Review Article

A Systematic Review on the Antihyperglycemic Property and Effect of Roselle (*Hibiscus sabdariffa* Linn.) Fruit Peel Extract in Diabetic Male Rats (*Rattus norvegicus*) Induced by Streptozotocin

Marycel Aison[1], Joshua Alvin Surisantos[2], Erin Anjella Chua[3], Ma. Danielle Kabiling[4], Kashima Mira Manalo[5], Edzyrel Ann Maravilla[6], Aldren Enrick Natividad[7], Winny Kyla Therese Medrano[8], Earl Adriane A Cano[1,2]

[1]Department of Medical Technology, Institute of Arts and Sciences, Far Eastern University, Manila, PHILIPPINES.
[2]The Graduate School, University of Santo Tomas, Manila, PHILIPPINES.

Submission Date: 26-04-2022; Revision Date: 01-06-2022; Accepted Date: 19-07-2022.

ABSTRACT

Aim/Background: Diabetes mellitus is a chronic disease that inhibits insulin production, which affects blood levels. Over-the-counter drugs regulate blood levels, while medicinal plants such as Roselle (*Hibiscus sabdariffa* Linn.) are used as a remedy. This systematic review aims to establish the antihyperglycemic properties of Roselle fruit peel extract, determine its effectiveness in diabetic male rats (*Rattus norvegicus*) induced by Streptozotocin, and evaluate the efficiency of Roselle fruit peel extract compared to over-the-counter diabetes medication; A comprehensive and systematic search of (1) Antihyperglycemic property and effect of *Hibiscus sabdariffa* Linn., (2) Samples used are diabetic male rats (3) Orally induced Streptozotocin given by medical professionals. **Materials and Methods:** The data were gathered through different databases, such as PubMed Central, the IOSR Journal of Pharmacy, EBSCOHost, Google Scholar, and ResearchGate; out of 100 studies retrieved, only 13 were utilized due to the elimination of the 87 by exclusion criteria. Diabetes is ranked 6th as the highest cause of death in the Philippines, ranking 9th worldwide. **Results and Conclusion:** In lieu of this, herbal or more organic forms of remedy are pursued by people who have diabetes. The review of studies shows that the *Hibiscus sabdariffa* Linn. plant possesses hypoglycemic, hyperlipidemic, and antioxidative properties due to the phytochemicals present. This review also solidifies the notion that Roselle extract and over-the-counter drugs have the same effect on blood sugar levels upon rat experimentation.

Keywords: Antihyperglycemic Property, Diabetes Mellitus, Streptozotocin, *Hibiscus sabdariffa* Linn., *Rattus norvegicus.*

Correspondence:
Joshua Alvin N Surisantos,
Department of Medical Technology, Institute of Arts and Sciences, Far Eastern University, Manila, PHILIPPINES.

Email: 2019138711@feu.edu.ph

INTRODUCTION

Diabetes mellitus is a disease that has affected more than 220 million worldwide (WHO, 2016).[24] This chronic disease affects the body's immune system, for it inhibits the production of insulin, which lowers the blood sugar level of humans.

SCAN QR CODE TO VIEW ONLINE

www.ajbls.com

DOI: 10.5530/ajbls.2022.11.41

According to Yusof *et al.* (2018), diabetes has long-term effects that can affect the cardiovascular system, making a heart attack

Higher.[26] Roselle *(Hibiscus sabdariffa)* is a plant used to make different processed products like wine (Maghirang, 2017).[16] According to Okur *et al.* (2021), Roselle is a plant rich in phytochemicals used in medical uses since it contains polyphenols, anthocyanins, organic acids, and polysaccharides. Its bioactive components can be therapeutic options for different diseases like hypertension, hepatoprotection, and even diabetes mellitus.[20]

Traditionally, people worldwide rely on medicinal plants as a remedy for different diseases. In connection to this, medicinal plants have been proven to have phytochemicals like tannins, saponins, glycosides, phenols, and others that contribute to the medicinal benefits that Roselle *(Hibiscus sabdariffa)* provides. Phytochemicals are naturally occurring bioactive compounds found in the parts of flowers like Roselle. These can be found in the flowers, leaves, fruits, seeds, and other parts of the plant. According to a study conducted by Adefolalu *et al.* (2019), *Hibiscus sabdariffa* contains significant phytochemical components that have hypoglycemic, hyperlipidemic, and hepatotoxic properties. The most potent and effective in lowering blood glucose levels would be alkaloids. Furthermore, this phytochemical has antidiabetic, anti-inflammatory, and antispasmodic properties, which are effective in curing diabetic patients.[1] On the other hand, flavonoids have antioxidant properties which are effective against cancerous cells. Saponins have cardiac depressants as well as anti-inflammatory properties.

Moreover, people are known to believe in traditional and herbal medicine since it has been used in the world for years. To further look for alternatives to over-the-counter drugs, this systematic review will define and discuss the different antihyperglycemic effects and properties of Roselle *(Hibiscus sabdariffa)* on lowering the blood sugar levels diabetic male rats. This article will help in people's lifestyle and nutritional diet. It discusses the effects of diabetes on the body and the corresponding effects of modern and traditional medicine on it. Through a systematic approach, the researchers will be able to provide a comparison between different findings on what works better in accordance with the body's metabolic functions. In addition to this, it will also urge the public to have a better nutritional lifestyle, especially with their nutrition and food intake. Lastly, this can help promote natural remedies for different diseases that are being studied in public health, as well as a possible alternative treatment compared to the over-the-counter drugs.

