Jurnal Ners Volume 10 Nomor 1 Tahun 2026 Halaman 1849 - 1855
JURNAL NERS
Research & Learning in Nursing Science
http://journal.universitaspahlawan.ac.id/index.php/ners

THE POTENTIAL OF SNAKE FRUIT PEEL EXTRACT AS A SUPPLEMENT TO METFORMIN FOR ANTIDIABETIC THERAPY AND FOR PREVENTING CELL APOPTOSIS: A *SYSTEMATIC REVIEW*

Anditri Weningtyas
Department of Medicine, Faculty of Medicine, Universitas Negeri Malang, Indonesia
anditri.weningtyas.fk@um.ac.id

Abstract

The white race, especially the adult population, has a prevalence of type 2 diabetes ranging from 3% to 6%. The diabetes frequency in Singapore has greatly escalated in the past ten years. Despite being called a tropical country, Indonesia is the world's second-largest contributor to biodiversity (following Brazil). Approximately 2,500 species of plants are classified as herbs in Indonesia, which has about 30,000 species. An example of these herbs is snake fruit that gives numerous pharmacological effects, such as immunostimulator, antioxidant, antidiabetic, and it improves lipid profile. A lot of types of snake fruit can be found in Indonesia, and their various content are likely to appear due to the different types of snake fruit's physical conditions, as indicated in the previous research. Phenolic compounds and flavonoid groups can inhibit the α-glucosidase enzymes due to being capable of neutralize free radicals, and eventually, pancreatic beta cell apoptosis can be prevented. Methods use Systematic Review by conducting literature searches using PubMed and Ebsco. The literature discusses snake fruit, antidiabetic and cell apoptosis. There are six studies, concluding that snake fruit can be antidiabetic and it prevents cell apoptosis. Snake fruit can be an antidiabetic alternative in the treatment of diabetes, particularly in preventing cell apoptosis.

Keyword: *Snake Fruit, Antidiabetic, Cell Apoptosis*

* Corresponding author : Anditri Weningtyas
Email : anditri.weningtyas.fk@um.ac.id

INTRODUCTION

The white race, particularly the adult population, has a prevalence of type 2 diabetes, ranging from 3% to 6%. The increasing frequency of diabetes in Singapore has considerably escalated in the past ten years. Besides, in the United States, those who suffering from diabetes have greatly increased, namely from 6,536,163 people in 1990 to 20,676,427 people in 2010. The occurrence of diabetes among Indonesians generally falls between 1.4% and 1.6%, although certain areas, such as Pekajangan (2.3%) and Manado (6%), report considerably higher rates [1]. While Papua records the lowest prevalence of diabetes mellitus (DM) at around 1.7%, the Ministry of Health's Basic Health Research (Riskesdas) Report states that DM affects about 5.7% of residents aged over 15 living in urban areas. While impaired glucose tolerance (IGT) averages about 10.2%, with reported figures stretching from as low as 4.0% in Jambi to as high as 21.8% in West Papua, the regions with the greatest overall prevalence are East Kalimantan and North Maluku, each reaching approximately 11.1% [2]. When considering both physician-confirmed cases and reported symptoms, diabetes mellitus in Indonesia affects about 2.1% of the population, whereas cases identified solely through a doctor's diagnosis represent only 1.5%. In DI Yogyakarta (2.6%), followed by DKI Jakarta (2.5%), North Sulawesi (2.4%), and East Kalimantan (2.3%), the doctor-diagnosed diabetes rate reaches its highest levels. In Sulawesi Tengah (3.7%), followed by Sulawesi Utara (3.6%), Sulawesi Selatan (3.4%), and Nusa Tenggara Timur (3.3%), the prevalence of diabetes, whether identified through medical diagnosis or reported symptoms, reaches its highest levels. Evidence indicated that men exhibit a lower prevalence of diabetes mellitus compared to women. Additionally, the prevalence of DM according to the doctor's diagnosis comprises 1.8%; meanwhile, the prevalence diagnosed by the doctors and symptoms comprises 2.3% [2].

