INTERNATIONAL CONFERENCE
ON LIFESTYLE DISEASES AND NATURAL MEDICINE (ICOLIFEMED)
Nomor ISSN: 3124-1115

The Effect Of Nanoemulsion Preparation Of Bay Leaf Extract (*Syzygium Polyanthum*) On Reducing Regenerating Islet-Derived Protein 3 Beta (Reg3β) And C-Reactive Protein (Crp) Levels In Wistar Rats With Diabetes Mellitus

Lintarisa Putri[1], Alinapiah Nasution[2], Maya Sari[3]
[1,2,3]Faculties Medicine , Dentistry and Knowledge Health , Universitas Prima Indonesia , North Sumatra

*E-mail : lintarisaputri@gmail.com

ABSTRACT

This study aims to evaluate the effect of bay leaf (*Syzygium polyanthum*) extract nanoemulsion preparations on reducing regenerating islet-derived protein 3 beta (REG3β) and C-reactive protein (CRP) levels in Wistar rats with diabetes mellitus. The method used includes the preparation of nanoemulsion preparations and measurement of REG3β and CRP levels as indicators of inflammation and pancreatic damage. Rats were divided into control and treatment groups, where the treatment group received bay leaf extract nanoemulsion preparations. The results showed that treatment with nanoemulsion significantly reduced REG3β and CRP levels compared to the control group. Nanoemulsion extract Bay leaves (*Syzygium Polyanthum)* contain secondary metabolites in the form of saponins, tannins, flavonoids, and triterpenoids which help repair pancreatic cells that experience inflammation due to diabetes mellitus. Administration of nanoemulsion extract Bay leaves (*Syzygium polyanthum)* at a concentration of 3.5% were effective in improving liver function in Wistar white rats (*Rattus norvegicus*) with diabetes mellitus. This improvement can be seen through CRP levels and liver histology structure which improved and resembled the control group . The results of histopathological observations of pancreatic tissue in treatment group 3 were as follows: nanoemulsion extract Bay leaves (*Syzygium Polyanthum)* with a concentration of 3.5% experienced the most significant improvement and approached the control group compared to the other groups. This finding indicates that bay leaf extract has potential as an anti-inflammatory agent and pancreatic protector in diabetes mellitus.

Keywords: *Nanoemulsi Leaf Greetings, REG3β, CRP*

INTRODUCTION

People with diabetes mellitus have system low immunity . So , it's easy caught infection . A number of study show that , there is *low grade chronic inflammation* of the endothelium can cause abnormalities vascular . This is reinforced with increasing inflammatory *markers* chronic *C-Reactive* Protein (Yeri *et al* ., 2015). *C-Reactive Protein* , too called with CRP is Wrong One inflammatory *markers* acute originating from from heart And often found on Lots related diseases with the occurrence of diabetes mellitus And disease cardiovascular . *C-Reactive Protein* (CRP), will increase tall in the inflammatory process And damage network (Kalma , *et al.* , 2018). REG3 β is a protein involved in the regeneration process

Nomor ISSN: 3124-1115

cells pancreas And functioning as indicator damage beta cells . Increased REG3 β levels are often associated with damage pancreatic beta cells in diabetes. On the side In other words , CRP is a phase protein . acute produced by heart as response to inflammation . High CRP levels show existence inflammation systemic , which is often happen on diabetes patients

CRP and REG3β can be quite sensitive *markers* in detecting inflammation related to *the progression* of *atherosclerosis.* The occurrence of cardiovascular disease can also be caused by increased CRP levels. CRP is an alpha-globulin produced in the liver, then its levels will increase significantly during the inflammatory process accompanied by tissue damage. The increase in CRP and REG3β levels in people with diabetes mellitus is caused by the inflammatory response of diabetes mellitus. CRP, one of the acute phase proteins present in normal serum, although in low concentrations. This CRP examination is useful to help detect inflammatory processes in the body (Kalma, ' *et al* .', 2018).

One herbal plant that can be used as a substitute for diabetes medication is the bay leaf (*Syzygium polyanthum).* The medicinal properties of the bay leaf are found in all parts of the plant, including the bark, roots, fruit, and leaves (Wijayakusuma, 2022). However, the leaves possess far more medicinal properties than any other part.