Furthermore, this review aims to establish the anti-hyperglycemic properties of Roselle (*Hibiscus sabdariffa)* fruit peel extract, determine its effectiveness in diabetic male rats *(Rattus norvegicus)* induced by Streptozotocin, and evaluate the efficiency of Roselle *(Hibiscus sabdariffa)* fruit peel extract compared to over-the-counter diabetes medication. The efficacy of Roselle in lowering blood glucose levels is assessed in this review by making a comprehensive approach to explicate the clinical trial results in the context of the accessible pharmacological, phytochemical, safety, and toxicity information looking into the physiologic and physical characteristics of rats. Through this comprehensive review, important information regarding the natural supplement or alternatives to insulin therapy is asserted, which in turn continues to enrich literature in this research area and the pharmaceutical field in the country.

METHODS

Search Strategy

Databases on the internet, such as PubMed Central, the IOSR Journal of Pharmacy, EBSCOHost, and electronic archives such as Google Scholar and ResearchGate, were used to obtain data. In addition, the query was conducted in February 2022 using a collection of terminologies such as (1) Antihyperglycemic, (2) Diabetic, (3) *Rattus norvegicus* or "Albino Rat" without further constraints that may cause a delay in our study that focuses on the antihyperglycemic property and effect of Roselle fruit peel extract in male rats that was induced by Streptozotocin.

Eligibility Criteria

The inclusion criteria established for this systematic review are the following: Articles published between 2009 to present from reliable research databases (e.g. PubMed, Google Scholar, and ResearchGate) containing topics related to (1) Antihyperglycemic property and effect of *Hibiscus sabdariffa* Linn., (2) Samples used are diabetic male rats (*Rattus norvegicus)*, (3) Induction of Oral Streptozotocin given by medical professionals such as Registered Medical Technologists and Biomedical Scientists, (4) Study designs that include in this systematic review are Experimental and Randomized Clinical Trial, and (5)Journal articles that were written in English. On the other hand, the exclusion criteria in this review are (1) Samples from humans, (2) Mice, (3) Female rats (*Rattus norvegicus),* (4) Rats with hepatitis infection, (5) Antibiotics administered intravenously, (6) Journal articles that were not written in English as well as those from predatory sites, (7) Articles published before 2009 (8) Journal articles that were not in full text, and (9) Secondary sources (e.g. Systematic Review, Review Paper).

Selection Strategy

The authors individually assessed all the studies, articles, and journals that may be included in this study. For this study, the authors looked through a wide range of related journal articles on the internet. They selected the most relevant journal articles based on the eligibility criteria that will help conduct this review. The authors reviewed the eligibility and discrepancies of selected studies. In

addition to this, the authors reviewed the title of the paper and the abstract before the whole text. Then they went over the testing procedure of the study to decide if it was included or not based on the eligibility criteria that they established beforehand. Lastly, the final assessment was submitted to their adviser for checking, mentoring, and validating the information and data provided.

Data Extraction

The authors (MVA, EAC, MGK, KMM, EAM, WKM, AEN, JAN) looked at a wide range of comparable journal papers and studies, taking into consideration factors such as (1) Primary Author, (2) Year of Publication, (3) Duration of Intervention, (4) Study Design, (5) Bioactivity, (6) Doses of Roselle Extract, (7) Sample Size/Number of Rats, (8) Route of Administration. Each accepted specific article is included in Table 1 below.

Results from the study selection for the narrative review

The initial data gathered by the proponents retrieved 100 journal articles and research studies. All of the journal articles and research studies were collected from reputable and reliable databases on the internet, such as PubMed Central, IOSR Journal of Pharmacy, EBSCOHost, and electronic archives, namely Google Scholar and ResearchGate. Duplicates were deleted from all of the studies and articles reviewed to obtain the relevant research studies and journal articles for this review. The 100 journals and retrieved studies were then assessed for relevance to this review study and their eligibility using the inclusion and exclusion criteria, with 87 being excluded as shown in Figure 1.

RESULTS

The Bioactivity of the Extract and Its Dosage.

Hibiscus sabdariffa Linn. extract have been identified as a potential source of bioactive compounds with substantial antioxidant, anti-inflammatory action, antihypertensive, antihyperlipidemic, anti-hepatotoxic, antidiabetic, and anti-inflammatory, according to studies. Hypertension, inflammation, diabetes, and metabolic syndrome have been successfully treated using Roselle extract. Different extraction procedures and its specified doses are listed in the given table in different research.

DISCUSSION

Safety and Toxicity

In the studies tested in animals, notably in male rats *(Rattus norvegicus)*, measurements linked to the Aspartate Aminotransferase (AST) and Alanine Aminotransferase (ALT) liver enzymes, as well as other analytes such as creatinine and blood urea nitrogen have typically shown either no change or decrease levels as presented in Table 2. However, at 300 mg/day of *Hibiscus sabdariffa* Linn. over 3 months, there was a detrimental effect on liver enzymes, notably *alanine aminotransferase* (ALT), suggesting that the extract might be hepatotoxic at extremely high levels. Since significant ALT levels have been found in male rats given extraordinarily high doses of *Hibiscus sabdariffa* Linn., a possible unfavorable impact might worsen or contribute to the development of liver diseases such as cirrhosis, liver cancer or hepatitis has been identified.

Fakeye (2009) found that *Hibiscus sabdariffa* Linn. extracts had a modest level of abrupt toxicity in rats, with an average fatal dosage ranging from 2000 to over 5000 mg/kg.[9] On the other hand, on the findings of Idris (2012) it showed that high dosage given to animals for several months without causing death; however, there will be detrimental effects on the testes and sperm count of the animal.[11] The differences in these results might be related to the different solvents employed, the technique and duration of treatment, and the variety and parts of *Hibiscus sabdariffa* Linn. utilized.

The Bioactivity of the Extract and Its Dosage

Several studies have shown that *Hibiscus sabdariffa* Linn's. (HSL) calyces extract as the potential source of bioactive molecules effectively lowered blood pressure, decreased blood cholesterol, had anti-inflammatory, antioxidant functions, antihyperlipidemic and antimicrobial properties.

