ORIGINAL ARTICLE

Potential of *Parkia Speciosa* Empty Pod Extract as A Topical Anti-inflammatory Orabase: In Silico Study

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ABSTRACT

Introduction: Inflammatory conditions are often found in oral cavity such as gingivitis, post tooth extraction, stomatitis, periodontitis, and oral abscess. Pharmacological therapy given is NSAIDs, but 78.8% of patients who consume NSAIDs feel gastritis as side effect. Therefore, it's necessary to optimize orabase (Ob)-based herbal medicine which have fast onset of action, avoid first pass metabolism, and mechanical barrier. Bitter bean peel extract (BBPE) (*Parkia speciosa*)-as the main waste-has good anti-inflammatory ability because it containing the highest concentration of flavonoid (Fl) (gallic acid, catechin, and ellagic acid). It was chosen because it's unspecified topically and minimum published. Objectives: To analyze potency of Ob Fl of BBPE in inhibiting COX-2. **Method:** Preparation of materials for Fl, control (arachidonic acid (AA) and celecoxib), COX-2 using PubChem and PDB databases. *In silico* carried out PASS to profiling probable anti-inflammatory, physicochemical to characterizing drug-likeness, ADMET to profiling pharmacokinetics, docking to simulating reaction, and visualization. **Result:** Fl of BBPE have potential as anti-inflammatory because they have Pa>0.3 and Pi<0.3 values. Fl has drug- like characteristics because they fulfill the 5 rules of Lipinski which reflects that compounds are easily absorbed and distributed to topical treatment targets, good pharmacokinetic abilities, and non-toxic to liver and topically. Fl was able to block the active site COX-2 on 371st peptide, because they had lower binding affinity (kcal/mol) (- 3.4, -4.9, and -4.6) than the control (-4.7, -3.3). **Conclusion:** Fl of BBPE has the potential as an anti-inflammatory for Ob because it has good inhibition against COX-2.
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Keywords: *Parkia speciosa* empty pod extract, Flavonoid, Orabase, COX-2 inhibitor, *In silico*.

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INTRODUCTION

Inflammation is the body's physiological response to an injury that would be considered a foreign body [1]. Inflammatory conditions are also often found in the oral cavity with 5 cardinal signs which include calor, tumor, dolor, rubor, and functio laesa (Cavaillon, 2021). Inflammatory conditions are often found in the oral cavity, some of which are periodontitis (74.1%), gingivitis (23.4%), oral abscesses (14%), stomatitis (8%), and swelling after tooth extraction (2.27%) [2]. The inflammatory process that occurs is mediated by strong inflammatory mediators such as prostaglandin E2 (PGE2) as a product of arachidonic acid (AA) bioconversion by the COX-2 enzyme (Das, 2021; Davis et al., 2020; Mahesh et al., 2021). Uncontrolled production of PGE2 will continuously encode the recruitment of immunocompetent cells which causes an increase in destructive responses to tissues, causing the inflammatory process to become chronic. Reviewing the activity of PGE2 which plays an important role in the inflammatory process, the therapy that is often given is anti- inflammatory drugs that inhibit COX-2 in converting AA to PGE2 such as Non- Steroid Anti-Inflammatory Drugs (NSAIDs) [3].

Nevertheless, NSAIDs can have gastritis side effects in

patients. Reporting from research conducted in 2021 showed that the prevalence of gastritis patients due to side effects of consuming NSAIDs was 78.8%. Decreased production of PGE2 in the stomach can eliminate the function of PGE2 as a gastroprotective, causing stomach irritation (gastritis). In addition, drug delivery using oral preparations can reduce the bioavailability of a drug thereby reducing the load absorbed by the body [4]. Reviewing this problem, researchers are also developing effective pharmaceutical preparations to distribute drugs to target locations in the body locally such as orabase [5]. Orabase has the advantage of being used topically because it can target specific locations locally so that the drug load received is also high. In addition, the time needed for the drug to reach the target location is faster than other drug preparations because it avoids first pass metabolism and gastric emptying time and the relatively shorter onset of action of the drug by acting immediately while the drug is applied topically [6].

