Solid lipid nanoparticle formulation and antihyperglycemic activity test of sea cucumber (Stichopus hermanii)

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**Keywords:**
- antihyperglycemic
- solid lipid nanoparticle
- Stichopus hermanii

**ABSTRACT**

This study aims to develop a formulation with the active ingredient Stichopus hermanii for antidiabetic treatment or function to lower blood glucose levels. The formulation approach taken is to design a formula in the form of solid lipid nanoparticles (SLN), where this system is expected to optimize absorption and improve the performance of the active substance. The SLN characterization includes particle size measurement, zeta potential, polydispersity index analysis, and morphology analysis using TEM. The antihyperglycemic activity test will be tested in vivo using male white rats using the glucose tolerance test method and induced by streptozotocin. The results of the TEM analysis showed that the sea cucumber spherical in shape. The particle size of the formula was found to be 0.25 nm. The polydispersion index (PDI) of the formulation was 67.5%, 2%, and 0.5%, respectively. In the same test, male rats were given treatment according to the group division, namely 50% glucose at a dose of 3 g/kg bw 30 minutes later and the blood sugar levels were measured at 30, 60, 90, and 120 minutes using a glucometer. In a follow-up test, the administration of test samples (days -3, 6, 9, 12, and 15) of CMC Na, metformin, and 25 mg/kg body weight of the test group showed that blood sugar level decreased with the highest decrease in positive control group. In conclusion, the results showed that sea cucumbers could be developed as a functional food product to help battle the onset of diabetes and diabetic complications.

**INTRODUCTION**

Diabetes mellitus is one of the diseases with the highest mortality rate globally with a significant increase in prevalence every year (IDF, 2017; WHO, 2020). It was recorded that in 2017 there were 425 million people suffering from diabetes and it is predicted that this will continue to increase to 629 million by 2045. The prevalence of diabetes has been rising in the last few decades, caused by the global rise in the prevalence of obesity. The premature morbidity, mortality, reduce life expectancy and financial and other costs to the patient with diabetes, their careers and the health service, make it an important public health condition (Forouhi & Wareham, 2010, 2019). Type 2 diabetes accounts for 85% of the total global prevalence. The prevalence of diabetes in Indonesia reaches more than 10 million people and is also one of the diseases that cause the highest number of people (Ligita et al., 2019; WHO, 2016).

Diabetes treatment using oral antidiabetics is carried out for a very long period of time, so there is a risk of unwanted side effects for the body. Alternative treatment using natural ingredients is an option to reduce the risk of side effects received (Qi et al., 2010). One of the uses of natural ingredients as an antidiabetic that has been carried out in previous research is the sea cucumber (Stichopus hermanii). Sea cucumber as an antidiabetic has been used empirically and is supported by its alpha glucosidase enzymes, alkaloids and saponins (Maryanti et al., 2017; Rasyid, 2012). A previous study tested the antihyperglycemic activity of the Ethanolic extract of Stichopus hermanii by measuring the blood sugar levels of rats after glucose and streptozotocin induction. From this research, it is known that sea cucumber ethanol extract dose of 800 mg/kg has the same activity as metformin (Rahmadani et al., 2020).

Recent research from the University of South Australia has found that processed dried sea cucumber with salt extracts can inhibit a compound that is associated with an increased risk of diabetes, thereby reducing the likelihood of the disease (Deo, 2023; Wong et al., 2023). The study found that processed dried sea cucumber...
with salt extracts and collagen can significantly inhibit Advanced Glycation End products (AGEs) by lowering a range of sugar-related metabolites in the body and reducing the risk of diabetes. AGEs form when proteins and/or fats combine with sugars in the bloodstream. When accumulated in high levels, they increase diabetic complications, including heart disease, Alzheimer's, Parkinson's, kidney disease, and cancer (Wong et al., 2023). The bioactive compounds in sea cucumbers can inhibit AGEs and protect against these diseases (McClure, 2023; Purwanto et al., 2019; Ramsey, 2023; Wang et al., 2020). These results provide sound evidence that sea cucumbers could be developed as a functional food product to help battle the onset of diabetes and diabetic complications.