In the various research, different extraction techniques were applied. The following procedures extracted dried petals from *Hibiscus sabdariffa* Linn.: aqueous, ethanol, and methanol. The extract was given orally in a dose-dependent approach on the findings of different studies, which are described in Table 3. *Hibiscus sabdariffa* Linn. therapeutic activity has been linked to anthocyanins, flavonols, and other phytochemicals (Alzubade, 2014).[4]

Eight out of thirteen studies show antihyperglycemic activity with methanol and aqueous methanol with different doses based on Table 3. In Streptozotocin-induced diabetic rats, *Hibiscus sabdariffa* Linn's. aqueous extracts were reported to significantly lower blood glucose levels and vascular endothelial damage and block the loss of endothelial cell viability and migration caused by high glucose. In addition to this, several studies mentioned the presence of phenolic substances such as 5-O-caffeoylshikimic acid, N-feruloylserotonin, quercetin-3-O-rutinose, and ellagic acid might be

Table 1: Characteristics of the included studies.

Primary Author	Year of Publication	Duration of Intervention	Study Design	Bioactivity	Doses of Roselle Extract	Sample Size/ Number of Rats	Route of Administration
D.O. Adeyemi[2]	2019	15 days	Experimental Design	Antihyperglycemic	1.75 g/kg	60	Oral
N.L. Yusof[27]	2018	2 months	Experimental Design	Antihyperglycemic	55 mg/kg	24	Oral
B. Niu[19]	2021	5 weeks	Experimental Design	Antihyperglycemic	60 mg/kg	24	Oral
J. A. Vega[12]	2020	15 days	Experimental Design	Antioxidant	400 mg/kg	45	Oral
N.L. Yusof[28]	2020	4 weeks	Experimental Design	Antihyperglycemic	100 mg/kg	24	Oral
N. N. Akhtar Husin[3]	2017	28 days	Experimental Design	Antioxidant, Antihyperglycemic	45 mg/kg	40	Oral
S. Pillai[21]	2015	60 days	Experimental Design	Antihyperglycemic	25 mg/kg	30	Oral
T. Andraini, S. Yolanda[5]	2014	5 weeks	Experimental Design	Antihyperglycemic, Antioxidant	100 mg/kgBW/d 200 mg/kgBW/d 400 mg/kgBW/d	25	Oral
B. Alzubade[4]	2014	28 days	Experimental Design	Antioxidant	25 mg/kgBW 50 mg/kgBW 100 mg/kgBW 200 mg/kgBW	30	Oral
F, J. Fatin[8]	2021	8 weeks	Experimental Design	Antihyperglycemic, antihypertensive, antihyperlipidemic	100 mg/kg	24	Oral
Mardiah[18]	2014	21 days	Experimental Design	Antioxidant	72 mg/day/ 200g bw	24	Oral
Mardiah[18]	2015	3 weeks	Experimental Design	Anti-Inflammatory	72 mg roselle / day / 200 g BW 288 mg / day / 200 g BW	24	Oral
O. Erukainure[7]	2015	2 weeks	Experimental Design	Antidiabetic	2.5 ml/kg bw 5 ml/kg bw	20	Oral

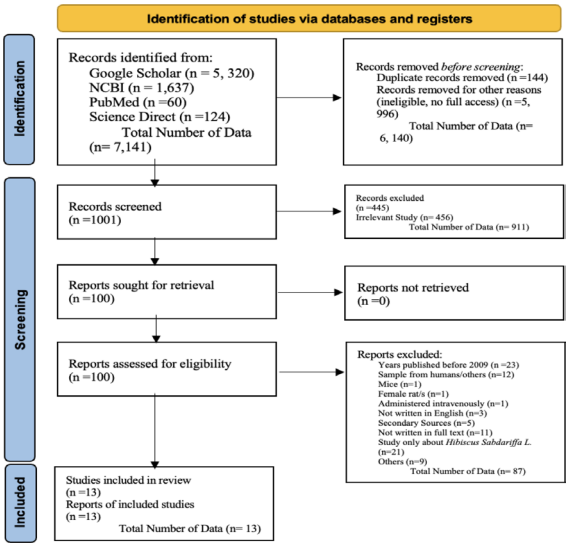

Figure 1: Flowchart of study selection for the narrative review.

primarily responsible for the hypoglycemic effect of Roselle. Antioxidant activity was seen in seven studies because of anthocyanins and flavonoids. According to Izquierdo-Vega *et al.* (2020), Delphinidin-3-O-sambubioside accounts for 85% of total anthocyanins and is thought to be the primary source of antioxidant capacity in *Hibiscus sabdariffa* Linn. extracts.[12] Antioxidants can protect the function of beta cells by fighting oxidative stress, which seeks to defend the beta cells. As a result, it can help to reduce diabetes-related problems and restore insulin sensitivity (Suresh *et al.*, 2021).[23] The antihypertensive activity was only present in Fatin, F.J., *et al.* (2021) study, where rats in Diabetes Mellitus with HPE supplementation and Diabetes Mellitus with metformin groups received 100 mg/kg with methanol extract.[8] In 2-kidney-1-clip rats (One renal artery is narrowed, reducing renal perfusion over time, whereas

Table 2: Safety and Toxicity on the effect of administration of *Hibiscus sabdariffa* Linn. extracts on creatinine, urea, aspartate aminotransferase, and alanine aminotransferase levels on male rats *(Rattus norvegicus).*

Primary Author, Year, Type of Study	Plant Part	Dose	Creatinine	Urea	Aspartate Aminotransferase	Alanine Aminotransferase
Lee, 2009,[15] Animal Studies	Flower	100mg	Not Significant	Decreased	Not Available	Not Available
Lee, 2009,[15] Animal Studies	Flower	200mg	Not Significant	Decreased	Not Available	Not Available
Kuo, 2012,[14] Animal Study	Flower	1% of extracted Roselle solution	Not Significant	Not Significant	Not Significant	Not Significant
Kuo, 2012,[14] Animal Study	Flower	2% of extracted Roselle solution	Not Significant	Decreased	Not Significant	Not Significant
Kuo, 2012,[14] Animal Study	Flower	5% of extracted Roselle solution	Not Significant	Decreased	Not Significant	Not Significant
Fakeye, 2009,[9] Animal Study	Calyx	300mg	Not Significant	Not Available	Not Significant	Increased

Legend: *NOT SIGNIFICANT* - when there is no changes on the level of the enzyme, *NOT AVAILABLE* - when there is no available data, *INCREASED* - when there is an elevation on the enzyme level, or *DECREASED* - when there is a depression on the enzyme level.

