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In Vitro Evaluation of Antidiabetic and Anti-Inflammatory Activities of Five Selected *Syzygium* Leaves Ethanolic Extract as Alpha-Glucosidase Inhibitors and Anti-denaturation of Bovine Serum Albumin

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Abstract
Background*: Diabetes mellitus (DM) has become a major health problem worldwide, with a continuous increase in mortality due to complications caused by hyperglycemia. Chronic hyperglycemia is often associated with inflammation due to increased production of free radicals.* ***Objective:*** *This study's main objective is to assess antidiabetic and anti-inflammatory properties in vitro of five particular Syzygium leaves extract (S. cumini, S.aqueum, S. malaccense, S. polyanthum, and S. aromaticum) using alpha-glucosidase and Bovine Serum Albumin (BSA).* ***Methods:*** *The five of selected Szygium leaves were macerated by using ethanol 96%, each extract was assessed in vitro for antidiabetic activity by analyzing the inhibitory of alpha-glucosidase using acarbose as strandard, and anti-inflammatory activity by analyzing the inhibitory denaturation of BSA Heat-induced and BSA induced by 2,2-diphenyl-1-picrylhydrazine (DPPH) with Sodium diclofenac as standard.* ***Results:*** *The IC_{50} of α-glucosidase inhibition was 76.235 µg/mL (strong) for S. malaccense and 0.241 µg/mL (very strong) for the acarbose standard. The greater IC_{50} of antidenaturation of BSA with heat-induced was S. polyanthum (95.7 µg/mL) and sodium diclofenac standard (59.25 µg/mL) both were strong inhibitor. Along with greater anti-denaturation of BSA, DPPH-induced S. malaccense (90.320 µg/mL) and sodium diclofenac standard (43.301 µg/mL), both of which are strong inhibitors.* ***Conclusion:*** *The ethanol extract of Syzygium leaves has the potential to be developed as an antidiabetic and anti-inflammatory herbal medicine, particularly S. malaccense and S. polyanthum leaf extracts, which provided greater activity in this study.*

Keywords*: α-glucosidase, anti-denaturation, antidiabetic, bovine serum albumin, syzygium*

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INTRODUCTION

The increasing prevalence and continuity of Diabetes Mellitus (DM) has become the main health problem in the world with a consistent increase in mortality due to complications of the disease (Zimmet *et al*., 2016). The IDF was reported 463 million adults are diabetes and the projection in 2045 will be estimated 700 million (International Diabetes Federation, 2019). The DM complications were predicted to be the cause of death of 4.2 million adults and its comparable to one mortality every eight seconds (Zimmet *et al*., 2016). The progress of Type-2 diabetes mellitus (T2DM) complications in chronic hyperglycemia induces oxidative stress and inflammation, simultaneously promoting complications including renal and cardiovascular diseases (Charlton *et al*., 2021; Yuan *et al*., 2019).

The increase in global spending on DM is reported to be more than 700 billion USD (International Diabetes Federation, 2019). The side effects of prolonged consumption of conventional drugs, as well as the less invasive prevention and therapeutics using natural medicine, are some of the problems in the success of DM therapy. The COVID-19 pandemic has also contributed to the increase in T2DM, so it is necessary to develop easy and inexpensive natural ingredient therapies to overcome the increased inflammation of T2DM so as to reduce diabetes complications.(Salleh *et al*., 2021). Most T2DM therapies are reported to have side effects of gastrointestinal disorders including the use of α-glucosidase Inhibitor (AGI) drugs due to the degradation of undigested carbohydrates by colon bacteria, causing excessive gas formation with a case percentage of 78% (Kumar *et al*., 2018). The result of Riset Kesehatan Dasar (Riskesdas) (2018) reported that, based on the doctor's diagnosis, the prevalence of DM in Indonesia aged over 15 years was 2%, an increase from the previous research results of 1.5% in 2013. Based on the blood sugar test findings, the prevalence of diabetes mellitus increased from 6.9% (2013) to 8.5% (2018). The pattern of increase of DM showed higher in the age ranged 56-64 years and 66-74 years (Kemenkes RI, 2020).

