Review of The Benefits of White Murbei as Antioxidants and α-Glucosidase Inhibitors in Diabetes Mellites Sufferers

Neng Risanti Al Masum[1] , Antan Saldaw[2] , Rhamal Amir[3] , Aden Dhana Rizkita[4]
[1]Bachelor of Pharmacy Program, Bogor Husada College of Health Sciences
Jl. Sholeh Iskandar No.4, RT.02/RW.03, Kedungbadak, Kec. Tanah Sereal, Bogor City, West Java 16164

Corresponding author
[1]adendhanarizkita@gmail.com

Abstract: Increased glucose levels in circulating blood are a sign of a chronic metabolic disease known as diabetes meliatus. In between countries around the world Indonesia is ranked 7th in terms of the number of diabetes mellitus sufferers . For help our diabetes treatment can use plant mulberry white , because has the ability to prevent α-glucosidase. Mulberry white own phenolic groups and antioxidant properties which is proven to inhibition of the glucosidase enzyme via the DPPH and ABTS methods. Journal reviews This aim For show potency Mulberry white (Morus Alba) as plants containing antioxidants and has activity inhibition enzyme glucosidase through ABTS and DPPH methods. For inhibition of the a-Glucosidase enzyme, the Ic50 value can be shown. It can be concluded that Morus alba can act as an antioxidant plant with an inhibitory value using the DPPH method of 16.83% - 43.95%, as well as an alpha-glucosidase inhibitor with an IC50 value of 550 μg/mL in the water extract and 241 μg/mL. mL on. ethanol extract. And the phenol value in white mulberry is 181, while the phenol value in red mulberry is 1422 and the phenol value in black mulberry is 1035.

Keywords: Diabetes mellitus, White Mulberry, antioxidants, α-Glucosidase

Introduction

Diabetes Mellitus is disease metabolic chronic that becomes world attention, disease this is marked with increasing glucose levels in blood circulation. Disease This become disease Sufficient health Serious because it is the cause of morbidity and mortality in people in various parts of the world especially in developing countries including Indonesia (diabetes care, 2014) . Therefore DM is still the world's concern today In 2015, the number of DM sufferers in the world reached 415 people and it is estimated that in 2040 it will reach 642 people. Meanwhile according to WHO Global Status Report on NCD data in 2014, there are 422 million people in the world suffering from DM and every year 1.5 million people die. Indonesia is a country that is ranked 7th in the number of DM sufferers in the world. According to the Indonesian Ministry of Health, in 2013, there were 12.1 million DM patients in Indonesia and it is estimated that the number will continue to increase (Ministry of Health , Republic of Indonesia, 2013).

Diabetes mellitus, also known as "diabetes" in society, is one of the "eternal" diseases that sufferers have to face every day. Patients experience the widespread impact of this disease due to its various complications that endanger their health and impact their social lives. In fact, the prevalence of diabetes mellitus throughout the world continues to increase every year. In 1995, prevalence reached 4.0% worldwide, and is expected to increase to 5.4% in 2025. In developing countries, including Indonesia, the number of diabetes mellitus sufferers in 1995 reached 84 million, and is expected to increase increasing to 228 million in 2025. (Kurniawan, A., 2005.)

There are two types of diabetes mellitus, type 1 which occurs consequence lack insulin production . Meanwhile type 2, DM occurs consequence inadequate use of insulin effective . DM patients are treated with insulin and or drug antidiabetic

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throughout his life (Brunton LL, et al 2010). For DM type 2, there is Lots type drug antidiabetic . A number of mechanism it works among other things, stimulating insulin secretion, decreases glucose blood, and inhibit absorption glucose . In Indonesia, medicine most antidiabetic used is glibenclamide , group sulfonylurea generation second . This medicine can give rise to effect side like nausea , vomiting , and illness yellow cholestatic (Dipiro , TJ, et al. 2008).

