Characterization of α-Glucosidase Inhibitor *Streptomyces* sp. IPBCC.a.29.1556 Aqueous Extract: An Endophyte of Indonesian *Ficus deltoidea*

Isra Janatiningrum[1*], Yulin Lestari[2,3], Dedy Duryadi Solihin[2], and Anja Meryandini[2]

[1]*Pharmacy Study Program, Faculty of Health Sciences, UIN Syarif Hidayatullah Jakarta, South Tangerang 15419, Indonesia*

[2]*Department of Biology, Faculty of Mathematics and Natural Sciences, IPB University, Jl. Agatis, Dramaga, Bogor 16680, West Java, Indonesia*

[3]*Tropical Biopharmaca Research Center, IPB University, Jl. Taman Kencana No. 3, Bogor 16128, West Java, Indonesia*

* ***Corresponding author:***

email: isra.janatiningrum@uinjkt.ac.id

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Abstract: *Filamentous bacteria have been known as actinobacteria which could produce various secondary metabolites, including an α-glucosidase inhibitor. The α-glucosidase inhibitor has been identified to be potentially valuable for the treatment of diabetes mellitus. Endophytic actinobacteria are able to produce bioactive compounds that are similar to their hosts. Indonesian* Ficus deltoidea *is one of the medicinal plants which has the activity of the α-glucosidase inhibitor. The α-glucosidase inhibitor has been characterized by optimizing compound production, fractionation, analysis using TLC and LC-MS, and identifying inhibitor mechanisms. The α-glucosidase inhibitor substance is present in* Streptomyces *sp. IPBCC.a.29.1556 aqueous extract. The aqueous extract was separated and fraction 1 had an* IC_{50} *value of 58.8 μg/mL, which is better than acarbose (*IC_{50} *= 90.4 μg/mL). Kinetic studies revealed that this fraction inhibited the enzyme through a non-competitive mechanism. Chemical profile based on LC-MS, fraction 1 showed the presence of Phenylpropynal, Butyric acid, 2-(2-Ethoxyethoxy)ethanolate, 1,1-Diethoxyethane acetate,* N,N*-dimethyl-3-oxide-1*H*-Benzotriazole-1-propanamine,* p*-coumaric acid, and isoquinolinium which might contribute individually or synergistically to the observed α-glucosidase inhibitor activity. These results suggest that fraction 1 from the aqueous extract of* Streptomyces *sp. IPBCC.a.29.1556 is the potential source to produce an α-glucosidase inhibitor for the management of postprandial hyperglycemia.*

Keywords: *α-glucosidase inhibitor; diabetes mellitus; endophytes;* Ficus deltoidei*;* Streptomyces

■ INTRODUCTION

Natural products are an important source of bioactive compounds in the world. One source of bioactive compounds is microorganisms, including actinobacteria. Actinobacteria are filamentous and advanced bacteria that have been known to produce various secondary metabolites [1-2]. These bacteria are important for human health, agriculture, industry, and biotechnology [3-5]. One of the secondary metabolites produced by actinobacteria is an α-glucosidase inhibitor.

The α-glucosidase inhibitor is one of the drugs for diabetes mellitus. This inhibitor works competitively to inhibit the action of the α-glucosidase enzyme, which is responsible for hydrolyzing carbohydrates to glucose. Carbohydrates will normally be converted into simple sugars or monosaccharides, which can be absorbed in the small intestine. Inhibition by the inhibitor compound can control blood sugar levels in patients with diabetes mellitus so that hyperglycemia does not occur. Acarbose is an α-glucosidase inhibitor compound isolated from soil actinobacteria in Kenya [6]. Acarbose has been commercialized for the treatment of diabetics. However, continuous use of acarbose may lead to some side effects, such as adverse gastrointestinal and liver

toxicity symptoms [7-8]. This is caused by the ability of acarbose, which is a competitive inhibitor and can inhibit all digestive enzymes of complex carbohydrates, interfering with all carbohydrate metabolisms. Therefore, a new inhibitor is needed to reduce the effects of weakness from acarbose. Hence, the α-glucosidase inhibitor from other sources is needed, such as actinobacteria, with lesser side effects.

