



THE ACTIVITY ANTIHIPERGLIKEMI FRAKSI- FRAKSI EXTRACT ETHANOL LEAVES SEMBUNG (BLUMEA BALSAMIFERA (L.) DC) IN RATS INDUCED STREPTOZOTOZIN NIKOTINAMID

Joseph Billi*, Mawaqit Makani

School of Farmasi, Sekolah Tinggi Ilmu Kesehatan Borneo Cendekia Medika, Jl. Sutan Syahrir No.11, Madurejo, Arut Selatan, Kotawaringin Barat, Kalimantan Tengah 74112, Indonesia

*billiro94@gmail.com

ABSTRACT

Diabetes mellitus (DM endokrinologis) is a disease or abnormality metabolic disorder is a group of heterogeneous where impaired insulin secretion can cause high blood glucose levels (abnormal settled) and glucose intolerance. It is characterized by abnormally high blood sugar (hiperglikemia). Hiperglikemia is a situation where patients fasting blood sugar levels rose above 110 mg / dl blood sugar levels and 2 hours after eating (PP) above 140 mg / dl. The discovery of herbal ingredients for antihyperglycemia is very necessary because diabetes is one of the most common diseases in the world. *Blumea balsamifera* leaf extract (BBLE) is known to be able to lower blood sugar levels because it has metabolite compounds that play a role in lowering blood sugar levels. Objective to evaluate the antihyperglycemic activity of ethanol extract and various fractions of sembung leaves (*Blumea balsamifera*) against streptozotocin-nicotinamide-induced rats. Method: This study used a randomized post-test only control group. Extraction was carried out using ethanol, then evaporated. Fractionation was carried out using the liquid-liquid extraction method, using water, ethyl acetate and n-hexane as solvents. For 10 days, 30 male Wistar rats were adapted, then their blood sugar levels were measured 2 hours after measuring their blood sugar levels, the test animals were given stz-na then left for 2 weeks after being given stz-na, when the blood sugar levels of the test animals were above 200 then given ethanol extract, water fraction, ethyl acetate fraction, n-hexane fraction and glibenclamide as positive controls and observed for 2 weeks until the blood sugar levels of the test animals could return to normal or below 200. Ethanol extract, n-hexane fraction, ethyl acetate fraction, water fraction and positive control are able to reduce blood sugar levels as seen from the following percentage reduction extract of 47.46 on day 17 and percentage reduction on day 24 of 75.62. n-hexane fraction of 46.19 on day 17 and percentage reduction on day 24 of 74.22. Ethyl acetate fraction of 51.22 on day 17 and percentage reduction on day 24 of 82.47. Water fraction of 56.46 on day 17 and percentage reduction on day 24 of 84.48. Positive control (glibenclamide) of 54.85 on day 17 and percentage reduction on day 24 of 83.17. Ethanol extract and fractions of sembung leaves (*Blumea balsamifera* (L.) DC) have antihyperglycemic activity against streptozotocin-nicotinamide-induced mice, and the best in reducing blood sugar levels in mice is the water fraction group followed by positive control and the next sequence is the ethyl acetate.

Keywords: antihyperglykemia; *blumea balsamifera*; sembung leaves; streptozotozin nikotinamide

How to cite (in APA style)

Billi, J., & Makani, M. (2024). The Activity Antihyperglykemi Fraksi- fraksi Extract Ethanol Leaves Sembung (*Blumea Balsamifera* (L.) DC) in Rats Induced Streptozotozin Nikotinamid. *Indonesian Journal of Global Health Research*, 6(S6), 1109-1118. <https://doi.org/10.37287/ijghr.v6iS6.5140>.

INTRODUCTION

Diabetes mellitus (DM endokrinologis) is a disease or abnormality metabolic disorder is a group of heterogeneous where impaired insulin secretion can cause high blood glucose levels (abnormal settled) and glucose intolerance. It is characterized by abnormally high blood sugar (hiperglikemia) (Soelistijo et al., 2019). Hiperglikemia is a situation where patients fasting blood sugar levels rose above 110 mg / dl blood sugar levels and 2 hours after eating (PP) above 140 mg / dl (World Health Organization, 2024). Based on the IDF, indonesia ranked fifth of ten countries with the highest number of diabetics. The prevalence of diabetes in indonesia reach 10,8 in 2021 % which means there will be more than 19,5 million people suffering from diabetes (Atlas, 2015). The survey (RISKESDAS) year 2018, the prevalence of

diabetes in central kalimantan of 1,14 %.According to provincial health department central kalimantan, in 2018 would continue to rise until 2025, With the third highest part of diabetes, it's a west kotawaringin of 2,520 people (Riskasdas, 2018).

