AESCULAPIUS MEDICAL JOURNAL

e-Journal **Aesculapius Medical Journal**
Vol. 6 No. 1 | Februari | 2026 | Hal. 273 – 283
E ISSN: 2808-6848
ISSN: 2829-0712

Terbit: 28/02/2026

The Potential of MIPGLE (Microencapsulation of *Psidium guajava* Leaf Extract) as a Natural Medicine for Tuberculosis

I Putu Anda Tresna Dananta[1*], Putu Prajata Vistara Putera[1]

Medical, Ganesha University Of Education, Bali, Indonesia

**Email: anda.tresna@student.undiksha.ac.id*

Abstract

Tuberculosis is an infectious disease caused by the bacterium Mycobacterium tuberculosis. Tuberculosis is one of the 10 diseases that cause the largest number of deaths in the world. Therefore, strategic steps to treat Tuberculosis are very necessary. One effort that can be made as an alternative treatment for Tuberculosis patients is the administration of natural medicine. Natural medicines can be produced through the use of natural ingredients such as guava leaves. Guava leaves contain antibacterial compounds, namely chalcone (flavonoid). This research is an experimental study intended to analyze the potential of chalcone in microencapsulation of Psidium guajava leaves extract as a natural medicine for tuberculosis in silico. The research results showed that microencapsulation phytochemistry showed positive results for flavonoid, tannin, phenol and saponin compounds with flavonoid levels of 201.513 mg/100mg QE. The SEM test results show that the Psidium guajava extract has been encapsulated in the maltodextrin-gelatine coating well and has a particle size of 115.442 µm. This research proven that chalcone has potential as an antibacterial agent through the results of PASS analysis with Pa of 0.284. chalcone with a single dose of drug 1048 mg/kg is known to be feasible as a drug substance with proven feasibility in various pharmaceutical aspects and 4th toxicity shows a low level of toxic impact to the body if this microencapsulation is consumed orally.

Keywords: *Microencapsulation, Natural Medicine, Psidium guajava, Tuberculosis*

Abstract

Tuberkulosis adalah penyakit infeksi yang disebabkan oleh bakteri Mycobacterium tuberculosis. Tuberkulosis merupakan salah satu dari 10 penyakit dengan angka kematian tertinggi di dunia. Oleh karena itu, langkah strategis dalam penanganan Tuberkulosis sangat diperlukan. Salah satu upaya yang dapat dilakukan sebagai pengobatan alternatif bagi pasien Tuberkulosis adalah pemberian obat alami. Obat alami dapat diproduksi melalui pemanfaatan bahan alam seperti daun jambu biji. Daun jambu biji mengandung senyawa antibakteri yaitu kalkon (flavonoid). Penelitian ini merupakan studi eksperimental yang bertujuan untuk menganalisis potensi kalkon dalam mikroenkapsulasi ekstrak daun Psidium guajava sebagai obat alami untuk Tuberkulosis secara in silico. Hasil penelitian menunjukkan bahwa fitokimia mikroenkapsulasi memberikan hasil positif terhadap senyawa flavonoid, tanin, fenol, dan saponin dengan kadar flavonoid sebesar 201,513 mg/100 mg QE. Hasil uji SEM menunjukkan bahwa ekstrak Psidium guajava telah terenkapsulasi dengan baik dalam lapisan maltodekstrin-gelatin dan memiliki ukuran partikel sebesar 115,442 µm. Penelitian ini membuktikan bahwa kalkon berpotensi sebagai agen antibakteri berdasarkan hasil analisis PASS dengan nilai Pa sebesar 0,284. Kalkon dengan dosis tunggal 1048 mg/kg diketahui layak sebagai bahan obat dengan kelayakan yang terbukti dalam berbagai aspek farmasi, serta uji toksisitas tingkat 4 menunjukkan tingkat dampak toksik yang rendah terhadap tubuh apabila mikroenkapsulasi ini dikonsumsi secara oral.

Kata kunci: *Mikroenkapsulasi, Obat Alami, Psidium guajava, Tuberkulosis.*

INTRODUCTION

Tuberculosis is an infectious disease caused by the bacterium *Mycobacterium tuberculosis*. There are several species of *Mycobacterium*, including *M. tuberculosis, M. africanum, M. bovis, M. Leprae* etc. Which is also known as Acid-Fast Bacteria (AFB). Tuberculosis mainly affects the lungs, making pulmonary disease the most common presentation, infection with the *Mycobacterium tuberculosis* causes inflammation of the lung parenchymal tissue, which is characterized by continuous coughing with phlegm, fever, shortness of breath, chest pain, and many more [1, 2, 3].

