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IN SILICO STUDY OF B-GLUCAN FROM INDONESIAN FERMENTED TRADITIONAL FOOD "Dangke" TO INCRASE IMMUNITY

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Abstract

The World Health Organization (WHO) defines a pandemic as a situation when the entire world population is has posibility to be infected with a disease, at the end of 2019 a new type of virus emerged that caused the death of thousands of residents of wuhan, china which was identified as a type of virus corona virus disease 19 (Covid-19). The body's immune system is one way to maintain the balance of the body from various infections, one of the things that we can consuming healthy and nutritious foods. Lactic acid fermentation products has a good effect on the body. In Adrian's research (2020), he explained that fermented food products can increase immunity. In a study reported by Wasser (2011), he was found that several exopolysaccharides synthesized by lactic acid bacteria has the potential to be used as additives in fermentation products as immunomodulators, one of which is β-glucan. β -glucan has been shown to be capable of immunomodulating macrophages in vitro and increasing the secretion of anti-inflammatory cytokines, another study reported by Tayo et al. (2018), showed that the exopolysaccharide produced by Weissella confuse (EPSWC) has immunomodulatory potential by stimulating IgG production in mice. Biological activity of lactic acid bacterial could be predicted with molecular docking and use score of binding affinity as a parameter for the ability on IgG. The steps consist of preparation of the target protein and ligand, molecular docking and drug likeness test. The results showed that the compound of lactic acid bacteria to increase immunity which had a binding affinity was -6.6

Keyword : Dangke, Lactic acid bacteria, Immunity

Introduction

The World Health Organization (WHO) defines a pandemic as a situation when the entire world population is has posibility to be infected with a disease. Throughout history there have been several types of viral pandemics worldwide, the Center for Research and Development for vectors and reservoirs of disease mentions 9 types of infections that have become world epidemics, namely PES, cholera, Spanish flu, Hong Kong flu, HIV/AIDS, SARS, swine flu, Ebola and at the end of the day. In 2019, a new type of virus emerged that caused the death of thousands of residents of Wuhan, China, which was identified as a type of Corona virus disease 19 (Covid-19).

The body's immune system is one way to maintain the balance of the body from various infections, one of the things that we can consuming healthy and nutritious foods. Lactic acid fermentation products have a good effect on the body. In Adrian's research 2020, he explained that fermented food products can increase immunity.

Dangke is the name for cheese from the Enrekang area, South Sulawesi. It is a traditional food that tastes similar to cheese, but looks and textures similar to tofu which is pure white to yellow soft in color. Dangke is made by heating it on low heat until it

boils, then adding a coagulant in the form of papaya latex (papain) so that clumping occurs, the usual preservation method is the addition of table salt. Dangke contains 55% water, 23.8% protein, 14.8% fat. The higher the heating temperature, the lower the protein and fat content, the higher the pH, the higher the lactic acid and the lower the lactose (Malaka, 2015).

Lactic acid bacteria can give affect local immunity by acting as part of the body's defense mechanism. Food that enters the digestive tract will be digested and distributed through the blood circulation, lactic acid bacteria can help kill bacteria, viruses, fungi so that in this way the bacteria in the intestine can protect the body from all kinds of pathogenic microorganisms.

In a study reported by Wasser (2011), it was found that several exopolysaccharides synthesized by lactic acid bacteria have the potential to be used as additives in fermentation products as immunomodulators, one of which is β-glucan. β-glucan has been shown to be capable of immunomodulating macrophages in vitro and increasing the secretion of anti-inflammatory cytokines. Another study reported by Tayo et al. (2018), showed that the exopolysaccharide produced by Weissella confuse (EPSWC) has immunomodulatory potential by stimulating IgG and IgM production in mice.

Materials and Method

1. **Ligand Preparation**
   The chemical structure beta glucan collected from literature study, IUPAC (2*S*,3*R*,4*S*,5*S*,6*R*)-2-[(2*R*,4*R*,5*R*,6*S*)-4,5-dihydroxy-2-(hydroxymethyl)-6-[(2*R*,4*R*,5*R*,6*S*)-4,5,6-trihydroxy-2-(hydroxymethyl)oxan-3-yl]oxyoxan-3-yl]oxy-6-(hydroxymethyl)oxane-3,4,5-triol, 3D structure, ligand SMILES C(C1C(C(C(C(O1)OC2C(OC(C(C2O)O)OC3C(OC(C(C3O)O)O)CO)CO)O)O)O)O is taken from Pubchem.
2. **Target Preparation**
   The protein structur collected in protein data bank (https://www.rcsb.org/) with pdb code2igd. The protein structure processed using pymol 2.5 to remove non-protein molecule. The target protein for this research is the IgG.
3. **Molekular Docking**
   Molekular docking performed with Vina wizard feature integrated in pyrx 0.8. the ligand is Beta glucan, the protein target is the IgG, Beta 1,4 D glucan is used as ligand control for docking process
4. **Molecular Visualization and Small Molecul Interaction**
   Interaction between ligand and protein target and control are visualized and analyzed with pymol 2.5
5. **Drug likeness test**
   Drug likeness test using physiochemical properties of ligand and matched with physiochemical of registered drugs. Drug likeness test using Lipinski rule