According to research by Suganda AG *et al.* (2015), bay leaf extract 3x350 mg/day was reported to be able to reduce fasting blood glucose levels and blood glucose levels 2 hours after eating, especially at levels of 200 mg/dl, although according to the statistical results obtained, it was not significant. However, in the research Tri Widiyati *et al* (2015) gave doses in the range of 250-500 mg/dl of dry methanol extract from bay leaves, which was proven to significantly reduce blood glucose levels. when. Bay leaves contain oil essential oils Which consists of from citral, eugenol, *triterpenoids, saponins, flavonoids,* and *tannin* . In addition, bay leaves also contain several vitamins, including vitamin A, vitamin C, vitamin E, *thiamin, riboflavin, niacin,* vitamin B6, Vitamin B12 and folate. The active compounds in bay leaves, *flavonoids,* have antioxidant properties that can potentially prevent the formation of free radicals. free And protect vessels blood from the damage that later can reduce cell damage and flavonoids contain antioxidants that have antidiabetic properties. There are also several Other active compounds, such as *saponins* , can prevent fat absorption in the intestines by increasing its secretion in the urine, preventing fat from accumulating in the blood vessels (Prahastuti S, 2019). These substances are found in bay leaves and are useful for managing dyslipidemia, diabetes mellitus, as an anti-inflammatory, and as an antibiotic (Anonymous, 2020).

Research conducted by (Widyawati P. S, 2016)regarding the effectiveness of bay leaf methanol extract on blood sugar levels in rats induced to hyperglycemia. The results obtained that bay leaf methanol extract with repeated administration of metformin and three doses of methanol extract, namely 250 mg, 500 mg and 1000 mg/kgBW for six days caused a significant decrease in STZ-induced diabetic rats. Then in 2017, Sri Wahjuni and Wita conducted a study testing the hypoglycemic and antioxidant effects of bay leaf ethanol extract on rats induced by alloxan. The results obtained that bay leaf ethanol extract can reduce blood glucose levels in rats induced by alloxan at a dose of 5 mg/kgBW (Wahjuni and Wita, 2017).

Objective in study This namely knowing the process of making bay leaf extract (*syzygium polyanthum)* in nanoemulsion preparations Knowing the content of active substances in bay leaf extract (*syzygium polyanthu* , knowing the effect of administering bay leaf extract nano preparations (*syzygium polyanthum*) with concentrations of 1.5%, 2.5% and 3.5% on Reducing Regenerating Islet-Derived Protein 3 Beta (REG3β) and C-Reactive Protein (CRP)

Nomor ISSN: 3124-1115

levels in Wistar rats with diabetes mellitus and analyzing the histopathological features of the pancreas after the treatment period, based on the above background, the researcher aims to evaluate the effect of bay leaf extract nanoemulsion preparations on reducing REG3 β and CRP levels in Wistar rats with diabetes mellitus. By understanding this mechanism, it is hoped that more effective therapies can be found to manage diabetes and its complications
From the description above, the conceptual framework in this research is as follows:

