Chayomed: Pharmacotheraputic Potential of Chayote (Sechium Edule) Peel Extract on Diabetes Mellitus and its Cancer Chemoprevention Property

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ABSTRACT

Recent statistics from the World Health Organization indicate that noncommunicable diseases such as cancer and diabetes mellitus remain major global health challenges, with cancer responsible for an estimated 9.7 million deaths worldwide in 2022 and diabetes directly causing about 1.6 million deaths in 2021, while also contributing to millions more through cardiovascular complications [18,19]. This study aims to determine the phytochemical, anti-angiogenic, and anti-hyperglycemic potential of Chayote (Sechium edule) peel extract. Ethanolic peel extract was subjected to phytochemical screening and tested for cytotoxicity, angiosuppressive activity, and blood glucose reduction. Secondary metabolites screening indicated the presence of alkaloids, flavonoids, saponins, phenols, and tannins, which possess known anti-oxidative and anti-inflammatory actions. Test for angiosuppressive activity using the Chorioallantoic Membrane (CAM) assay revealed a significant anti-angiogenic property at 25%, 50%, and 75% concentrations of the S. edule peel extract with all inhibiting the growth of blood vessels. These results were comparable to the positive control, methotrexate. The Brine Shrimp Lethality Assay revealed an LC_{50} value of 505.14 µg/mL. Since this value is greater than 100 µg/mL which indicates that the extract maybe non-toxic to human cells. Analysis of glycemic activity showed that the extract significantly reduced blood glucose levels in mice, particularly at 200 µg/mL, which performed at par with the positive control. The results proved that S. edule peel extract exhibits promising phytonutraceutical, anti-angiogenic, and anti-diabetic properties, representing a potential novel approach for cancer prevention and diabetes management. Isolation of potent bioactive compounds responsible for the aforementioned claims should be done as well as in vivo testing should be conducted to further validate the results of the study.

Keywords: angiosuppressive, cancer, cytotoxicity, diabetes milletus, phytonutraceutical.

INTRODUCTION

Diabetes mellitus and cancer represent two of the most significant global health challenges, characterized by complex biological mechanisms that often require aggressive and expensive treatments [14]. Diabetes is a group of endocrine diseases marked by sustained hyperglycemia, affecting millions globally and ranking as a top cause of mortality in the Philippines [3]. Simultaneously, cancer remains a devastating disease defined by the abnormal and uncontrolled growth of cells that can invade various organs [9]. While these conditions appear distinct, they are both impaired by oxidative stress and disruptions in cellular homeostasis, creating a need for versatile therapeutic agents that can address multiple pathological fronts.

Chayote (Sechium edule) is known for its rich nutritional profile, providing essential vitamins, minerals, and dietary fiber that support overall health. It is particularly abundant in vitamin C, which enhances immune function, and B-complex vitamins that play a crucial role in energy metabolism. In addition, chayote contains important minerals such as potassium, which helps regulate blood pressure, as well as magnesium and calcium that contribute to bone health [2]. The high fiber content of chayote further promotes digestive health, aids in weight management, and helps regulate blood sugar levels. Grown widely in tropical and subtropical regions, chayote is a versatile and easy-to-cultivate vegetable that thrives in warm climates with adequate support for its climbing vines, making it an accessible dietary component with potential relevance to metabolic health and disease prevention.

Management of diabetes relies on regulating blood sugar levels to prevent systemic complications [16]. Chayote (Sechium edule) is a nutrient-dense vegetable known for its high fiber content and low glycemic index, which can slow sugar absorption and prevent glucose spikes. However, beyond its dietary fiber, the peel of the Chayote contains potent bioactive compounds that are reported to enhance insulin sensitivity and inhibit carbohydrate-digesting enzymes. This suggests that the extract may serve as a natural anti-hyperglycemic agent capable of reducing blood glucose levels effectively [1].

On the other hand, fighting against cancer focuses on inhibiting the proliferation of malignant cells and preventing angiogenesis, the process by which tumors develop their own blood supply to grow and spread [13]. Phytochemicals found such as flavonoids and phenols are known to modulate cell signaling pathways and induce apoptosis. By demonstrating angiosuppressive properties, a natural extract can potentially starve tumors of necessary nutrients, offering a novel, non-toxic lead for cancer prevention and treatment that mimics the effects of conventional anticancer medications without the associated adverse side effects.

