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The Histopathological Picture of The Pancreas in Hyperglycemic Obese White Rats After Giving Virgin Coconut Oil and Extra Virgin Olive Oil

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ABSTRACT

The pancreas is a glandular organ that has a crucial role in the body's digestive and metabolic systems. This study investigated the histopathological effects of virgin coconut oil (VCO) and extra virgin olive oil (EVOO) on the pancreas of hyperglycemic obese white rats. This study used a post-test only with control group design, involved 20 male Wistar rats were divided into four groups: negative control without treatment, negative control with alloxan induction, VCO treatment, and EVOO treatment. The rats were subjected to a high-fat and high-carbohydrate diet, followed by alloxan induction to induce hyperglycemia. VCO and EVOO were administered orally for 14 days. Histopathological analysis revealed that the negative control group 1 exhibited intact pancreatic tissue, while negative control group 2 showed significant damage. VCO administration resulted in improved pancreatic structure, but EVOO demonstrated superior efficacy, significantly enhancing the area, diameter, and density of the islets of Langerhans and the number of endocrine cells. As conclusion, statistical analysis confirmed significant differences among the groups, particularly highlighting EVOO effectiveness over VCO. The findings suggest that both oils have protective effects on pancreatic health, with EVOO being more effective in promoting beta cell regeneration.
Keywords: virgin coconut oil; extra virgin olive oil; pancreatic histopathology; hyperglycemia; obesity

INTRODUCTION

The pancreas is a glandular organ that has a crucial role in the body's digestive and metabolic systems, functioning in the production of digestive enzymes and the hormone insulin which regulates blood glucose levels. Pancreatic insufficiency can occur due to damage caused by various clinical conditions, including pancreatitis, diabetes, and obesity.[1] Diabetes mellitus, characterized by elevated blood sugar levels, is often caused by inadequate insulin secretion or insulin resistance, and its prevalence continues to increase globally.[2,3] Obesity and hyperglycemia are interrelated and can lead to serious metabolic disorders, including type 2 diabetes and cardiovascular disease.[4,5] Research shows that a diet rich in healthy fats, such as extra virgin olive oil (EVOO), can reduce the risk of metabolic diseases and improve lipid profiles.[6,7] EVOO is rich in monounsaturated fatty acids and phenolic compounds that have antioxidant and anti-inflammatory properties, contributing to the reduction of inflammation and oxidative stress, which are major risk factors in the development of pancreatic disease.[8,9]

Virgin Coconut Oil (VCO) is also known as a source of healthy fats that can help with weight management and blood sugar levels. VCO contains medium-chain fatty acids, such as lauric acid, which can increase metabolism and reduce body fat.[10] Research shows that VCO can contribute to the reduction of blood glucose levels and improvement of lipid profiles in experimental animals experiencing hyperglycemia.[11] Although these two oils have significant health benefits, their mechanisms of action and histopathological effects on the pancreas may differ. Previous research has shown that EVOO consumption can reduce pancreatic inflammation and improve beta-cell function, while VCO can affect lipid and glucose metabolism in different ways.[12,13]

This study aimed to analyze the comparison of pancreatic histopathology in hyperglycemic obese white rats after administration of VCO and EVOO, with the hope of gaining a better understanding of the impact of these two types of oil on the structure and integrity of pancreatic tissue. The general objective of this study is to analyze the effect of VCO and EVOO on the histopathological picture of the pancreas, with specific objectives including measurement of the area, diameter, and density of the islets of Langerhans and the number of pancreatic endocrine cells after administration of placebo in non-obese and hyperglycemic obese white rats, as well as after administration of VCO and EVOO.