Result and Discussion

1. **Ligand Preparation**
   Ligand after being download from PuChem website, the ligand should be corvert from SDF to PDB/Cif format to make the molecular docking process easier. The 3D structur of ligand show in figure 1.

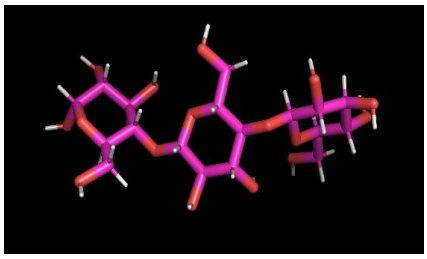

Figure 1. visualization 3D of Beta Glucan

2. Target Preparation

The target used in this research is IgG with PDB code 2igd. IgG IgG is a type of antibody commonly found in body fluids and blood. IgG protects the body from infection by binding to viruses and bacteria. The 3D structur of protein target show in figure 2.

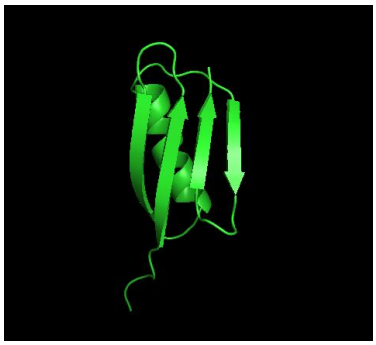

Figure 2. visualization D from protein target IgG

3. Molecular Docking Result

Molecular docking using computation method to predict potential activity from a compound before it is being tested. Binding affinity of IgG with ligands is greater than binding affinity of IgG with control. Binding affinity result of Dangke Food are shown in table 3 and 4.