Increased production of free radicals, particularly reactive oxygen species (ROS), can result from hyperglycemia and lead to oxidative stress. The disproportion between ROS and antioxidant defenses not only causes direct cell damage but also inflammation, which results in tissue damage. Diabetes is often associated with inflammation when biochemical changes in diabetes affect the increase in TNF-α and IL-1β, which leads to an increase in ROS by mitochondria. Emerging therapeutic strategies address this pathway in a different way, ranging from enhancing free radical scavenging (antioxidants and Nrf2 activators) to reduce ROS production such as NADPH oxidase inhibitors and XO inhibitors or inhibiting associated inflammatory pathways (NLRP3 inflammation inhibitors, lipoxins, GLP, receptor -1 agonists and AT-1 receptor antagonists) (Asmat *et al*., 2016; Oguntibeju, 2019; Zhang *et al*., 2021). Oxidative stress reported to trigger the development of micro- and macrovascular damage complications in T2DM and hyperglycemia, as well as being responsible for DNA, lipid and protein damage associated with ROS production (Oguntibeju, 2019).

Natural ingredient therapy is currently in great demand because it is relatively cheaper and easier to obtain to become one of the options for the treatment of DM, especially T2DM. Natural medicines are projected to play a role in overcoming DM complications and the side effects of conventional drug consumption, especially if used for a long period of time. *Syzygium*, a genus of plants from the *Myrtaceae* family, is one of the largest genera of flowering plants with a total of 1800 species and is distributed in areas that mainly have a tropical climate, including Indonesia. (Abdullah *et al*., 2021; Kavitha & Poonguzhali, 2021). Plants of the Myrtaceae family are reported to be the 20 largest ethnomedicinal families in Indonesia with 5 (five) species of the *Syzygium* genus (Hidayat, 2021). Some of the species of the genus *Syzygium* studied were *S. polyantum*, *S. aromaticum*, *S. aqueum*, *S. cumini*, and *S. malaccensis*. The *Syzigium* group of plant species is reported to have been used for generations in traditional Ayurvedic medicine in India (Cock & Cheesman, 2018).

Studies conducted by Zaen & Ekayanti (2022) and Aklimah & Ekayanti (2022) on antioxidants from leaf extracts of several *Syzygium* genus plants showed very strong antioxidants in ethanol extracts of *Syzygium* plant leaves with IC_{50} values *Syzygium aromaticum* 3.026± 1.699 µg/ml, *Syzygium polyanthum* 3.555± 2.776 µg/ml, *Syzygium aqueum* 5.416± 2.588 µg/mL, *Syzygium malaccense* 3.297± 2.595 µg/mL and *Syzygium cumini* 2.416± 1.543 µg/mL (Aklimah & Ekayanti, 2022; Zaen & Ekayanti, 2022). A phenetic study of each of the five *Syzygium* species was conducted as an initial screening for further investigation of pharmacological activities and ROS-related mechanisms. The purpose of this study was to analyze the α-glucosidase inhibition test and anti-denaturation of Bovin Serum Albumin (BSA) protein of several *Syzygium* leaf extracts as a therapy for T2DM and inflammation through the mechanism of increasing antioxidant defense, regulating carbohydrate metabolism and inhibiting inflammatory pathways. The novelty of this study is the anti-denaturation BSA induced 2,2-

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diphenyl-1-picrylhydrazil (DPPH) activity of five *Syzygium* leaf extracts. This study is expected to support and improve references in the development of herbal medicine as an antidiabetic and anti-inflammatory agent. The α-glucosidase enzyme inhibition and protein anti-denaturation of *Syzygium* genus plant species is limited to one activity test, while diabetes is associated with inflammation; therefore, it is necessary to analyze the potential of natural medicines with antidiabetic and anti-inflammatory activities.