All animal procedures were conducted in strict accordance with national and institutional guidelines for the care and use of laboratory animals. The experimental protocols for the antihyperglycemic test involving Albino mice were approved by the Institutional Animal Care and Use Committee (IACUC) under Protocol Number 2025-ACL-AS-002. The study adhered to the principle of minimizing animal distress throughout the 14-day acclimation and 5-day induction periods.

Methods and Experimental Details

Ethanolic Extraction

Five hundred grams of peels were soaked in 1000 ml of 95% ethanol at room temperature. After 48 hours, the extract was filtered using filter paper. The collected ethanolic crude extract was subjected for rotary evaporation in PHILEXPORT Quality Control Laboratory, General Santos City, Philippines to obtain the pure extract.

Figure 1. Soaking of Sechium edule and Its Crude Extract

Phytochemical Screening

Bioactive compound of Sechium edule was determined following the protocols of Tiwari et al. in 2011.

a. Test for Alkaloids (Wagner's Test)

One (1) ml of S. edule was treated with Wagner's reagent and was added along the sides of the test tube. The presence of reddish or brown precipitates indicates the presence of alkaloids.

b. Test for Flavonoids

One (1) ml of the plant extract was treated with sodium hydroxide solution. The formation of intense yellow color until it becomes colorless on addition of hydrogen chloride (dilute acid) indicates the presence of flavonoids.

c. Test for Saponins (Foam test)

One (1) ml of extract was diluted with 2 ml distilled water. The suspension was shaken in a graduated cylinder for 15 minutes. If the foam persist for ten minutes indicates the present of saponins.

d. Test for Tannins

One (1) ml of the extract was diluted with 1% gelatin solution containing 10% NaCl. The presence of white precipitates indicates the presence of tannins.

e. Test for Phenols

One (1) ml of extract was treated with 3-4 drops of ferric chloride solution. The formation of bluish black color indicates the presence of phenols.

Duck Chorioallantoic Membrane (CAM) Assay

The angiosuppressive activity was determined using CAM assay by Cruz et al. in 2022 where eight (8) - day old duck egg was used. Each egg went through candling to determine the embryo's position. Using sterile forceps, small holes were carefully made around the airspace, and then sealed with parafilm to prevent contamination. The eggs were treated with 25%, 50%, 75% concentration of S. edule extracts diluted to distilled water in 1mL quantities which are obtained using the C1V1=C2V2 formula, anticancer drug (positive control), and distilled water (negative control). The eggs were treated with 0.1mL of the treatments respectively and incubated at 37.5 ^{0}C for 48 hours.

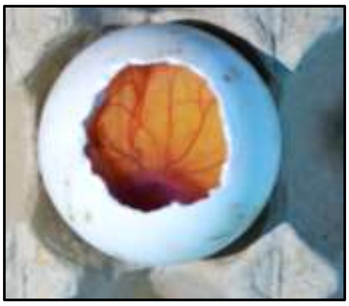

Figure 2. CAM of an 8-day Old Duck Embryo

Brine Shrimp Lethality Assay

The cytotoxicity assay was performed using the Artemia salina lethality test following the protocol of Sarah et al. (2017). Brine shrimp eggs were hatched in an aerated rectangular aquarium containing artificial seawater prepared by dissolving 25 g of table salt per liter of distilled water (≈25 ppt salinity). The setup was maintained at 28–30 °C under continuous illumination for 20–24 hours to allow hatching of photophilic nauplii. After hatching, live nauplii were separated from egg shells by turning off aeration and light. Ten nauplii were transferred into test tubes containing artificial seawater and exposed to varying concentrations of the plant extract (0, 100, 500, and 1000 µg/mL). After 24 hours of exposure, surviving nauplii were counted, and percentage lethality was calculated using percentage of death formula.

$$\%\text{Death} = \frac{\text{Number of dead nauplii}}{\text{Number of dead nauplii} + \text{Number of live nauplii}} \times 100$$