Actinobacteria are predominantly free living and are found in diverse environments, including plant tissue. Microbes that live on plant tissues without causing harm effects to the host are called endophytes [9]. In recent years, such microbial endophytes are beginning to attract researchers' attention due to their ability to produce various compounds with a pharmacological value similar to their hosts. Actinobacteria have been developed to be a member of the plant microbiome because they produce various secondary metabolites. Previous reports showed that endophytic actinobacteria have α-glucosidase inhibitor activity, such as *Tinospora crispa*. Interestingly, it was observed that endophytic actinobacteria (BWA65) that are similar to *Streptomyces diastaticus* produced the inhibitor, which showed doubled activity than its host plant *T. crispa* [10]. Endophytic actinobacteria isolated from antidiabetic medicinal plants *Leucas ciliata* and *Rauwolfia densiflora* also exhibited α-amylase inhibitor activity. The α-Amylase inhibitor demonstrated antidiabetic activity similar to the α-glucosidase inhibitor [11]. The high diversity of bioactive compounds produced by endophytic actinobacteria makes the study of endophytic actinobacteria important.

Ficus deltoidea is a medicinal plant popular in Indonesia. *F. deltoidea* was used traditionally to treat diabetes [12]. In addition, several studies have proven that *F. deltoidea* has antidiabetic activity [13-15]. The ability of *F. deltoidea* to produce α-glucosidase inhibitors is suggested to be related to the presence of endophytic microbes, including actinobacteria. Previous studies showed that the abundance of actinobacteria in the tabat barito plant tissue is quite numerous and varied [16]. One of the actinobacteria that have been isolated from *F. deltoideia*, *Streptomyces* sp. IPBCC.a.29.1556 has ability to produce α-glucosidase inhibitors (IC_{50} values of 159.25 μg/mL) [17]. The capability of tabat barito to produce α-glucosidase inhibitors is related to the presence of actinobacteria. *Streptomyces* sp. IPBCC.a.29.1556 are expected to be able to substitute medicinal plants as a drug specifically for antidiabetic. Thus, the purpose of this study was to obtain and characterize a new α-glucosidase inhibitor compound from *Streptomyces* sp. IPBCC.a.29.1556 that have been isolated from *F. deltoidea*.

■ EXPERIMENTAL SECTION

Materials

Streptomyces sp. IPBCC.a.29.1556 isolate (IPB Culture Collection), mammalian (rat), α-glucosidase enzymes from rat intestinal acetone powder (Sigma, St. Louis), and *p*-Nitrophenyl α-D-glucopyranoside (PNPG) (Sigma, St. Louis) were employed in this study.

Instrumentation

Instrumentations used in this work were UV/Vis Microplater Spectrophotometer (Biotec Epoch), TLC Silica gel (Merck 60G F_{254} 25 Glass plates 20 × 20 cm), Linomat spotting TLC (CAMAG Linomat 5), and liquid chromatography-mass spectrometry (ACQUITY UPLC®H-Class System (Waters, USA).

Procedure

Preparation of isolates

Endophytic actinobacteria *Streptomyces* sp. IPBCC.a.29.1556 were isolated from *F. deltoidea* leaves as previously reported [16]. The isolates were then inoculated using (ISP) 4 agars for 7 d at 25 °C. The isolates were then used as the primary culture for the production of α-glucosidase inhibitors.

The α-glucosidase inhibitor assay

Rat intestinal acetone powder (200 mg) was dissolved in 4 mL phosphate buffer (50 mM) in an ice bath. The solution was sonicated for 15 min at 4 °C and then vortexed for 20 min. Afterward, the solution was centrifuged at 10000 rpm at 4 °C for 30 min. The supernatant from centrifugation was made into a stock of enzymes. The test reaction was carried out by mixing 10 μL enzyme solution (0.5 U/mL) with 50 μL phosphate

buffer and 20 µL test sample. The mixture was incubated for 5 min at 37 °C. Subsequently, 20 µL PNPG as a substrate was added and reincubated for 30 min at 37 °C. The reaction was terminated by the addition of 500 µL Na_2CO_3 (0.1 M). Inhibition activity was examined using microplate spectrophotometers at 410 nm wavelength [18]. As a comparison, acarbose was used as a positive control. The inhibition of the activity of the α-glucosidase enzyme is determined by the formula:

$$\text{Inhibition } (\%) = \frac{\text{AC} - (\text{AS1} - \text{AS0})}{\text{AC}} \times 100\%$$

where AC: absorbance control, AS0: absorbance of the sample without enzymes, and AS1: absorbance of the sample.