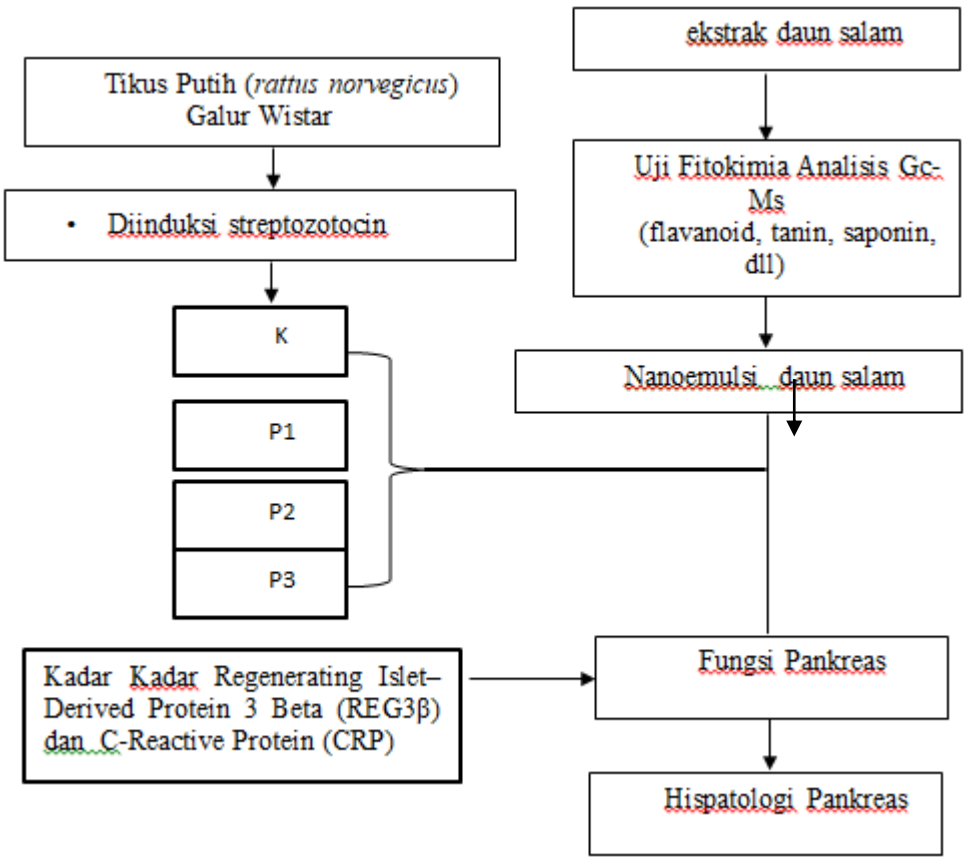


Figure 1. Conceptual Framework

METHODS

This research is a True experimental research, with the research design used is *Post Test Only Control Group Design* , which is a type of research that only observes the control and treatment groups after being given an action. The research design uses *a post-test with control group design* or controls the sample based on the treatment group to analyze the activity test of bay leaf extract nanoemulsion (*syzygium polyanthum*) on reducing levels of regenerating islet-derived protein 3 beta (reg3β) and c-reactive protein (crp) in wistar rats with diabetes mellitus. This research was conducted at the Laboratory of the Department of Pharmaceutical Pharmacology, Faculty of Medicine, University of North Sumatra and the Anatomical Pathology Laboratory, University of North Sumatra. This research was conducted from June to August 2025. Ethical Clearance will be submitted to the Health Research Ethics Commission (KPEK) of Prima Indonesia University and is still in process .
Based on the sample calculation above, each group must have a minimum of 6 test animals. In this study, researchers used 6 Wistar rats for each group, resulting in a total of 24 test animals. The test animals were randomly assigned to 4 test groups.

Nomor ISSN: 3124-1115

Acclimatization is the process of adjusting to a new environment. All male Wistar rats underwent seven days of acclimatization in the Laboratory of the Department of Pharmaceutical Pharmacology, Faculty of Medicine, University of North Sumatra before receiving treatment. The rats had sufficient time to adjust to their new environment, food, and water. The rats were fed and watered according to their standard requirements (*ad libitum*) . After 14 days of adaptation, on the first day of the experiment an injection was carried out. streptozotocin 55 mg/kgBW intraperitoneally in mice. After injection streptozotocin, in time 24 O'clock mouse given sucrose 10% through probe And given Eat Which Enough For prevent hypoglycemic conditions . Then, body weight measurements were taken every 2 days, namely on the 3rd day and blood glucose measurements were taken every 6 days, namely on the 7th day, for determine mouse diabetes mellitus with criteria level glucose >300mg/dl. Before making the nanoemulsion, bay leaves must first be converted into an extract using a maceration method. 2 kg of the collected bay leaves are then taken to be used as an extract. The collected bay leaves are then cleaned and dried. Once the bay leaves are dry, they are ground to a fine powder (simplicia) of 600 g.

Next, the powdered simplicia is mixed with 96% ethanol in a ratio of 1:10, then left for 24 hours and stirred every 6 hours. The maceration results are separated and the previous steps are repeated with the same amount of 96% ethanol. The resulting macerate is then placed in *a rotary vacuum evaporator* and evaporated to obtain a crude extract. Next, take 0.2 ml of the extract into vial and add 5 ml of 75 µM 2,2-Diphenyl-1-Picrylhydrazyl (DPPH) solution. Then let the mixture stand for 30 minutes in a light-free room . Bay leaf nanoemulsion was obtained by the *water-titration method* . The oil phase was made from a mixture of virgin coconut oil *and* tween 80 as a surfactant, and *polyethylene glycol* 400 (PEG 400) as a co-surfactant in a ratio of 1: 8.5: 0.5. Then water at a temperature of 70 ^{o}C was added to the oil phase by titration, stirring continuously until a homogeneous nanoemulsion was obtained. The nanoemulsion was then assessed through organoleptic tests, pH, stability, and particle size. In addition, the nanoemulsion was also assessed physically through color, aroma, and several homogeneity parameters. The particle size used in this study was 33 nm (Hanifah *et al.* , 2021).