METHODS

The research design was a true experimental study with a post-test only with control group.[14] Male Wistar rats (*Rattus norvegicus*), aged 2-4 months and weighing 200-300 grams, were used as the research population. The study was conducted at the Laboratory of the Faculty of Medicine, Universitas Muslim Indonesia, from June to July 2024. A total of 20 rats were divided into four groups: (1) negative control without treatment, (2) negative control with alloxan induction, (3) VCO treatment group, and (4) EVOO treatment group. The inclusion criteria were healthy male rats weighing ≥200 grams and glucose levels >135 mg/dl after alloxan induction, while exclusion criteria included rats weighing <200 grams, glucose levels <135 mg/dl, or

morphological abnormalities. The sampling technique used was purposive sampling, ensuring only rats meeting the criteria were included.

Rats were fed a high-fat and high-carbohydrate diet using duck egg yolk at a dose of 1.8 grams per 200 grams of body weight daily. Hyperglycemia was induced by intraperitoneal administration of alloxan at a dose of 30 mg/200 grams of body weight. VCO and EVOO were administered orally at doses determined based on previous literature, with VCO given at 2 ml/200 grams of body weight and EVOO at 1 ml/200 grams of body weight daily for 14 days. Histopathological analysis was performed to evaluate the area, diameter, density of the islets of Langerhans, and the number of pancreatic endocrine cells. Measurements were conducted using ImageJ software on images captured with a light microscope, and staining was performed using hematoxylin and eosin (H&E). To minimize bias, the histopathological assessment was conducted blindly, with the researcher unaware of the group identities during analysis.

Normality was tested using the Shapiro-Wilk test, homogeneity of variance was assessed using Levene's test, and group comparisons were performed using One-Way ANOVA followed by post-hoc tests (e.g., LSD or Tukey) for significant differences.[15,16] The study adhered to ethical guidelines, with approval obtained from the Faculty of Medicine and the laboratory. The results are expected to provide insights into the therapeutic potential of VCO and EVOO in managing pancreatic damage in hyperglycemic obese conditions, contributing to the development of alternative therapies for obesity and diabetes.

RESULT

In negative control group 1, which was not given a high-fat diet, alloxan, or VCO/EVOO treatment, the histopathological picture of the pancreas showed intact and healthy tissue structure. The islets of Langerhans appeared normal with uniform size and high density, as well as a homogeneous distribution of endocrine cells, with no visible damage (Figure 1).

Negative control group 2, which was given a high-fat diet and alloxan, showed damage to the structure of pancreatic tissue. The islets of Langerhans appeared to shrink with a decrease in endocrine cell density. Some endocrine cells showed signs of pyknosis, indicating cellular damage, as well as areas of degeneration with irregular cytoplasm (Figure 2).

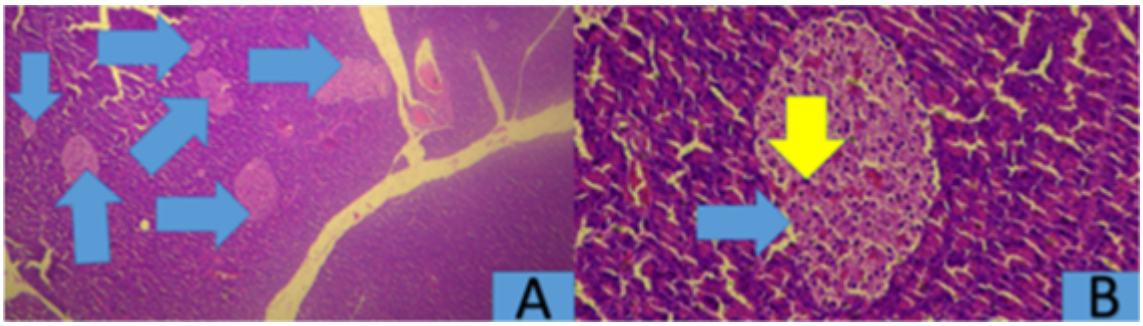

Figure 1. Histopathology of the pancreas of white mice with hematoxylin and eosin (H&E) staining, at 40x (A) and 400x (B) magnification, in mice in the negative control group 1. The blue arrow indicates the islets of Langerhans, and the yellow arrow indicates endocrine cells.