MATERIALS AND METHODS

Materials

Alpha-glucosidase from Bacillus stearothermophilus, 4-Nitrophenyl α-D-glucopyranoside and Bovine Serum Albumin (BSA) were purchased from Sigma-Aldrich; ethanol, aluminum trichloride, potassium acetate, Methanol, Citric acid, ethyl acetate, formic acid, and silica gel F254 TLC plates were purchased from Merck; and DPPH (2,2-Diphenyl-1-Picryl hydrazine) was from Himedia. Leaves of five ground *Syzygium* (*S. aromaticum*, *S. polyanthum*, *S. aqueum*, *S. malaccense*, and *S. cumini*) were collected from Balai Penelitian Tanaman Rempah dan Obat (Bogor, Indonesia). Each of the five *Syzygium* plants was used to identify plant species at the Research Center of Biosystematics and Conservation (Bogor, Indonesia).

Methods

Plant extraction

Five *Syzygium* leaf powders were weighed 500 g and extracted by the maceration method with 96% ethanol (1:10 w/v), soaked for three days, and stirred periodically. The filtrate from the first maceration was filtered twice. The filtrate from maceration and repetition was evaporated at 50 ºC by using a vacuum rotatory evaporator (DLAB Rotary Evaporator RE-100 Pro) (Wahyulianingsih *et al*., 2016).

Determination of anti-diabetic activity by inhibition of α-glucosidase (Akmal et al., 2023)

Initial enzyme activity assay: A total of 60µL of 0.1M phosphate-buffered saline (pH6.8) was added to 50µL of 0.07 U/mL enzyme solution and incubated in a 96 well micro plate at 37 ℃ for 20 min. After pre-incubation, 50 µL of 2mM *p*NPG was added to the microplate and then incubated again at 37 ℃. The last stage was stopped by adding 160 µl of sodium carbonate solution to the micro-plate well and evaluating the absorbance with a wavelength of 425 nm. Enzyme activity assay - *Syzygium* leaf extract: A total of 60µL of 0.1M of each *Syzygium* leaf ethanol extract was added to 50 µl of 0.07 U/mL enzyme solution and incubated in a 96 well micro plate at 37 ℃ for 20 min. After preincubation 50 µL of 2mM *p*NPG was added into the microplate and then incubated again at 37 ºC. The final stage was stopped by adding 160 µL of sodium carbonate solution to the microplate and measuring the absorbance at a wavelength of 425 nm.

Acarbose-enzyme activity assay: A total of 60µL acarbose was added to 50 µL of 0.07 U/mL enzyme solution and incubated in a 96 well micro plate at 37 ℃ for 20 min. After pre-incubation, 50 µl of 2mM *p*NPG was added to the microplate and incubated again at 37 ℃. The last stage was stopped by adding 160 µL of sodium carbonate solution to the cuvette and measuring the absorbance at a wavelength of 425 nm. The assay of initial enzyme blank activity and enzyme inhibition (BEA and BIE): A total of 60µl of phosphate solution of each *Syzygium* leaves extract and acarbose standard was added to 50µL of 0.07 U/mL enzyme solution and incubated in a 96 well micro plate at 37 ºC for 20 minutes. After preincubation 50 µL of 2mM PNPG was added into the micro plate and then incubated again at 37 ºC. The last stage was stopped by adding 160 µL of sodium carbonate solution and reading the absorbance with a wavelength of 425 nm by using Biotek Epoch Microplate Spectrophotometer.

Determination of anti-inflammatory activity by inhibition denaturation of heat-induced bovine serum albumin (Williams *et al*., 2008)

The assay of anti-inflammatory activity five selected *Syzygium* extracts were conducted using a heat-induced Bovine Serum Albumin (BSA) denaturation assay. Tris-buffer Saline 0.05 M was used to create the stock solutions of BSA 5% (w/v), which was then adjusted to pH 6.8 using glacial acetic acid. 100 µL-aliquots of the BSA stock solution and distilled water were mixed with varying test tube of the extract to create 1.0 mL sample that included the extract at different dilutions. The samples were heated in a waterbath for seven minutes at 70°C to cause protein denaturation. The solutions cooled to room temperature. Spectrophotometry UV-Vis (PG-Instrument) was used to quantify the turbidity of the solutions at wavelength of 517 nm. As controls, solutions with distilled water in place of the extract were used; values obtained with these preparations were interpreted as indicating 100% protein denaturation. BSA-free samples served as blanks and Diclofenac's anti-denaturing properties served as positive control in concurrent studies. The following formula was used to determine the percentage inhibition of denaturation, where Abs control is the absorbance of the controls, Absorbance (Abs) of sample of the *Syzygium* leaves extract or diclofenac samples, and Abs blank of the blank.