Lately, there has been a report informing that herb is categorized as a drug and it is greatly demanded. Based on the information presented in the document *Promoting the Role of Traditional Medicine in Health System: Strategy for the African Region*, it is noted that nearly 80% of the population in WHO member states across Africa rely on traditional medicine for their healthcare needs. Citing data from the WHO Regional Office for the Americas (AMOR/PAHO), the report highlighted that in Chile nearly 71% of residents, and in Colombia about 40%, make use of herbal medicinal products [3]. In the meantime, Indonesia is categorized as a tropical country and it occupies the second ranking (after Brazil) of the most enormous countries in the world, having vast biodiversity. Additionally, there are approximately 30,000 plant species that people can encounter in Indonesia in which there are roughly 2,500 species from those plants that emerge as herbs [4]. The example of those herbs is snake fruit, containing numerous pharmacological effects such as immunostimulator, antioxidant, antidiabetic, and it improves profile lipid.

The results of phytochemical test indicated that snake skin and flesh evidenced the emergence of the alkaloid group of compounds, flavonoids, hydroquinone, steroids, and tannins. Besides, saponins are contained in some certain types of snake fruits. The study utilized snake fruit that was attained from Cililin, Tasikmalaya and Taman Buah Mekarsari, and the test of the extracts was conducted for the antidiabetic through α-glucosidase inhibition test [5]. In Indonesia, a lot of types of snake fruit can be found. Additionally, the emersion of various content is likely to happen. The underlying reason of these differences is because of the physical conditions of the snake fruit types, as mentioned in the previous study. Phenolic compounds and flavonoid groups can be functioned to inhibit α- glucosidase enzymes since they have the capability in terms of neutralizing free radicals; as a consequence, pancreatic beta cell apoptosis that generates insulin can be prevented [6]. This review aimed at determining the benefits of snake fruit as an antidiabetic alternative in preventing cell apoptosis.

METHODS

The method used in the Systematic Literature Review was PRISMA-P (Preferred Reporting Items for Systematic Reviews and Meta-Analyses Protocols) Checklist 2015 [7]. Quality Assessment was applied to assist in

assessing the methodological quality of a journal, and the JBI Critical Appraisal Checklist table was utilized in the assessment process [8]. PICO method was employed for journal searches through PubMed and Ebsco, and six journals were attained.