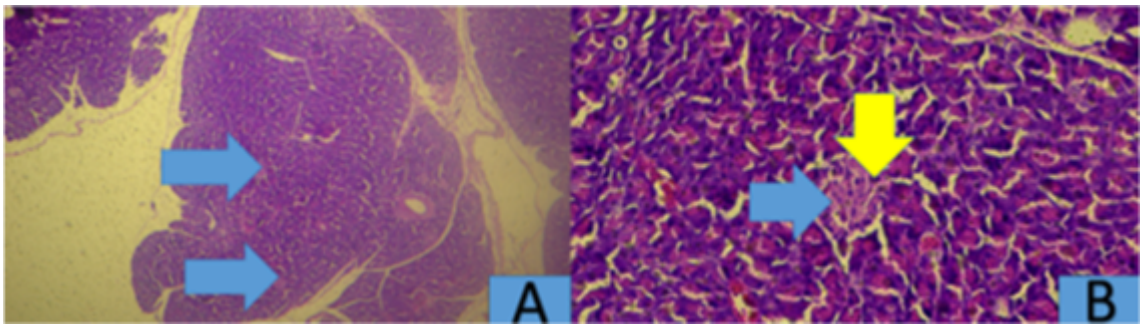

Figure 2. Histopathology image of the pancreas of a white rat with HE staining, at 40x (A) and 400x (B) magnification, in the negative group 2 rats. The blue arrow indicates the islets of Langerhans, and the yellow arrow indicates endocrine cells.

In the group given virgin coconut oil (VCO) after alloxan induction, there was an improvement in the structure of the pancreatic tissue compared to the negative control group 2. The islets of Langerhans appear larger, although they have not yet returned to normal. Endocrine cells show signs of regeneration with increased area and density, although there are still areas of degeneration (Figure 3).

The group given extra virgin olive oil (EVOO) after alloxan induction showed a more significant improvement in pancreatic tissue than the VCO group. The islets of Langerhans in the EVOO group showed an increase in size and density, with an organized endocrine cell core and uniform cytoplasm, indicating better tissue recovery (Figure 4).

Histopathological observations show significant differences between the four groups. Negative control 1 has the best islet of Langerhans structure, while negative control 2 is severely damaged. The VCO group shows moderate improvement, while the EVOO group shows better improvement, indicating a stronger protective effect on pancreatic tissue (Figure 5).

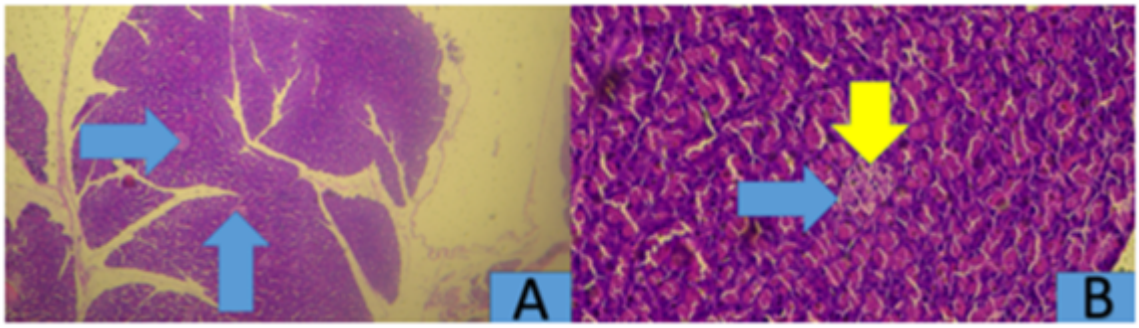

Figure 3. Histopathology image of the pancreas of white mice with HE staining, at 40x (A) and 400x (B) magnification, in mice in the virgin coconut oil (VCO) group. The blue arrow indicates the islets of Langerhans, and the yellow arrow indicates endocrine cells.