Indonesia is a country that has a very broad agricultural sector with an area of agricultural land reaching 10.45 million hectares per year by 2022 with the main agricultural commodities being biopharmaceutical plants. One of the biopharmaceutical plants that thrives in Indonesia is the bitter bean plant (*Parkia speciosa)* with production in Indonesia reached 387,691 tons with the highest distribution in the provinces of Central Java (108,378 tons). Bitter bean peel waste has high levels of flavonoids of 55-270 g/kg from 1 kg of bitter bean peel waste. In 270 g/kg of flavonoids, active compounds were found which predominated including gallic acid (23.31 g/kg), ellagic acid (8.91 g/kg) and catechin (5.82 g/kg). This was proven in previous studies that examined the anti-inflammatory effects of the flavonoid compounds of bitter bean peel extract. The results showed that the administration of bitter bean peel extract was able to reduce the production of IL-1, IL-1β, TNF-α, and IL-6. In addition, bitter bean peel extract was able to reduce the expression of NF-κB p65 and VCAM-1. Nevertheless, the existing research has not yet answered the mechanism or the specific anti- inflammatory ability of the bitter bean peel waste extract against COX-2 [7].

Along with the development of bioinformatics and medical technology, a lot of research has been carried out to develop pharmaceutical preparations and explore new drug compounds (drug discovery) using in silico biocomputing technology. This aims to increase the effectiveness, efficiency, and optimize the therapeutic process. This research focuses on discovering the potential of bitter bean peel waste extract as orabase when viewed through in silico tests. This research is expected to be able to provide specific descriptions and predictions regarding the inhibition ability of the bitter bean peel waste extract against COX-2 when applied via orabase preparations [8,9].

MATERIALS AND METHODS

Research Materials

This study used the active compound of bitter bean peel waste extract which was downloaded and prepared in 2 dimensions from the PubChem website (https://pubchem.ncbi.nlm.nih.gov/). The active compounds used in the waste banana peel extract are flavonoid compounds with the highest levels including gallic acid/GA (CID 370), ellagic acid/EA (CID 5281855) and catechin/Cat (CID 9064). As a comparison, the researchers used 2 comparator compounds, namely the active compounds of COX-2 selective inhibitor anti-inflammatory drugs, namely celecoxib (CID 2662) and arachidonic acid (CID 444899) as native ligands of COX-2. The target of this study was the COX-2 enzyme with PDB ID 5IKR which was downloaded and prepared for its 3-dimensional structure from the RCSB Protein Data Bank page (https://www.rcsb.org/). Selection of COX-2 with PDB ID 5IKR is based on enzyme sources isolated from humans, has a resolution of more than 2E, namely 2.34E, and has the most favorable region value of 90% in the Ramachandran range which is effective for protein docking targets [8,10].

PASS Prediction

PASS prediction is carried out by entering the canonical SMILES or SMILES sequences of GA, EA, and Cat test compounds obtained from the PubChem website into the Way2Drug website to predict their bioactivity. After that, the Probable to Active (Pa) and Probable to Inactive (Pi) values will be obtained [11,12].

Physicochemical Test

Physicochemical tests were carried out by uploading the 2-dimensional conformations of the test compounds GA, EA, and Cat to the Lipinski Rule of Five page to determine their drug-likeness characteristics. The Lipinski test results contain 5 parameters including molecular mass, Log P, donor hydrogen bonds, acceptor hydrogen bonds, and molar refractivity. A compound is categorized as a drug-like compound if it fulfills 2 of the 5 Lipinski parameters, namely molecular mass <500 dalton (Da), Log P <5, donor hydrogen bonds <5, acceptor hydrogen bonds <10, and molar refractivity in the range of 40-130 [13].

ADME Prediction

ADME or pharmacokinetic prediction is done with the help of the PkCSM website. This prediction is the same as the PASS prediction which utilizes the SMILES sequence or the canonical SMILES as a marker for the compound to be predicted. After the SMILES sequence is inputted into the column, the ADME prediction will take place. The prediction results displayed contain each parameter, namely administration, distribution, metabolism, and excretion. Because the research being conducted wanted to know the ability of the active compounds when distributed topically, the ADME parameters

used must also be specific. Some of them are for the administration aspect the water solubility parameters (in numeric) and skin permeability (in numerical) are taken, the distribution aspect uses the human fraction unbound parameter (in percentage), the metabolism aspect uses the CYP2D6 parameter of substrates and inhibitors, and the excretion aspect uses the total clearance parameter (in numeric) [14].