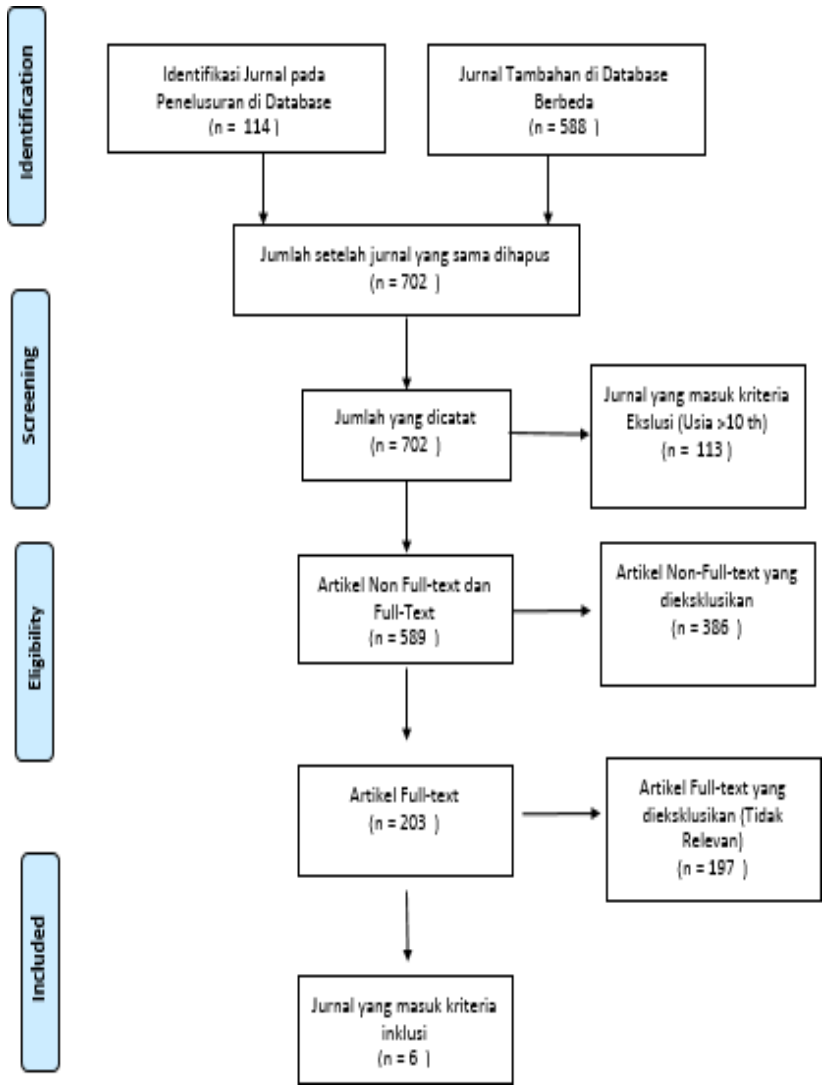

Figure 1. PRISMA Flow Diagram

RESULT AND DISCUSSION

This study discussed snake fruit as antidiabetic and prevention of cell apoptosis.

Based on the journals reviewed, the following table is obtained:

No	Title	Author	Year	Result
1	Anti-Diabetic Effect of Snake Fruit Skin Extract in Alloxan-	Marzuki, Girsang, Nasution, Lister	2022	SFSE indicated the antihyperglycemic effects

	Induced Wistar Rat			
2	Potensi Ekstrak Etanol Kulit Buah Salak Terhadap Histopatologi Pankreas Tikus Putih Jantan Diabetes Melitus	Utami, Sariani, Tandi	2022	Ethanol extract of salak fruit peel was effective in regenerating rat pancreatic cells
3	Aktivitas Antidiabetes Ekstrak Kulit Buah Salak Manonjaya dengan Ikan Zebra (Danio rerio) Sebagai Hewan Model	Rohaeti, Nurafifah, Batubara	2022	The ethyl acetate fraction provided the most active spot as an α glucosidase inhibitor.
4	Efek Pemberian Ekstrak Buah Salak (Salacca zalacca) dalam Menurunkan Kadar Glukosa Darah Pada Tikus Model Diabetes Melitus	Datu, Lebang, Suoth	2023	Snake fruit extract significantly affected blood glucose profiles and body weight
5	Literature Review: Pengaruh Kulit Salak (Salaca Zalacca) Terhadap Glukosa Darah	Suntara	2023	Salak bark helps lower the level of blood sugar, emerges as an inhibitor of α-glucosidase, regeneration of β pancreatic cells, and an increase in insulin sensitivity.
6	Efektivitas Ekstrak Etanol Kulit Salak (Salacca zalacca) Terhadap Penurunan Berat Badan Dan Kadar Gula Darah Tikus Putih (Rattus norvegicus)	Valentino et al.	2021	The dose of EEKS gave the highest effects on lowering the KGD.

Discussion

Numerous phytochemical constituents, including alkaloids, steroids or triterpenoids, flavonoids, and tannins, were found to be present in the ethanolic extract of snake fruit peel, according to the findings obtained in this study. The presence of phenols, flavonoids, tannins, monoterpenoids, saponins, steroids/triterpenoids, and alkaloids in snake-fruit peel extract, as reported in other studies, is also confirmed by the findings of the present research. Among the various benefits associated with the phytochemical compounds found in the ethanolic extract of snake-fruit skin is their function as antioxidants or skin-brightening agents. The antihyperglycemic action of SFSE is not only associated with its phytochemical constituents but is also supported by the extract's superior overall quality [9]. Antioxidant and inhibitory effects that are contained in saponins and flavonoids affect glucosidase enzymes. The effects given by inhibitory of the-glucosidase enzymes are capable of absorbing glucose in the digestive tract, and eventually the level of postprandial blood glucose can be reduced. Additionally, the antioxidant effects offered by SFSE ethanol give a contribution to antidiabetic effects. It is linked to the pancreatic damage mechanisms resulted from alloxan. GSH then reduces alloxan, forming unsteady dialuric acids. Besides, it will ultimately go through autoxidation

so that alloxan radicals can be formed [10].