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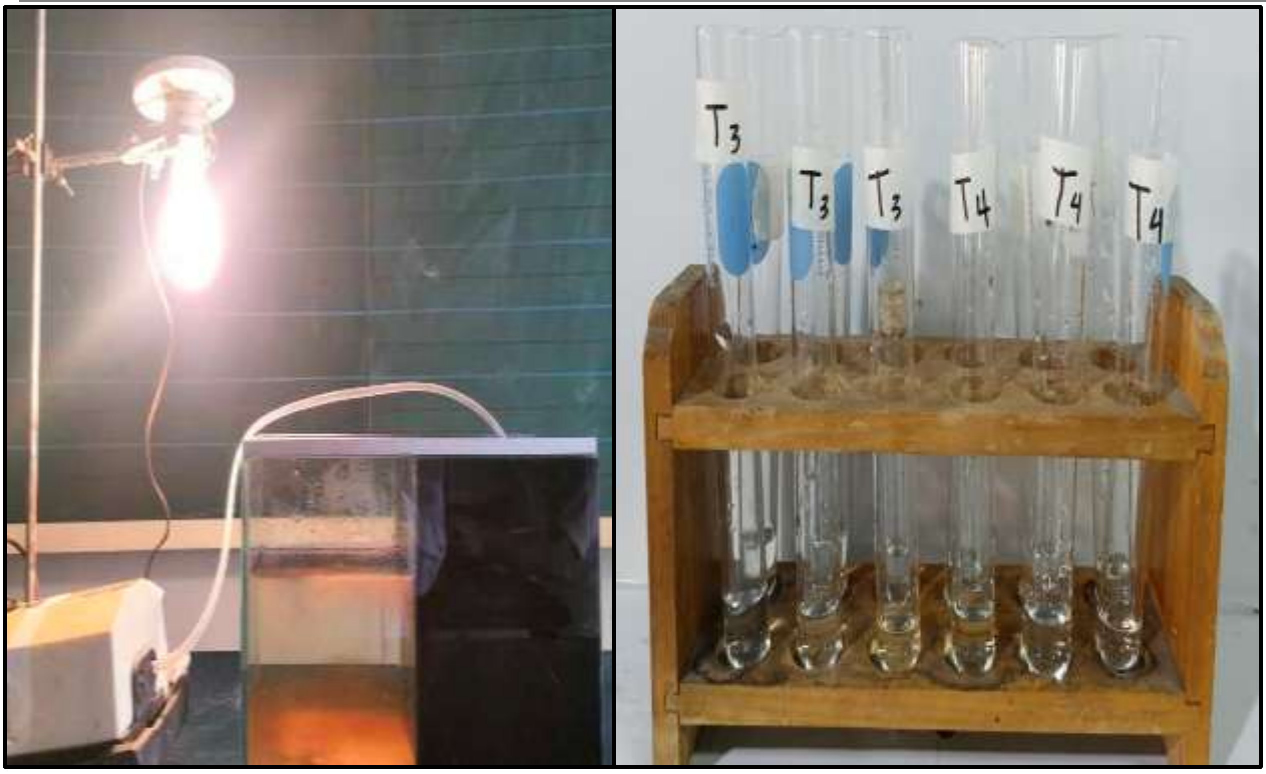

Figure 3. Brine Shrimp Collection Set-up and Cytotoxicity Testing

Antihyperglycemic Test

The antihyperglycemic activity test was done following the protocol of Kifle ZD et al. (2020). For two (2) weeks, the laboratory mice were acclimated in preparation for the antihyperglycemic activity test. The mice were fasted for six (6) hours, and the next day, their basic blood sugar levels were measured using a digital glucometer. The blood glucose was then recorded to serve as baseline for the test. To raise the blood glucose levels, the mice were then induced with dexamethasone at a dose of 20 µg/mL/kg once a day for five (5) days. Once the mice were induced with hyperglycemic drug, they were assigned into 5 groups, with 3 replicates each. The positive control (Metformin), the negative control (distilled water), and the experimental group of S. edule peel extract in varying concentrations were then administered. After an hour, the blood glucose was then measured and recorded for statistical analysis.

Figure 4. Inducing hyperglycemia to Albino Mice

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RESULTS AND DISCUSSION

Phytochemical Screening

Phytochemical analysis of the ethanolic peel extract of S. elude revealed the presence of bioactive compounds including alkaloids, flavonoids, saponins, phenols, and tannins. These substances exert antidiabetic effects by enhancing insulin sensitivity, inhibiting carbohydrate-digesting enzymes, and reducing oxidative stress [8].

Additionally, they demonstrate anticancer activity by modulating cell signaling pathways and inducing apoptosis in malignant cells through antioxidant and anti-inflammatory actions [6].