Safety and Toxicity on the effect of administration of Hibiscus sabdariffa Linn. *extracts on creatinine, urea, aminotransferase, and alanine aminotransferase levels on male rats (Rattus norvegicus).* The administration of *Hibiscus sabdariffa Linn* extracts to the male rats *(Rattus norvegicus)* has been classified from the part of the Roselle and from the extracted dose utilized in the male rats. Moreover, creatinine, urea, aspartate aminotransferase, and alanine aminotransferase are the enzymes linked to the safety and toxicity of the extracts of *Hibiscus sabdariffa Linn.*

Table 3: *The Bioactivity of the Extract and Its Dosage.*

Bioactivity	Extract	Doses	Reference
Antihyperglycemic	70% Methanolic	1.75 g/kg	D.O. Adeyemi[2]
	Aqueous	55 mg/kg	N.L Yusof[25]
	Methanolic	60 mg/kg	B. Niu[19]
	Methanolic	100 mg/kg	N.L Yusof[26]
	Aqueous	45 mg/kg	N. N. Akhtar Husin[3]
	80% Ethanol	25 mg/kg	S. Pillai[21]
	Aqueous Ethanol	100 mg/kgBW/d	T. Andraini and Y. Sophie[5]
	Aqueous Ethanol	200 mg/kgBW/d	T. Andraini and Y. Sophie[5]
	Aqueous Ethanol	400 mg/kgBW/d	T. Andraini and Y. Sophie[5]
	Methanol	100 mg/kg	F, J. Fatin[8]
Antioxidant	Aqueous	400 mg/kg	J. A. Vega[12]
	Aqueous	45 mg/kg	N. N. Akhtar Husin[3]
	Aqueous Ethanol	100 mg/kgBW/d	T. Andraini and Y. Sophie[5]
	Aqueous Ethanol	200 mg/kgBW/d	T. Andraini and Y. Sophie[5]
	Aqueous Ethanol	400 mg/kgBW/d	T. Andraini and Y. Sophie[5]
	Aqueous	25 mg/kg B.W.	B. Alzubade[4]
	Aqueous	50 mg/kg BW	B. Alzubade[4]
	Aqueous	100 mg/kg BW	B. Alzubade[4]
	Aqueous	200 mg/kg B.W.	B. Alzubade[4]
	Methanol	100 mg/kg	F, J. Fatin[8]
Antihypertensive	Methanol	100 mg/kg	F, J. Fatin[8]
Antihyperlipidemic	Methanol	100 mg/kg	F, J. Fatin[8]
Anti-Inflammatory	Aqueous	72 mg roselle/day/ 200 g BW	Mardiah, *et al*.[17]
	Aqueous	288 mg/day/kg BW	Mardiah, *et al*.[17]
Antidiabetic	40% roselle calyx Aqueous	2.5 and 5 mL/kg B.W.	O. Erukainure *et al*.[7]

the other kidney is untouched), HS aqueous extract demonstrated antihypertensive and cardioprotective effects. With this, anthocyanins, particularly Cyanidin-3-sambubioside and Delphinidin-3-O-sambubioside, are thought to be the active components responsible for the antihypertensive and hypocholesterolemic effects of *Hibiscus sabdariffa* Linn. possibly due to their abundance in aqueous extracts (Izquierdo-Vega *et al.,*

2020).[12] Diabetes causes the walls of your blood vessels to stiffen, leading diabetes to harm your body's small blood vessels. This raises the pressure, resulting in hypertension. Only one study found antihyperlipidemic effects, and it used Methanol to extract the data. The hypolipidemic potency of *Hibiscus sabdariffa* Linn. extract (HSE) has been demonstrated in several trials, suggesting that Roselle could be used as an anti-obesity drug. Obesity is caused by an energy imbalance and high-fat consumption, diabetic complications such as hypertension, hyperlipidemia, insulin resistance, and fatty liver. *Hibiscus sabdariffa* Linn. have potential therapeutic properties and could be useful in this pathology since they have several impacts on obesity affecting human health (Riaz and Chopra, 2018).[22] According to Yang *et al.* (2010), the antihyperlipidemic effect of aqueous Roselle extract reduces hepatocyte lipid content via fatty acid synthase HMG-CoA reductase activation.[25] As with anti-inflammatory activity, which was only demonstrated in one analysis, this study used an aqueous method with two dose variables. Inflammatory compounds (IL-6, hs-CRP, IL-18, and TNF-) are produced by diabetes (Riaz and Chopra, 2018).[22] To determine the effect of Roselle extract on Streptozotocin-induced diabetic rats, Mardiah *et al.* (2014) found that a dose of "72 mg Roselle/day/200 g B.W. and 288 mg/day/200 g B.W." reduced the amount of tumor necrosis factor (TNF-); thus, Roselle has anti-inflammatory properties.[17] In addition, antidiabetic characteristics that have only been discovered in one research, with two controls using an aqueous approach and antidiabetic properties identified only in one study, are treated with two controls that use an aqueous approach. According to Erukainure (2015), HSL extract administration lowered blood glucose levels, high-density lipoprotein cholesterol levels, and most suitable serum insulin levels in diabetic rats, implying an antidiabetic potential.[7]

Liver and kidney to Total Body Weight Ratio

As shown in Figure 2, there are differences in the dosages of the extract in *Hibiscus sabdariffa* Linn., with distinct ratios in the liver and kidney. It is common knowledge that any modifications to a human's weight can signify damage to the usual body organ functions; the organ-body weight ratio can be an indication of cell inflammation, as well as cell constriction (Alzubade, 2014).[4] In addition, ALT is a liver enzyme whose concentration is associated with liver tissue and hepatic condition. A change in the value of this enzyme is considered an indication of liver damage or excessive pressure on the liver.