Optimization of α-glucosidase inhibitor production

Time optimization. The production curve is used to determine the optimum time used to produce large amounts of α-glucosidase inhibitors. *Streptomyces* sp. IPBCC.a.29.1556 isolates were inoculated in ISP 2 medium. The culture was tested for its inhibitory activity against the α-glucosidase enzyme every 5 d.

Medium optimization. Optimization of production media was done by testing α-glucosidase inhibitors on three different medium i.e., ISP 2 (malt extract 2%, yeast extract 0.4%, dextrose 0.4%), Yeast Starch (YS) (soluble starch 1%, yeast extract 0.4%, K_2HPO_4 0.05%, $MgSO_4{\cdot}7H_2O$ 0.05%), and ISP 4 (soluble starch 1%, K_2HPO_4 0.1%, $MgSO_4{\cdot}7H_2O$ 0.1%, NaCl 0.1%, $(NH_4)_2SO_4$ 0.2%, $CaCO_3$ 0.2%, $FeSO_4{\cdot}7H_2O$ 0.001%, $MnCl_2{\cdot}7H_2O$ 0.001%, $ZnSO_4{\cdot}7H_2O$ 0.001%). *Streptomyces* sp. IPBCC.a.29.1556 isolates were inoculated on each medium and incubated for 10 d at 25 °C. Then each culture was examined for its inhibitory activity against the α-glucosidase enzyme. The results of the highest inhibition values indicate the best production medium.

Extraction of bioactive compounds. ISP 2 medium was prepared. Then, under aseptic conditions, 3 inoculars (0.9 cm) of purified culture *Streptomyces* sp. IPBCC.a.29.1556 inoculating to 100 mL ISP 2 broth medium. After that, the culture was incubated for 7 d at 25 °C. After 7 d, the culture was ready for use as a starter culture for the fermentation process. The 1% of the starter culture was put into ISP 2 medium for large amounts of fermentation. The fermentation process was done for 10 d at 25 °C with an aerobic condition in a shaker at 110 rpm. After that, the culture was centrifuged to separate the supernatant and biomass (5000 rpm, 30 min). The supernatants were completely evaporated using an evaporator and the extract was ready to be tested.

Fractionation of bioactive compounds with preparative thin layer chromatography (TLC). The mobile phase (eluent) is optimized before fractionation using Preparative TLC. Separation is performed using silica TLC plate as stationary phase. The first test was carried out using a single eluent with a polar-non-polar gradient. After the two best single eluents were obtained, then the single eluent was mixed with different concentration gradients. The best combination of eluent was used as an eluent in the separation with preparative TLC [19].

The selected endophytic actinobacterial extract of 0.1 g was dissolved with 10 mL methanol (1% w/v), and then 1 mL of the extract was placed on a silica glass plate (20 × 20 cm) using CAMAG Linomat 5. Then, it was separated using eluents that had been optimized before. The spots formed were then collected and eluted using methanol. The elution was concentrated by evaporating at 30 °C. The fraction obtained from spot elution was then tested for α-glucosidase inhibitor activity. The method is described above.

Liquid chromatography-mass spectrometry (LC-MS) analysis. Fractions with the highest inhibitory activity were characterized using LC-MS. The selected fraction of 0.1 g was dissolved with 10 mL of methanol. The fraction (1 µL) was injected into the LC-MS using Ultra Performance Liquid Chromatography (UPLC) system and C18 column (1.8 µm 2.1 × 50 mm) BEH. The MS condition used the ES system (electrospray ionization), Collision 4 V energy, Collision Ramp energy 25–70 V, with a mass analysis in a m/z range of 50–1500. The LC-MS chromatogram was analyzed using the Masslynx V4.1 program. Analysis was carried out to determine the similarity, relative abundance, and spectrum of compounds. Then to determine the possible compounds, the spectrum was compared with compound mass weight data on the Chemspider website.

Determination of inhibition mechanism

The effect of substrate concentration was used to predict the type of inhibitor of the fraction compound. Determination of the type of inhibitor was carried out by testing the inhibitor activity at various substrate concentrations, i.e., 20, 10, 5, 1 and 0.5 mM. The type of inhibition was determined from the Lineweaver-Burk plot. The plot is made of substrate concentration on the horizontal axis and velocity on the vertical axis [20].