The treatment of disease DM is expensive to the need alternative drug of a cheap , hence developed alternative treatment using traditional medicinal plants. One of the plants that could be used as an alternative to traditional treatment dm sembung as a. Plant sembung (*Blumea balsamifera*) is one of the plants used in folk medicine, the drugs are often used as its leaves, we do that corporate sembug leaves used as a pain, diarrhea, the itch (Nursamsu & Firmansyah, 2017). Traditionally, plant sembung used in indonesia for rheumatism, painful menstruation, flu, swollen, bone pain, diarrhea, an ulcer, asthma, angina, cholera, abdominal pain, loss of appetite, chest pain, heart disease, fever, bronchitis, epitaksis. The community usually use leaves sembung to treatment by cutting its leaves smaller into pieces, boiled until the very last, and drink it (Rahardjo, 2016).

Blumea balsamifera having more than 100 secondary as these volatile oil, flavonoid, alcohol, dihidroflavon, sterol, an organic acid, monoterpen, seskuiterpen, triterpen. Most existing research examining the effects of volatile oil bioaktif flavonoid and in vitro and in vivo. Flavonoid component is the main non-volatil *blumea balsamifera* (Naipospos et al., 2022) (Jiang et al., 2014). The flavonoid content sembung leaves extract *Blumea balsamifera* (L.) the village of hasangi 89,2971 mg qe / g and simangalam village of 83,9828 mg qe / g (Maslahat et al., 2013). *Blumea balsamifera* is volatile oil in a yellow greased with a unique. The volatile oil *blumea balsamifera* mostly found in leaves and branches, having the nature and the antioksidant an anticancer. Poor *blumea balalamifera* origin, tawangmangu and bogor containing tannin, flavonoid, L-camphor, borneol, caryophene, β -caffeine and α -humulene (Atikawati; et al., 2019) .

Extract ethanol leaves sembung may reduce blood glucose levels white male rats diabetes with dosage of 200 mg / kg bb highest have an effect. A combination of herbs preparation leaves slobber (*Plectranthus scutellarioides* (L.) R.BR.), leaves menyran (*Phyllanthus niruri* L.), leaves sembung (*Blumea balsamifera* (L.) DC) and leaves catnip (*orthosiphon aristatus* (B.)) Miq. At 570 mg/200 mg/KgBB dose could reduce blood glucose of 60,1975 % glibenklamid in doses equivalent to 0,49 mg / kg weight of 63,1650 %. The extract leaves hidroetanol *Blumea balsamifera* (hebb) 300 and 600 mg dose kg-1 diabetes in rats induced streptozotocin (STZ) significant decreasing blood glucose compared to rats given glibenklamid control diabetes (Atikawati; et al., 2019) (Abdel Aziz et al., 2020) (Xia et al., 2014).Research antihyperglycemic activity of ethanol extract sembung leaves already exists so researchers develop up to fractions-. Research on the antihyperglycemic activity of ethanol extract of sembung leaves already exists so that researchers develop it to its fractions. This study aims to determine whether the ethanol extract fractions are able to reduce blood sugar levels in rats that have been induced by stz-na and to see which fraction is most effective in reducing blood sugar levels in rats

METHOD

Material used in this research as sembung leaves, kloralhidrat, xylen solvent, absolute ethanol, ammonia, chloroform, hydrochloric acid, mayer reagents, dragendroff reagents, magnesium, hydrochloride acid, amyl alcohol, sodium hydroxide, fec13 % 1, formalin, lieberman reagents burchard, cmc, glibenklamid as a positive control.An instrument used in this research are maceration equipment consisting of a bottle maceration, a beaker glass, a flannel, ayakan mesh 40, alluminium foil, a funnel, an oven, kolorimeter, squash 50 ml measures, pipet hematokrit, stems the mixer, a weigh, sterling-bidwell, moisture-ballance, the

evaporators, tweezers, pipet drops, paper weigh, filter paper, vial, rat home, cutter, spuit, piknometer, the glass and needle. In this study the experimental animal used was a male white rat with a wistar strain (*ratus norvegicus*) age 16 weeks at a weight of 150 to 250 grams. The number of rats used by 30 and grouped into 6 groups of treatment with groups of 5 rats. Previously on rat were acclimatized for seven days. Before being used for research, Animals tried to be fasting 18 hours but were still given a drink.