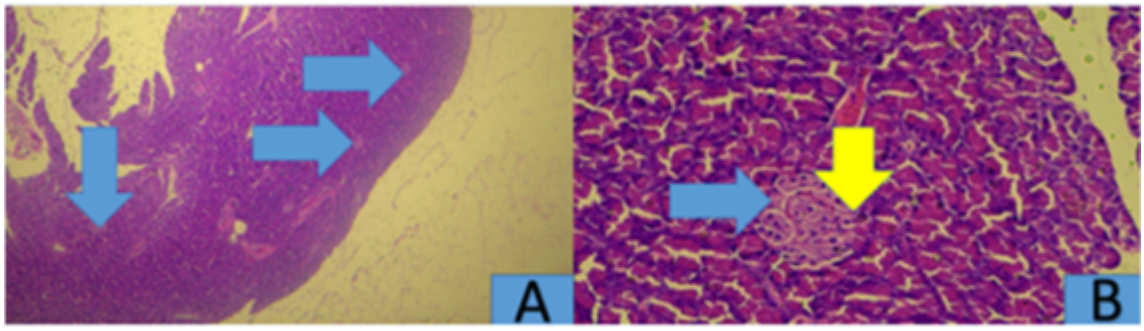

Figure 4. Histopathology image of the pancreas of white mice with HE staining, at 40x (A) and 400x (B) magnification, in mice of the extra virgin olive oil (EVOO) group. The blue arrow indicates the islets of Langerhans, and the yellow arrow indicates endocrine cells.

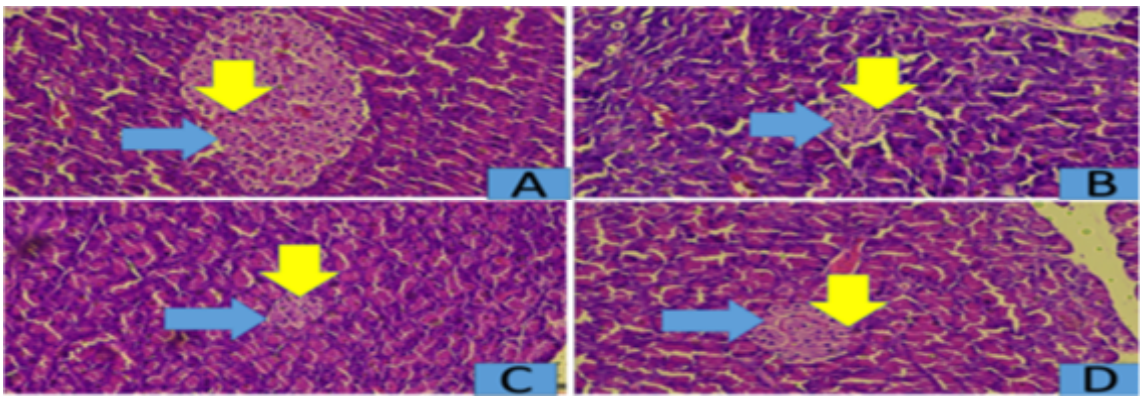

Figure 5. Histopathological image of the pancreas of white mice with HE staining at 400x magnification: A (negative control group 1), B (negative control group 2), C (VCO group), D (EVOO group), blue arrow indicates islets of Langerhans, and yellow arrow indicates endocrine cells.

Table 1 presents the results of the data analysis for the count of endocrine cells (beta cells) across different experimental groups. The negative control group 2 exhibited a mean count of 3.33 with a standard deviation of 1.36, indicating a significant reduction in beta cell numbers. In contrast, the negative control group 1 showed a higher mean of 7.00. The groups receiving treatment with VCO and EVOO had mean counts of 4.80 and 7.33, respectively. Notably, the ANOVA test revealed significant differences among the groups ($p = 0.002$).

