

IN SILICO STUDY OF THE POTENTIAL OF GAMBIR LEAF CATECIN COMPOUNDS (*Camellia sinensis* L.) AS ANTI-BACTERIAL AGAINST *Mycobacterium tuberculosis* IN InHA

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ABSTRACT

Isoniazid is an anti-tuberculosis pro-drug by inhibiting mycolic acid in bacterial cell walls which requires activation by inhA and the presence of mutations in the Kat-G gene increases resistance to isoniazid. The disadvantages is that high humidity can cause bacteria to grow quickly. Pathogenic bacteria are one of the causes of infection, both gram-positive bacteria and gram-negative bacteria. One of the diseases caused by bacteria is tuberculosis, which is caused by *Mycobacterium tuberculosis*.

The four compounds of the catechin group from gambir plants, namely Epikatekin (EC), Epigallo catechin (EGC), Epikatekin gallate (ECG), and Epigallokatekin gallate (EGCG), three of which meet the criteria of Lipinski's five laws, namely in EC, ECG and EGC with one violation, namely Hydrogen Bond Donor > 5 where Lipinski's criteria for compounds are said to be good if HBD < 5.

Keywords : Catechin, Isoniazid, InhA, KatG

INTRODUCTION

The disadvantages is that high humidity can cause bacteria to grow quickly. Pathogenic bacteria are one of the causes of infection, both gram-positive bacteria and gram-negative bacteria. One of the diseases caused by bacteria is tuberculosis, which is caused by *Mycobacterium tuberculosis*. Tuberculosis (TB) is an ancient disease that still exists and causes significant global health problems. Nearly half a million cases have a multidrug resistance (MDR) form of the disease. The World Health Organization (WHO) plans to eliminate TB by 2030 worldwide. (WHO.2021)

Catechin compounds are known to have antibacterial activity. Chinese green gambir leaf extract was found to strongly inhibit the growth of the major food-borne pathogens, *Escherichia coli* O157:H7, *Salmonella typhimurium* DT104, *Listeria monocytogenes*, *Staphylococcus aureus*, and the diarrheal food poisoning pathogen *Bacillus cereus*, by 44-100%. with the highest activity against *Staphylococcus aureus* and the lowest against *E. coli* O157:H7.

Bioassay-guided fractionation technique was used to identify the main active components. A simple and efficient reversed-phase high-speed countercurrent chromatography (HSCCC) method was developed for the separation and purification of four bioactive polyphenolic compounds, epicatechin gallate (ECG), epigallocatechingallate (EGCG), epicatechin (EC), and caffeine (CN). The structures of these polyphenols were confirmed by mass spectrometry. Among the four compounds, ECG and EGCG is compound the most active than another catechins compound, particularly EGCG against *Staphylococcus aureus*. The activity of gambir polyphenols, particularly EGCG on antibiotic-resistant *Staphylococcus aureus* strains, suggests that these compounds are potential natural alternatives for controlling bovine mastitis and food poisoning caused by *Staphylococcus aureus*. (Si.W. et.al.2006).

METHODS

This research is a computational-based pre-experimental design. aims to find data that can provide a definition or explanation related to the concept used, namely the in-silico method of catechin compounds from *Camellia sinensis* L. through the mechanism of inhibition of InHA

and KatG as mycolic acid receptors on the Mycobacterium tuberculosis cell wall. Using Autodock Vina and Biovia Discovery Studio software.

RESULTS

A. Prediction of Bioactivity

Tabel 2. Result of Antibacteria Phytochemical Bioactivity Catechin

Compounding	Pa	Pi
EC	0,385	0,031
ECG	0,392	0,035
EGC	0,369	0,033
EGCG	0,327	0,032
Isoniazid	0,870	0,003

DISCUSSION

Pa is Probability to be Active and Pi is Probability to be in active. The value in the table above shows that the Pa value as an antibacterial on catechin compounds is less than 0.5 so it can be interpreted as less fulfilling as an antibacterial.

A. Lipinski Rule of Five

The parameters observed for the determination of ligand affinity to the receptor are bond free energy, amino acid residues, and the number of hydrogen bonds (Pratama, 2016). The Lipinski Rule of Five parameter states that a compound is predicted to be easily absorbed, has good permeability and good bioavailability if it meets the parameters of molecular weight <500, Log P value <5, number of Hydrogen Bond Donors <5, number of Hydrogen Bond Acceptors (HBA) <10.

HBA and HBD values are related to the biological activity of drug molecules. Biological activity can be influenced by changes in the physico-chemical properties of compounds, for example boiling point, melting point and solubility in water can be caused by the number of hydrogen bonds (Ruswanto, 2015). Based on the results of physicochemical prediction of compounds using pkCSM Online Tool, the data in table IV.1 illustrates that of the four catechin components studied, there is only one that fulfills Lipinski's Law of Five, namely the EC compound (Epikatekin) and the comparison compound, INH.

The ECG and EGC compounds have one failure at the HBA (Hydrogen Bond Acceptor) value > 5. While in EGCG there are two failures, namely at the HBA and HBD values.

B. Antibacterial Potential of Catechins

The results of predicting the phytochemical bioactivity of catechin and INH compounds through www.way2drug.com/PASSOnline are illustrated in table IV.4. Pa-value is Probability to be Active and Pi-value is Probability to be inactive. The terms of the meaning of the Pa value are as follows: $Pa > 0.7$ means that the compound has a high potential to become a bioactive compound in in vivo and in vitro experimental tests, as well as having a high level of similarity with drug compounds with the same bioactivity. Whereas a value of $0.5 < Pa < 0.7$ means that the compound has a high potential to become a bioactive compound in invitro and in vivo tests and has the potential to become a scaffold for the development of new drugs with the relevant bioactivity. $Pa < 0.5$ means that the compound has low potential to become a bioactive compound in in vitro and in vivo experimental tests and if forced it will not be successful to be developed. While Isoniazid as a comparator substance has a Pa-value of 0.720 as an antituberculosis. The high Pa potential of catechin is as an antioxidant, which is 0.710.

CONCLUSION

The four compounds of the catechin group from gambir plants, namely Epikatekin (EC), Epigallo catechin (EGC), Epikatekin gallate (ECG), and Epigallokatekin gallate (EGCG), three of which meet the criteria of Lipinski's five laws, namely in EC, ECG and EGC with one violation, namely Hydrogen Bond Donor > 5 where Lipinski's criteria for compounds are said to be good if HBD < 5.

While EGCG does not meet the criteria of Lipinski's law with two violations, namely HBD and HBA.

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