Antidiabetic Activity of Catechin from Cinnamon (Cinnamomun Burmanii) by Inhibiting Alfa Glucosidase Enzyme

by Turnitin Indonesia

Submission date: 13-Mar-2023 11:00PM (UTC-0700)
Submission ID: 2036827057
File name: 24796-Article_Text-80359-1-10-20230110.pdf (386.89K)
Word count: 2245
Character count: 12603

OPEN ACCESS International Journal of Applied Biology

ISSN : 2580-2410
eISSN : 2580-2119

Antidiabetic Activity of Catechin from Cinnamon (*Cinnamomun Burmanii*) by Inhibiting Alfa Glucosidase Enzyme

Zohrah Hasyim[1], Ismayniar[2], Natalia Ratu[2], Emi Eka putri[2], St Zaenab[3*]

[1] Post Graduate School, Hasanuddin University, Makassar, Indonesia
[2] Departemen of Biologi, Faculty of Mathematics and Natural Sciences, Hasanuddin University, Makassar, Indonesia
[3] Study Program of Aquaculture, Faculty of Fisheries, Cokroaminoto Makassar University, Makassar, Indonesia

Abstract

Diabetes mellitus (DM) is a chronic disease that occurs when the body experiences insulin resistance. One of the treatment for DM is by inhibiting the performance of the -glucosidase enzyme which is located on the smooth wall. Indonesia is famous for having various types of herbal plants that are often used as traditional ingredients, one of which is cinnamon (*Cinnamomun burman* II) which has compounds such as catechins that are useful as antioxidants. This research method a docking simulation, the ligand was downloaded in the Pubmed database and the androgen receptor macromolecule was downloaded in the Protein Data Bank (PDB), the ligand structure preparation, the test ligand docking simulation and the comparison uses the pymol,pyrx program, and Lipinski test, toxicity test using the PREADMET program. The results of binding affinity for the test compound, namely catechin compounds, obtained a binding affinity of -8.0 kcal/mol, while the comparative test, metformin, obtained a binding affinity of -3.3 kcal/mol and Lipinski qualifies as non-carcinogens but can be mutagens. These results indicate that catechin compounds have greater inhibition on alpha glucosidase receptors that cause type 2 diabetes mellitus compared to metformin compounds.

Article History
Received November 20, 2022
Accepted December 14, 2022

Keyword
Diabetes mellitus;
Cinnamomun burmanni;
α-glicosidase;
Catechin;
Docking

Introduction

Catechins are natural polyphenolic compounds flavan-3-ols (or flavanols), belonging to the flavonoid family. They are found in abundant concentrations in a variety of fruits, vegetables and plant-based beverages. The name catechin is derived from Cutch tree (*Acacia catechu* L.f). Catechin chemically consists of two benzene rings (A- and B-rings) and a dihydropyran heterocycle (the C-ring) with a hydroxyl group on carbon 3. There are two chiral centers on the molecule on carbons 2 and 3.

Catechin stereoisomers in cis ((-)-epicatechin) or trans ((+)-catechin) configuration, with respect to carbons 2 and 3, are flavan -3 - ol compounds. Through esterification with gallate groups, flavanols can form gallic acid conjugates epicatechin gallate (ECG),

CONTACT : ST ZAENAB nhenhabsitti@gmail.com

epigallocatechin (EGC), dan epigallocatechin gallate (EGCG). Condensed catechins are obtained via catechin polymerization. The most common oligomers derived from epicatechin are A-type and B-type procyanidins. In A type dimers, the monomers are linked by both a 4→8 carbon–carbon and a 2→O7 ether bond, and the monomers of the B-type dimers are linked through 4→8 carbon–carbon bonds (Bernatoniene and Kopustinskiene, 2018).

The antioxidant efficacy of catechins is exerted through direct mechanisms scavenging ROS, chelating metal ions; and indirect mechanisms inducing antioxidant enzymes, inhibiting pro-oxidant enzymes, and producing phase II detoxification enzymes and antioxidant enzymes.