Generation of ethanol extracts of sembung leaves

Leaf dust weighed a thousand grams, inserted in a dark - colored container, added 7,5 litres of ethanol 96 %. Then stir the dust and closed immediately, It was kept in a room that was spared the sun's rays and held for 72 hours, with occasional snitching. After 72 hours, maserer filtered with flannel fabric, filtrate is held in a glass beamer and rounded up using rotary evaporator. Extract results used for ethanol-free testing and extract rendement calculations.

Fractionation of extract ethanol sembung leaves

Extract ethanol sembung leaves of 20 g's slightly dissolved with hot water, Then partitioned with water 50 ml and solvent n-heksana 50 ml into a separated funnel was repeated three times. The n-heksana fraction is the upper filtrate and the water fraction is the lower filtrate. The n-heksana fraction is separated from the held water fraction and thickened using the rotary evaporator at 80⁰c temperatures. Remaining water fraction of the n-hexane fraction then re-defraction with ethyl acetate solvent 50 ml using a separating funnel this process is repeated as many as 3 times. Ethyl acetate fraction separated from water fraction then attached with rotary evaporator with evaporative temperature 500⁰c. Fractionated residual filtrate with ethyl acetate is a water fraction, Then it is thickened with water bath until it is thick.

Identification of chemical content sembung fraksi-fraksi extract and leaves

- a. An alkaloid identification. Sample detection in 60 f254 silica gel, put in a vessel containing saturated: ethyl toluene phases of the motion, acetic: dietilamin (7:2:1) elution until a raised and dried, then sprayed with dragendorff reagent. An alkaloid test used dragendorff give color orange or brown after heated for 5-10 minutes at a temperature of 100c. The analysis shows patche of color orange.
- b. Identification terpenoid / steroid. Used the quiet phase of its motion with silica gel f254 n-heksan: ethyl acetate (7:3). Can be seen in uv lamp stain 254 nm and 366 nm dark green and detection rays looked use bouchard liberman reagents.
- c. Flavonoid identification. Make a spot sample on silica plate gel f254. Silica plate gel are then inserted into saturated vessels containing etyl acetate phase motion: formiatic acids: glacial acetate acid: water (100: 11: 11: 27) and then implemented to the limit, plate dried and observed in uv light. Detection of flavonoid compounds performed with cytroborate reagent. Once heated for 5 minutes at 100⁰c temperatures, there will be yellow fluorescence greenness at uv 366 nm. Quersetin as a comparison because it's a flavonoid group that's often found in plants because of biological activity. This flavonoid and quersetin compound can form a complex with an orange-colored AlCl₃
- d. Identification saponin. Silent phase used silica gel f254 with the mobile phase kloroform-metanol-air by comparison with 6:3:1. Can be seen in lamp uv 254 nm and 366 nm green. Reagent spray anisaldehyd with result the color purple and under visible light were a blue.

The preparation of the test animals

Rats and used in this research as many as 30 tail. Adapted for 1 week. After that is induced by stz-na rats for 10 days. After the experience blood sugar levels high (≥ 200) for 10 days and after that divided into 6 groups on the basis of ranking blood sugar levels and sorted a spiral

rata-rata so as to have the same blood sugar levels. Each test group consists of 5 rats. Grouping of test animals as follows:

- Kelompok I : Positive control (Glibenklamid 0,9 mg/Kg BB tikus)
- Kelompok II : Negative control (larutan CMC-Na 1 %)
- Kelompok III : DM rats given ethanol extract of sembung leaves (400 mg/Kg BB)
- Kelompok IV : DM rats given n-hexane fraction of sembung leaves (100 mg/Kg BB)
- Kelompok V : DM rats given ethyl acetate fraction of sembung leaves (100 mg/Kg)
- Kelompok VI : DM rats given water fraction of sembung leaves (100 mg/KgBB)