Toxicity Test

Toxicity tests are carried out with the help of the pkCSM website and or ToxTree. This prediction is the same as the PASS and ADME predictions which use the SMILES sequence or the canonical SMILES as a marker for the compound to be predicted. After the SMILES sequence is inputted into the column, the prediction of toxicity will take place. The prediction results displayed include each parameter, namely AMES toxicity, human maximum tolerated dose, lethal dose of 50, hepatotoxicity, and skin sensitization [15].

Molecular Docking Test

The molecular docking test was carried out by uploading the test compound, comparator compound, and target protein to the PyRx application. After uploading, run the PyRx program to find out the results of binding affinity in units of kcal/mol, mode, RMSD lower bound and upper bound (Ji et al., 2020; Pantsar & Poso, 2018; Pinzi & Rastelli, 2019; Saikia & Bordoloi, 2019). Visualization of the docking results was carried out to profile the location, type, and number of bonds formed between the test compound and the target protein. The visualization process utilizes the PyMol and Biovia applications. Visualization is done by uploading the docked conformation that is inserted into the target protein. After that it can be known the location, type, and number of bonds formed [10].

RESULT

PASS Prediction Result

Table I.

The PASS analysis outcomes demonstrated EA compound revealed a 0.749 probability of being active as an anti-inflammatory, with a 0.010 probability of inactivity. The results show that the Es compound has the highest chance of being active as an anti-inflammatory among the other 3 compounds while outperforming celecoxib's chance of being active as an anti-inflammatory agent.

Table I. PASS prediction result of the active compound of bitter bean peel waste extract

Compound	GA*	Cat*	EA*	Celecoxib
Pa	0.548	0.548	0.749	0.663
Pi	0.044	0.044	0.010	0.021
ΔP (Pa-Pi)	0.504	0.504	0.739	0.642

*GA : Gallic Acid, Cat : Catechin, EA : Ellagic Acid

Physicochemical Test Result

Table II.

The results of the physicochemical tests indicated that GA compounds conformed to Lipinski's criteria, possessing a molecular mass of 170 Da, 4 donor hydrogen bonds, 5 acceptor hydrogen bonds, a log P of -0.18, and a molar refractivity of 32.57. Similarly, the subsequent findings for Cat compounds met Lipinski's standards, with a molecular mass of 290 Da, 5 donor hydrogen bonds, 6 acceptor hydrogen bonds, a log P of 1.09, and a molar refractivity of 68.13. Moreover, the subsequent data for EA compounds satisfied Lipinski's parameters, exhibiting a molecular mass of 302 Da, 4 donor hydrogen bonds, 8 acceptor hydrogen bonds, a log P of 0.20, and a molar refractivity of 58.00.

Table II. Physicochemical test results of the active compound of bitter bean peel waste extract.

Compound	Molecular Mass (Da)	Hydrogen Bond Donor	Hydrogen Bond Acceptor	Log P	Molar Refractivity
Standard	**≤500 Da**	**≤5**	**≤10**	**≤5**	**40-130**
GA*	170	4	5	-0.18	32.57
Cat*	290	5	6	1.09	68.13
EA*	302	4	8	0.20	58.00

*GA : Gallic Acid, Cat : Catechin, EA : Ellagic Acid

ADMET Prediction Result

Table III.

GA compounds have a mucosa permeability value of 2.23, water solubility -2.56, human fraction unbound of 61.7%, negative against CYP2D6, and have an excretion rate of 3.30 ml / min. Cat compounds have a mucosa permeability value of 2.46, water solubility -3.117, human fraction unbound of 23.5%, negative against CYP2D6, and have an excretion rate of 1.52 ml / min. EA compounds have a mucosa permeability value of 2.48, water solubility -3.181, human fraction unbound of 8.3%, negative against CYP2D6, and have

Table III. ADME prediction results of the active compound of bitter bean peel waste extract.