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$$\% \text{ inhibition of denaturation} = [\{\{\text{Abscontrol} - (\text{Abssample} - \text{Absblank})\} / \text{Abscontrol}\} \times 100\%]$$

Table 1. Yield percentages of five *syzygium* leaves extracts

Sample	Yield (%)
Syzygium cumini	24.380
Syzygium aqueum	18.556
Syzygium malaccense	23.756
Syzygium polyanthum	30.19
Syzygium aromaticum	32.90

Determination of anti-inflammatory activity by inhibition denaturation of DPPH-induced bovine serum albumin (Alam *et al*., 2022)

The anti-inflammatory activity of five selected *Syzygium* extracts was analyzed by a modified method using a DPPH-induced BSA denaturation assay. The radical scavenging activity (RSA) adopted to measure anti-inflammatory activity using the DPPH method. Briefly, 2 mL of extract solution (1–100 µg/mL) in methanol and BSA stock solutions (prepared as the same method above) was added to 2 mL of DPPH (0.1 mM) solution. The mixtures were kept aside in a dark area for 30 min and absorbance was measured at λmax 517 nm against an equal amount of DPPH and methanol as a blank. The percentage of DPPH• scavenging (% Scavenging of DPPH) was estimated using the equation:

$$\% \text{ Scavenging of DPPH} \bullet = [(A0 - A1)/A0] \times 100$$

Statistical analysis

All the experiments for the determination of inhibitory activity of alpha-glucosidase and denaturation of BSA Heat-induced, and denaturation of BSA by using DPPH-induced have been conducted triplet (n=3). The values are expressed as the mean ± standard deviation (SD).

RESULTS AND DISCUSSION

Syzygium is a genus of plants from Myrtaceae family which is one of the largest genera of flowering plants with total 1800 species and distributed in regions mainly have a tropical climate including Indonesia (Abdullah *et al*., 2021). The five fresh leaves of *Syzygium* were determined at the Research Center of Biosysthematics and Conservation (Bogor, Indonesia) and it was validated as *Syzygium aromaticum*, *S. polyanthum*, *S. aqueum*, *S. malaccense*, and *S. cumini*. The extract of five leaves of *Syzygium* was done by cold extraction method (maceration). The crude extract of five Syzygium leaves was green-brownish with a distinctive aroma, and the result of the higher yield percentage was *Syzygium aromaticum* (32.90%) and *Syzygium polyanthum* (30.19%) shown in Table1. The yield percentages of five *Syzgygium* extracts obtained fulfilled the quality requirements of the extraction standard as values above 10% (Kementrian Kesehatan RI, 2017).