Because of medicine antidiabetic This must consumed lifetime alive , patient will worrying effect side therapy this and prepare the cost . Therefore that is necessary therapy available alternatives same effect , effect more side less , and costs more A little For disease This . One of herbal plants that have been used for a long time as therapy especially in China and many available in Indonesia is leaf mulberry (Morus alba) (Mudra.M., et al. 2007).

Mulberry is one of plant with the genus Morus of family Moraceae . Mulberry has 24 species and one subspecies and at least 100 varieties is known . Mulberry comes from from area subtropical. The genus Morus has around nine mercy species trees and the most common species planted is mulberry white (*Morus alba L*). Mulberry white own a number of part , like leaves , flowers , fruit , stems , and growth fast in time short . Because many efficacy biologically useful , mulberry white (*Morus alba L.*) has used in treatment traditional China during many years . Originate from mulberry white , have ability For inhibits α-glucosidase , and can used For control concentration postprandial glucose . Research result about extract mulberries in diabetes mellitus sufferers show excellent results , because group the phenolic , mulberry own characteristic antioxidants and has various activity biochemistry , incl antioxidant , antimutagenic , and anticarcinogenic , as well ability For change gene expression . (Machii et al, 2000).

Mulberry used For various function medical , incl carminative , diaphoretic , diuretic , antipyretic , palpitation , hypotensive , diabetes mellitus , laxative , vertigo, cholesterol high fever , elephantiasis, hepatitis, antitussive , febrile , and plasmodium malariae . The juice also contains Lots antioxidant . (Mohammadi and Prakash, 2008) (Wang et al, 2013). Mulberry own characteristic Antioxidants are one of them because exists group phenolic . mulberry own characteristic antioxidants and has various activity biochemistry , incl antioxidant , antimutagenic , and anticarcinogenic , as well ability For change gene expression . (Nakamura et al, 2003).

Antioxidants are actually able to slow or inhibit oxidation of substances that are easily oxidized even in low concentrations . Antioxidants are also appropriately defined as protective compounds cell from harmful effects from radical free . Every molecules that have One or more electron No pair called as radical free . Free radicals can cause cancer , stroke, heart disease , and aging early . Caused exists radical free in body . What compound ward off radical free named antioxidant . Reactive oxygen free radicals if they are related to disease, these free radicals can come from body metabolism and other external factors a. Free radicals is an unstable species because it has unpaired electrons and looks for electron pairs in biological macromolecules. Proteins, lipids, and DNA from healthy human cells are good sources of electron pairs. Oxidation conditions can cause damage to proteins, DNA, cancer , aging, etc other diseases . The chemical components that act as antioxidants are phenolic and polyphenolic compounds. Compounds in this group are widely found in nature, especially in plants, and have the ability to capture free radicals. Antioxidants that are found in many foods include vitamin E , vitamin C , and Cartenoid . (Rahman, Malik, and Ahmad

Materials and Methods

This research focuses show potency Mulberry white (Morus Alba) as plants containing antioxidants and has activity inhibition enzyme glucosidase through ABTS and DPPH methods.

Results and Discussion

Discussion

1. Mulberry

1.1 Content Mulberry

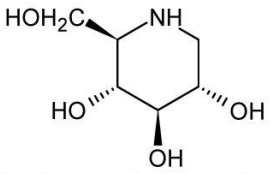
Morus Alba leaves contains , Ecdysterone , lupeol, inocosterone , betasitosterol , moracetin , alpha-hexenal, isoquersetin , scolopoletin , benzayldehid , cislamda-hexenol , benzayldehyde , eugenol, linalool, benzyl alcohol , amino acids , trigoneline , choline , adenine , copper , zinc , vitamins (A, B1, C, and carotene), and acids chlorogenic , acid fumaric , acid folate , and acid formyltetrahydrofolic Twigs contain tannins and vitamin A. Mostly study show that skin root contain compound originating active from flavones mulberin , mulberochromen , cyclomulberin , cyclomulberochromen , morusin , and mulberrofuran A. In addition , some study show that skin root contain sour betulinic , scopoletin , alpha- amirin , alpha-amirin , undecaprenyl, and dodocaprenyl . urease is present in seed mulberry . Fruit mulberry contain component component like alkaloids , flavonoids, saponins, phenolics , and terpenoids , besides That extract leaves and fruit mulberry have activity anti- bacterial power . Including bacteria pathogen consequence content compound phenolic . (Ferlinahayati, 2012).