Statistical analysis

Statistical analysis was performed as means ± standard deviation (SD) from three independent replicates. One ways analysis of variance (ANOVA) was applied for comparison of the mean values with 95% confidence levels. Linear regression analysis was performed using Microsoft Excel 2013.

■ RESULTS AND DISCUSSION

Time Optimization for α-Glucosidase Inhibitor Production

Endophytic actinobacterial isolate from *F. deltoidea* has the same α-glucosidase inhibitor activity as its host. In a previous study, *Streptomyces* sp. IPBCC.a.29.1556 isolate has an inhibitory activity to rat intestinal α-glucosidase [17]. The α-glucosidase played an important role in modulating postprandial hyperglycemia, which broke down α-1,4-glucosidic linkages of disaccharides, resulting in monosaccharides. The α-glucosidase inhibitor interfered with enzymatic action in the brush border of the small intestine. Inhibition of α-glucosidase enzyme would control blood sugar levels. It could inhibit the liberation of D-glucose from oligosaccharides and disaccharides, resulting in delaying glucose absorption and decreasing postprandial plasma glucose levels. Before extraction of an α-glucosidase inhibitor compound, the endophytic actinobacteria were first optimized for time and production medium.

The production of secondary metabolites in microbes is influenced by nutrition as a limiting factor for growth. Actinobacteria growth is influenced by nutritional sources present in the medium and requires a certain amount of time to reach optimum growth to produce secondary metabolites. The results showed that

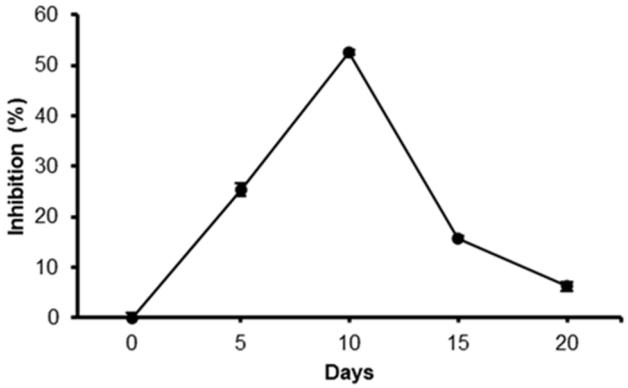

Fig 1. Time optimization of α-glucosidase inhibitor production from *Streptomyces* sp. IPBCC.a.29.1556. Values are expressed as the mean ± standard deviation (n = 3)

10 d was the optimum time for α-glucosidase inhibitor production (Fig. 1). The production time of secondary metabolites from *Streptomyces* sp. IPBCC.a.29.1556 is in accordance with several previous reports. The most optimum antibiotic production from *Streptomyces afghaniensis* VPTS3-1 was over a period of 9 d [21]. Antifungal from *Streptomyces rochei* AK 39 was optimum on 8–11 d and decreased on 12 d [22]. This shows that on average secondary metabolites are produced after incubation of 8–11 d. Over period 12 d, the production of secondary metabolites will decrease due to the depletion of nutrients in the fermentation medium and entering the death phase.

Medium Optimization for α-Glucosidase Inhibitor Production

The growth medium is very influential on the secondary metabolites production of actinobacteria [23-24]. In this study, three different types of media were used, i.e., ISP 2, YS, and ISP 4. The results showed that ISP 2 medium is the best medium for producing secondary metabolites, especially the α-glucosidase inhibitor (Fig. 2). The ISP 2 medium has dextrose and malt extract as carbon sources. The simple sugar structure of dextrose makes it easier to be consumed by microbes. Antibiotic production in *Streptomyces albidoflavus* is optimum when the media contain dextrose as a carbon source [21]. Dextrose is the best carbon source for *Streptomyces noursei* ATCC 11455 in