Several species of *Syzygium*, including *S. cumini*, *S. polyanthum*, *S. aqueum*, *S. aromaticum*, and *S. malaccense*, have been shown to exhibit enzymatic inhibitory action (Zulcafli *et al*., 2020). The absorbanse measurement results then calculate to percentage inhibition value. The activity of the *Syzygium* extracts mostly inhibited 50% of the enzyme activity at 100-200 µg/mL unless *S. malaccense* inhibited <100 µg/mL. The result of th α-glucosidase enzyme inhibition study showed *S. malaccense* was the greater inhibitory activity with IC_{50} value 76.235 µg/mL (Table 2). The concentration 200 µg/mL of *Syzygium cumini* obtained percentage of inhibition 63.261±0.178% (Figure 1). The inhibitory activity of acarbose is greater compared to each *Syzygium* extracts with IC_{50} values 0.241 µg/mL. Acarbose acts by competitive and reversible inhibition of α-amylase and α-glucosidase from the pancreas (Glittenberg, 2012). It is well known that flavonoids derived from plants have antidiabetic effects (Najafian *et al*., 2012; Yoshikawa *et al*., 1998). Ethanolic extract of *Syzygium* leaves reported have high flavonoid content (Aklimah & Ekayanti, 2022; Zaen & Ekayanti, 2022). Flavonoid and other polyphenols are reported potentially inhibit α-amylase and α-glucosidase without adverse gastrointestinal effects and useful to T2DM therapy (Barber *et al*., 2021). Many flavonoids have a higher inhibition of α-glucosidase and leading to slow-release effect that of α-amylase which may be favoured over acarbose to decrease postprandial glucose without uncomfortable side effects (Barber *et al*., 2021). The active substances myricetin-3-O-rhamnoside and europetin-3-O-rhamnoside, which were separated from *S. aqueum*, inhibited α-glucosidase (Manaharan *et al*., 2012). Maslinic acid (MA) and Oleanollic acid (OA) produced from *S. aromaticum* were observed to decrease the expression of α-glucosidase, and α-amylase in the small intestines of STZ-induced diabetic rats (Khathi *et al*., 2013). The active component of *S. cumini* and *S. malaccense*, myricitrin, was found to inhibit α-glucosidase and α-amylase (Khathi *et al*., 2013).

The strong antioxidant activity of some *Syzygium* leaves extract reported in the previous study (Aklimah & Ekayanti, 2022; Zaen & Ekayanti, 2022), a problem-solving approach as well as a therapeutic strategy for DM and inflammation through the mechanism of increasing antioxidant defenses, improving carbohydrate metabolism profiles and inhibiting inflammatory pathways so as to reduce the risk of hyperglycemia

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complications(Akmal et al., 2023; Shaw *et al*., 2017). According to Ekayanti *et al* (2018) Phenolic components in natural materials are known to bind to proteins of enzymes and form enzyme-inhibitor bonds, thereby reducing enzyme activity (Ekayanti *et al*., 2018). Polyphenols are also reported to have therapeutic effects on DM vascular dysfunction (Nor *et al*., 2022). The antioxidant activity of ethanol extract of *Syzygium* plant leaves is expected to overcome the ROS imbalance that triggers oxidative stress in T2DM (Oguntibeju, 2019). Further studies in the development of T2DM and inflammation therapy need to be carried out by analyzing the α-glucosidase enzyme inhibitory activity and anti-denaturation of Bovine Serum Albumin (BSA) protein in ethanol extracts of the leaves of several *Syzygium* plants. Alpha Glucosidase Inhibitor (AGI) is one of the effective therapeutic groups used as T2DM treatment in improving metabolic profiles and potentially reducing the risk of long-term hyperglycemia complications (Akmal et al., 2023). The α-glucosidase is an enzyme secreted from the epithelium of the small intestine that is responsible for carbohydrate degradation by hydrolyzing complex carbohydrates into simple glucose that can eventually be absorbed (Syabana *et al*., 2022).

The production of free radicals leads to protein denaturation in the body, which triggers the release of inflammatory mediators and triggers inflammatory pathways (Shaw *et al*., 2017). The method used to reduce BSA volume and stock solutions of compounds or extracts was used to assess anti-denaturation (anti-inflammatory) activity. The results presented in Table 3 and Figure 2 represent *Syzygium* ethanolic extract and sodium diclofenac as a positive control. An anti-denaturation protein assay using heat induction increased the kinetic energy and caused the molecules to vibrate and move quickly, disrupting hydrogen bonds and non-polar hydrophobic interactions of the protein. Sodium diclofenac is a non-stereoidal anti-inflammatory drug that is non-selective and has better solubility in water and organic solvents. The concentrations of sodium diclofenac used were 5, 15, 25, 50, and 75 µg/mL. The concentrations of the *Syzygium* ethanolic extracts were 25, 50, 75, 100, and 200 µg/mL. The concentrations of *Syzygium* leaf extract inhibited protein denaturation by >50% in the range of 100-200 µg/mL. The inhibitory activity of protein denaturates is attributed to the presence of bioactive compounds. The inhibition of BSA denaturation induce by heating resulted the higher IC_{50} for *Syzygium polyanthum* (95.7 µg/mL) compared to standard (sodium diclofenac) was 59.25 µg/mL. *Syzygium* extract was reported rich of polyphenol compound (Sobeh *et al.*, 2018). Polyphenol, phenyl propanoids and the disulphides interacting with the aliphatic regions around the lysine residue on the BSA and reported suitable as an anti-oxidants, anticancer, and anti-glycation (Williams *et al*., 2008).