Parameters for examining pancreatic function are the enzymes amylase and lipase. Amylase works by hydrolyzing carbohydrates and forming simple sugars, while lipase works by hydrolyzing fats to form fatty acids. Amylase and lipase are enzymes secreted by the exocrine part of the pancreas. Amylase and lipase levels are used as biochemical markers of pancreatic dysfunction. On the 15th day, the mice were anesthetized and then blood samples were taken through the orbital vein with a capillary pipette of 3 cc, collected into an EDTA (*Ethylenediamine Tetraacetic Acid*) tube and placed in a cool box. The blood samples were then examined at the University of North Sumatra Laboratory.

RESULTS AND DISCUSSION

Results of Rat Body Weight Measurement

This research used test animals in the form of white rats (*Rattus norvegicus*). Male Wistar strain with a body weight of 200-300 grams. The test animals were divided into 4 groups. group, control group which was only given base cream, treatment group 1 given nanoemulsion extract bay leaf (*Syzygium Polyanthum)* with concentration Which different, that is 1.5%, 2.5 %, And 3.5%. Calculation sample based on on formula ferderer For 4

Nomor ISSN: 3124-1115

group And obtained results as much as 6 mice per group, so the total sample in this study was 24 mice. Following characteristics of research test animals

Table 1. Characteristics of test animals

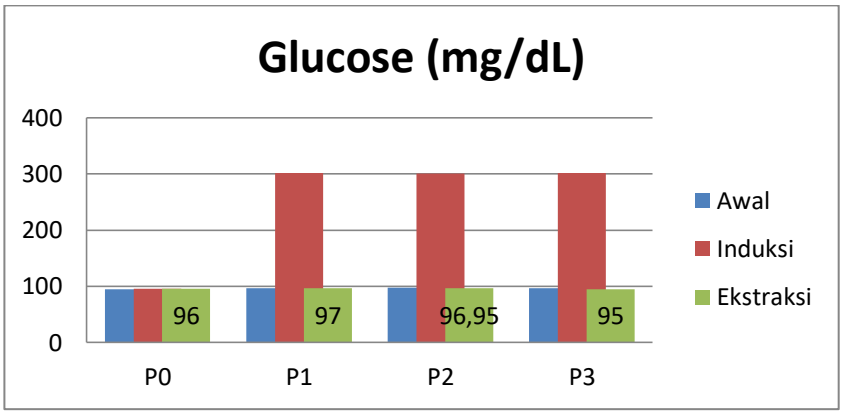
Komponen	Kelompok			
	K	P1	P2	P3
Jenis Tikus	*Rattus norvegicus* putih galur wistar			
Jenis Kelamin	Jantan			
Keadaan Umum	Warna bulu putih, sehat, dan aktif			
Rata-rata Berat Badan Awal	243gr	245gr	245gr	244gr

Description of Blood Sugar Level Measurement Results

Table 2. Average Blood Glucose Levels (BGL) mg/ dL of Mice Before and After Streptozotocin Induction and Bay Leaf Extract Treatment

Kelompok	KGD Awal (H0)	KGD (mg/dL) Setelah Diinduksi Streptozotocin (H14)	KGD (mg/dL) Setelah diberi perlakuan ekstrak (H28)	Selisih KGD (setelah induksi aloksan-diberi perlakuan)
Kontrol	95	95,25	96	-0,75
Perlakuan 1 (P1)	96,55	301,25	97	- 204,25
Perlakuan 2 (P2)	97,5	300,5	96,95	-203,55
Perlakuan 3 (P3)	97	301,8	95	-206,8

So the test results above show the success rate of the bay leaf extract nanoemulsion (*Syzygium Polyanthum)* on reducing blood glucose levels in mice with diabetes mellitus . The comparison can be seen in the following graph:



In group P0, diabetes induction treatment was not given so that this group had stable glucose levels, whereas in groups P1, P2 and P3, this group was induced by streptozotocin so that post-induction observations showed that all groups had glucose levels >300 mg/dL, but after

Nomor ISSN: 3124-1115

being given the extraction treatment Bay leaf extract nanoemulsion (*Syzygium Polyanthum)* was seen to decrease the blood glucose levels of mice until groups P1, P2 and P3 entered the normal blood glucose criteria for mice.