The incidence of diabetes mellitus (DM) is increasing every day in the world. Based on a report from the International Diabetes Federation, there are 463 million people (20-79 years) who currently suffer from diabetes and is expected to increase to 700 million in 2045. The proportion of people with type 2 diabetes is increasing in most countries and 79% of them live in poor and developing countries. As many as 374 million people are currently at risk for type-2 diabetes. DM is a chronic metabolic disorder caused by insulin deficiency or resistance. In type 1 DM there is damage to beta cells in the pancreas resulting in insulin deficiency and in type 2 DM there is resistance or decreased insulin secretion. There are several drug therapies used to treat type 2 DM, namely sulfonylureas, thiazolidinediones, GLP-1 receptor agonists, DPP-4 inhibitors, SGLT2 inhibitors, GLP-1 receptor agonists or basal insulin, drug selection is based on the specific effects of the drug or the patient's condition. glibenclamide., Glibenclamide has an action to increase insulin secretion, (Mrabti et al., 2018).

The glucokinase enzyme is known as hexokinase (HK) type IV from a member of the hexokinase family of enzymes. The function of the glucokinase enzyme is to catalyze reactions in glucose metabolism, namely the phosphorylation of glucose to glucose phosphate.

Anti-inflammatory, cancer and rheumatic analgesic. Kaempferol itself is known as an antioxidant, anti-inflammatory, anticancer by inducing apoptosis and is known as a phytoestrogen. Apart from gandarusa, kaempferol is also contained in Ginkgo biloba, Tilia spp., Equisetum spp., Moringa oleifera, Sophora japonica and propolis (Nuraisyah, 2018).

Other glucose for type 2 diabetes mellitus Metformin hydrochloride, a biguanide, is the most popular oral glucose-lowering drug in most countries, widely viewed as the 'baseline therapy' for individuals with newly diagnosed type 2 diabetes mellitus. This reputation results from its effective glucose lowering capabilities, low cost, weight neutrality, safety profile good overall (especially the lack of hypoglycemia as a side effect). The minimum effective dose of metformin is 500 mg daily and maximum efficacy is achievedat a dose of 2000 mg daily. While some pa]\tients may benefit from doses as high as 2500 mg daily, in the present study, overall, there were no major differences in fasting plasma glucose and HbA1c when compared to the lower daily dose of 2000 mg. At 500 mg, metformin lowered fasting plasma glucose by an adjusted mean of 1.1 mmol/l and HbA1c by 0.9% (9.8 mmol/mol; placebo reduction); at 2000 mg, the corresponding reductions were 4.3 mmol/l and 2.0% (21.9 mmol/mol; p ÿ 0.01) (Sumaryada, 2014).

Materials and Methods

Materials and tools

The material used in this docking simulation is a two-dimensional structure of the reference ligand in the form of bichalutamide and catechin test ligands and their analogues which can be downloaded at the Pubmed database (PMID:18775680) (http://www.ncbi.nlm.nih.gov/pubmed). While the selected macromolecules are androgen receptors with the code Pdb 3B67, which can be downloaded at the Protein Data Bank (PDB) (http://www.rscb.org/pdb/). The tools used are hardware and software.

Ligand Structure Preparation

Preparation of the ligand structure of the test compound and the ligand of the comparison compound is the first step that must be carried out. Bicalutamide, ketamine compounds, and their analogues (PMID: 18775680) were prepared in a two-dimensional (2D) structure and then transformed into a three-dimensional (3D) structure with the Marvinsketch 6.0 program package.

Test and comparison ligand docking simulations

The test ligands were in the form of catechins and their analogues, and the reference ligands in the form of pubchem in pdb format were converted into *.pdbqt format through the https://www.rcsb.org/ . The docking method is carried out by tethering each ligand to a catechin compound. Each ligand is in a flexible state which will interact with biomacromolecules in a rigid condition. *Phmol,pyrx* used in the docking simulation of the test and comparison ligands for catechin compounds (Arwansyah, et al., 2014).

Lipinski Rule Analysis and toxicity test

Lipinski's rule is calculated using the swissadmet web (http://www.swissadme.ch/index.php#). Lipiski parameters include MlogP≤4,15, molecular weight ≤500Da, hydrogen bond donor ≤5 and hydrogen bond acceptor≤ 10. Absorption and distribution tests. and analysis of the toxicity properties of secondary metabolites of cinnamon plants using web PREADMET (https://preadmet.webservice.bmdrc.org/toxicity).