Table 2. Inhibitory percentages and IC_{50} values of α-glucosidase

Sample	**Inhibitor Percentages (%)**					**IC_{50} values (µg/mL)**
	1	**2**	**3**	**4**	**5**	
Acarbose	36.057	61.305	70.687	93.731	96.930	0.241±0.478
S. cumini	6.667	17.609	29.457	44.094	63.261	123.239±0.224
S. aqueum	28.659	37.391	43.804	48.225	56.087	169.676±0.237
S. malaccense	35.000	43.841	49.638	54.565	60.870	76.235±0.234
S. polyanthum	31.486	38.261	43.768	48.949	52.790	198.222±0.392
S. aromaticum	2.826	17.283	27.971	40.109	58.370	144.698±0.186

Values are mean ± SD (n=3). Acarbose concentrations (0.1, 0.5, 1.0, 5.0, and 10.0 ppm), Sample extract concentrations (25, 50, 75 100, 200 ppm)

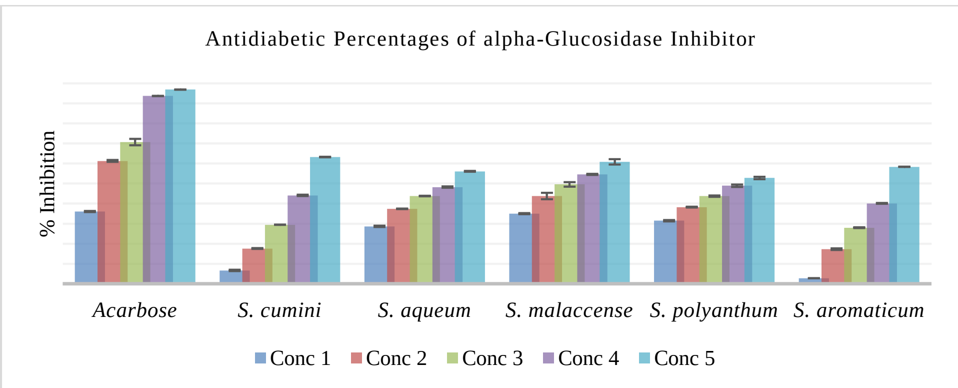

Figure 1. α-Glucosidase inhibitor of five leaves *syzygium* extract

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Table 3. Inhibitory percentages and IC_{50} values of Anti-denaturation BSA protein heat-induced

Sample	**Anti-Denaturation Percentages BSA Protein Heat-Induced (%)**					**IC_{50} (µg/mL)**
	1	**2**	**3**	**4**	**5**	
Sodium diclofenac	22.459	26.089	47.289	63.771	82.720	59.25±0.557
S. cumini	6.968	17.608	33.380	40.301	50.964	200.270±1.331
S. aqueum	8.061	13.724	32.054	41.363	51.727	198.26±0.398
S. malaccense	13.876	28.469	40.072	50.598	55.801	182.73±0.143
S. polyanthum	20.754	34.330	42.883	58.194	65.670	95.7±0.448
S. aromaticum	27.213	39.533	43.002	44.797	59.988	164.15±0.717

Values are mean ± SD (n=3), Sodium diclofenac concentrations (5, 15, 25, 50, and 75 ppm), Sample extract concentrations (25, 50, 75, 100, 200 ppm)