Making Nanoemulsion of Bay Leaf Extract (*Syzygium Polyanthum)*

Before making the nanoemulsion, bay leaves must first be converted into an extract using a maceration method. The collected bay leaves are then cleaned and dried. Once dry, grind them to a fine powder (simplicia) of 600g.

Figure 3. Making Nanoemulsion Bay Leaf Extract

The results of the bay leaf extract nanoemulsion production were analyzed for organoleptic, pH, stability, and particle size. Furthermore, the nanoemulsion was also physically evaluated for color, aroma, and several homogeneity parameters.

Table 3. Test Evaluation Organoleptic nanoemulsi leaf regards

	Testing	
P1 (1.5 %)	- Aroma	- Smell Typical
	- Color	- Green pale
	- Form	- Emulsion
	- Homogeneity	- Homogeneous
P2 (2.5 %)	- Aroma	- Smell Typical
	- Color	- Green pale
	- Form	- Emulsion
	- Homogeneity	- Homogeneous
P3(3.5 %)	- Aroma	
	- Color	- Smell Typical
	- Form	- Green concentrated
	- Homogeneity	- Emulsion
		- Homogeneous

The results of the pH measurement table, it can be concluded that the bay leaf extract nanoemulsion with a concentration of 1.5% obtained pH measurement results with an average of 6.45, the bay leaf extract nanoemulsion with a concentration of 2.5% obtained pH

Nomor ISSN: 3124-1115

measurement results with an average of 6.31 and the bay leaf extract nanoemulsion with a concentration of 3.5% obtained pH measurement results with an average of 6.25.

Phytochemical Screening of Bay Leaf Extract (*Syzygium Polyanthum)*

Table 4. Phytochemical Test

Metabolit Sekunder	Pengujian	Warna	Hasil
Flavonoid	Wilstater	Merah	+
Saponin	Forth	Biru dan berbuih	+
Tannin	FeCl3	Hijau kehitaman	+
Alkaloid	Wagner	Kuning	+
Triterpenoid	Lieberman – Burchard	Merah	+

Keterangan: (+) = Mengandung golongan senyawa yang diuji
(-) = Tidak mengandung senyawa yang diuji

Secondary metabolite testing is carried out to determine the content of organic compounds. there is on extract Bay leaf. Table on prove Bay leaf extract has been shown to contain active compounds such as alkaloids, flavonoids, saponins, tannins, terpenoids, and steroids. Therefore, it can be said that this extract has many health benefits due to its content. antioxidants that can used as antidiabetic , anticancer and can repair damaged pancreas function.

RP Level Results

C-reactive protein) levels in healthy mice typically range from 0 to 1 mg/L. These levels can vary depending on the testing method and the specific condition of the mouse. In good health, CRP levels tend to be very low. However, during inflammation or infection, CRP levels can increase significantly. Normal CRP (C-reactive protein) levels in mice induced by streptozotocin (STZ) can vary depending on the time of sampling and the stage of the disease. However, generally, after stz induction, CRP levels can increase significantly in response to the resulting oxidative stress and inflammation. In studies involving stz-induced mice, CRP levels can range from 1 to 10 mg/L or more, depending on the degree of inflammation and time post-induction.

Table 5. Results Analysis Descriptive CRP Levels

KADAR CRP	Kelompok (n=6) Rerata-standar deviasi			
	K	P1	P2	P3
Kadar CRP awal	0,69±0,07	0,687±0,076	0,73±0,048	0,677 ±0,066
Kadar CRPsetelah induksi streptozotocin	0,71±0,069	4,367±0,3265	4,635±0,646	5,102±1,219
Kadar CRP setelah diberi perlakuan	0,706±0,068	0,738±0,063	0,778±0,066	0,845±0,0099

Table in on show that The average CRP level will increase under streptozotocin (STZ) induction conditions. Streptozotocin is a compound used to induce diabetes mellitus in experimental animal models, and this induction process will trigger oxidative stress