	Administration	Distribution	Metabolism	Excretion
Compound	Water Solubility	Log K_{ow}	CYP2D6 substrate daninhibitor	Total clearance(ml/min)
GA*	-2.56	2.23	Negative	3.30
Cat*	-3.117	2.46	Negative	1.52
EA*	-3.181	2.48	Negative	3.44

*GA : Gallic Acid, Cat : Catechin, EA : Ellagic Acid

an excretion rate of 3.44 ml/min. Furthermore, GA compounds are negative for AMES toxicity, so they are considered not to cause genetic mutations, have a maximum dose threshold of 5,020 mg / kg body weight, lethal dose 2,218 mol / kg, and do not cause mucosal / skin irritation because they are negative for skin sensitization. Cat compounds are negative against AMES toxicity, so they are considered not to cause genetic mutations, have a maximum dose threshold of 2,740 mg / kg body weight, lethal dose 2,428 mol / kg, and do not cause mucosal / skin irritation because they are negative for skin sensitization. EA compounds are negative for AMES toxicity, so they are considered not to cause genetic mutations, have a maximum dose threshold of 2,990 mg / kg body weight, lethal dose 2,399 mol / kg, and do not cause mucosal / skin irritation because they are negative for skin sensitization.

Molecular Docking Test Results

Table IV.

The results of the molecular docking test determine the ability and anti- inflammatory potential of bitter bean peel waste extract compounds reviewed through their ability to inhibit COX-2 compared to comparison compounds. GA compounds in mode and RMSD 0 have binding affinity values of -3.4 kcal / mol, this value is not lower than celecoxib but lower than arachidonic acid. Cat compounds in mode and RMSD 0 have binding affinity values of -4.9 kcal/mol, this value is lower than celecoxib and arachidonic acid. EA compounds in mode and RMSD 0 have binding affinity values of -4.6 kcal / mol, this value is not lower than celecoxib but lower than arachidonic acid.

Table IV: Molecular docking test results of the active compound of PsEPE and comparator compound against COX-2 at the active site of the 371st peptide.

Target	Compounds	Binding affinity (kcal/ mol)	RMSD		
			Mode	Lower bound	Upper bound
COX-2 PDBID 5IKR	Gallic Acid	-3,4	0	0	0
	Catechin	-4.9	0	0	0
	Ellagic Acid	-4,6	0	0	0
	Celecoxib	-4,7	0	0	0

Visualization Results

Fig 1.

The visualization results of molecular docking tests between the test compound and the comparison compound against the target protein showed identical bond locations. This is indicated by the location of the compound binding to peptides in the COX-2 enzyme. The types of bonds formed include hydrogen bonds and van der waals bonds. The precise bond types and locations are described in the following table.

Table V.

The visualization results are attached in detail to the table

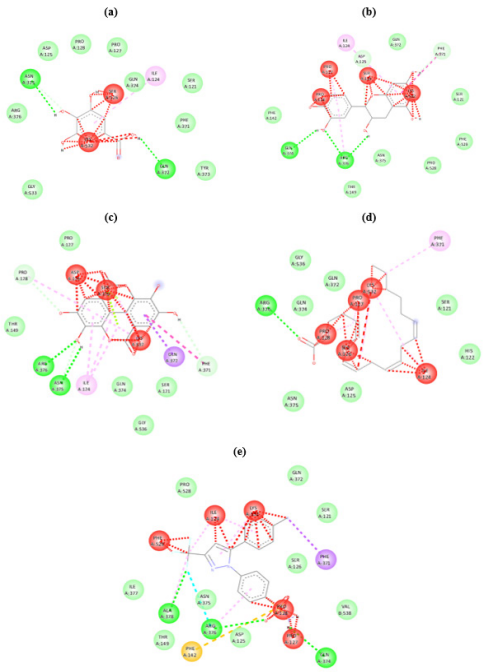

Fig 1 : The visualization results of the active compound of (Parkia speciosa). The bond formed between the active compound of PsEPE consisting of gallic acid (a), catechin (b), ellagic acid (c) and the comparator compound arachidonic acid (d) and celecoxib (e) against COX-2 at the active site of the 371st peptide. Different colors and lines indicate the formation of the type of bond between the test compound and the enzyme peptide. Light green indicates the formation of a van der Waals bond, dark green indicates the formation of conventional hydrogen bond, red indicates the formation of an unfavorable bump bond, dark purple indicates the formation of a pi-sigma bond, light purple indicates the formation of a pi-alkyl bond, yellow indicates the formation of a pi-sulfur bond, and pink indicates the formation of alkyl bonds.