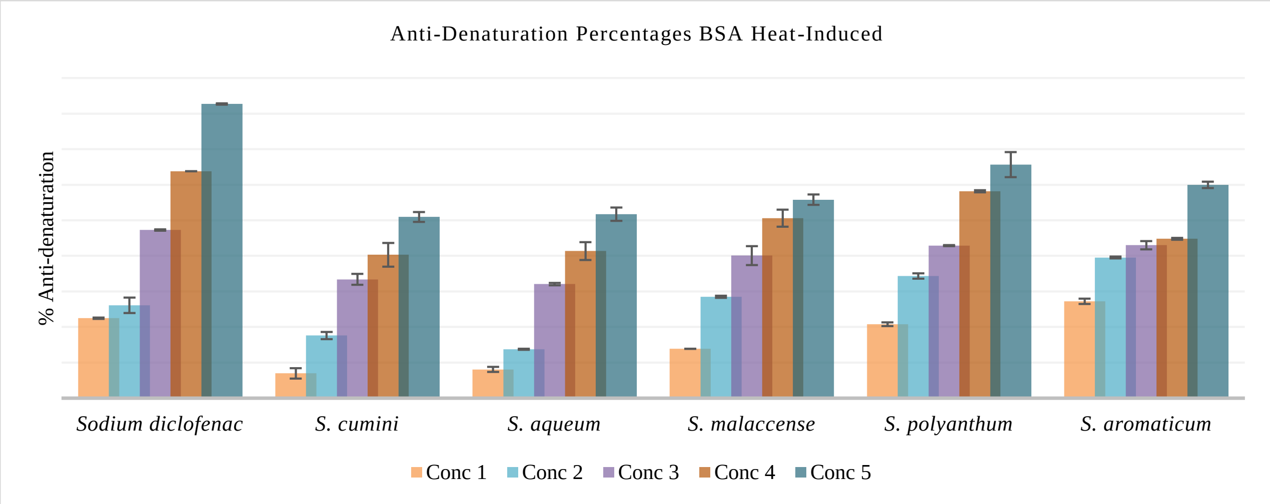

Figure 2. Anti-Denaturation BSA of five leaves *syzygium* extract heat-induced

Table 3. Inhibitory percentages and IC_{50} values of Anti-denaturation BSA protein DPPH-induced

Sample	**Anti-Denaturation Percentages (%)**					**IC_{50} (µg/mL)**
	1	**2**	**3**	**4**	**5**	
Sodium diclofenac	13.427	31.841	49.916	56.432	61.338	43.301±0.422
S. cumini	20.103	27.890	36.710	49.066	63.886	117.233±1.120
S. aqueum	16.530	29.006	35.322	43.353	56.179	180.320±1.282
S. malaccense	8.782	18.306	40.198	52.628	62.400	90.320±1.076
S. polyanthum	13.417	22.075	28.900	44.150	51.404	196.470±0.405
S. aromaticum	11.817	18.760	32.722	45.008	59.165	171.596±0.479

Values are mean ± SD (n=3), Sodium diclofenac concentrations (5, 15, 25, 50, and 75 ppm), Sample extract concentrations (25, 50, 75, 100, 200 ppm)

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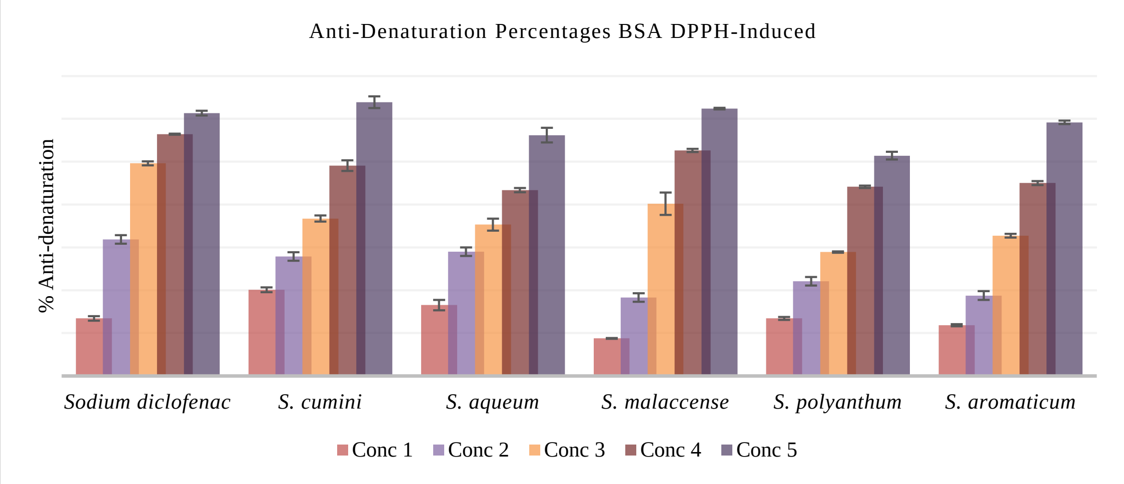