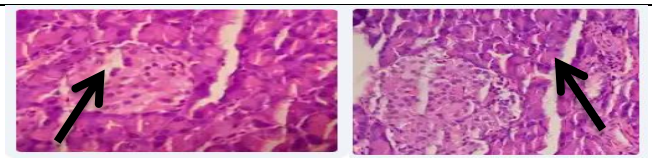
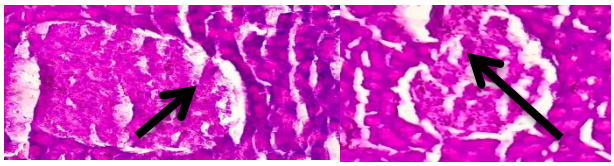
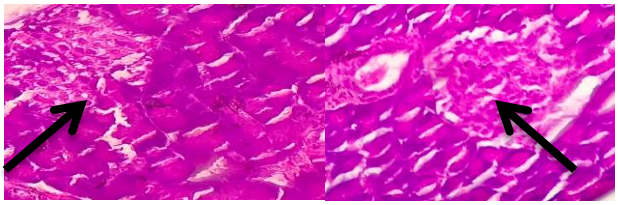
Nomor ISSN: 3124-1115

characterized by an increase in CRP levels. This can be seen in the average and deviation in the control group 0.71±0.069, treatment 1 4.367±0.3265, treatment 2 4.635±0.646 and treatment 3 5.102±1.219.

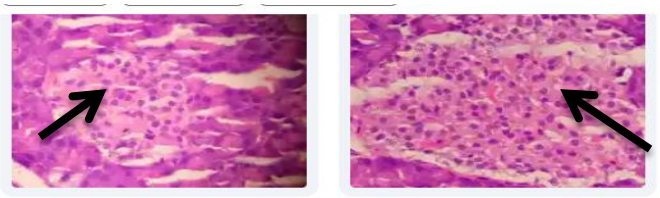
After being induced by streptozotocin, the mice were then treated with bay leaf nanoemulsion to reduce CRP levels for 2 weeks and after that they would be observed again. From the table it can be concluded that CRP levels decreased in treatment group 1 with the administration of 1.5% bay leaf extract nanoemulsion with a mean and standard deviation of 0.738 ± 0.063, treatment group 2 with the administration of 2.5% bay leaf extract nanoemulsion with a mean and standard deviation of 0.778 ± 0.066 and treatment group 3 with the administration of 3.5% bay leaf extract nanoemulsion with a mean and standard deviation of 0.845 ± 0.0099. Based on results test normality that has been done use *Kolmogorov-Smirnov Test.* obtained results significance of 0.965 on all group on moment beginning acclimation mice , after induced 0.236 and after given treatment 0.983. Data said normally distributed if p value > 0.05. So from that , can concluded that the data is normally distributed . After the data is known to be normally distributed, a homogeneity test is carried out using the *Levene test* to determine whether each variant of the research population group is the same or homogeneous.

Histopathological Observation Results

Table 6. Histopathological Description of Pancreatic Tissue

No	Group	Histopathological Image of Pancreatic Tissue
1	Control (Aquades)	 A score of 0 was obtained because no degenerative changes , no necrotic changes , and no inflammatory cells were found throughout the pancreatic interstitial space. This group was not induced and was not given extract treatment.
2	Treatment 1	 Score 3 because the number of inflammatory cells is between 51-100 in the entire interstitial space of the pancreas, number of cells with degree of damage (51% - 75%) of the entire LP (Visual Field).
3	Treatment 2	 Score 2: if the number of degenerative cells with a degree of damage (26-50%) of the entire LP (Visual Field), the number of necrotic cells < 25% of the entire LP and the number of inflammatory cells between 11-50 in the entire pancreatic interstitial space.

Nomor ISSN: 3124-1115

4	Treatment 3		Score 1 because amount cell degenerative with degrees damage (< 1-25%) of entire LP (Field of View), total cell necrotic < 25% of all LP. and amount cell inflammation < 10 on all over pancreatic interstitial space

REG3β levels in histopathology can be significantly increased in the treated group compared to the control group, indicating anti-inflammatory or regenerative effects. Comparison between various concentrations (1.5%, 2.5%, and 3.5%) can show different dose responses, where higher concentrations may result in higher levels of REG3β **Normal expression (control)** : REG3β mRNA expression: **very low or almost undetectable** Protein: only detected in small amounts, < **10 pg/mg** tissue (in healthy conditions). The results of histopathological observations conducted using a light microscope showed a significant reduction in the degree of damage across the entire visual field and an improvement in the number of inflammatory cells throughout the pancreatic interstitial space in the treatment group given bay leaf nanoemulsion. This demonstrates the effectiveness of the treatment in protecting the pancreas from damage.