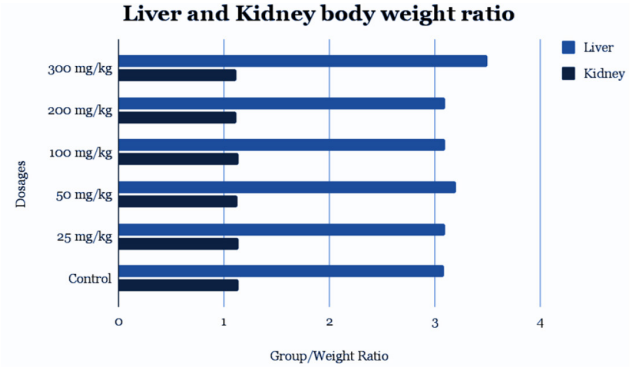

Figure 2: Liver and kidney to Total Body Weight Ratio.
The analysis indicated that during the trial period of 28 days, administration and ingestion of aqueous extract of *Hibiscus sabdariffa Linn* in male rats at all dosages (25,50,100,200 mg/kg body weight) exhibited no significant (P 0.05) effect on liver and kidney to body weight ratio compared to the control.

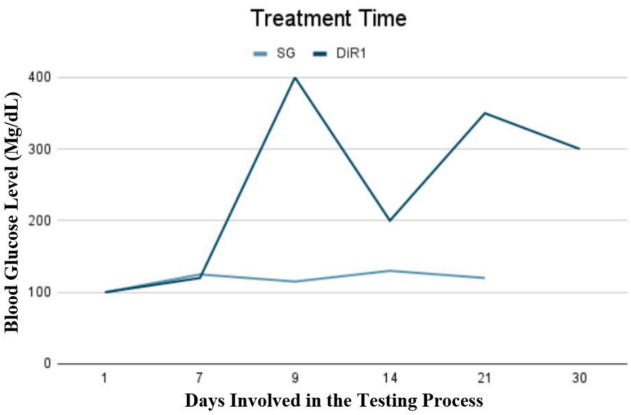

Figure 3: Fasting Blood Glucose.
Average blood sugar levels of induced rats: first blood glucose level on day 1; Streptozotocin induction on day 7; Roselle extract treatment on days 9-21 (DiR1); Control (SG).

However, various studies associated with the administration of aqueous extract of *Hibiscus sabdariffa* Linn. in male rats *(Rattus norvegicus)* exhibited non-significant changes in terms of liver and kidney to body weight ratio in accordance with the ingestion of the aqueous plant extract in (*Hibiscus sabdariffa* Linn.) several dosages (25,50,100,200 mg/kg body weight) which are presented in Figure 2, the extract did not induce severe tissue damage in the male rats. It also means that protein excretion through the kidney is not affected. Thus, these results indicate that the aqueous plant extract which contains 200 mg of the dried *Hibiscus sabdariffa Linn* flowers were boiled in 1000 mL distilled water did not cause any constriction or inflammations to the liver and kidney cells as long as high dosages are not administered (Alzubade, 2014).[4]

Fasting Blood Glucose Level

There is a comparison among rats with blood glucose groups in several studies which indicates that the high

fructose diet group showed a significant increase in blood glucose levels than the control group. Moreover, the fasting blood sugar levels were significantly lower in rats fed a high fructose diet containing *Hibiscus sabdariffa* Linn. extracts (Andraini and Yolanda, 2014).[5]

Several studies have shown that increased blood glucose levels were a sign of diabetes. The average blood sugar level of the four rats was calculated throughout the treatment period to obtain the blood glucose data. (Figure 3). Figure 3 indicates that the rats were hyperglycemic after 2-3 days of Streptozotocin induction, as confirmed by a blood glucose rise of g>200 mg/dl. Figure 3 shows that rats fed 72 mg/ml/200g Roselle extract exhibited a drop in blood glucose on the 14th day; however, after that it increased at the end of the studies. Between the 14th day and the end of the studies, rats fed Roselle extracted 288 mg/ml/200g wb, indicating lower blood glucose levels. Negative control rats had lower blood glucose levels on the 7th and 14th days treatment period, but their blood glucose levels rose again at the end of the study. The blood glucose level, on the other hand, was shown to be increased on day 21 and then decreased at the end of the study. As a result, it confirms that the rats' blood glucose levels decrease after suffering from hyperglycemia for 2-3 days.

Phytochemical Therapeutic Effects of *Hibiscus Sabdariffa* Linn.

As shown in Table 4, several studies showed that Roselle (*Hibiscus Sabdariffa* Linn.*)* has different therapeutic benefits that affect the blood glucose level of the rats being tested. These include antioxidant potential, antihyperlipidemic properties, improved resistance to insulin, and its preventive potential against cardiac dysfunction.