The research discusses the results of the development of pharmaceutical preparations with the active ingredient Stichopus hermanii for antidiabetic treatment or function to lower blood glucose levels. The formulation approach taken is to design a formulation in the form of solid lipid nanoparticles (SLN), where this system is expected to optimize absorption and improve the performance of the active substance. SLN is an alternative carrier system to carry other colloids (emulsions, liposomes and micro or nanoparticle polymers) that can be used to increase the bioavailability of drugs or other active compounds (Mehnert & Mäder, 2012; Mukherjee et al., 2009). Sea cucumber formulated in the form of SLN will be characterized by looking at the shape and size of the particles. The antihyperglycemic activity test will be tested in vivo using male white rats using the glucose tolerance test method and induced by streptozotocin.

METHOD

Chemicals and Instruments

The ingredients used in this study included sea cucumber (Stichopus hermanii), 96% ethanol, streptozotocin, Na-CMC, metformin (Merck), lecithin, glyceryl monostearate (GMS), tween 80, and distilled water. The tools used in this study include laboratory glassware, blender, desiccator, drying cabinet, analytical balance, microscopy, water bath, rotary evaporator, oven, water bath, vortex, magnetic stirrer, stirrer bar, pH meter, transmission electron microscope (TEM), particle size analyzer (PSA), glucometer and strip.

Material Collection and Extraction

Using experimental research design, sea cucumbers were collected from Pramuka Island, Thousand Islands, Jakarta Bay, Padang Beach, and Eastern Indonesian Waters. The results of the collection of materials were identified by the Laboratory of Animal Systematics, Department of Biology, Faculty of Mathematics and Natural Sciences, University of North Sumatra, Medan, Indonesia. The identification results obtained stated that the sample was a marine animal with the species Stichopus hermanii.

The collected samples were cleaned first by washing with running water until clean, then cleaned the internal organs until the meat remained. The clean samples were cut into 3x3 cm in size and dried using a drying cabinet. The sample is declared dry if the water content has reached <10%. The dry sample was then blended until a powder sample was obtained (Husni et al., 2020; Pertiwi et al., 2020).

Extracts were made by maceration using 96% ethanol as solvent, by mixing 300 g of simplicia powder with 2.25 liters of 96% ethanol in a sealed vessel and tightly closed. Store in a place protected from light for 5 days while shaking frequently. Then it is filtered, squeezed and the dregs are washed with liquid filter, stored in a cool place for several days, the liquid is poured and filtered. Performed at a higher temperature at room temperature, which is 40–60°C. Furthermore, the extract was evaporated using a rotary evaporator until a thick extract was obtained, then the extract was dried using a freeze dryer (Azwanida, 2015).

Formulation

SLN is made by solvent emulsification method. The manufacturing process of this method was initially based on fat deposition in an o/w emulsion. The lipophilic phase is dissolved in an organic solvent which is immiscible with water and emulsified in the aqueous phase. Then the removal of the organic solvent from the emulsion is carried out by evaporation. After the removal of the solvent, the nanoparticles are formed by the deposition of lipids in an aqueous medium (Hou et al., 2003; Mehnert & Mäder, 2012). The manufacture of SLN refers to the SLN resveratrol formulation where the formula is designed in various combinations of the amount of GMS solid fat, namely GMS 0.5%, 1%, 1.5%, 2%, and 2.5% w/w to obtain the optimal formula with the best characteristics. Each formula was further characterized to obtain the best SLN formula. The preparation of sea cucumber SLN begins with dissolving the sea cucumber extract in homogenized ethanol using a magnetic53 stirrer, then the GMS is melted and added with lecithin dissolved in dichloromethane. The two solutions were then homogenized at 30,000 rpm using Ultra Turax at a maximum of 24,000 rpm for 5 minutes plus 50g aqua demineralized solvent. Furthermore, the tween 80 solution was added to the mixture and then homogenized at 24,000 rpm for 5 minutes and the remaining aqua demineralized solvent was added to 100g. The SLN formation process was followed by stirring using a 3,000 rpm magnetic stirrer for 5 hours (Kovacevic et al., 2011; Mappamasing et al., 2015). The composition of the formula can be seen in Table 1.
**Evaluation of Characteristic Preparation**

SLN characterization includes particle size measurement, zeta potential, polydispersity index analysis, and SLN morphology analysis using TEM. Particle size, zeta potential, polydispersity index analysis. Particle size, zeta potential, and SLN polydispersity index were measured by photon correlation spectroscopy, Dynamic Light Scattering (DLS), Nano Zeta sizer, malvern instrument using disposable plain folded capillaries at 25°C. Prior to measurement, all samples were diluted using distilled water and a vortex for 30 seconds to produce a suitable scattering intensity. Each SLN measurement was repeated three times at 25°C. The refractive indices of particles and water are 1.54 and 1.33, respectively, which are used to calculate the particle size distribution, zeta potential, and polydispersity index. Interpretation of the results of the measurement of the particle size distribution, namely the distribution of particle sizes accompanied by the number or volume of these sizes. The particles range from 10-200 nm (Garud et al., 2012; Silva et al., 2011).