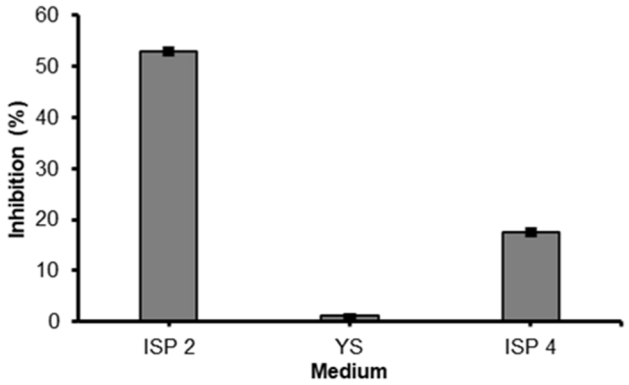

Fig 2. Medium optimization of α-glucosidase inhibitor production from *Streptomyces* sp. IPBCC.a.29.1556. The optimization medium using International Streptomyces Project 2 (ISP 2) Medium, Yeast Starch (YS) medium, and International Streptomyces Project 4 (ISP 4) Medium. Values are expressed as the mean ± standard deviation (n = 3)

producing nystatin [24]. Malt extract is a dried cereal extract from germinated cereal grain. Malt extract contains carbon and nitrogen sources. The abundant carbon source is maltose; the percentage of maltose in malt extract is 60–63%. Maltose is a disaccharide that can increase the production of secondary metabolites [21]. Malt extract the increases shelf life of *Streptomyces rimosus* strain c-2012 [25].

Determination of Bioactive Compounds

Fractionation of Streptomyces *sp. IPBCC.a.29.1556 extract*

The selection of eluents in the TLC process was carried out by performing several eluent combinations. The combination of eluent was carried out by trying different polarity gradient solvents. *Streptomyces* sp. IPBCC.a.29.1556 aqueous extract can be separated well with a combination of eluent methanol:ethanol (1:9). This extract was successfully fractionated and formed 5 different spots with a Retention factor (Rf) value of 0.04, 0.43, 0.74, 0.86, 0.92.

The fraction obtained from preparative TLC was then tested in terms of its inhibitory activity on the α-glucosidase enzyme. The test results in the form of absorbance values were obtained from the reaction between PNPG and α-glucosidase. It produces *p*-nitrophenol (yellow color), which is not inhibited by the active fraction. This value shows an inverse relationship with the inhibitory activity of the α-glucosidase enzyme. A lower absorbance value means high inhibitory activity. If the substrate concentration increases, the inhibitory activity of the α-glucosidase enzyme decreases. The inhibition test results showed that almost all fractions have inhibition in varying percentages. Based on the IC_{50} values, fraction 1 was found as the most active fraction because of its lowest IC_{50} value of 58.8 μg/mL. IC_{50} is a quantitative measure that indicates how much of a particular inhibitory substance is needed to inhibit 50% of biological processes such as enzyme reactions. A lower IC_{50} value indicates the activity of the substance is more effective. Furthermore, the fraction 1 IC_{50} value is better than acarbose (90.4 μg/mL) (Fig. 3).

Identification of α-glucosidase inhibitor compounds using LC-MS

Analysis of chromatogram data in fraction 1 contained 5 peaks with the highest abundance (Fig. 4). At the first peak (Rt = 14.34), in its MS spectrum, major fragments were observed as Phenylpropynal. Phenylpropynal is a β-lactamases inhibitor. This compound is a specific irreversible inactivator of β-lactamases [26-27]. The second (Rt = 15.95) peak has a similarity with butyric acid, 2-(2-Ethoxyethoxy)ethanolate, and 1,1-Diethoxyethane acetate. Butyric acid is a fatty acid naturally present in

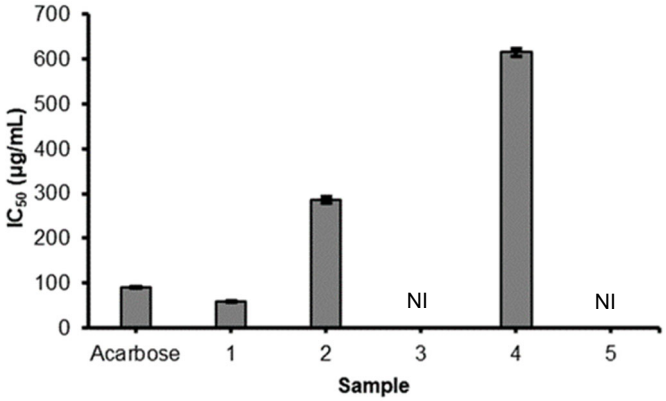

Fig 3. IC_{50} value of α-glucosidase inhibitory activities from fractionation using preparative TLC. NI: No Inhibition. Values are expressed as the mean ± standard deviation (n = 3)