Table 2 presents the results of the statistical analysis comparing the endocrine cell count (specifically beta cells) between different treatment groups, utilizing the Least Significant Difference (LSD) test. The p-values indicate the significance of the differences observed between the groups. A p-value of 0.002 between negative control 2 and negative control 1 suggests a statistically significant difference in beta cell counts, indicating that the treatments or conditions applied to these groups had a notable impact on beta cell preservation or regeneration. In contrast, the comparison between negative control 2 and VCO yielded a p-value of 0.180, indicating no significant difference, suggesting that VCO did not have a substantial effect on beta cell counts compared to negative control 2. However, the comparison between Negative Control 2 and EVOO showed a significant p-

value of 0.001, highlighting EVOO effectiveness in enhancing beta cell counts. The comparison between negative control 1 and VCO yielded a p-value of 0.050, which is on the threshold of significance, suggesting a potential benefit of VCO that warrants further investigation. Conversely, the comparison between negative control 1 and EVOO (p = 0.744) indicates no significant difference, suggesting that EVOO effect may not be as pronounced in this specific context. Lastly, the comparison between VCO and EVOO resulted in a p-value of 0.026, indicating a significant difference, with EVOO likely demonstrating superior efficacy in enhancing beta cell counts compared to VCO.

Table 1. Results of data analysis of endocrine cell count (beta cells)

	Statistics test					
	Frequency	Mean	SD	Normality test (p)	Homogeneity test (p)	Anova (p)
Negative control 2	6	3.33	1.36	0.093	0.100	0.002
Negative control 1	6	7.00	1.54	0.456		
VCO	5	4.80	1.09	0.135		
EVOO	6	7.33	2.50	0.907		

Table 2. Statistical analysis test for comparison of endocrine cell count (beta cells) between groups

Comparison between groups	p value
Negative control 2 & negative control 1	0.002
Negative control 2 & VCO	0.180
Negative control 2 & EVOO	0.001
Negative control 1 & VCO	0.050
Negative control 1 & EVOO	0.744
VCO & EVOO	0.026

a = Least Significant Difference (LSD) test results

Table 3. Results of analysis of islet average area data

Group	Statistics test					
	Frequency	Mean	SD	Normality test (p)	Homogeneity test (p)	Kruskal Wallis Test (p)
Negative control 2	6	0.0006	0.00042	0.069	0.000	0.050
Negative control 1	6	0.0019	0.00169	0.084		
VCO	5	0.0003	0.00023	0.219		
EVOO	6	0.0004	0.00033	0.023		

Table 4. Statistical analysis test for comparison of mean area of Langerhans islets between groups

Comparison between groups	p value
Negative control 2 & negative control 1	0.150
Negative control 2 & VCO	0.234
Negative control 2 & EVOO	0.337
Negative control 1 & VCO	0.028
Negative control 1 & EVOO	0.030
VCO & EVOO	0.522

a = Mann-Whitney test results

Table 3 presents the results of the analysis of the average area of pancreatic islets across different treatment groups, including statistical tests for normality, homogeneity, and the Kruskal-Wallis test. The data show that the mean islet area varies among the groups, with negative control 1 having the highest mean (0.0019) and VCO the lowest (0.0003). The standard deviation (SD) values indicate variability within each group, with negative control 1 showing the highest variability (SD = 0.00169) and VCO the lowest (SD = 0.00023). The normality test results (p-values) suggest that the data for all groups, except EVOO (p = 0.023), are normally distributed, as their p-values exceed the 0.05 threshold (negative control 2: p = 0.069; negative control 1: p = 0.084; VCO: p = 0.219). However, the homogeneity test yielded a p-value of 0.000, indicating that the variances across groups are not equal, necessitating the use of the non-parametric Kruskal-Wallis test. The Kruskal-Wallis test result (p = 0.050) suggests a borderline significant difference in the average islet area among the groups, implying that the treatments or conditions may have varying effects on islet size.