TEM (Transmission Electron Microscopy) was used to find the shape and surface morphology of the SLN. A drop of diluted sea cucumber SLN was placed on the surface of the carbon-coated copper network after removal of excess fluid using a hydrophilic filter membrane. Then dried at a temperature of 25 °C for up to one minute, the lattice with a mesh size of 300 was then marked negative by giving 2% uranyl acetate for one minute and allowed to dry at room temperature. The SLN sample is placed on the sample handle, then examined using a transmission electron microscope and then the image is taken after selecting a certain part of the object (sample) and the desired magnification so that a good and clear photo is obtained (Abbasalipourkabir et al., 2012; Jores et al., 2004).

PSA (Particle Size Analysis) is a particle size test with a range of 2-7000 nm using the principle of dynamic light scattering and Brownian motion. The particle size was calculated based on the Stokes-Einstein correlation function and the Brownian motion was defined as the translational diffusion coefficient. Brownian movement speed is influenced by size, viscosity, common and laplace methods, where each system produces a size distribution in intensity, number and volume. The test was carried out by means of 2 drops of SLN sample mixed into 5 ml of distilled water, 3 ml was taken and put into a cuvette for analysis (Gupta et al., 2016).

**Antihyperglycemic Activity Test**

Glucose tolerance test in rats was carried out using various doses of SLN. Male white rats were checked for initial blood sugar levels, then given treatment according to groups. After 30 minutes all rats from each group were given 50% glucose as much as 1% orally. Furthermore, blood sugar levels were measured again at 30, 45, 60, 90, and 120 minutes (Herlina et al., 2018; Rahmadani et al., 2020; Sridhar et al., 2011). From the results of the tolerance test, several variations of the best dose were taken that had the greatest effect. Furthermore, it will be used for the dose of the antidiabetic effect test by the streptozotocin induction method.

Antidiabetic effect test with streptozotocin induction method was performed after getting the best dose variation from glucose tolerance test in diabetic male rats. Streptozotocin induction was administered intraperitoneally to each rat. Then 3 days after being induced, the blood glucose levels of male white rats were measured. The test was carried out for 15 days. After induction, blood was drawn on days 3, 6, 9, 12, 15 (Windari et al., 2019; Zhang et al., 2008). All in vivo pharmacological test treatments carried out in this study received ethical approval from the research ethics committee of the Faculty of Medicine, University of North Sumatra and Central General Hospital H. Adam Malik, Medan, Indonesia.

**Data Analysis**

The data were analyzed by using Paired Samples Test Statistics to see the real difference between the control group and the treatment group, followed by the one-way ANOVA test with a 95% confidence level to determine the 59 mean differences between treatments. If there is a difference, it is continued by using the Post Hoc Tukey test to determine the difference between the treatment groups. This statistical analysis uses the SPSS (Statistical Product and Service Solution) program.
RESULTS AND DISCUSSION
Solid Lipid Nanoparticle of Sea Cucumber Characteristics
SLN is made in various combinations of the amount of solid fat GMS, each formula is then characterized to obtain the best SLN. The results of the characterization can be seen in Table 2.