The DNA framework of pancreatic β-cells can be disrupted and the thiol groups of the glucokinase enzyme can be blocked as a result of alloxan-derived radicals, which ultimately leads to β-cell injury. A decrease in insulin release occurs when ATP generation in pancreatic β-cells is disrupted by the inhibition of the glucokinase enzyme's thiol group; meanwhile, the impairment of β-cell DNA structure can lead these cells to undergo death. Stemming from the mechanism of the alloxan actions, the SFSE that consists of saponins and flavonoids has an ability to give antioxidant effects through the donation of electrons to the constructed alloxan radicals; as a result, alloxan compounds that are more stable can eventually be generated, in the meantime, the dangers of the alloxan in pancreatic tissues can ultimately be reduced. It is denoted in the result of the study, indicating that an improvement in the pancreatic structures is found by escalating or adding the doses of the mangrove leaf extract [11].

The distinction of the content can be caused by the various types of snake fruit physical conditions, grounded in the previous study. Phenolic compounds and flavonoid groups can serve as the inhibitory of α-glucosidase enzymes due to being capable of neutralizing free radicals so that the damages in pancreatic beta cells in producing insulin can be avoided [12].

Grounded in the study conducted by Utami et al. (2022), particularly in the results of the damage score pancreatic β cells in 6 groups, it was mentioned that based on the samples that were attained, the damage score for the "normal controls" group was 0; it can be viewed in the picture showing that cell damage in Langerhans or exocrine cells was not found. It occurred because the normal group did not receive streptozotocin; it ultimately damages the pancreas. Besides, it merely suspended functional Na-CMC serving as a solution stabilizer, and it did not affect the sugar blood level. Conversely, the highest damage score was attained by the negative control group, in which the high score was with average damage, namely three. Moreover, it was proven that the occurrence of serious damage indeed happened, showing that apoptosis, lysis, and atrophy were undergone by Langerhans cells; on the contrary, in exocrine cells, it turned to be necrotic, and there was an increase in the apoptosis (cell death) [13].

As denoted in the results of Mann-Whitney analysis in table 4.4, it was indicated that the doses comprising 140 and 280 mg/kg BW significantly differ from the negative control, demonstrating that pancreatic beta cells can be regenerated by the extracts of the snake fruit skin. It occurs due to having active substances contained in both doses that are capable of regenerating pancreatic beta cells. Additionally, the two doses emerge as high doses; hence, it reaches the desired therapeutic limit. In the meantime, at a dose of 70 mg/kg BW, it does not significantly differ from the negative control, indicating that this dose and the negative control have no differences. For this reason, it can be conveyed that the doses do not give any effects on regenerating pancreatic beta cells due to having the smallest doses; therefore, the desired therapeutic index limit is not reached. Meanwhile, when using doses of 70, 140 and 280 mg/kg BW, it significantly differs from the positive control, representing that the entire three doses are dissimilar to the positive control. It demonstrates that the whole three doses have effects on regenerating pancreatic beta cells; the effects shown, however, are not capable of reaching the level of antidiabetic drug administration that serves as the positive control. It occurs due to owning natural ingredients, in which the therapeutic effects are considered weaker and slower than chemical drugs. At the dose of 70, 140, and 280 mg/kg BW, it significantly differs from the normal control, indicating that these three doses are dissimilar to the normal control. Hence, it demonstrates the deep effects on regenerating pancreatic beta cells; nonetheless, the shown effects have not reached the normal control. The reason of this occurrence is that it is hard for the impaired organs to be back to their normal forms [13].

In the meantime, grounded in the study carried out by Rohaeti et al. (2022), it was mentioned that if viewed in a statistical way, the drug metformin functioning as a positive control and the extract of salak fruit peel has an ability in terms of lessening the level of blood sugar in zebrafish that suffers from diabetes. The group of crude extracts and active fractions emerges as the group that significantly gives effects on the reduction of blood sugar levels in zebrafish. The emergence of hypoglycemic activity in the extract of snake fruit peel occurs due to the fact that there are α-glucosidase inhibitor compounds contained

in the snake fruit skin. These compounds have a pivotal role to inhibit carbohydrate digestion complex into glucose, and eventually the glucose intake from the intestines into the blood is likely to be lessened. The regeneration of pancreatic β-cells can enhance insulin secretion, a process that flavonoids are known to promote. Additionally, flavonoids can be functioned as antioxidants, capturing the production of free radicals after the induction by utilizing alloxan. It is also believed that flavonoids are capable of having an induced hypoglycemia activity in testing animals. Alloxan comes from the group of iflavone and flavone glycos contained in the extracts of salak fruit peel [5].