Figure 1. White Mulberry

1.2 Benefits of Mulberries

Based on data from the International Diabetes Federation (IDF), diabetes mellitus type 2 is the cause of 90% of DM sufferers . 1 Diabetes mellitus type 2 is annoying metabolism endocrine , causes insulin secretion is reduced , which causes hyperglycemia (Soelistijo SA , 2019). Diabetes mellitus type 2 requires long lasting treatment , esp pharmacological (Santhanakrishnan I, 2014). Treatment pharmacology in diabetes mellitus type 2 has various effect side , incl hypoglycemia heavy even death.Wrong One preparation drug antihyperglycemic injection have a weekness non use comfortable (Margaret Chan , 2016 **)** Mulberry has more than 150 species, including white mulberry (Morus alba) which can lower blood sugar. 12,13 White mulberry grows quickly with a short life span. 14 White mulberry leaves contain 1-deoxynojirimycin (DNJ).15,16 Deoxynojirimycin is a glucosidase inhibitor (Wilson RD, 2015).

1-deoxynojirimycin (DNJ), ingredient active main mulberry , is a polyhydroxylated alkaloid piperidine (derivative tertrahydroxy piperidine). This alkaloid can depicted as a glucose analogue with replace group amine for oxygen atoms in ring pyranose . (Zhang W et al, 2019) DNJ inhibits intestinal α- glucosidase , which reduces absorption glucose , lowering rate glucose blood . Apart from having role in modulate metabolism glucose and insulin, DNJ also shows activity lipid regulator and anti- obesity , inhibits adipogenesis, and possibly own effect neuroprotective . Apart from that , he Possible is component important in prevent change pathology brain in suffering patients Alzheimer's disease . (Chen Z et al, 2018)



(2R,3R,4R,5S)-2-(hydroxymethyl)piperidin-1-ium-3,4,5-triol

Figure 2. Structure 1-deoxynojirimycin (DNJ).

Supplementation powder mulberry in Long term dapt increase regulation of metabolism with modulate expression of the conferring protein track insulin signal . Additionally , improvements function mitochondria after DNJ supplementation of leaf mulberry . Dysfunction mitochondria cause decline ATP production and increase production species oxygen reactive , and its consequences develop insulin resistance . Therefore it , improves function mitochondria is element important in preventing and treating type 2 diabetes . More studies carry on show that extract leaf mulberry and DNJ improve insulin resistance with change

track Insulin signaling in muscle frame mouse db /db. (Kang CW et al, 2020)

2. Extraction Mulberry

The maceration extraction method is widely used in several studies. This method has weaknesses, namely that it requires quite a long extraction time and produces less than optimal results. So from it's in use extraction method alternative one of them uses ultrasonic waves. Ultrasonic bath extraction using ultrasonic waves is extraction by propagating energy through waves using liquid as a propagation medium which can increase the intensity of energy transfer so that the extraction process is more optimal than conventional extraction methods. (kuldikole , J, 2002)

From method extraction using an ultrasonic bath is obtained results antioxidant IC50 extract fruit mulberry, result treatment ratio material solvent and extraction time range between 291.76 – 219.27 ppm. Chart average activity antioxidant IC50 due to various treatment ratio ingredients: solvent (w/v) and extraction time can seen in Figure 3 below This .