<table>
<thead>
<tr>
<th>Formula</th>
<th>Particle Size (nm)</th>
<th>Polydispersity Index</th>
<th>Zeta Potential (mV)</th>
</tr>
</thead>
<tbody>
<tr>
<td>SLN GMS 0.5%</td>
<td>298.6</td>
<td>0.472</td>
<td>-21.9</td>
</tr>
<tr>
<td></td>
<td>281.9</td>
<td>0.448</td>
<td>-20.9</td>
</tr>
<tr>
<td></td>
<td>251.9</td>
<td>0.552</td>
<td>-21.4</td>
</tr>
<tr>
<td>Average</td>
<td>277.47 ± 23.66</td>
<td>0.4907 ± 0.0545</td>
<td>-21.40 ± 0.50</td>
</tr>
<tr>
<td>SLN GMS 1%</td>
<td>217.0</td>
<td>0.599</td>
<td>-19.0</td>
</tr>
<tr>
<td></td>
<td>206.6</td>
<td>0.673</td>
<td>-19.0</td>
</tr>
<tr>
<td></td>
<td>220.6</td>
<td>0.618</td>
<td>-19.0</td>
</tr>
<tr>
<td>Average</td>
<td>214.73 ± 7.27</td>
<td>0.6300 ± 0.0384</td>
<td>-19.00 ± 0.00</td>
</tr>
<tr>
<td>SLN GMS 1.5%</td>
<td>311.6</td>
<td>0.429</td>
<td>-25.7</td>
</tr>
<tr>
<td></td>
<td>343.7</td>
<td>0.421</td>
<td>-23.2</td>
</tr>
<tr>
<td></td>
<td>277.2</td>
<td>0.565</td>
<td>-16.2</td>
</tr>
<tr>
<td>Average</td>
<td>310.83 ± 33.26</td>
<td>0.4717 ± 0.0809</td>
<td>-21.70 ± 4.92</td>
</tr>
<tr>
<td>SLN GMS 2%</td>
<td>740.5</td>
<td>0.631</td>
<td>-23.3</td>
</tr>
<tr>
<td></td>
<td>602.6</td>
<td>0.715</td>
<td>-22.1</td>
</tr>
<tr>
<td></td>
<td>603.7</td>
<td>0.735</td>
<td>-21.7</td>
</tr>
<tr>
<td>Average</td>
<td>648.93 ± 79.30</td>
<td>0.6937 ± 0.0552</td>
<td>-22.37 ± 0.83</td>
</tr>
<tr>
<td>SLN GMS 2.5%</td>
<td>424.3</td>
<td>0.683</td>
<td>-16.5</td>
</tr>
<tr>
<td></td>
<td>444.9</td>
<td>0.616</td>
<td>-16.0</td>
</tr>
<tr>
<td></td>
<td>404.9</td>
<td>0.785</td>
<td>-16.2</td>
</tr>
<tr>
<td>Average</td>
<td>424.70 ± 20.00</td>
<td>0.6947 ± 0.0851</td>
<td>-16.23 ± 0.25</td>
</tr>
</tbody>
</table>

TEM analysis was performed to determine the morphology and size of the SLN. The results of the TEM analysis showed the sea cucumber SLN particles were spherical in shape. The results of the sea cucumber TEM analysis can be seen in Figure 1.

The results of the characteristic analysis show that the greater the concentration of GMS, the greater the particle size. This shows that the addition of GMS concentration affects the particle size of a preparation. The particle size has a value that corresponds to the Solid Lipid Nanoparticle (SLN) size range. This will affect the higher absorption of the drug in the body (Jahanshahi & Babaei, 2008).

The PDI (polydispersity index) value is the sum calculated from two simple parameters for correlation data (Cumulants). The results showed that the PDI value close to 1 means it has a very wide size distribution and contains large particles or aggregates that can undergo sedimentation. Particles with a size above 500 nm and having a PDI value above 0.5 are said to be large and agglomerated. Particle Size Analyzer (PSA) is a particle size test with a size between 2-7000 nm using the principle of Dynamic Light Scattering (DLS) and Brownian motion. The results of PSA analysis show that the amount of fat added in the formula has an effect.
on particle size and the value of the Polydispersity Index (PDI). Polydispersity index is the level of heterogeneity of a collection of particles as a measure of particle size distribution. The PDI value is in the range of 0-0.6. If the PDI shows a value > 0.6, it indicates that the sample has a wide size distribution. The smaller the PDI value (close to zero) illustrates that the more homogeneous the particle size distribution. The greater the amount of fat, the larger the particle size tends to be. This is because the increase in the fat composition and the constant amount of surfactant will form a larger particle size because the surface area that can be covered by the surfactant does not increase, while the increased amount of fat results in the presence of a fat surface that cannot be covered by the surfactant so that the fat will agglomerate and resulting in a larger particle size (ISO, 2001; Jores et al., 2004).

The results of the characterization of the SLN formula, then all formulas meet the nano size. Zeta potential measurement provides information on the stability of a colloid during storage, provides information on the charge of colloidal particles related to the electrostatic repulsion between particles in SLN suspension, so as to prevent colloidal particle aggregation. Zeta potential can predict the gelation phenomenon. The sample has a potential value of -25 mV. While the zeta potential value of -15 mV indicates the start of the gelation phenomenon. Gelation phenomenon is one of the factors that influence the incorporation of active substances in SLN, which is the phenomenon of changing the viscosity of SLN from liquid to viscous resembling a gel. This gelation phenomenon is related to the modification of fat crystals which results in an increase in the surface area of the particles, so that the surfactant is unable to cover the new surface formed, so fat aggregation occurs. A good zeta potential value is greater than +30 mV or less than -30 mV. The more positive or negative the zeta potential value indicates that the greater the repulsive force between particles with the same charge, the smaller the tendency between the particles to aggregate (ISO, 2001; Mehnert & Mäder, 2012).