Results and Discussion

Results

Table 1. The active compounds of catechins and antidiabetic metformin compounds (drugs)

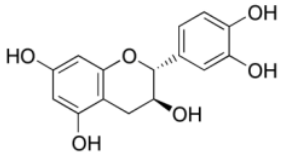
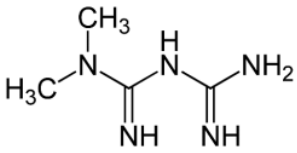
Active Compound Structure	Comparison Ligand Macromolecular Identity
	
Catechin	Metformin
C15H14O6	C4H11N5

Table 2. Molecular docking test results

Ligand name	Binding affinity(kcal/mol)	The atoms play a role	The role of atoms in ligands
catechin	-8.0	O=H	acceptor H
Metformin	-3,3	H=O	donor H

Table 2 shows the molecular docking results of catechin compounds against α-glucosidase (GAA), namely a binding affinity of -8.0kcal/mol, while the results of molecular docking of metforming compounds obtained a binding affinity of -3.3kcal/mol. These results indicate that the catechin contained in cinnamon (*Cinnamomum burmannii*) exhibits interactions with the α-glucosidase (GAA) ligand site.

Table 3. Results of drug-like properties analysis based on Lipinski's rule

compound	Lipinski's rule				
Catechin	Massa molekul≤500Da	MlogP ≤4,15	Akseptor ikatan hydrogen ≤10	Donor ikatan hydrogen≤ 5	Description
	290.27	0,24	6	5	fullfill

Table 4 result Farmakokinetika Test (Absopstion, Distribution) and toxicity

compound	Farmakokinetika			Toksisitas
	Absorption	Distribusi		
		BBB	PPB	
Catechin	High	No	Yes	Non Carsinogenik. Mutagen

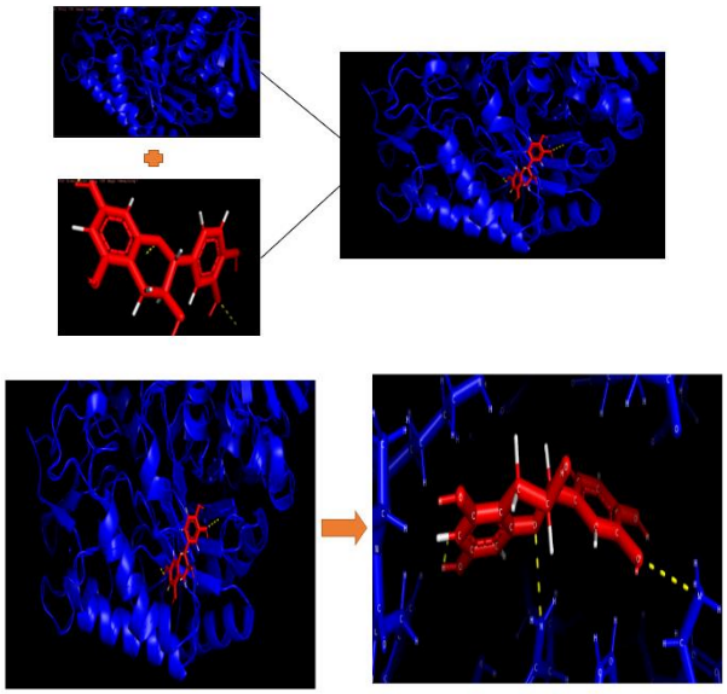


Figure 1. Interaction of catechins with the enzyme α-glucosidase (GAA)

Figure 1. above shows the active site where the protein enzyme α-glucosidase (GAA) and catechin compounds bind well where it can be seen that the atoms that play a role are O=H