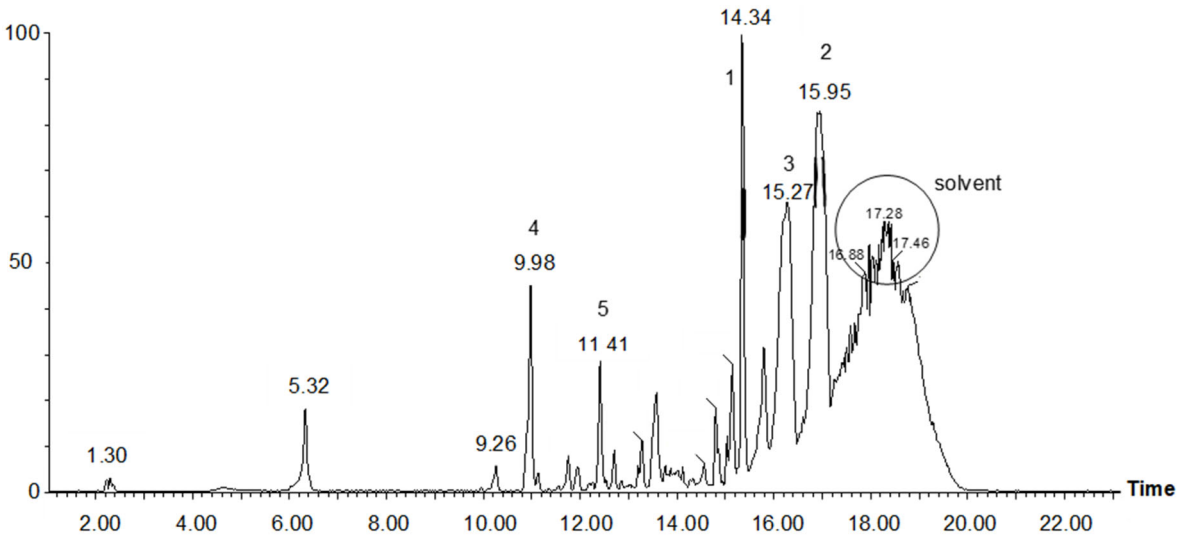

Fig 4. Chromatogram identification of fraction 1 compounds using LC-MS

the body of mammals, produced in the intestinal lumen from the fermentation process of a type of carbohydrate by bacteria. The presence of butyric acid provides various positive effects on the health of intestinal function [28-29]. Butyric acids function as probiotics, anticancer, anti-inflammatory, affecting cellular proliferation, differentiation and apoptosis [30-32]. Balan et al. [33] reported that the 2-allylamino-4-methylsulfanylbutyric acid (AMSB) exhibited α-amylase and α-glucosidase activities.

The third (Rt = 15.27) peaks have similar major fragments with butyric acid, 2-(2-Ethoxyethoxy)ethanolate, and *N*,*N*-Dimethyl-3-oxide-1*H*-benzotriazole-1-propanamine. The propanamine group has been reported to have antimicrobial and antimalarial activity [34-35]. However, research on antidiabetic has never been reported before. The fourth peak (Rt = 9.98) is a *p*-coumaric acid compound with a major fragment at *m/z* 165.058 (Table 1). Some herbs containing *p*-coumaric acid content are known to have α-amylase and α-glucosidase inhibitor activities [36-37]. The fifth peak (Rt = 11.41) is similar to 2-{2-[1-(1,3-Benzodioxol-5-ylmethyl)-2,5-dimethyl-1*H*-pyrrol-3-yl]-2-oxoethyl}isoquinolinium. Isoquinolinium is an alkaloid compound. Berberine from *Berberis vulgaris* is an isoquinoline alkaloid that has antidiabetic activity with α-glucosidase and α-amylase inhibitory activity [38].