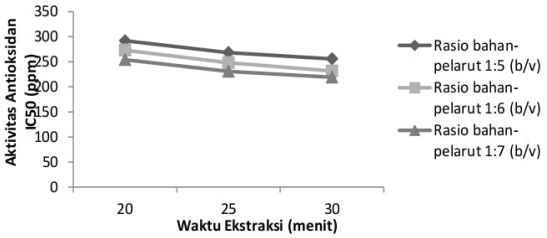


Figure 3. Extraction results antioxidant

Average activity antioxidant IC50 increases with the more many ratio Ingredients: solvent (w/v). Average _ activity antioxidant highest found in the treatment duration of 30 minutes and the ratio material from solvent 1:7(w/v) of 219.27 ppm. Meanwhile the average activity antioxidant Lowest obtained from treatment time 20 minutes with ratio material: solvent 1:5(w/v) of 291.76 ppm.

Figure 3 shows that activity antioxidant extract tend increase with the more forever time extraction with an ultrasonic bath, meanwhile the more tall ratio material the solvent will too increase activity antioxidants in the indicated extracts with the more low IC50 value . Increased activity antioxidant along increasing time extraction , due to rate anthocyanins included in the flavonoid group that can role as antioxidant (widyastuti , N, 2010).

Principle activity arrest radical free with DPPH method viz exists activity antioxidants in the sample cause happen change color DPPH solution in ethanol from colored purple concentrated become unit pale (Permana , Takayama, 2003). Mechanism inhibition activity radical DPPH free by anthocyanin is with donating hydrogen atoms from part group the hydroxyl to compound radical DPPH free so form compound radical more DPPH free stable (DPPH-H).

3. Antioxidant Test

Morus Phenol Total Flavonoid Total Fk

Table.1 Ascorbic acid , total phenols , total flavonoids in *Morus alba* , *Morus nigra* , and *Morus rubra (Elcisli and Emine, 2007).*

Morus	Total phenol	Total Flavonoids	Flavonoids/ phenols	Ascorbic acid
Alba	181ppm	29ppm	0.16	22.4 ppm
Nigra	1422ppm	276ppm	0.19	21.8ppm
Rubra	1035ppm	219ppm	0.21	19.4ppm

Table 2. total phenols and activity antioxidant *morus alba (perez . et al, 2008)*

Variable	Clone			
	Mall	Ma2	Ma3	Ma4
Total Phenol	13.46 ± 0.27ppm	12.81 ± 0.14ppm	13.16 ± 0.41ppm	15.50 ± 0.56ppm
ABTS	11.63 ± 0.23ppm	11.34 ± 0.19ppm	10.82 ± 0.32ppm	12.00 ± 0.24ppm
DPPH	12.64 ± 0.22ppm	12.34 ± 0.30ppm	11.89 ± 0.21ppm	11.17 ± 0.01ppm

Table.3 IC 50 against inhibition *alpha- glucosidase (yang et al, 2011)*

Variable	Clone			
	Mall	Ma2	Ma3	Ma4
Total Phenol	13.46 ± 0.27ppm	12.81 ± 0.14ppm	13.16 ± 0.41ppm	15.50 ± 0.56ppm
ABTS	11.63 ± 0.23ppm	11.34 ± 0.19 ppm	10.82 ± 0.32ppm	12.00 ± 0.24ppm
DPPH	12.64 ± 0.22ppm	12.34 ± 0.30ppm	11.89 ± 0.21ppm	11.17 ± 0.01ppm

On the third type mulberry have the same total flavonoids and phenolics The same high, however For content sour superior ascorbate is inside type mulberry white . Extract mulberry white own content polyphenol properties antioxidant . Phenolic compounds are capable of donating hydrogen well hydrogen This produce initiated antioxidants with reaction neutralization radical free is stage beginning from the oxidation process . Antioxidant results from relative polyphenols tall