The measurement of blood glucose levels animals test

Measurement of blood sugar levels by the god-pap method and absorbansi read of spektrofotometer uv-vis at wavelengths 500 nm. Fasting rats for 18-20 hours while still being given a drink before taking the blood. The volume of the blood is drawn orbitalis 1 ml with pipe capillary then stored in a tube plastic eppendorf dmembeku and allowed to have perfect with blood serum. Blood stored in a tube plastic eppendorf disentrifugasi for 15-20 minutes with speed 3000 rpm. Has a serum that have been stored in a refrigerator at a temperature 2-80c that were. After that the sugar content of measured by means of 10 µl serum coupled with a mixture of reagents god lap as many as 1000 µl then divortek for 1 minutes until a perfect. Having left for 20 minutes at a temperature of 20-250c absorbansi not spektrofotometer uv-vis at wavelengths 500 nm then calculated the glukoa (mg /) dl blood

Analysis of results

Quantitative data expressed as the result of this research mean (mean) (±) standard deviations (SD). Significance statistic computed by using analysis variance one direction (anova) followed by t-test. The effect of anti hiperglikemik analysis is measured by the standard of trust 95 % correlative. The considered statistically significant when p-result less than 0,05 (p<0,05).

RESULT

Extraction methods in this study used masseration methods because the active compounds of the sembung leaves have antihyperglychemic activity are generally not a substance that can't withstand warming and is volatile. That's it maseration does not cause the degradation of non-resistant metabolites. While for filtering solution is used ethanol 96 % because it can attract the active substances needed in an optimal study such as steroids, triterpen, flavonoid, alkaloid and sponin. Generate data extracting ethanol of a bundle leaf can be seen on table 1.

Tabel 1.

Rendemen ekstrak etanol leaves sembung

| Weight of powder (g) | Weight of extract (g) | Rendement ekstrak (%) |
|----------------------|-----------------------|-----------------------|
| 750 | 166,55 | 22,20 |
| 750 | 173,06 | 23,07 |
| Average | 22,63 | |

Average rendemen extract ethanol leaves sembung % 22.63 is obtained.

Result the determination water content of extract sembung leaves

Water is a medium the growth of fungi, mildew and invading microorganisms, that can undermine simplisia plant. The presence of water in simplisia can lead to contamination and reaction enzimatis so as to affect simplisia purity of the impact on the quality and khasiatnya. This needs to be done in order to give the moisture content of the maximum limits to the size of the moisture content of simplisia interested in. The determination of the moisture content of this use of distillation xylene with sterling-bidwell. Xylene are liquids

bearer who ca not miscible with water due to the boiling point and the specific gravity greater. Thus when processing heating, water will be more volatile and into a pumpkin top volume has then measured for a while. The determination of the moisture content of the leaves sembung can be seen in table 2.

Table 2.

| Result the determination of the moisture content of extract sembung leaves | | |
|--|---------------------|-------------------|
| Sampling weight (g) | Volume on the scale | Water content (%) |
| 20 | 1,8 | 9,00 |
| 20 | 1,5 | 7,50 |
| 20 | 1,1 | 5,50 |
| Average | 7,33 ± 1,76 | |

From table 2 seen that the percentage of the moisture content of extract leaves sembung % 7,33 amounted to. The shows that extracts leaves sembung compliant with the the moisture content of less than 10 %.

The results of the determination of the specific gravity of extract ethanol

Specific gravity of can be defined as the tension of a substance to voltage water, the values of both substances are determined at the same temperature. The aim determination of the specific gravity of which is to see the volume of a union of water with a substance. The determination of the specific gravity of, is a special parameter to see the purity of a substance is already same as water. The determination of the specific gravity of calculated using a piknometer. Extract used is extract sembung leaves that uses a solvent ethanol 96 % and obtained the ml / 1.1 g.

The result of creating fractions from extract sembung leaves ethanol

Making fractions-fractions extract ethanol sembung leaves in a leaf sembung use method liquid-liquid extraction by means of a separating funnel. Organic solvents used to fractionate this is n-heksana, ethyl acetate and water, where the third organic solvents that diverse polarity having the nature of. It is meant to make compounds chemical be inside leaves extract sembung and having antihyperglykemi activity can be separated by polarity. The principle of solubility is described by like-dissolved like or In other words, solvent will attract same compounds, for example polar solvents will attract polar compounds, and semipolar compounds will attract those that are semipolar. Likewise, non-polar solvents will also attract non-polar compounds. The results of calculating the yield for each fraction can be seen in

Tabel 3.

| Weight of extract (g) | Weight of faction (g) | | | The number of faction (g) | Rendement (%) | | | Results of the whole faction (%) |
|-----------------------|-----------------------|-------------|-------|---------------------------|---------------|-------------|-------|----------------------------------|
| | n-heksan | etil asetat | air | | n-heksan | etil asetat | air | |
| 120 | 12,25 | 35,60 | 15,20 | 63,05 | 10,20 | 29,67 | 12,67 | 53,54 |