Roselle contains a phytochemical property called anthocyanin, which helps in the production of antioxidative and hypolipidemic properties of Roselle through increasing the fatty acids and free radicals in the body systems of the mice that have high blood glucose levels (Yolanda, 2014).[5] It was proven in several studies that there had been a difference in the lipid peroxide level and glucose concentration. In patients with high glucose levels or even diabetes mellitus, there is a significant increase in the lipid peroxide level. It is a clear indication that the usage of blood sugar lowering tea can decrease the production of radicals. In the study conducted by Kangralkar *et al.* (2010),[13] tea treatment and metformin were given to the treatment groups to lower their lipid peroxidation levels, thus suggesting the antihyperlipidemic function of Roselle.

Table 4: *Phytochemical Therapeutic Effects of Hibiscus Sabdariffa* Linn.

Bioactivity	Extract
Antioxidative	Due to its polyphenolic components, including protocatechuic acid, catechins, caffeic acid, and epigallocatechin-gallate, *Hibiscus sabdariffa* Polyphenol-rich Extract (HPE) was discovered to have potent antioxidant activity (Yusof, 2018).[26]
Antihyperlipidemic	HPE has an antihyperlipidemic effect, lowering lipid profile markers such as plasma T.G., cholesterol, and the Triglycerides or High-Density Lipoprotein (TG/HDL) risk ratio in diabetic rats. As a result, by lowering hyperlipidemia with HPE supplementation, type 1 diabetes-related cardiac dysfunction and anatomical abnormalities would be reduced (Yusof, 2018).[25]
Improved Insulin Resistance	Insulin resistance appeared to have increased significantly in rats treated with a single dose (2.5 ml/kg bw) of the produced beverage, followed by the untreated diabetic rats; diabetic rats given 5.00 ml/kg bw of the produced beverage have the lowest resistance value (Erukainure, 2015).[7]
Improved Insulin Sensitivity	Reduced insulin sensitivity was observed in rats treated with a single dose (2.5 ml/kg bw) of the produced beverage, followed by the untreated diabetic rats; diabetic rats given 5.00 ml/kg bw of the produced beverage have the highest resistance value (Erukainure, 2015).[7]
Prevention of Cardiac Dysfunction	HPE has therapeutic significance in preventing diabetic cardiac dysfunction by inhibiting cardiac ROS overexpression, reducing type 1 diabetes-induced cardiac dysfunction, and structural remodeling (Yusof, 2018).[25]

Legend: HPE - *Hibiscus sabdariffa* Polyphenol-rich Extract, TG - Triglycerides, HDL - High Density Lipoprotiens

According to studies that were conducted by Gurrola-Diaz that were focused on the effects of *Hibiscus sabdariffa* Linn on the lipid profiles of rats with or without any metabolic defects, Roselle showed potential in its hyperlipidemic properties wherein the rats that were given the treatments from the said plant had an improvement in lowering the cholesterol levels of the test subjects.[10] In line with this, there was also a decrease in the rats' blood sugar level, suggesting an antihyperglycemic potential of Roselle.

In addition to this, according to a study performed by Erukainure (2015),[7] the single-dose treatment group

had a somewhat high serum insulin level, which could indicate hyperinsulinemia due to insulin resistance. The high Homeostatic Model Assessment of Insulin Resistance (HOMA-IR) and lowered Quantitative Insulin-Sensitivity Check Index (QUIKI) scores, which indicate reduced insulin sensitivity. An increase in beta cell function is observed in treated rats which correlates with increased insulin level, demonstrating that hypoglycaemic hypoglycemia can reverse beta cell dysfunction activity.

Several studies confirm that Roselle contains therapeutic benefits that include lowering the body's blood sugar level. Therefore, this confirms that Roselle has antihyperglycemic effects since it was affected by several other factors in the body.

CONCLUSION

During the review, the authors consolidated the information that the extracts of Roselle (*Hibiscus sabdariffa* Linn.) contain significant phytochemical components such as hypoglycemic and antidiabetic properties, which effectively lower the blood sugar level and cure diabetic patients.

The Roselle (*Hibiscus sabdariffa* Linn.) should be studied further to assess its functional properties and mechanisms of action toward the body to lower blood sugar levels. It is also important to determine the factors such as pharmacological, phytochemical, safety, and toxicity information as well as the physiologic and physical characteristics of rats that may affect the efficiency and potency of Roselle (*Hibiscus sabdariffa* Linn.) because it will determine the effectiveness of its properties in lowering the blood sugar of the patient, thus, helping in controlling and treating diabetes.

To address the increasing prevalence of diabetes, numerous plant regimens have been studied across the world; unfortunately, only a few are demonstrated to lower blood glucose, boost insulin production, and improve insulin resistance, thus, resulting in a high prevalence of people diagnosed with diabetes (Brutsaert, 2022).[6] As a proposition, the application of Roselle (*Hibiscus sabdariffa* Linn.) extract is a viable option to manage diabetes to decrease blood glucose. Moreover, extensive research on probable antihyperglycemic properties against diabetes is a candidate for follow-up studies. Comparative studies using male and female rats can be included since they both have significant reference values, which can be compared to the conditions encountered in human studies. Other recommendations would include testing Roselle with the addition of other medicinal plants to check out their effectiveness.

The biomedical applications of Roselle (*Hibiscus sabdariffa* Linn.) with potential antidiabetic and hypoglycemic properties like their ability to control the blood sugar levels in response to diseases associated with diabetes may be included in the future. Moreover, future researchers may also want to study other medicinal herbs or plants with antihyperglycemic properties like Roselle (*Hibiscus sabdariffa* Linn.). These studies are important for they might potentially decrease the prevalence of diabetes in local and international settings.

ACKNOWLEDGEMENT

We are grateful to our parents, whose love, understanding, and inspiration are always there for us.

The authors are also especially indebted to Mr. Earl Adriane Cano, who has demonstrated unwavering patience and a strong dedication to the group. His professional counsel motivates us to improve our work continually. We are fortunate to have the opportunity to learn from and work alongside you.