as a hydrogen donor or electrons and capabilities polyphenols can stabilize electrons that don't pair . Activity antioxidant from mulberry white can seen from a number of method , with use mulberry 2,2-azinobis-3-Ethlybenzoathiazoline-6-Sulfonic Acid (ABTS) method white and mulberry red capacity its antioxidants seen similar , but When using 2,2-diphenyl-1-picrylhydrazyl (DPPH) method produces that capacity antioxidant in mulberry white more tall compared to with mulberry red, p This showing difference capacity antioxidant can influenced from factor genotype from mulberry , environment , and protocol extraction his . A high positive correlation ($r = 0.81$, $p \leq 0.05$) between Total Plate Count (TPC) and antioxidant capacity measured by the ABTS • + method was observed. In contrast, TPC had only a weak negative correlation with DPPH • ($r = -0.22$, $p \leq 0.05$) . (Mena et al., 2011).

Compound phenolic to response antioxidant in each capacity test antioxidant experience difference in contribution from each the compound . Measurement antioxidant use DPPH method will seen If exists change color because exists activity antioxidants , such as color purple pale changed become color yellow . As for the system inhibition from DPPH method with anthocyanin is exists hydrogen atom donation from some clusters the hydroxyl into the compound DPPH radical , with method This so will produce more compounds stable . Antioxidant from compound phenolics given to diabetics with a number of mechanism can reduce complications of diabetes with reduction of oxidative stress , Reactive Oxygen Species (ROS) , and Tumor Necrosis Factor Alpha (TNF-α) . (Tiwari and Rao, 2002)

In diabetics it will experience damage oxidative like diabetes complications and worsening condition when oxidative stress influence increase in ROS inside mitochondria the sufferer , for prevent damage oxidative so need there is action for normalizing ROS is one of them with usage antioxidant (Widowati, 2008) . Known enzymes with Alpha- Glucosidase capable cut bond glossydic with modify number , position , or configuration group hydroxyl on the sugar molecule , because matter the condition hyperglycemia happen fixation glucose high in diabetics , inhibition alpha- glucosidase enzyme will help overcome condition hyperglycemia Because amount absorbed monosaccharides from the intestines will reduce . Inhibition alpha-glucosidase enzyme can also seen from where is the value of Ic_{50} ? concentration compound capable inhibit 50% against something given system . When looking at the Ic_{50} value based on research conducted by Syahrir et al (2009), was carried out testing extract leaf mulberries in mice , pregnant compound deoxynojirimycin (DNT). The DNT compound is ready For hinder movement a-glucosidase catalyst in the small intestine , esp with replaces the linked dynamic site on the compound glucosidase so that can prevent solution bond glycosidic substrate become monosaccharides .

4. Enzyme Inhibitor Test

As additional to its function as antioxidants , phenolics found in Morus alba have ability For stop alpha- glucosidase enzyme , which can influence diabetes mellitus sufferers . Alpha-glucosidase enzyme cut bond glycosidic depending on number , position , and configuration group hydroxyl on the sugar molecule . (Halpern et al, 2010) . Therefore , inhibition alpha glucosidase enzyme can help overcome hyperglycemia , a condition in which the blood sugar concentration high in diabetes sufferers . This is because amount monosaccharides absorbed by the intestine are reduced . (Febrinda et al, 2013) .

5. IC50 test

IC50 value, defined by IUPAC as concentration compounds that have ability For inhibits 50% of the enzyme alphaglucosidase to system certain , yes used For show inhibition enzyme alphaglucosidase . Based on IC50 value , which is found in research by Yang et al. (2011), Morus alba shows activity in hinder enzyme alphaglucosidase with fraction ethyl acetate amounting to 171 g/ mL.

Conclusions

Can be concluded that seen results from a number of journal obtained . Fruit mulberry white can role as plant antioxidant with mark Power resistor use

DPPH method of 16.83%-43.95%, as well as alpha-glucosidase inhibitor with IC50 value of 550 µg/mL in the extract the water and 241 µg/ mL. in extract ethanol . And value phenols in mulberries white is 181, whereas mark phenols in mulberries red is 1422 and value phenols in mulberries black is 1035. So mulberry red proven can helps diabetes sufferers .

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