The identification of chemical content fraksi-fraksi and extract leaves sembung use chromatography thin layer

Identification uses thin layer chromatography with silica gel f254, for flavonoid tests use chloroform motion phases: acetate etyl (6: 4), saponin test uses chloroform phase: methanol: water (64: 50: 1), alkaloid test uses toluen motion phase: etyl acetate: dietil amin (7: 2: 1), terpenoid test uses n-hexan motion phase: etyl acetate (93: 7). The solvent destination selected because each solvent has a different pattern so that the compounds with different patterns are expected to be separated from the person. The results are seen after the clet plate

is sprayed with a cytroborate suppression to show stains or stains. Color-blue stains or stains can be seen below lamp uv 366.

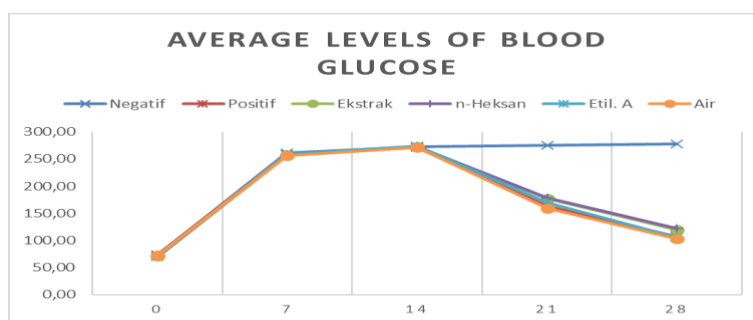
Tabel 4.
The result of identification of chemical content fraksi-fraksi and extract leaves sembung use chromatography thin layer

| Secondary metabolite compounds | Results after spraying | | Result | | | |
|--------------------------------|------------------------|-----------------|----------------|-----------------|--------------------|------------|
| | 254 nm | 366 nm | Esktrak etanol | Fraksi n-heksan | Fraksi etil asetat | Fraksi air |
| Flavonoid | Greenish yellow | Greenish yellow | + | - | + | + |
| Alkaloid | Cokelat jinga | Cokelat jinga | + | - | + | + |
| Saponin | Biru | Biru | - | - | + | + |
| Terpenoid | Merah keunguan | Merah keunguan | + | - | + | - |

Flavonoid identification shows results of yellowish-green color is present in ethanol extract, ethyl acetate fraction and water fraction. On the identification of alkaloids shows the result of yellowish brown color is found in ethanol extract, water and ethyl acetate. On the identification of saponin shows results of blue or young blue color on water and ethyl acetate fractions. On the identification of terpenoid compounds shows the result of purplish red in ethanol extract, ethyl acetate fraction and water fraction.

Result measurements levels of blood glucose

Blood glucose measurements are done five times, That's on the zeroth day (H0) as the initial blood take., On day 3 (H1) to measure the condition of animal hyperglycemia test after stz-na delivery, On the 10th day (H2) after stz induction to trigger pancreatic cell damage so that dm conditions can be achieved, where dm conditions can be achieved by measuring the blood glucose levels 200 mg / dl, Day 17 (H3) and day 24 (H4) to know the degree of blood glucose after being treated. Blood glucose measurements can be seen at table 5.



Picture 1. The measurement result average animal testing blood sugar level

DISCUSSION

Flavonoid, alkaloid, saponin, and terpenoid as compound is often identified from simplisia and extract sembung leaves and the potentially as antihyperglycemia and antihyperlipidemia. The most abundant compound in the sembung leaves as flavonoid . A compound derived contained in a plant flavonoid sembung include blumeatin (5,3',5' trihydroxy-7-methoxy-dihydro-flavone), velutin, tamarixetin, dihidrokuersetin- 7,4' -dimetil ether, ombuine, rhamnetin, luteolin-7-metil ether, luteolin, kuersetin, 5,7,3', 5' tetrahidroksiflavanon, and dihidrokuersetin-4' methyl ether. (Ruhardi & Handoyo, 2021). Flavonoid and terpenoid activity reported to have the effects of hypoglycemia antidiabetic drug, or as an antioxidant. An alkaloid glukoneogenesis have an effect of hypoglycemia and sent down glucose levels in the blood and down, saponin can increase insulin secretion in pancreas langerhans (Pang et