Figure 3. Anti-denaturation BSA of five leaves *syzygium* extract DPPH-induced

Low doses of BSA have been found as a channel for broad-spectrum *in vitro* study to analyze possible therapeutic prototypes (Williams *et al.*, 2008). The modified method of anti-denaturation BSA was designed to be relevant to chronic hyperglycemia conditions, which are caused by an increase in free radicals and oxidative stress. In this method, BSA was desaturated by DPPH-inducing and plays role as free radicals and denaturation agent as well. DPPH is used as a substrate to evaluate antioxidant activity; it is a stable free radical that can accept one electron or hydrogen. The greater anti-denaturation BSA DPPH-induced was *Syzygium malaccense* with IC_{50} values is 90.320 µg/mL (Table 3) and the percentage chart showed at Figure 3. *Syzygium* leaf extract inhibited BSA denaturation, which was induced by DPPH at a range of 100-200 µg/mL >50% inhibition. The IC_{50} value less than 50 Sodium diclofenac (positive control) was categorized as having a strong inhibitory effect on protein denaturation. The ability of blocking the Cyclooxygenase (COX) and Lipoxygenase-5 (LOX-5) pathways was one of the pathways to overcome inflammation. Flavonoid substances are known to have anti-inflammatory properties, while tannin and saponin compounds maintain membranes by attaching to cations. Flavonoids and saponins have been shown to have anti-inflammatory properties via scavenging free radicals. The erythrocyte membranes from hypotonic solutions could be stabilized by free radical inhibitors (Shalihah *et al*., 2021).

CONCLUSION

Diabetes mellitus (DM) has become the main health problem worldwide, with a consistent increase in mortality due to disease complications. The chronic hyperglycemia is often associated with inflammation due to increase production of free radicals thus lead to oxidative stress. *Syzygium* leaves have the potential to be developed into antidiabetic and anti-inflammatory drugs. The greater result of IC_{50} value for α-glucosidase inhibition was 76.235 µg/mL (strong) for Syzygium malaccense and 0.241 µg/mL (very strong) for the acarbose standard. The greater antidenaturation of BSA with heat-induced was *Syzygium polyanthum* (95.7 µg/mL) and sodium diclofenac standard was 59.25 µg/mL both were strong inhibitor. Along with anti-denaturation of BSA, DPPH-induced *Syzygium malaccense* (90.320 µg/mL) and sodium diclofenac standard (43.301 µg/mL) were strong inhibitors. Further research is needed to confirm the antidiabetic and anti-inflammatory activities of *Syzygium* extract using different in vitro and in vivo methods.

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AUTHOR CONTRIBUTIONS

Conceptualization: M.E.; Methodology, M.E.; Software, F.S.; Validation, M.E.; Formal Analysis, M.E.; Investigation, M.E.; Resources, M.E.; Data Curration;

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F.S.; Writing - Original Draft, M.E.; Writing - Review and Editing, M.E.; Visualization, F.S.; Supervision: M.E.; Project Administration, F.S.; Funding Acquisition, M.E.

CONFLICT OF INTEREST

The authors declare that they have no conflicts of interest.

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