Table 4 presents the results for the comparison of the mean area of Langerhans islets between different groups using the Mann-Whitney test. The comparison between negative control group 2 and negative control group 1 yielded a p-value of 0.150, indicating no significant difference in islet area. Similarly, comparisons between negative control group 2 and both the VCO (p = 0.234) and EVOO (p = 0.337) groups also showed no significant differences. However, significant differences were observed between negative control group 1 and the VCO (p = 0.028) and EVOO (p = 0.030) groups, suggesting that both treatments positively influenced islet area compared to the negative control. The comparison between the VCO and EVOO groups did not reveal significant differences (p = 0.522).

Table 5. Results of data analysis of mean islet of Langerhans density

Group	Statistics test					
	Frequency	Mean	SD	Normality test (p)	Homogeneity test (p)	Kruskal Wallis test (p)
Negative control 2	6	1.833	1.602	0.001	0.054	0.016
Negative control 1	6	6.167	3.868	0.368		
VCO	5	4.200	2.167	0.272		
EVOO	6	7.500	1.870	0.961		

a = Normality test results; homogeneity; Kruskal-Wallis

Table 5 presents the results of the data analysis for the mean density of Langerhans islets across different experimental groups. The negative control group 2 exhibited a mean density of 1.833, indicating a significantly

lower density compared to the other groups. In contrast, the negative control group 1 had a mean density of 6.167, while the VCO group showed a mean density of 4.200. The EVOO group demonstrated the highest mean density at 7.500. The Kruskal-Wallis test indicated significant differences among the groups (p = 0.016), suggesting that the treatments had a notable impact on the density of Langerhans islets.

Table 6. Statistical data analysis results comparison of mean Langerhans island density between groups

Comparison between groups	p value
Negative control 2 & negative control 1	0.068
Negative control 2 & VCO	0.031
Negative control 2 & EVOO	0.004
Negative control 1 & VCO	0.598
Negative control 1 & EVOO	0.582
VCO & EVOO	0.043

a = Results of the Mann-Whitney test

Table 7. Results of data analysis of mean islet diameter

Group	Statistics test					
	Frequency	Mean	SD	Normality test (p)	Homogeneity test (p)	Kruskal Wallis test (p)
Negative control 2	6	0.028	0.01127	0.567	0.000	0.014
Negative control 1	5	0.049	0.02700	0.147		
VCO	5	0.017	0.00654	0.387		
EVOO	6	0.014	0.00082	0.091		

a = Normality test results; homogeneity; Kruskal-Wallis

Table 8. Statistical data analysis results comparison of mean islet of langerhans diameter between groups

Comparison between groups	p value
Negative control 2 & negative control 1	0.143
Negative control 2 & VCO	0.170
Negative control 2 & EVOO	0.043
Negative control 1 & VCO	0.032
Negative control 1 & EVOO	0.005
VCO & EVOO	0.707

a = Mann-Whitney Test Results

The comparison between negative control group 2 and negative control group 1 yielded a p-value of 0.068, indicating no significant difference in islet density. However, significant differences were observed when comparing negative control group 2 with both the VCO group (p = 0.031) and the EVOO group (p = 0.004), suggesting that both treatments effectively increased islet density compared to the negative control. Comparisons between negative control group 1 and the VCO (p = 0.598) and EVOO (p = 0.582) groups did not show significant differences. Notably, the comparison between the VCO and EVOO groups revealed a significant difference (p = 0.043), indicating that EVOO may have a superior effect on islet density compared to VCO (Table 6).

The negative control group 2 exhibited a mean islet diameter of 0.028, while the negative control group 1 had a larger mean diameter of 0.049. The VCO group showed a mean diameter of 0.017, and the EVOO group had the smallest mean diameter at 0.014. The Kruskal-Wallis test indicated significant differences among the groups (p = 0.014), suggesting that the treatments had a notable impact on islet diameter, with variations observed in the effects of VCO and EVOO compared to the control groups (Table 7).