al., 2014). Based on the average blood glucose levels in table 5 and figure 1 and with statistical analysis using one way anova followed by the tukey post hoc test showed significant results ($p < 0.05$) which means there is a significant difference between treatment groups. The results of the analysis can be seen in glucose measurements on the 7th and 14th days after the test material treatment showed that the ethyl acetate fraction and water fraction were comparable to the positive control of glibenclamide which can be interpreted that the ethyl acetate fraction and water fraction already have strength comparable to the positive control even when viewed from table 5 and figure 1 can be said to be better than the positive control. In ethanol extraction, and n-hexane fractions each differ significantly to the positive control which can be interpreted that the ethanol extract and n-hexane fraction have the ability to lower blood sugar levels in test animals but not as good as the ethyl acetate fraction, water fraction and positive control.

It is suspected that there is a role of chemical compounds in sembung leaves that can work as antihyperglycemia, for example flavonoid compounds that can lower blood glucose levels. Flavonoids contained in plants are thought to be able to improve insulin receptor sensitivity (Klara, 2023). Other studies have shown that flavonoid compounds contained in sembung leaves have antioxidant activity. Antioxidant properties protect organs from cell damage caused by free radicals and slow down the aging process. Synthetic and natural antioxidants (from various plants) can control blood sugar levels and prevent complications of diabetes (Widowati, 2008) (Jiang et al., 2014). Flavonoids play a role in pancreatic tissue damage caused by DNA alkylation, because they can improve the morphology of the pancreas in mice. Flavonoids have been reported to have antidiabetic effects and regenerate cells in the islets of Langerhans. When pancreatic tissue improves, the amount of insulin in the body increases, blood sugar enters the cells, and blood sugar levels in the body decrease (Suryani et al., 2013). In relation to the healing mechanism of diabetes, flavonoids are thought to play a significant role in increasing antioxidant enzyme activity and are able to regenerate damaged pancreatic β cells so that insulin deficiency can be overcome (Dita et al., 2023) (Rahmi et al., 2021) (Nessa et al., 2003).

Glibenclamide is a class of drugs that are already on the market that have activity as antidiabetics. Glibenclamide stimulates glucose uptake, suppresses excess hepatic glucose production, and reduces glucose absorption in the intestine. Glibenclamide given to mice as a positive control has a mechanism in increasing insulin sensitivity, therefore this study is in line with research conducted by which states that the mechanism of positive control, namely glibenclamide, can increase insulin sensitivity. Thus, glucose levels will decrease when given glibenclamide (Depkes, 2005). Based on previous research, a combination of herbal medicine preparations from iler leaves (*Plectranthus scutellarioides* (L.) R.BR.), menyran leaves (*Phyllanthus niruri* L.), sembung leaves (*Blumea balsamifera* (L.) DC.) and catnip leaves (*Orthosiphon aristatus* (B.) Miq.) at a dose of 570 mg/200 gBW can reduce blood glucose by 60.1975% or equivalent to glibenclamide at a dose of 0.49 mg/kg body weight of 63.1650% (Nurhayati, 2023). Studies show tea giving *B. balsamifera* leaves at 50 mg/kgBB; 100 mg/kgBB and 150 mg/kgBB can affect adropin *Mus musculus* blood sugar at 120 minutes with a percentage of 62%, 73%; 72.34% and 80,06% (Novi et al., 2023). Administration of hydroethanol leaf extract of *Blumea balsamifera* (HEBB) at doses of 300 and 600 mg kg⁻¹ in diabetic rats induced by streptozotocin (STZ) showed a significant decrease in blood glucose compared to diabetic control rats given glibenclamide. Ethanol extract of sembung leaves can reduce blood glucose levels in male diabetic white mice and a dose of 200 mg/kg BW has the highest effect (Eriadi et al., 2017). Other studies also stated that the combined extract of *C. grandis* and *B. balsamifera* showed increased antidiabetic activity through improving oxidative stress, β -cell regeneration, and increasing insulin expression (Putra et al., 2024).

CONCLUSION

Ethanol extract and fractions of sembung leaves (*Blumea balsamifera* (L.) DC) have antihyperglycemic activity against streptozotocin-nicotinamide-induced mice, and the best in reducing blood sugar levels in mice is the water fraction group followed by positive control and the next sequence is the ethyl acetate.

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