Based on the identification of compounds with LC-MS, fraction 1 was found to contain several compounds that have previously been reported to have α-glucosidase

Table 1. Identification of fraction 1 compounds

Peak	Relative abundance (%)	Compound	*m/z*	Similarity (%)
1	4.86	Phenylpropynal	131.05	97.5
		Butyric acid	89.0599	100
2	18.57	2-(2-Ethoxyethoxy)ethanolate	133.086	99.58
		1,1-Diethoxyethane acetate	177.112	
		Butyric acid	89.0574	99.82
3	12.31	2-(2-Ethoxyethoxy)ethanolate	133.085	100
		N,*N*-dimethyl-3-oxide-1*H*-Benzotriazole-1-propanamine	177.1103	46.82
4	3.65	*p*-Coumaric acid	165.058	100
5		2-{2-[1-(1,3-Benzodioxol-5-ylmethyl)-2,5-dimethyl-1I-pyrrol-3-yl]-2-oxoethyl}isoquinolinium	399.1749	98.55

inhibitor activity. It can be concluded that the group of compounds, i.e., butyric acid, Isoquinolinium, and *p*-coumaric acid are the predicted compounds that contribute to the inhibition of α-glucosidase in fraction 1. There was also an α-amylase inhibitor, which is an enzyme working together with an α-glucosidase inhibitor to hydrolyze carbohydrates. If both enzymes are inhibited, they can control hyperglycemia in diabetics. In addition to these two inhibitors, other compounds with antioxidant and antimicrobial activities were also found. This can then be further developed and investigated to determine their relationship with the inhibition of the α-glucosidase enzyme.

Determination of Inhibition Mechanism

The enzyme kinetics have several parameters that can be tested, K_m and V_{max}. The determination of these two parameters is based on the relationship between substrate concentration [S] and enzyme activity. Based on the tests that had been conducted, the velocity was linear with the concentration of PNPG at low concentrations. The reaction rate would be close to the maximum at high PNPG concentrations, as shown in Fig. 5. The velocity of an enzymatic reaction will increase with the addition of substrate concentration [S], but it will reach the maximum velocity (V_{max}) even though the [S] keeps increasing.

Determination of the type of inhibitor mechanism using Lineweaver Burk plot (Fig. 6). The Km value indicates the substrate concentration needed to reach half of the maximum velocity. The presence of fraction 1 at 250 µg/mL in the experiment did not change the K_m

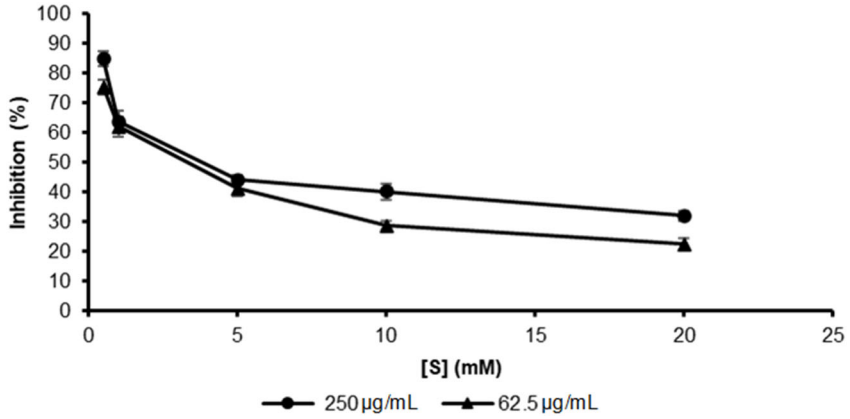

Fig 5. Effect of substrate PNPG concentration on α-glucosidase inhibitor activity of fraction 1 at 250 and 62.5 µg/mL. The values shown are the means of triplicate assays ± standard deviation (n = 3)