CONCLUSION

1. Administration of nanoemulsion extract Bay leaves (*Syzygium polyanthum)* at a concentration of 3.5% were effective in improving liver function in Wistar rats (*Rattus norvegicus*) with diabetes mellitus. This improvement was evident in CRP levels and liver histology, which improved and resembled the control group.
2. The results of histopathological observations of pancreatic tissue in treatment group 3, namely nanoemulsion extract Bay leaves (*Syzygium Polyanthum)* with a concentration of 3.5% experienced the most significant improvement and were closer to the control group compared to the other groups.
3. Nanoemulsion extract Bay leaves (*Syzygium Polyanthum)* contain secondary metabolites in the form of saponins, tannins, flavonoids, and triterpenoids which help repair pancreatic cells that experience inflammation due to diabetes mellitus.

ACKNOWLEDGEMENT

The Faculty of Medicine, Dentistry, and Health Sciences, as well as the directors of study programs, are acknowledged by the authors for their support of this research at Universitas Prima Indonesia. Additionally, we appreciate the supervisors' insightful comments. The University of North Sumatra, the Faculty of Pharmacy, the Pharmacology Laboratory, and the Nanomedicine Laboratory are all acknowledged by the authors for their invaluable support of this study.

Nomor ISSN: 3124-1115

REFERENCES

Anonymous, 2020. *General Standard Parameters for Medicinal Plant Extracts.* . Jakarta: Directorate General of POM, Ministry of Health, Republic of Indonesia. Indonesia Introduction. Jurnal Persada Husada Indonesia, 5(16), 45 – 52.

Aliviameita, A., & Puspitasari. (2019). Textbook of Hematology Course. In Textbook of Hematology Course. https://Doi.Org/10.21070/2019/978- 623-7578-00-0

Aliviameita, A., Puspitasari, P., & Purwanti, Y. (2021). Correlation of Blood Profile with Serum CRP in Diabetes Mellitus Patients with Diabetic Ulcers. The Journal of Muhammadiyah Medical Laboratory Technologist, 4(1), 40. https://Doi.Org/10.30651/Jmlt.V4i1.7242

Bordon, J., Aliberti, S., Fernandez-Botran, R., Uriarte, S.M., Rane, M.J., Duvvuri, P., Peyrani, P., Morlacchi, L.C., Blasi, F., & Ramirez, J.A. (2013). Understanding the role of cytokines and neutrophil activity and neutrophilapoptosis in the protective versus deleterious inflammatory response to pneumonia. International Journal of Infectious Diseases, 17(2), e76 – e83. https://doi.org/10.1016/j.ijid.2012.06.006

Budiastuti, D., & Bandur, A. (2018). Validity and Reliability of Research. In the North Sumatra Provincial Health Office. (2018). Health Profile of North Sumatra Province in 2018. Ministry of Health of the Republic of Indonesia, 138 – 139.

Eka, SM, & Evi, P. (2022). Description of C-Reactive Protein Levels in Controlled and Uncontrolled Type 2 Diabetes Mellitus Patients at the Mojoagung Jombang Community Health Center.

Fatimah, RN (2016). Type 2 Diabetes Mellitus. Indonesian Journal of Pharmacy,
27(2), 74 – 79. Https://Doi.Org/10.14499/Indonesianjpharm27iss2pp74

Iriani, N., Dewi, AKRSD, & Sudjud, S. (2022). Research Methodology. Rizmedia Pustaka Indonesia.

Kalma, K. (2018). Study of C-Reactive Protein (CRP) Levels in Type 2 Diabetes Mellitus Patients. Journal of Health Analysis Media, 1(1). Https://Doi.Org/10.32382/Mak.V1i1.222

Ministry of Health of the Republic of Indonesia. (2020). Infodatin Stay Productive, Prevent, and Overcome Diabetes Mellitus 2020. In Data and Information Center of the Ministry of Health of the Republic of Indonesia (pp. 1 – 10).

Ministry of Health of the Republic of Indonesia. (2019). Signs and Symptoms of Diabetes. Directorate of Prevention and Control of Non-Communicable Diseases, Directorate General of Disease Prevention and Control. https://P2ptm.Kemkes.Go.Id/Artikel-Sehat/Tanda-Dan-Gejala-Diabetes

Ministry of Health of the Republic of Indonesia. (2020). Stay Productive, Prevent and Treat Diabetes Mellitus. In the Data and Information Center of the Ministry of Health of the Republic of Indonesia.