Lastly, we would like to thank Mr. Bernadino Hagosojos and Ms. Princess Tolenada, our research professors, for providing valuable insights and a strategic writing approach to completing this article.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

ABBREVIATIONS

ALT: Alanine Aminotransferase**; AST:** Aspartate Aminotransferase; **CRP:** C-Reactive Protein; **IL:** Interleukin; **HDL** High Density Lipoprotein; **HMG-CoA:** Hydroxymethylglutaryl-coenzyme; **HOMA-IR:** Homeostatic Model Assessment of Insulin Resistance; **HPE:** *Hibiscus sabdariffa* Polyphenol-rich Extract; **HS:** *Hibiscus sabdariffa;* **HSE:** *Hibiscus sabdariffa Linn* extract; **HSL:** *Hibiscus sabdariffa Linn;* **TG:** Triglycerides; **TNF:** Tumor Necrosis Factor; **QUIKI:** Quantitative Insulin-Sensitivity Check Index.

SUMMARY

Based on the results, the extracts of *Hbiscuss sabdariffa* Linn. showed a significant effect on lowering the blood sugar level of the rats. However, there are some negative effects shown on the results, particularly when the dosage used is more than 300 mg over the span of more than 3 months, in which it will be harmful for the liver. Thus, the administration of *Hibiscus sabdariffa* Linn. can

be therapeutic on proper use and dosage and improper administration can be hepatotoxic.