The comparison between negative control group 2 and negative control group 1 yielded a p-value of 0.143, indicating no significant difference in islet diameter. However, significant differences were observed when comparing negative control group 2 with the EVOO group (p = 0.043), suggesting that EVOO treatment resulted in a smaller islet diameter compared to the negative control. Additionally, significant differences were noted between negative control group 1 and both the VCO group (p = 0.032) and the EVOO group (p = 0.005), indicating that both treatments influenced islet diameter. The comparison between the VCO and EVOO groups did not reveal significant differences with p-value = 0.707 (Table 8).

DISCUSSION

Effect of Alloxan on the Histopathology of the Pancreas

The results showed that alloxan induction can increase blood glucose levels and damage the ultrastructure of pancreatic beta cells, in line with findings confirming beta cell damage due to alloxan induction.[17] Alloxan mimics the structure of glucose and is transported by the GLUT2 transporter into beta cells, triggering the production of Reactive Oxygen Species (ROS) through redox reactions. The accumulation of ROS causes damage to cell membranes, DNA, and intracellular organelles such as mitochondria, which ultimately leads to cell death.[18] Further research confirms that alloxan contributes to the destruction of pancreatic beta cells, so that the effect of alloxan on the pancreas creates a consistent histopathological picture in various studies. This demonstrates the importance of understanding the impact of oxidative stress in the pathogenesis of diabetes.

The Effect of VCO on Beta Cell Improvement

The results showed that the administration of VCO was able to increase the area of the islets of Langerhans and the density of pancreatic beta cells in alloxan-induced rats, with a protective effect that can be attributed to the lauric acid, polyphenol, and tocopherol content in VCO, which has antioxidant and anti-inflammatory properties. Previous research indicates that VCO, which is rich in these components, contributes to the protection of pancreatic beta cells from damage due to oxidative stress, as well as increasing cellular energy metabolism which supports pancreatic tissue regeneration. In addition, VCO not only improves the histopathological profile of beta cells, but also increases the

number of beta cells in alloxan-exposed mice, supporting findings that indicate broader regenerative potential, including accelerated wound healing and increased fibroblast proliferation. Thus, VCO functions as a promising therapeutic agent in improving pancreatic health in conditions of obesity and hyperglycemia.[19–21]

The findings confirm that alloxan is a potent inducer of pancreatic beta cell damage, primarily through oxidative stress mechanisms. This underscores the critical role of oxidative stress in the pathogenesis of diabetes and highlights the need for therapeutic strategies that target ROS production and its damaging effects. While alloxan is a valuable tool for studying diabetes in animal models, its use should be carefully controlled to ensure consistent and reproducible results. Future research should explore ways to mitigate alloxan-induced damage while maintaining its utility in diabetes research.

The Effect of EVOO on Beta Cell Enhancement

The results showed that polyphenols in EVOO can increase insulin secretion and glycemic control in type 2 diabetes patients, as well as increase insulin sensitivity through PPAR-γ pathway activation, which plays an important role in improving pancreatic endocrine function. In addition, the fatty acid composition in EVOO plays an important role in the characterization of olive oil, which can affect the biochemical and molecular effects on pancreatic health. Thus, EVOO not only enhances beta-cell regeneration but also has the potential to reduce insulin resistance in diabetic models, making it a better choice than VCO in this context.[6,22–25]

The results suggest that VCO has significant potential as a therapeutic agent for improving pancreatic health, particularly in conditions of hyperglycemia and oxidative stress. Its antioxidant and anti-inflammatory properties, attributed to components like lauric acid and polyphenols, make it a promising candidate for protecting and regenerating beta cells. However, further clinical studies are needed to validate these findings in humans and to determine optimal dosages and long-term effects. VCO's affordability and accessibility also make it a viable option for populations in resource-limited settings.