Table 1: Results of Phytochemical Analysis of Sechium Edule Peel Extract

Bioactive Compounds	Leaf Extract
Alkaloids	+
Flavonoids	+
Saponins	+
Phenols	+
Tannins	+

(+): present; (-): absent

Cytotoxicity Test

Table 2: Brine Shrimp Lethality Assay of S. edule Peel Extract

Treatment	REPLICATES			Average Mortality rate	probit	LC50
	R1	R2	R3			
1000	20	10	10	13	3.87	505.14
500	10	10	10	10	3.72	
100	0	10	10	7	3.52	
0	0	0	0	0	-	

Table 2 shows the percentage mortality and LC_{50} of Sechium edule peel extract. The extract was found active at 100µg/ml against the brine shrimps. Results show that the computed LC_{50} is 505.14 µg/mL which is greater than 100 µg/mL. This indicates that the Sechium edule peel extract is considered as nontoxic toward human cells. This suggests that the extract will not have adverse effect upon medicinal applications.

Chorioallantoic Membrane Assay

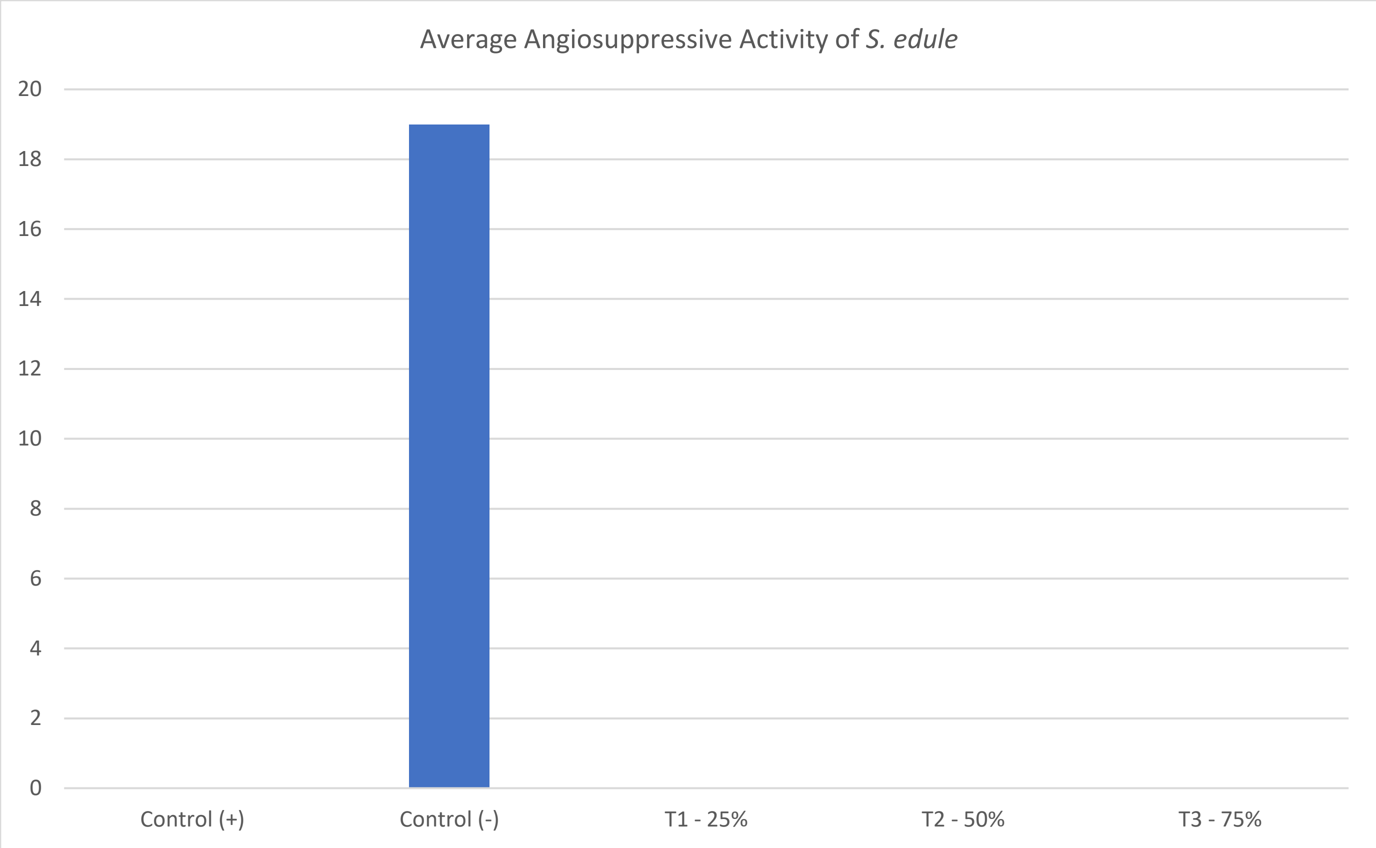

Figure 5. Results of Angiosuppressive Activity of Sechium elude Peel Extract

Figure 5 shows the average angiosuppresive ability of Methotrexate (positive control) and S. edule peel extract. The S. edule peel extract demonstrated significant anti-angiogenic activity.