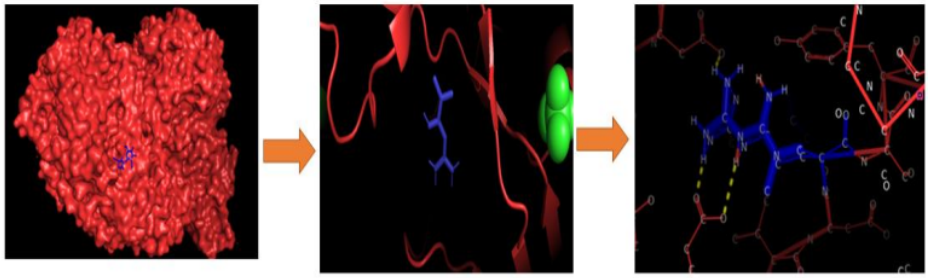


Figure 2. Interaction of metformin (drug) with the enzyme α-glucosidase (GAA)

Figure 2. above shows the active site where the protein enzyme α-glucosidase (GAA) and the compound metformin bind well where you can see the atom that plays a role, namely H=O.

Discussion

One of the plants that can be used as herbal medicine is cinnamon (*Cinamomun Burmanii*) (Arrafi and Amanatie, 2018). The use of cinnamon plants as a medicine for gout, high blood pressure, ulcers, hermia, asthma, canker sores, constipation, and diabetes mellitus (Syarif et al., 2015)

Molecular docking is a computation to predict a relationship whether the compound has activity before being tested. This experiment with molecular docking was to see if the diabetes mellitus drug in circulation had activity in inhibiting the aldose reductase enzyme. Molecular docking can be done with many paid and free software. This study uses PyRx software for docking and uses the pymol programs (Karisma et al., 2016).

Based on the results of docking between the ligand and the receptor, it is obtained from the conformation of the ligand with the lowest energy. Binding affinity is a measure of the ability of a drug to bind to a receptor. The lower the binding affinity value, the higher the affinity between the ligand receptors and vice versa, the greater the binding affinity value, the lower the affinity between receptors (Karisma et al., 2016).

In the results of the pymol and pyrx program (Table 2), the results of the binding affinity for the test compound, namely the catechin compound, obtained a binding affinity of -8.0 kcal/mol, while in the comparator test, namely metformin, a binding affinity result of -3.3 kcal/mol. These results indicate that the catechin compound has greater inhibition to the alpha glucosidase receptor causing type 2 diabetes mellitus compared to the metformin compound.

Table 3. above catechins have a molecular mass of ≤ 290.27, MlogP ≤ 0.24, hydrogen bond acceptors ≤10, and hydrogen bond donors ≤ 5 where these results meet the requirements of the Lipinski rule.

Table 4. Catechin absorption exhibits high permeability in penetrating cell membranes. While the results of the distribution of PPB values indicate good absorption in the human body and a good level of absorption in the human intestine. The BBB value indicates the drug's ability not to penetrate the blood-brain barrier. Meanwhile, the toxicity profile was examined through mutagenicity and carcinogenicity parameters using the PREADMET web. PREADMET is widely used to assess the mutagenic potential of a compound using bacteria. The results above indicate that catechin compounds are not carcinogenic but can act as mutagenic and non-carcinogenic.

Conclusion

Catechin has the lowest affinity energy, which is -8.0 kcal/mol compared to the metformin test ligand, which is -3.3 kcal/mol, and Lipinski qualifies as non-carcinogens but can be mutagens. so that catechin is the most widely tested ligand potential as an antidiabetic drug compared to metformin. These results still need to be tested further using experimental tests.

References

Ahmad Naufal Arrafi and Amanatie. Uji aktivitas antidiabetes infusa kulit batang kayu manis (Cinnamomun burmanii) pada mencit putih jantan secara in Vivo. Jurnal Kimia Dasar. 2018;7(2).

Arwansyah, Ambarsari L, Sumaryada TI. 2014. Simulasi Docking Senyawa Kurkumin Dan Analognya. Current Biochemistry. Volume 1 (1): 11-19

Bernatoniene J, and Kopustinskiene DM. The Role of Catechins in Cellular Responses to Oxidative Stress. Molecules. 2018;23(4):1-11. doi:10.3390/molecules23040965

Karisma Enggar S, Nurul F, Erwinda K, Dedy P, dan Broto S. 2016. Docking molekular potensi antidiabetes melitus tipe 2 turunan zerumbon sebagai inhibitor aldosa reduktase dengan autodock vina. Chimica et Natura Acta. 4(1): 2016.16-20.