REFERENCES

1. Adefolalu FS, Salawa JS, Gara TY, Abubakar AN. Hypoglycemic and hypolipidemic effect of methanol extract of *Hibiscus sabdariffa* seed in alloxan induced diabetic albino rats [internet]. Nig J Bas App Sci. 2019;27(2):[151-6]. doi: 10.4314/njbas.v27i2.20.
2. Adeyemi DO, Adewole OS. *Hibiscus sabdariffa* renews pancreatic β-cells in experimental type 1 diabetic model rats [internet]. Morphologie. 2019;103(341 Pt 2):[80-93]. doi: 10.1016/j.morpho.2019.04.003, PMID 31101500.
3. Nazratun Nafizah AH, Budin SB, Zaryantey AH, Mariati AR, Santhana RL, Osman M, *et al*. Aqueous calyxes extract of roselle or *Hibiscus sabdariffa* Linn supplementation improves liver morphology in streptozotocin induced diabetic rats [internet]. Arab J Gastroenterol. 2017;18(1):[13-20]. doi: 10.1016/j.ajg.2017.02.001, PMID 28336227.
4. Alzubade B. Effects of aqueous extract of *Hibiscus sabdariffa* L. on some biochemical indices of liver and kidney function in male albino rats. Vol. 6(2); 2014. Magazin of al-Kufa University for biology [internet] [cited Apr 18 2022]. Available from: https://www.iasj.net/iasj/download/511a240d314d5da7.
5. Andraini T, Yolanda S. Prevention of insulin resistance with *Hibiscus sabdariffa* Linn. extract in high-fructose fed rat [internet]. Vol. 23(4). p. 192-4; 2014 [cited Apr 18 2022]. Available from: https://sci-hub.ee/10.13181/mji.v23i4.848.
6. Brutsaert EF. Diabetes mellitus (DM); 2020. MSD manual consumer version [internet] [cited Apr 18 2022]. Available from: https://www.msdmanuals.com/home/hormonal-and-metabolic-disorders/diabetes-mellitus-dm-and-disorders-of-blood-sugar-metabolism/diabetes-mellitus-dm.
7. Erukainure OL, Okafor O, Ajayi A, Obode O, Ogunji A, Okporua T, *et al*. Developed beverage from roselle calyx and selected fruits modulates β-cell function, improves insulin sensitivity, and attenuates hyperlipidaemia in diabetic rats [internet]. Beni-Suef University Journal of Basic and Applied Sciences. 2015;4(4):[307-13]. doi: 10.1016/j.bjbas.2015.11.007.
8. Fatin F, J, *et al*. Potential of *Hibiscus sabdariffa* Linn. Polyphenol-rich Extract in Improving diabetes-induced Vascular Functional and structural Abnormalities in Rats [internet]. Vol. 50(7): [1959-1970]; 2021 [cited Apr 18 2022]. Available from: https://www.ukm.my/jsm/pdf_files/SM-PDF-50-7-2021/11.pdf.
9. Fakeye TO, Pal A, Bawankule DU, Yadav NP, Khanuja SPS. Toxic effects of oral administration of extracts of dried calyx of *Hibiscus sabdariffa* Linn. (Malvaceae) [internet]. Phytother Res. 2009;23(3):[412-6]. doi: 10.1002/ptr.2644, PMID 19003943.
10. Gurrola-Díaz CM, García-López PM, Sánchez-Enríquez S, Troyo-Sanromán R, Andrade-González I, Gómez-Leyva JF. Effects of *Hibiscus sabdariffa* extract powder and preventive treatment (diet) on the lipid profiles of patients with metabolic syndrome (MeSy) [internet]. Phytomedicine. 2010;17(7):[500-5]. doi: 10.1016/j.phymed.2009.10.014, PMID 19962289.
11. Idris MH, Budin SB, Osman M, Mohamed J. Protective role of *Hibiscus sabdariffa* calyx extract against streptozotocin induced sperm damage in diabetic rats [internet]. EXCLI J. 2012;11(11):[659-69]. Available from EXCLI J.; 11:659-669. PMID 27847454, PMCID PMC5099906.
12. Izquierdo-Vega J, Arteaga-Badillo D, Sánchez-Gutiérrez M, Morales-González J, Vargas-Mendoza N, Gómez-Aldapa C, *et al*. Organic Acids from Roselle (*Hibiscus sabdariffa* L.)—A Brief Review of Its Pharmacological Effects [internet]. Biomedicines. 2020;8(5):[100]. doi: 10.3390/biomedicines8050100.
13. Kangralkar, *et al*. Acute toxicity and hypoglycemic properties of ethanolic root extract of *Vermonia amygdalina* (bitter leaf) in alloxan-induced diabetic rat [internet]. Vol. 4(4). p. 612-5; 2011 [cited Apr 18 2022]. Available from: https://indianjournals.com/ijor.aspx?target=ijor:rjpt&volume=4&issue=4&article=029.
14. Kuo CY, Kao ES, Chan KC, Lee HJ, Huang TF, Wang CJ. *Hibiscus sabdariffa* L. Extracts reduce serum uric acid levels in oxonate-induced rats[internet]. Journal of Functional Foods. 2012;4(1):[375-81]. doi: 10.1016/j.jff.2012.01.007.
15. Lee WC, Wang CJ, Chen YH, Hsu JD, Cheng SY, Chen HC, *et al*. Polyphenol extracts from *Hibiscus sabdariffa* Linnaeus attenuate nephropathy in experimental Type 1 diabetes [internet]. J Agric Food Chem. 2009;57(6):[2206-10]. doi: 10.1021/jf802993s, PMID 19219995.
16. Maghirang R. Every important fact you need to know about Roselle [internet]; 2017 [cited Apr 18 2022]. Available from: https://www.agriculture.com.ph/2017/11/28/roselle/.
17. Mardiah. The Effect of Roselle Extract (*Hibiscus sabdariffa* Linn.) On blood glucose Level and Total Antioxidant Level on Diabetic Rat Induced By streptozotocin [internet]. Vol. 4(10). p. 08-16; 2014 [cited Apr 18 2022]. Available from: http://www.iosrphr.org/papers/v4i10/B041008016.pdf.
18. Mardiah, Zakaria FR, Prangdimurti E, Damanik R. Anti-inflammatory of purple Roselle extract in diabetic rats induced by streptozotocin [internet]. Procedia Food Science. 2015;3:[182-9]. doi: 10.1016/j.profoo.2015.01.020.
19. Niu B. *Hibiscus sabdariffa* (Roselle) polyphenol-rich Extract Averts Cardiac Functional and Structural Abnormalities in Type 1 Diabetic Rats [internet]. p. 2-27; 2018 [cited Apr 18 2022]. Available from: https://sci-hub.ee/10.1139/apnm-2018-0084.
20. Okur ME, Özbek H, Polat DÇ, Yılmaz S, Arslan R. Hypoglycemic activity of *Capparis ovata* desf. var. palaestina zoh. methanol extract [internet]. Braz J Pharm Sci. 2018;54(3):[01-9]. doi: 10.1590/s2175-97902018000318031.
21. Pillai SS, Mini S. Polyphenols rich *Hibiscus rosa* sinensis Linn. petals modulate diabetic stress signalling pathways in streptozotocin-induced experimental diabetic rats [internet]. Journal of Functional Foods. 2016;20:[31-42]. doi: 10.1016/j.jff.2015.10.007.
22. Riaz G, Chopra R. A review on phytochemistry and therapeutic uses of *Hibiscus sabdariffa* L [internet]. Biomed Pharmacother. 2018;102:[575-86]. doi: 10.1016/j.biopha.2018.03.023, PMID 29597091.
23. Suresh V, Reddy A, Muthukumar P, Selvam T. Antioxidants: Pharmacotherapeutic boon for diabetes[internet]; 2021 [cited Apr 18 2022]. Available from: https://www.intechopen.com/chapters/77150.
24. World Health Organization. Global report on diabetes [internet]. p. 01-86; 2016 [cited Apr 18 2022]. Available from: https://apps.who.int/iris/bitstream/handle/10665/204871/9789241565257_eng.pdf;jsessionid=F173755DDAC0AA37459AFC234EEDB647?sequence=1.
25. Yang MY, Peng CH, Chan KC, Yang YS, Huang CN, Wang CJ. The hypolipidemic effect of *Hibiscus sabdariffa* polyphenols via inhibiting lipogenesis and promoting hepatic lipid clearance [internet]. J Agric Food Chem. 2010;58(2):[850-9]. doi: 10.1021/jf903209w, PMID 20017484.
26. Yusof N, *et al*. *Hibiscus sabdariffa* (Roselle) polyphenol-rich extract averts cardiac functional and structural abnormalities in type 1 diabetic rats [internet]. Vol. 43(12): [1224-1232]; 2018 [cited Apr 18 2022]. Available from: https://pubmed.ncbi.nlm.nih.gov/29726706/.
27. Niu B, Xie X, Xiong X, Jiang J. Network pharmacology-based analysis of the anti-hyperglycemic active ingredients of roselle and experimental validation [internet]. Comput Biol Med. 2022;141:104636. doi: 10.1016/j.compbiomed.2021.104636, PMID 34809966.
28. Yusof NL. *Hibiscus sabdariffa* Linn. (Roselle) polyphenols-rich Extract Prevents hyperglycemia-induced Cardiac Oxidative Stress and mitochondrial Damage in Diabetic Rats [internet]. Vol. 49(10). p. 2499-506; 2020 [cited Apr 18 2022]. Available from: http://www.ukm.my/jsm/pdf_files/SM-PDF-49-10-2020/15.pdf.

Cite this article: Aison M, Surisantos JA, Chua EA, Kabiling MD, Manalo KM, Maravilla EA, Natividad AE, Medrano WKT, Cano EAA. A Systematic Review on the Antihyperglycemic Property and Effect of Roselle (*Hibiscus sabdariffa Linn*) Fruit Peel Extract in Diabetic Male Rats (*Rattus norvegicus*) Induced by Streptozotocin. Asian J Biol Life Sci. 2022;11(2):308-16.