Table V: The results of the type and location of the bonding between the active compound of PsEPE and the comparator compound on the active site of the 371st COX-2 peptide.

Protein Target	Compounds	Types and Locations of Bonding
COX-2 PDBID 5IKR	GA*	- Hydrogen Bonding: **ASN375**, GLN372 - Van der Waals Bonding: **ARG376**, ASP125,PRO128, PRO127,**GLN374**, SER121,PHE371, TYR373, GLY533
	Cat*	- Hydrogen Bonding: **GLN374**, **ARG376** - Van der Waals Bonding: PHE142, GLN372,SER121, PHE529, PRO528, **ASN375**, THR149
	EA*	- Hydrogen Bonding: **ARG376**, **ASN375** - Van der Waals Bonding: PRO127, SER121,GLY536, **GLN374**, THR149
	AA*	- Hydrogen Bonding: **ARG376** - Van der Waals Bonding: GLY536, GLN372,**GLN374**, SER121, HIS122, ASP125, **ASN375**
	Cele*	- Hydrogen Bonding: ALA378,**ARG376**, **GLN374** - Van der Waals Bonding: PRO528, GLN372,SER121, SER126, VAL538, ASP125, **ASN375**,THR149, ILE377

*GA: gallic acid, Cat: Catechin, EA: ellagic acid, AA: arachidonic acid, Cele: celecoxib

above so that it can find out the location of the same peptide bond between one compound and another. GA, Cat, EA, AA, and Cele compounds have the same peptide bond location, namely ASN375 (Asparagine 375), ARG376 (Arginine 376), and GLN374 (Glutamine 374).

Fig 2.
Test compounds and comparison compounds that have been simulated molecular docking are visualized simultaneously at the active site of COX-2 (peptide 371). The results showed that all five simulated compounds occupying at the same bonding location were shown with mutually superimposed structures in figure c.

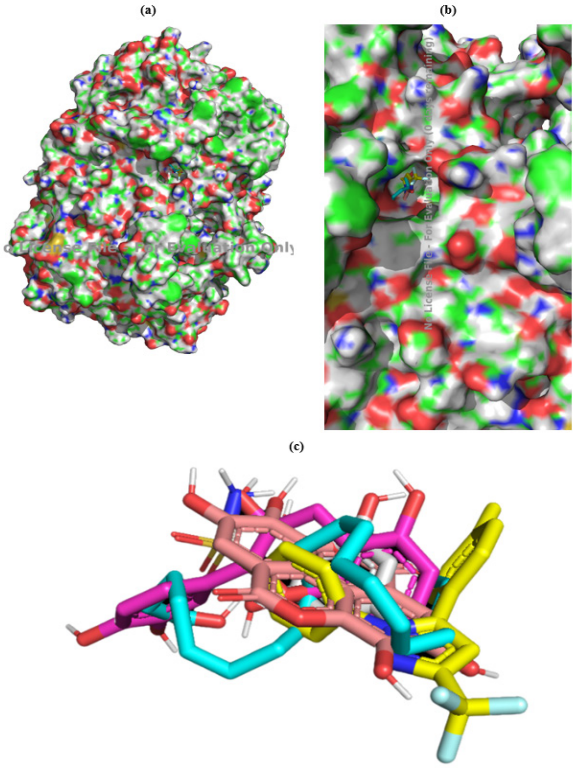

Figure 2 : Comprehensive visualization of the bond between the active compound of PsEPE and the comparator compound on the active site of the 371st peptide COX-2. Visualization run into 3 difference perspective such as full enzyme visibility (a), active site-specific visibility (b), and superimposed test ligand at active site (c)