Mrabti HN, Jaradat N, Fichtali I, et al. Separation, identification, and antidiabetic activity of catechin isolated from Arbutus unedo L. Plant roots. Plants. 2018 ;7(2). doi:10.3390/plants7020031

Nuraisyah F. Faktor Risiko Diabetes Mellitus Tipe 2. J Kebidanan dan Keperawatan Aisyiyah. 2018.13(2):120-127. doi:10.31101/jkk.395

Sumaryada TI. Simulasi Docking Senyawa Kurkumin Dan Analognya Sebagai Inhibitor Enzim 12-Lipoksigenase. Curr Biochem. 2014. 1(1):11-19.

Syarif, P., Suryotomo, B., & Soeprapto, H. 2015. Diskripsi dan manfaat tanaman obat di pedesaan sebagai upaya pemberdayaan apotik hidup (studi kasus di Kecamatan Wonokerto). Pena Jurnal Ilmu, 13. Retrieved from http://jurnal.unikal.ac.id/index.php/pena/arti cle/view/49

Antidiabetic Activity of Catechin from Cinnamon (Cinnamomun Burmanii) by Inhibiting Alfa Glucosidase Enzyme

ORIGINALITY REPORT

19%	9%	11%	8%
SIMILARITY INDEX	INTERNET SOURCES	PUBLICATIONS	STUDENT PAPERS

PRIMARY SOURCES

1	A. Bordoni, C. Boesch, C. Malpuech-Brugère, C. Orfila, L. Tomás-Cobos. "The role of bioactives in energy metabolism and metabolic syndrome", Proceedings of the Nutrition Society, 2019 Publication	5%
2	Cesar G. Fraga, Patricia I. Oteiza. "Dietary flavonoids: Role of (−)-epicatechin and related procyanidins in cell signaling", Free Radical Biology and Medicine, 2011 Publication	2%
3	dpom.gilead.org.il Internet Source	1%
4	Awik Puji Dyah Nurhayati, Andis Rihandoko, Arif Fadlan, Shabrina Syifa Ghaissani, Nurul Jadid, Edwin Setiawan. "Anti-cancer potency by induced apoptosis by molecular docking P53, caspase, cyclin D1, cytotoxicity analysis and phagocytosis activity of trisindoline 1,3 and 4", Saudi Pharmaceutical Journal, 2022 Publication	1%

5	Submitted to Institute of Technology, Sligo Student Paper	1 %
6	springeropen.altmetric.com Internet Source	1 %
7	Submitted to Liverpool John Moores University Student Paper	1 %
8	ojs.unud.ac.id Internet Source	1 %
9	Inmaculada Guerrero Fernández de Alba, Antonio Gimeno-Miguel, Beatriz Poblador-Plou, Luis Andrés Gimeno-Feliu et al. "Association between mental health comorbidity and health outcomes in type 2 diabetes mellitus patients", Scientific Reports, 2020 Publication	1 %
10	Theopilus Watuguly, Yohanes Bare, Dewi Ratih Tirt, Indranila Kustarini. "In silico Study Phytosterol Cymbopogon citratus and Curcuma longa as Inhibitor Agent 3C-Like Protease SARS-CoV-2", Pakistan Journal of Biological Sciences, 2022 Publication	1 %
11	Submitted to University of Glamorgan Student Paper	1 %

12	Submitted to University of Birmingham Student Paper	1 %
13	journal.unj.ac.id Internet Source	<1 %
14	melysajournal.com Internet Source	<1 %
15	molpharm.aspetjournals.org Internet Source	<1 %
16	patents.google.com Internet Source	<1 %
17	edoc.unibas.ch Internet Source	<1 %
18	gproteindb.org Internet Source	<1 %
19	mafiadoc.com Internet Source	<1 %

Exclude quotes	Off	Exclude matches	Off
Exclude bibliography	Off		