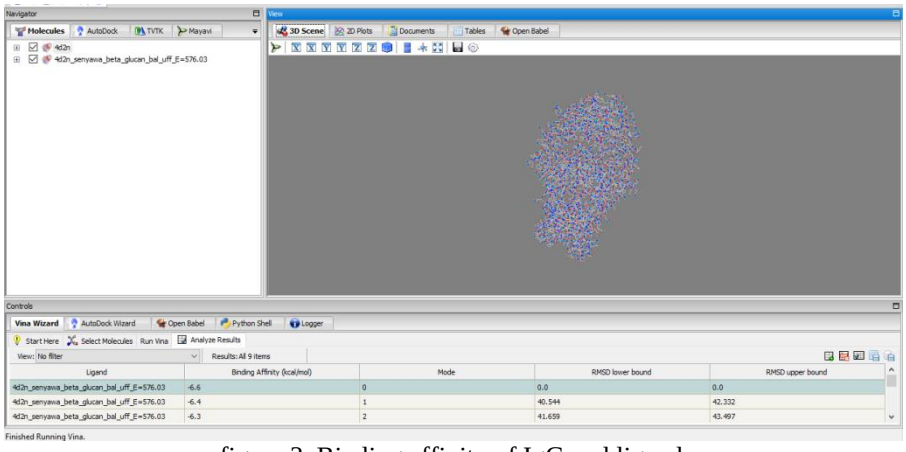

figure 3. Binding affinity of IgG and ligand

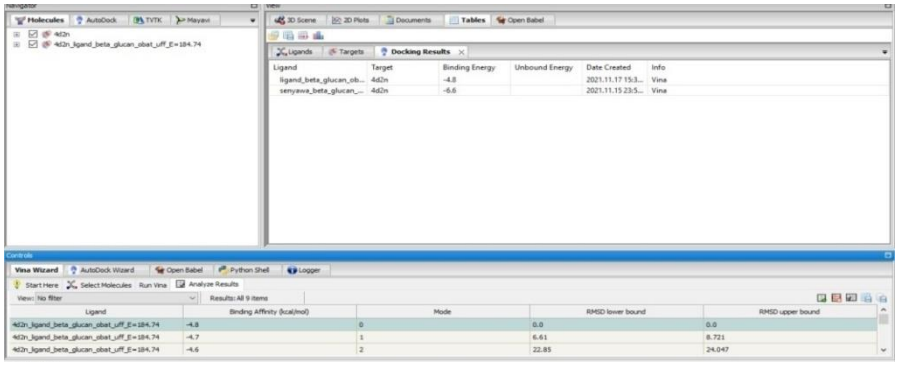

figure 4. Binding affinity of IgG and control

4. Ligand Macromolecule Interaction Visualization

Ligand- Macromolecule interaction visualization result shown figure 5

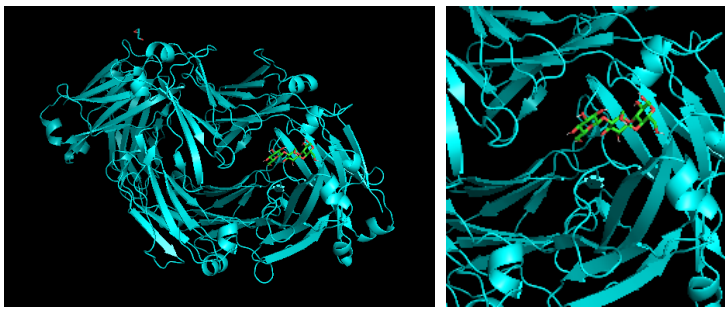

Figure 5. visualization IgG and ligand

5. Drug Likeness Test

After molecular docking process, the next step is the drug likeness test. Drug likeness test is term to explain how physiochemical of a compound effect molecular properties in vivo. The majority rule for drug likeness test using physiochemical properties of molecular structure and match with the registered drug. Lipinski rule which is the molecular weight is ≤500 kDa, LogP is ≤5, hydrogen bond donor is ≤5 and hydrogen bond accertor is ≤10, these a similar with good drug oral bioavaibility. The molecular weight of more than 500 kDa cannot diffuse through the cell membrane. The high low P indicate the more hydrophobic of the molecule, the negative log P value is also not good because molecul cannot pass through the lipid bilayer membrane (Sulfahri, 2019). The result of drug likeness for each compound are shown in table 6.

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Toxicity		
Human Ether-a-go-go-Related Gene Inhibition	Weak inhibitor	0.9517
	Non-inhibitor	0.8283
AMES Toxicity	Non AMES toxic	0.8628
Carcinogens	Non-carcinogens	0.9551
Fish Toxicity	Low FHMT	0.8951
Tetrahymena Pyriformis Toxicity	Low TPT	0.7547
Honey Bee Toxicity	High HBT	0.6701
Biodegradation	Not ready biodegradable	0.6632
Acute Oral Toxicity	IV	0.6266
Carcinogenicity (Three-class)	Non-required	0.6495

Figure 6. drug likeness test of ligand

6. Toxicity Test

The results of the toxicity test show that the ligands of the compounds are not toxic, the result show in figure 7.

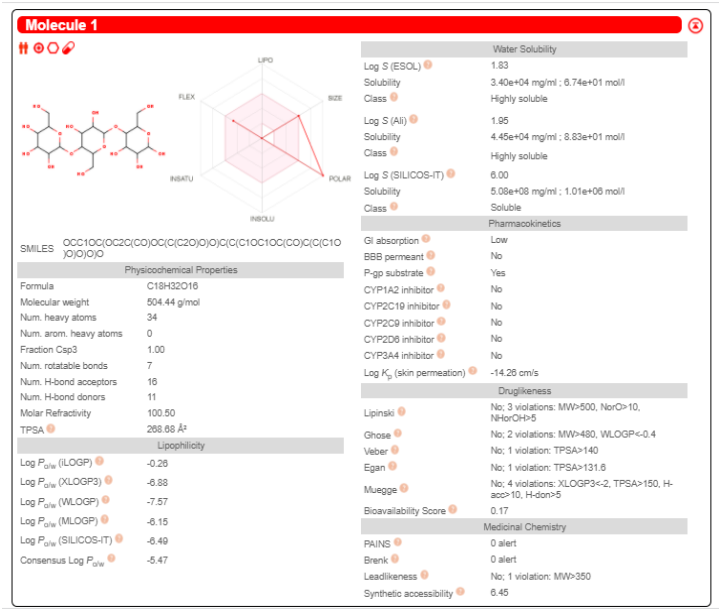

Figure 7. Toxicity test of ligand

CONCLUSION

The B-glucan compound has an binding affinity for IgG protein with a value of -6.6 and is not toxic, B-glucan can increase immunity defenses by binding to bacteria or viruses on the body, but the druglikeness test showed that the B-glucan compound was >500 kDa which means that diffucult diffuse through the cell membrane.

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