Quantitative analysis of the duck embryos after 48 hours of administration showed a complete degeneration of blood vessel branch points in all treated concentrations. It is found that concentrations >25% exhibits toxicity toward the duck eggs leading to death. The concentrations have comparable result with the positive control.

Table 3: Descriptives of Angiosuppressive Activity of S. edule Peel Extract

Treatments	N	Mean	Std. Deviation
Control +	3	.0000	.00000
Control -	3	18.6667	1.52753
25%	3	.0000	.00000
50%	3	.0000	.00000
75%	3	.0000	.00000
Total	15	3.7333	7.75027

Table 3 shows the descriptive result of treatments. The negative control has the mean of 18.6667 with the standard deviation of 1.52753. Positive control and the concentrations have .0000 on both. This suggests that Sechium edule peel extract have similar results with the positive control. Therefore, S.edule peel extract exhibits angiosuppressive property.

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Table 4: Analysis of Variance of Angiosuppressive Activity of S. edule Peel Extract

	Sum of Squares	df	Mean Square	F	Sig.
Between Groups	836.267	4	209.067	448.000	.000
Within Groups	4.667	10	.467		
Total	840.933	14			

[a.] 0.05 Level of Significance

Table 4 presents the results of Analysis of Variance of the angiosuppressive activity of S. edule peel extract. Result shows that the computed p-value is 0.000 which is lower than the standard 0.05 confidence level. This implies that there is a significant difference between the comparison of number of blood vessel branch points in the treatments. This indicates that the S. edule peel extract has angiogenic property based on the table above.

Table 5, on the other hand, shows the multiple comparisons among the treatments. The p-value found between the negative control and the other treatments is 0.000, which indicates that there is a significant difference between and are comparable for its significant value is lower than the standard significant level at 0.05.

On the other hand, the positive control and 25%, 50%, and 75% concentrations of S. edule peel extract have comparable results in terms of its angiosupressive activity with a p-value of 1.000.

Thus, there is no significant difference and are comparable. The results revealed that concentrations >25% of the peel extract is at par with the result of the positive control in causing degeneration of the blood vessels in the duck embryo leading to death.

Table 5: Multiple Comparisons of the Angiosuppressive Activity of S. edule Peel Extract

Antihyperglycemic Activity Test

Table 6: Results of Antihyperglycemic Activity Test of S. edule Peel Extract

Treatments	Mean Baseline Blood Glucose Level	Mean Induced Blood Glucose Level	Mean Treated Blood Glucose Level	Mean Difference Blood Glucose Level
Positive Control	74.0	147.0	90.7	56.3
Negative Control	88.3	180.7	175.7	5.0
50 µ/mL	93.0	123.7	91.7	32.0
100 µ/mL	86.3	122.3	87.0	35.3
200 µ/mL	88.3	156.3	102.7	53.7

Table 6 presents the mean baseline, induced, and treated blood glucose levels of laboratory mice subjected to different treatments. Following glucose induction, all groups exhibited elevated blood glucose levels, confirming successful induction of hyperglycemia.

The negative control group showed minimal reduction in glucose levels after treatment, indicating the absence of spontaneous glucose normalization. In contrast, mice treated with the extract demonstrated notable reductions in blood glucose levels, particularly at concentrations of 100 µ/mL and 200 µ/mL. The 200 µ/mL group exhibited

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a mean glucose reduction (53.7 mg/dL) comparable to that of the positive control (56.3 mg/dL), suggesting a strong glucose-lowering effect.