The results of the zeta potential analysis showed that all formulas had a zeta potential close to -30 mV, as in SLN GMS 0.5%, SLN GMS 67 1.5%, SLN GMS 2% showed that the formula had a stable tendency during storage and had no tendency to the gelation phenomenon. The results showed that the higher the concentration of sea cucumber extract, the larger the particle size. This can happen because the higher the collision between the particles which is directly proportional to the increase in concentration. The increase in particle size can be caused by collisions between particles which can cause particle aggregation. The addition of lecithin has the effect of increasing the zeta potential value of SLN, this results in variations in the zeta potential value of the formula even though the lecithin composition is added to the entire formula (Mehnert & Mäder, 2012; Silva et al., 2011).

### Antihyperglycemic Activity

In this study, 51 male white rats were divided into 17 groups, each group consisting of 3 rats, namely group 1 CMC Na 0.5% dose 1% bw; group 2 Metformin, group 3 to group 17 SLN doses of 50, 100, 200 mg/kg bw. Before the experiment, male white rats were fasted for ± 20-24 hours, then the weight of each male white rat was weighed and marked on the tail. Each male white rat was measured its fasting blood sugar level using a glucometer to determine the initial blood sugar level. Then the male white rats were given treatment according to the group division, namely 50% glucose at a dose of 3 g/kg bw 30 minutes later and the blood sugar levels of male white rats were measured at 30, 60, 90, and 120 minutes using a glucometer. The effect of dose on blood sugar levels of male white rats oral glucose tolerance test (n=3) can be seen in Table 3. In the same test on SLN, male white rats were divided into 5 groups, each group consisting of 3 tails, group 1 (control) CMC Na 0.5%; group 2, 3, 4 (test group) SLN dose of 700 mg/kg body weight, 750 mg/kg body weight; and 800 mg/kg bw, and group 5 metformin 65 mg/kg bw. Before being induced with streptozotocin, male rats used in the previous experiment were acclimatized again for one week, then fasted, then weighed each, marked on the tail and measured fasting blood sugar levels using a glucometer. The results of the average blood sugar levels of male white rats after being induced by streptozotocin can be seen in Table 4.

<table>
<thead>
<tr>
<th>Groups</th>
<th>Glucose Level (mg/dl) ± SD</th>
<th>Normal</th>
<th>Minute 0</th>
<th>Minute 30</th>
<th>Minute 60</th>
<th>Minute 90</th>
<th>Minute 120</th>
</tr>
</thead>
<tbody>
<tr>
<td>Negative Control</td>
<td></td>
<td>84.67 ±</td>
<td>199.00 ±</td>
<td>205.33 ±</td>
<td>185.67 ±</td>
<td>137.33 ±</td>
<td>105.33 ±</td>
</tr>
<tr>
<td>Positive Control</td>
<td></td>
<td>84.33 ±</td>
<td>150.33 ±</td>
<td>147.67 ±</td>
<td>118.00 ±</td>
<td>96.33 ±</td>
<td>88.33 ±</td>
</tr>
<tr>
<td>SLN GMS 0.5% 50 mg/kg</td>
<td></td>
<td>82.00 ±</td>
<td>180.00 ±</td>
<td>193.67 ±</td>
<td>144.67 ±</td>
<td>109.33 ±</td>
<td>100.00 ±</td>
</tr>
</tbody>
</table>

Table 3. The Results of the Average Blood Sugar Levels of Rats on Glucose Tolerance Method

Indonesian Journal of Multidisciplinary Science, Vol. 3, No. 1, October 2023
The bioactive compounds contained in sea cucumber decrease gluconeogenesis so that blood sugar levels and insulin requirements decrease. Alkaloids are also contained which can prevent the oxidation of pancreatic beta cells due to alloxan induction so that damage can be minimized (Prawitasari et al., 2021; Rahmadani et al., 2020). The bioactive compounds contained in sea cucumbers are alkaloids and the enzyme -glucosidase. Alkaloids work by stimulating the hypothalamus and glucosidase. Alkaloids decrease blood sugar levels in rats. Thus, for further research, SLN GMS 2.5% doses of 50, 100 and 200 mg/kg bw diabetic rats were used. In a follow-up test with streptozotocin induction, the administration of test samples (days 3, 6, 9, 12, and 15) of CMC Na, metformin, and 25% SLN according to their respective doses showed that blood sugar levels decreased with the highest decrease in positive control group.