CONCLUSION

Secondary metabolites such as flavonoids, saponins, and phenolic compounds are present in the ethanol-based extracts derived from the peel of snake fruit (*Salacca zalacca*). They have the effects of regenerating pancreatic β cells streptozotocin induction and are considered effective in regenerating pancreatic β cells.

REFERENCES

S. Ndraha, "Diabetes Melitus Tipe 2 Dan Tatalaksana Terkini," Medicinus, Vol. 27, No. 2, Hal. 9–16, 2014

S. A. Soelistijo Et Al., Konsensus Pengendalian Dan Pencegahan Diabetes Melitus Tipe 2 Di Indonesia 2015. Jakarta: Pb Perkeni, 2015.

Kemendagri, "Obat Herbal Tradisional," War. Ekspor, No. September 2014, Hal. 1– 20, 2014.

S. Dalimartha Dan F. Adrian, Ramuan Herbal Tumpas Penyakit. Jakarta: Penebar Swadaya, 2013.

Rohaeti, E., Nurafifah, D. And Batubara, I. (2022) 'Antidiabetic Activity Of Manonjaya Snakefruit Skin Extract With Zebra Fish (Danio Rerio) As Animal Model', *Jurnal Jamu Indonesia*, 7(3), Pp. 102–110. Available At: Https://Doi.Org/10.29244/Jji.V7i3.201.

Zahid, H.F., Ali, A., Ranadheera, C.S., Fang, Z., Dunshea, F.R., Ajlouni, S. 2022. In Vitro Bioaccessibility Of Phenolic Compounds And Alpha-Glucosidase Inhibition Activity In Yoghurts Enriched With Mango Peel Powder, Food Bioscience 50, Part A, 102011, Https://Doi.Org/10.1016/J.Fbio.2022.102011

Shamseer L, Moher D, Clarke M,Ghersi D, Liberati A, Petticrew M, Et Al.Preferred Reporting Items For Systematic Review And Meta-Analysis Protocols(Prisma-P) 2015: Elaboration AndExplanation. Bmj [Internet].2015;349(January):1–25. Available From: Http://Dx.Doi.Org/Doi:10.1136/Bmj.G7647

Munn Z, Moola S, Lisy K, Riitano D Tc. Methodological Guidance For SystematicReviews Of Observational Epidemiological Studies Reporting Prevalence And Incidence Data. 2015;1–5. Available From: Https://Joannabriggs.Org/Critical_AppraisAl_Tools

Datu, O.S., Lebang, J.S. And Suoth, E.J. (2023) 'Efek Pemberian Ekstrak Buah Salak (Salacca Zalacca) Dalam Menurunkan Kadar Glukosa Darah Pada Tikus Model Diabetes Melitus', *Jurnal Mipa*, 12(1), Pp. 30–33. Available At: Https://Doi.Org/10.35799/Jm.V12i1.44267.

Marzuki, M. *Et Al.* (2022) 'Anti-Diabetic Effect Of Snake Fruit Skin Extract In Alloxan-Induced Wistar Rat', *International Journal Of Health And Pharmaceutical (Ijhp)*, 3(1), Pp. 146–153. Available At: Https://Doi.Org/10.51601/Ijhp.V3i1.143.

Suntara, D.A. (2023) 'Literature Review: Pengaruh Kulit Salak (Salaca Zalacca) Terhadap Glukosa Darah', *Jurnal Ilmiah Hospitality*, Viii(I), Pp. 1–19.

Valentino, A. *Et Al.* (2021) 'Efektivitas Ekstrak Etanol Kulit Salak (Salacca Zalacca) Terhadap Penurunan Berat Badan Dan Kadar Gula Darah Tikus Putih (Rattus Norvegicus)', *Jurnal Ilmu Kedokteran Dan Kesehatan*, 8(3), Pp. 279–285. Available At: Https://Doi.Org/10.33024/Jikk.V8i3.4883.

Utami, I.K., Sariani, N.P. And Tandi, J. (2022) 'Potensi Ekstrak Etanol Kulit Buah Salak

Terhadap Histopatologi Pankreas Tikus Putih Jantan Diabetes Melitus', *Farmakologika: Jurnal Farmasi*, 19(1), Pp. 21–30. Available At: Http://Jfarma.Org/Index.Php/Farmakologika/Article/View/341%0ahttp://Jfarma.Org/Index.Php/Farmakologika/Article/Download/341/77.