. (2019). Diabetes. www.who.int. https://www.who.int/health-topics/diabetes

[126]. Yang, Y., Laval, S., & Yu, B. (2021, January 1). Chemical Synthesis of Saponins. Advances in Carbohydrate Chemistry and Biochemistry. https://doi.org/10.1016/bs.accb.2021.10.001