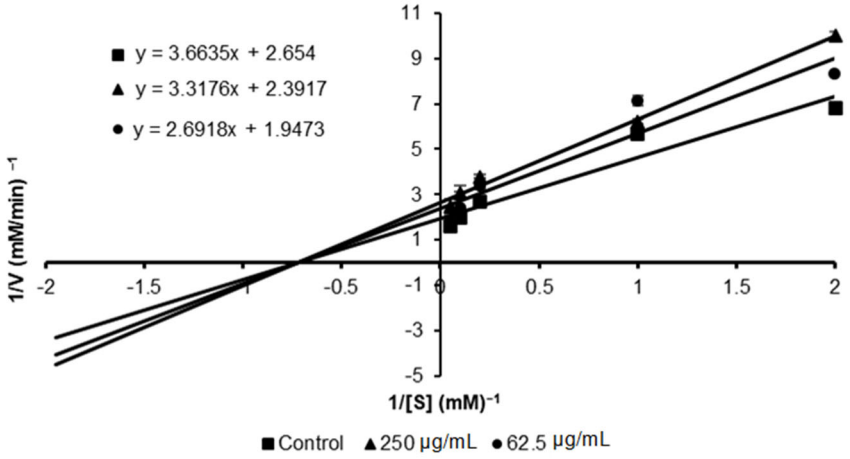

Fig 6. Lineweaver-Burke plot of α-glucosidase activity. Concentration of fraction 1 at 250 and 62.5 µg/mL. The data are expressed as the mean reciprocal of initial velocity for n = 3 replicates at each substrate concentration

value of 1.38 mM, whereas the V_{max} value decreased from 0.52 to 0.40 mM/min (Table 2). Based on these results, it can be concluded that the inhibitor of the fraction is a non-competitive inhibitor. Most competitive inhibitors came from phytochemical compounds such as triterpenoids, flavonoids, and phenols [39-41]. Non-competitive inhibitors are reversible and can bind to enzymes or enzyme-substrate complexes. This type of inhibitor is not influenced by the amount of substrate that exists because it does not bind to the active side of the enzyme. However, it can change the structure of the active side, thus, the inhibitor reduces the enzyme activity. Acarbose, a commercial α-glucosidase inhibitor, is a type of competitive inhibitor. This means that acarbose competes with substances to inhibit the enzyme. So, while substrate concentration was high, it required a higher concentration of acarbose. Diabetics, when eating heavy high glucose, need more acarbose. In contrast to a non-compressive inhibitor, as much as any substrate, in this case, the glucose put into the body will not interfere with inhibitory activity [42].

p-Coumaric acid is commonly found in plants. This compound is a type of phenolic compound that has an aromatic ring and a hydroxy group (OH) and is a precursor for the synthesis of flavonoid compounds. Phenol and flavonoid compounds are groups of compounds that have been widely reported as non-competitive inhibitors for α-glucosidase. The flavonoid compounds have been shown to be effective in reducing the risk of type 2 diabetes in people with prediabetes [43]. Prediabetes is a condition where people at high risk of developing type 2 diabetes are characterized by blood glucose levels exceeding the normal limit but not yet high enough for the Diabetes category. This prediabetes condition must be maintained to anticipate the occurrence of DM. Prediabetes is treated by using supplements that contain α-glucosidase inhibitors before meals. In addition, the combination of acarbose consumption with flavonoid and phenol compounds could reduce the use of acarbose by 62.5% [44]. Growing evidence shows that the combination of α-glucosidase inhibitors from natural product compounds with acarbose shows synergistic inhibition. This synergistic effect will increase the effectiveness of acarbose [45]. Based on this report, *Streptomyces* sp. IPBCC.a.29.1556 aqueous extracts may also be developed into supplementary supplements to reduce the dose of acarbose used.

Table 2. Kinetic properties of fraction 1 on rat α-glucosidase

Sample	Sample (μg/mL)	V_{max} (mM/min)	K_m (mM)
Control		0.52 ± 0.002	1.38 ± 0.022
Acarbose	250	0.52 ± 0.017	6.61 ± 0.279
	62.5	0.52 ± 0.003	2.73 ± 0.021
Fraction 1	250	0.40 ± 0.040	1.38 ± 0.028
	62.5	0.40 ± 0.038	1.38 ± 0.008

Values are expressed as the mean ± standard deviation (n = 3)

■ CONCLUSION

Endophytic actinobacterial isolate from Indonesian *F. deltoidea* has the same α-glucosidase inhibitor activity as its host. Aqueous extract from *Streptomyces* sp. IPBCC.a.29.1556 isolates had α-glucosidase inhibitor activity. Fraction 1 had the highest activity, with an IC_{50} value of 58.8 μg/mL which was stronger than acarbose. Fraction 1 contains several compounds such as Phenylpropynal, Butyric acid, 2-(2-Ethoxyethoxy)ethanolate, 1,1-Diethoxyethane acetate, *N*,*N*-dimethyl-3-oxide-1*H*-Benzotriazole-1-propanamine, *p*-coumaric acid, and isoquinolinium. These results suggest that several compounds in fraction 1 are potential effective α-glucosidase inhibitors for the management of postprandial hyperglycemia.

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