DISCUSSION

Physicochemical Analysis

The PsEPE's major active compound (GA, EA, and Cat) is known to have been categorized in the drug-like category because it meets Lipinski's rules and is listed in table 2. These results show that these compounds can likely penetrate cell membranes due to their moderate molecular size. PsEPE's major active compound possesses favorable characteristics for passive diffusion to reach its target site efficiently according to the result of number of hydrogen bond donor and acceptor (26). A drug-like compound has specified characteristic of pharmacokinetics indicates that compounds with values below 5 (Log P) exhibit favorable polarity, enabling them to distribute through the bloodstream efficiently that facilitate dissolution and systemic circulation through the blood vessels. From the physicochemical test analysis also known the ability to maintain their bonding position with the target protein. The PsEPE's major active compound shows molar refractivity values of 68.13 and 58.01, ensuring its ability to uphold the bond with the target protein. However, GA compounds fall below the normal molar refractivity range at 32.57, suggesting that Cat and EA compounds may better maintain the strength and binding position with the target protein. Overall, based on the five physicochemical test parameters, all PsEPE's major active compound exhibit drug-like characteristics as they meet at least two predetermined criteria (27).

ADME Prediction Analysis

(Table III). ADME prediction plays an important role in determining whether the active compounds of bitter bean peel waste extract can be applied topically in orabase preparations. Judging from the administrative aspect, the active compound of bitter bean peel waste extract has water solubility values of - 2.56, -3.11, and -3.18 respectively. From the results of the administrative aspect, the active compound of bitter bean peel waste extract is able to dissolve in water solvents so that it can be circulated throughout the body where the majority

is composed of water and is easy to distribute. The next parameter is skin permeability. This parameter can indicate that a compound can be distributed topically through the skin. However, the mucosal structure in the oral cavity has a structure that is not the same as the histological structure of adnexal skin in general. In addition to its different histological structure, the density of the diameter of the pores of the oral mucosa (Log K_{ow} <0.5) has the narrowest pore diameter value compared to mucosal pores (Log K_{ow} ~0.5) or skin in general (Log K_{ow} ~0.7-0.8) [18].

Therefore a compound that can be predicted to diffuse passively to enter through the oral mucosa is a compound with a value of MW <300 Da. Compounds that have MW <300 Da (Log MW <2.48) have excellent hydrophilic properties and have an optimal Log P value of less than 5. The bitter bean peel waste extract compound has MW log values of 2.23, 2.46, and 2.48 respectively. This value is categorized as still included in the threshold range of MW log values, a compound that is able to penetrate the mucous membrane of the oral cavity. Thus, from the MW log value obtained from the bitter bean peel waste extract compound, it can be predicted that it can be applied in topical form of orabase [19].

Generally, all drug compounds consumed by humans will be bound by plasma proteins in the blood which will later form an inactive formation called drug plasma binding protein. The greater the FU value or the closer to 1, the more drug fractions that are active and can be distributed to the target so that they can cause pharmacological and therapeutic effects. From the results of pharmacokinetic analysis of FU, as many as 61.7% of gallic acid compound partitions, 23.5% of catechin compounds, and 8.3% of ellagic acid compound partitions are predicted to be active compounds and able to cause pharmacological responses [20].

Normally the body will metabolize drugs that enter the body through xenobiotic metabolic mechanisms. The three *Parkia speciosa* compounds (gallic acid, catechin, and ellagic acid) have negative values against CYP2D6 which means that these active compounds are predicted not to interfere with xenobiotic metabolism and interact with other drugs. The last parameter is excretion. Through prediction pkCSM is also able to predict the rate of excretion of active compounds absorbed by the body. Based on data obtained from the database, gallic acid, catechin, and ellagic acid compounds will be excreted from the body through urine with successive excretion rates of 3.3, 1.52, and 3.44 ml/minute [11].