Table 7: Descriptives of Antihyperglycemic Activity of S. edule Peel Extract

Treatments	N	Mean	Std. Deviation
Positive control	3	38.114	3.7044
Negative control	3	2.763	.9388
50 µ/mL	3	25.876	12.7821
100 µ/mL	3	28.924	13.5896
200 µ/mL	3	33.475	8.2421
Total	15	25.831	14.9145

[a.] 0.05 Level of Significance

Table 7 summarizes the mean blood glucose reduction across treatment groups, expressed with standard deviation. The positive control group recorded the highest mean glucose reduction, serving as a standard for effective anti-diabetic activity. Among the extract-treated groups, increasing concentrations resulted in progressively higher mean reductions, with the 200 µ/mL group showing a mean value (33.48) closest to the positive control (38.11).

The negative control group exhibited the lowest mean reduction, reinforcing the lack of therapeutic effect. This descriptive result further suggests that the extract exhibits measurable anti-diabetic effects, which become more consistent at higher concentrations.

Table 8: Analysis of Variance of Antihyperglycemic Activity of S. edule Peel Extract

	Sum of Squares	df	Mean Square	F	Sig.
Between Groups	2253.006	4	563.251	6.540	.007
Within Groups	861.193	10	86.119		
Total	3114.198	14			

a. 0.05 Level of Significance

Table 8 presents the results of the Analysis of Variance on the blood glucose–lowering effect of S. edule peel extract. The results show that the computed p-value is 0.007, which is lower than the standard 0.05 confidence level. This implies that there is a significant difference among the treatments in terms of mean blood glucose reduction. This indicates that the S. edule peel extract exhibits significant anti-diabetic activity based on the table above.

The extract-treated groups demonstrated a dose-dependent reduction in blood glucose levels. The 200 µg/mL group exhibited a mean reduction of 53.7 mg/dL, which is statistically comparable ($p > .05$) to the 56.3 mg/dL reduction observed in the Metformin (positive control) group.

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Table 9: Table for Multiple Comparison for the Antihyperglycemic Activity

(I) group	(J) group	Mean Difference (I-J)	Sig.
positive control	negative control	35.35084*	.001
	50 u/ml	12.23802	.137
	100u/ml	9.19002	.253
	200u/ml	4.63865	.554
negative control	positive control	-35.35084*	.001
	50 u/ml	-23.11282*	.012
	100u/ml	-26.16082*	.006
	200u/ml	-30.71219*	.002
50 u/ml	positive control	-12.23802	.137
	negative control	23.11282*	.012
	100u/ml	-3.04800	.696
	200u/ml	-7.59937	.340
100u/ml	positive control	-9.19002	.253
	negative control	26.16082*	.006
	50 u/ml	3.04800	.696
	200u/ml	-4.55137	.561
200u/ml	positive control	-4.63865	.554
	negative control	30.71219*	.002
	50 u/ml	7.59937	.340
	100u/ml	4.55137	.561

On the other hand, table 9 below shows the multiple comparisons among the treatments. The p-value obtained between the negative control and the extract-treated groups (50 µ/mL, 100 µ/mL, and 200 µ/mL) is less than 0.05, which indicates that there is a significant difference among these treatments and that their effects are comparable in terms of statistical significance since the values are lower than the standard significance level of 0.05. On the other hand, the positive control and the extract-treated groups showed comparable results in terms of blood glucose reduction, as their computed p-values were greater than 0.05. This means that there is no significant difference and the treatments are considered comparable. The results revealed that the S. edule peel extract, particularly at higher concentrations, is at par with the positive control in reducing blood glucose levels, indicating its potential anti-diabetic property.

CONCLUSION

The results of the study supported the phytochemical, anti-angiogenic, and anti-diabetic properties of the Sechium edule peel extract. The bioactive compounds alkaloids, flavonoids, saponins, phenols, and tannins indicate a promising source of phytonutraceuticals as they can be applied for further pharmacological use, such as enhancing insulin sensitivity and inhibiting the proliferation of malignant cells. Cytotoxicity analysis revealed that S. edule peel extract is considered non-toxic toward human cells, suggesting it will not have an adverse effect upon medicinal applications. The extract exhibited angiosuppressive and antihyperglycemic activities comparable to standard treatments, indicating its potential for cancer prevention and diabetes management. However, further isolation of its bioactive compounds is necessary to validate these findings and support future pharmacological applications. It is concluded that the extract operates through separate but complementary mechanisms: metabolic regulation of blood glucose and structural inhibition of tumor-related angiogenesis.

These findings suggest that S. edule peel extract is a promising, non-toxic lead for the development of phytonutraceuticals aimed at chronic disease management.

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