EVOO ability to enhance insulin secretion, improve glycemic control, and reduce insulin resistance makes it a superior choice for managing diabetes compared to VCO. The high concentration of polyphenols in EVOO, such as tyrosol and caffeic acid, provides robust protection against oxidative stress and supports beta cell regeneration. These findings highlight the importance of dietary interventions in diabetes management and suggest that EVOO should be incorporated into the diets of individuals at risk of or living with diabetes. However, its higher cost and limited availability in some regions may restrict its widespread use.

Comparison of the Effectiveness of VCO and EVOO on Beta Cell Improvement

The results showed that both VCO and EVOO have a protective effect on the pancreas, but EVOO showed more significant results in increasing the number of beta cells. This advantage is most likely due to the higher phenolic concentration in EVOO, which provides stronger protection against oxidative stress. Previous research indicates that the lauric acid content in VCO can stimulate GLP-1, which plays a role in improving beta cell function, while polyphenols in EVOO, such as tyrosol and caffeic acid, can protect beta cells from apoptosis and increase glucose sensitivity. The superiority of EVOO in increasing the number of beta cells may be related to the higher concentration of polyphenols, which provide stronger protection against oxidative stress. Nevertheless, VCO remains an attractive alternative due to its wider availability and more affordable price, especially in developing countries.[19,22,26–28]

While both VCO and EVOO demonstrate protective effects on pancreatic beta cells, EVOO higher phenolic content gives it an edge in terms of efficacy, particularly in reducing oxidative stress and enhancing beta cell regeneration. However, VCO remains a valuable alternative due to its affordability and accessibility, especially in developing countries. The choice between VCO and EVOO may ultimately depend on individual circumstances, including cost, availability, and specific health needs. Future research should focus on optimizing the use of both oils in combination to maximize their therapeutic benefits.

Research Limitations

This study has several limitations that should be acknowledged. First, the sample size of 20 rats, while sufficient for preliminary analysis, may limit the generalizability of the findings. A larger sample size could provide more robust data and enhance the statistical power of the results. Second, the study was conducted over a relatively short treatment period of 14 days, which may not fully capture the long-term effects of VCO and EVOO on pancreatic health. Future studies should consider longer treatment durations to assess the sustained impact of these oils. Additionally, the research focused solely on male Wistar rats, which may introduce gender bias; including female rats in future studies could provide a more comprehensive understanding of the effects of VCO and EVOO. Furthermore, while histopathological analysis was performed, the study did not explore the underlying molecular mechanisms by which these oils exert their effects on pancreatic tissue, which could provide valuable insights into their therapeutic potential. Lastly, the study's reliance on animal models may limit the applicability of the findings to human subjects, necessitating further clinical trials to validate the results in a human population. Addressing these limitations in future research will enhance the understanding of the therapeutic roles of VCO and EVOO in managing obesity and diabetes.

CONCLUSION

Based on the results of the study on the comparison of the histopathological picture of the pancreas in hyperglycemic obese white rats after administration of VCO and EVOO, it can be concluded that the administration of VCO resulted in an improvement in the pancreas, with an increase in the number of endocrine cells, area, diameter, and density of the islets of Langerhans, while EVOO showed a more significant improvement. There were significant differences in the number of endocrine cells, diameter, and density of the islets of Langerhans between the EVOO group and the other groups, which showed that EVOO was more effective than VCO in improving the histopathological picture of the pancreas.

For further research, it is advisable to explore variations in the doses of VCO and EVOO, using test animals with more diverse health conditions, as well as developing molecular studies related to the mechanisms of action of both oils. In the context of clinical applications, clinical trials in humans are needed to confirm the safety and effectiveness of VCO and EVOO as adjunctive therapies, as well as research into their interactions with standard diabetes therapies. In addition, public education about the benefits of natural oils such as VCO and EVOO should be enhanced, and the public is encouraged to integrate the consumption of these two oils into their daily diets as a preventive measure against obesity and diabetes, paying attention to safe dosages.

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