Nomor ISSN: 3124-1115

Ministry of Health. (2019). Consensus on Management and Prevention of Type 2 Diabetes Mellitus in Indonesia 2011 Indonesian Endocrinology Association.Ptpm.Kemkes.Id, 1.

Khodijah, S. (2021). Overview of Leukocyte Count in Patients with Uncontrolled Type II Diabetes Mellitus. 6.

Lestari, Zulkarnain, & Sijid, SA (2021). Diabetes Mellitus: Review of Etiology, Pathophysiology, Symptoms, Causes, Examination, Treatment, and Prevention. Uin Alauddin Makassar, November, 237–241 . http://Journal.Uin-Alauddin.Ac.Id/Index.Php/Psb

Maria, I. (2021). Nursing Care for Diabetes Mellitus and Nursing Care for Stroke. Deepublish.

Muflikhatur SR, MH, 2018. Differences in the Effect of Extract and Decoction of Bay Leaves (Eugenia polyantha) on Total Cholesterol Levels in Sprague Dawley Rats.. *Journal of Nutrition College.* , 3(1), pp.42-149.

Nugrahani, F. (2014). Qualitative Research Methods in Language Education Research (Vol. 1, Issue 1). Penggabean, D. (2020). Scientific Paper: Description of C-Reactive Protein (CRP) in Type 2 Diabetes Mellitus Patients.

Permatasari, ND, Rachmawati, B., Riansari, A., & Limijadi, EKS (2020). The Relationship Between Hba1c and Crp in Type-2 Diabetes Mellitus Patients with Obesity and Without Obesity. Journal of Nutrition College, 9(4),267 – 272. Https://Doi.Org/10.14710/Jnc.V9i4.29011

Prahastuti S, TSHE, 2019. Effect of Bay Leaf Infusion (Syzgium polyanthum(wight) Walp) on Reducing Total Blood Cholesterol Levels in Wistar Rats with Dyslipidemia Model. *Jurnal Medika Planta* , 1(4), pp.28-32.

Praptomo, AJ, Anam, K., & Raudah, S. (2017). Health Research Methodology. Deepublish.

Prasetyoningtiyas, NW (2018). Description of Leukocyte Count in Patients with Uncontrolled Type 2 Diabetes Mellitus (Study. Photosynthetica, 2(1), 1 – 13.

Roflin, E., Liberty, IA, & Pariyana. (2021). Population, Sample, Variables in Medical Research (Nasrudin (Ed.); 1st Ed.). Nem.

R. (2019). Periodontitis and the Risk of Coronary Heart Disease. In S. Wulansari (Ed.), Pt Penerbit IPB Press.

Santoso, S., Rachmawati, B., & Retnoningrum, D. (2018). Differences in the Absolute Number of Leukocytes, Neutrophils, and Lymphocytes in Patients with Controlled and Uncontrolled Type 2 Diabetes. 7(2), 854 – 862.

Situmeang, MM (2018). C-Reactive Protein Description in Type 2 Diabetes Mellitus Patients Treated at Haji Adam Malik General Hospital, Medan. Kti Poltekkes Medan, Health Analyst Department.

Situmorang, PR (2017). The Effect of Ethanol Extract of Chayote (SechiumEdule Jacq.Swartz) Fruit on Interleukin 6 Levels and Pancreatic Histopathology of Streptozotocin (Stz)-Induced Hyperglycemic Mice. 15 – 25.

Sukendra, IK, & Atmaja, IKS (2020). Research Instruments. In Journal Academia.

Nomor ISSN: 3124-1115

Sun, H., Saeedi, P., Karuranga, S., Pinkepank, M., Ogurtsova, K., Duncan, BB,Stein, C., Basit, A., Chan, JCN, Mbanya, JC, Pavkov, ME,Ramachandaran, A., Wild, SH, James, S., Herman, WH, Zhang, P.,Bommer, C., Kuo, S., Boyko, EJ, & Magliano, DJ (2022). Idf DiabetesAtlas: Global, Regional And Country-Level Diabetes Prevalence EstimatesFor 2021 And Projections For 2045. Diabetes Research And Clinical Practice, 183, 109119. Https://Doi.Org/10.1016/J.Diabres.2021.109119

Syahza, A. (2021). Research Methodology Book. Ur Press Pekanbaru.

Wijayakusuma, H., 2022. *Indonesian Medicinal Plants: Spices, Rhizomes, and Tubers.* Jakarta: Prestasi Instan Indonesia.