Toxicity Test Analysis

From the results of pkCSM analysis regarding toxicity aspects (Table IV), it was found that the three active compounds of Parkia speciosa gave negative results for AMES toxicity. AMES toxicity is a state of cellular mutation caused by the activity of chemicals in the body. If a compound is said to be positive for AMES toxicity, then the compound when consumed and in the body will be a mutation factor and trigger mutations (Marnett, 2019). Dose is the quantity of a compound that researchers use to become a drug and will eventually be consumed by humans. The benefit of knowing the dosage threshold is to determine the therapeutic dose of a drug compound so that it does not become a toxic dose for the body. The three *Parkia speciosa* compounds showed maximum tolerated dose values of 5.020, 2.740, 2.990 mg/kgBB, respectively. From this information, it will be able to be the basis for determining therapeutic doses, drug use doses, and lethal doses before in vitro and in vivo analysis [21].

PASS Prediction Analysis

Biological activity is qualitatively considered as active or inactive in the PASS program. The results of the PASS prediction are presented as a ranking list of various biological activities with calculated probabilities Pa ("active") and Pi ("becoming inactive"). The following are the predicted results of PASS compounds in *Parkia speciosa* (Gallic Acid (GA), Catechin, and Ellagic Acid (EA)), and celecoxib mapped as anti- inflammatory in table I [11,12].

Based on PASS prediction result (Table I), gallic acid, catechin, and celecoxib compounds have a Pa value of 0.5<Pa<0.7 with a value of Pa>Pi as an anti-inflammatory compound. The Pa values of gallic acid and catechins are 0.548 and 0.548 respectively. While ellagic acid compounds have a Pa>0.7 and Pa>Pi values of 0.749 which indicates that ellagic acid compounds have a high chance of being active as anti- inflammatory (Table I). This shows that compounds in Parkia speciosa have the potential to be active as anti-inflammatory compounds with the greatest chance of active compounds being ellagic acid, gallic acid, and catechins [12].

Molecular Docking Test Analysis

Based on the results of molecular docking tests results (Table V), gallic acid compounds, catechins, and Ellagic acid extracts of bitter bean peel waste have good anti-inflammatory abilities. Gallic acid, catechin, and ellagic acid compounds have lower affinity binding values than celecoxib and arachidonic acid. Gallic acid, catechin, ellagic acid compounds require successive bond energies of -3.4; -4.9 and -4.6 kcal/mol. This value reflects that the compounds contained in bitter bean peel waste extract are able to become anti- inflammatory agents because they are able to block the formation of bonds between the native ligand of arachidonic acid to the active site of COX-2. In the other hand, binding affinity value of bitter bean peel compounds with celecoxib is equally negative, but the affinity values of celecoxib tend to be lower in almost all groups than the affinity of gallic acid and ellagic acid compounds. This does not indicate that GA and Ea compounds do not have

good anti-inflammatory abilities, but this deviation in affinity values indicates that GA and EA compounds are predicted to have a low binding ability below celecoxib [22].

Docking Visualization Analysis

Based on the results of molecular docking test visualization, gallic acid, catechin, and ellagic acid compounds of bitter bean peel waste extract have similar molecular activity with comparison compounds because of the location of the identical binding to peptides in the COX-2 enzyme so that it has good anti- inflammatory abilities (Figure 3). Test and comparison compounds/ ligand have the same bond location, namely ASN375 (Asparagine 375), ARG376 (Arginine 376), and GLN374 (Glutamine 374) and superimpose on the same orbital bag (Figure 2 and 3). The location of the same bond indicates similar bound proteins so that the value of bond affinity and mode interaction is not much different. The same binding location and low binding affinity of the test compound also indicate its ability to be a competitive inhibitor of the COX-2 peptide. The bond of the test compound on COX-2 peptide consists of 2 types of bonds, namely strong hydrogen bonds and weak van der walls (Table VI). Gallic acid has 1 hydrogen bond, while catechins and ellagic acids have 2 hydrogen bonds. The number of hydrogen bonds is aligned with the binding affinity value of the test compound, where catechins with the lowest binding affinity value have 2 hydrogen bonds, while gallic acid with a large binding affinity value only has 1 hydrogen bond and higher energy to binding (Table VI) [8–10].

CONCLUSION

Flavonoid compounds of bitter bean peel waste extract has the potential as an anti-inflammatory for orabase because it has good inhibition against COX- also predicted to be able to be distributed topically orally As a suggestion, further studies are needed in vitro and in vivo studies that specifically determine the anti-inflammatory ability of bitter bean peel waste extract where information can be taken from this study.

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