The decrease in blood sugar levels by giving SLN is caused by the presence of bioactive compounds contained which can prevent the oxidation of pancreatic beta cells due to alloxan induction so that damage can be minimized (Prawitasari et al., 2021; Rahmadani et al., 2020). The bioactive compounds contained in sea cucumbers are alkaloids and the enzyme -glucosidase. Alkaloids decrease blood sugar levels in rats. Thus, for further research, SLN GMS 2.5% doses of 50, 100 and 200 mg/kg bw diabetic rats were used. In a follow-up test with streptozotocin induction, the administration of test samples (days 3, 6, 9, 12, and 15) of CMC Na, metformin, and 25% SLN according to their respective doses showed that blood sugar levels decreased with the highest decrease in positive control group.

The table shows that the rats experienced a decrease in blood sugar levels. In the SLN GMS group 2.5%, the dose of 200 mg/kg bw in 120 minutes was not significantly different from the positive control. SLN 2.5% at a dose of 200 mg/kg bw resembles t the dose of 200 mg/kg bw in 120 minutes was not significantly different from the positive control p>0.05.

<table>
<thead>
<tr>
<th>Groups</th>
<th>Blood Glucose Level (mg/dl) + SD</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Day 3</td>
</tr>
<tr>
<td>Negative Control</td>
<td>1.8933 ± 0.90743</td>
</tr>
<tr>
<td>Positive Control</td>
<td>17.8800 ± 4.79691</td>
</tr>
<tr>
<td>SLN GMS 2.5% 50 mg/kg</td>
<td>5.7867 ± 2.28596</td>
</tr>
<tr>
<td>SLN GMS 2.5% 100 mg/kg</td>
<td>8.4133 ± 1.32455</td>
</tr>
<tr>
<td>SLN GMS 2.5% 200 mg/kg</td>
<td>10.9567 ± 1.83129</td>
</tr>
</tbody>
</table>

The table shows that the rats experienced a decrease in blood sugar levels. In the SLN GMS group 2.5%, the dose of 200 mg/kg bw in 120 minutes was not significantly different from the metformin group and the CMC Na group in decreasing KGD. SLN 2.5% at a dose of 200 mg/kg bw resembles the antidiabetic effect of metformin and can reduce blood sugar levels in rats. Thus, for further research, SLN GMS 2.5% doses of 50, 100 and 200 mg/kg bw diabetic rats were used. In a follow-up test with streptozotocin induction, the administration of test samples (days 3, 6, 9, 12, and 15) of CMC Na, metformin, and 25% SLN according to their respective doses showed that blood sugar levels decreased with the highest decrease in positive control group.

The decrease in blood sugar levels by giving SLN is caused by the presence of bioactive compounds contained which can prevent the oxidation of pancreatic beta cells due to alloxan induction so that damage can be minimized (Prawitasari et al., 2021; Rahmadani et al., 2020). The bioactive compounds contained in sea cucumbers are alkaloids and the enzyme -glucosidase. Alkaloids work by stimulating the hypothalamus and decreasing gluconeogenesis so that blood sugar levels and insulin requirements decrease. Alkaloids are also proven to have the ability to regenerate damaged pancreatic cells. Alkaloids have the potential as anti-diabetic agents.
by inhibiting the work of the -glucosidase enzyme. and saponins that can prevent complications of diabetes (Agrawal et al., 2013; Rasouli et al., 2020). Currently, GLUT 4 is often used as a variable in research on the improvement or recovery of type 2 diabetes mellitus (Safitri et al., 2019; Tiong et al., 2013).

CONCLUSION

The SLN particles were spherical in shape, and the best formula was SLN GMS 1%. The antihyperglycemic activity test showed that SLN GMS 1% had a significant effect on reducing blood glucose levels in rats. The study provides evidence that sea cucumber formulated in the form of SLN could be developed as a functional food product to help battle the onset of diabetes and diabetic complications. Further research is needed to determine the safety and efficacy of sea cucumber SLN in humans. SLN was able to reduce the KGD of male white rats and had an antidiabetic effect against streptozotocin-induced male white rats. SLN of sea cucumber ethanol extract was able to reduce the KGD of male white rats induced by streptozotocin.

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