Tuberculosis is one of the 10 diseases that cause the largest number of deaths in the world. Based on the 2019 Global tuberculosis Report, the morbidity rate for tuberculosis in 2018 reached 10,000,000 people. Meanwhile, cases of tuberculosis deaths reached 1,500,000 people. Globally, an estimated 10 million (range 8.9 - 11 million) people fell ill with tuberculosis in 2019. Eight countries accounted for two-thirds of the global total: India (26%), Indonesia (8.5%), China (8.4%), Philippines (6.0%), Pakistan (5.7%), Nigeria (4.4%), Bangladesh (3.6%) and South Africa (3.6%) [4].

The usual therapeutic approach to tuberculosis is by giving multiple types of drugs such as Isoniazid (H), para-amino salicylic acid (PAS), Streptomycin (S), Ethambutol (E), Rifampicin (R) and Pyrazinamide (P). The treatment of Tuberculosis consists of 2 steps including initial stage and advanced stage. The initial stage consists of administering medication every day under direct supervision to prevent drug resistance, which if administered correctly, the patient becomes non- infectious within 2 weeks and the conversion of positive AFB TB blood to negative within 2 months. In the advanced stages, patients receive fewer types of medication, but over a longer period of time, in the advanced stages it is important to kill persistent germs thereby preventing recurrence [5].

This usual approach to Tuberculosis is cumbersome, because of the poor, expensive, less- effective, and toxic alternatives to the first-line drugs. Not only that, excessive use of conventional chemical medicine can have side effects for the patients such as unexplained loss of appetite, nausea or vomiting, brown urine, or jaundice (yellowing of skin or eyes), persistent tingling, numbness, or burning of hands or feet, persistent weakness, fatigue, fever, or abdominal tenderness, easy bruising or bleeding, and blurred vision or changed vision [6,7].

Apart from conventional treatment with medical drugs, tuberculosis can also be treated with natural alternative medicines using bioactive compounds derived from plant parts, one of which comes from the *Psidium guajava* plant. *Psidium guajava* is a plant that is easily found in Indonesia, especially on the island of Bali. However, the part of this plant that is often used is only the fruit, compared to the leaves of this plant which generally have many useful bioactive compounds. *Psidium guajava* leaves have various potentials, including being anti-bacterial, anti-inflammatory and anti- oxidant. This potential comes from the bioactive compounds contained therein. One of the compounds contained in many *Psidium guajava* leaves is chalcone [8].

Chalcone compounds and their derivatives are one of the natural substances that possess numerous pharmacological activities, including antibacterial, anti-inflammatory, antimalarial, anticancer, antifungal, and antioxidant properties. In addition to having various pharmacological activities, chalcone compounds also serve as precursors for the biosynthesis of flavonoids and iso flavonoids [9]. The chalcone compound has α, β unsaturated ketone groups which act as antibacterials because they can damage bacterial cell walls. The presence of hydroxyl groups also plays an active role in inhibiting bacterial growth [10].

Based on the description above, the researcher wants to know the potential of microencapsulation of *Psidium guajava*

leaf extract as a natural medicine for tuberculosis by in-silico method.

METHOD

Types, Time, and Location Research

This research uses experimental research methods using an in-silico approach or calculations using computing technology that produces quantitative data. This research will start from 12 November 2024 to 03 January 2025 in several places. Experiments were carried out in the Biomedical Laboratory of Undiksha, the MERO Foundation Chemistry Laboratory, and Laboratory of Basic Sciences, Faculty of Agriculture, Warmadewa University, Denpasar. Meanwhile, in- silico analysis was carried out in the Computer Laboratory of Undiksha.

Several variables were analyzed in this research. The independent variable in this study was microcapsules based on guava leaves extract (*Psidium guajava).* The dependent variable in this research is the potential and effectiveness of guava leaves extract (*Psidium guajava)* in microcapsule form as an alternative therapy for tuberculosis. The control variable in this study was guava leaves (*Psidium guajava).*

Research Materials and Tools

The materials needed in this research are guava leaves (*Psidium guajava),* maltodextrin, gelatine, and organic solvents. The tools needed to carry out this research experiment are; blender, beaker, scale, stir bar, thermometer, filter paper, medical gloves, 40 mesh and 30 mesh filter, oven, petri dish, glass funnel, and capsules.

Experiment

Guava leaves (*Psidium guajava)* that have been picked are followed by a washing process and then blanched in boiling water at a temperature of 100°C for ± 3 minutes. Then drained and dried in the sun until dry. After it dries, it will continue with the extraction of guava leaves (*Psidium guajava).* The guava leaves are blended to produce a coarse powder which is then filtered using a 30-mesh sieve and followed by filtration using a 40-mesh sieve to produce finer guava leaves powder. From the guava leaves powder that has been obtained, proceed with boiling the guava leaves powder in a dose of 2 grams and 200 ml of water at a temperature of 70° C. After that, the powder is filtered using a paper filter which aims to filter out any remaining lumps so that the liquid does not leave any remaining lumps so the guava leaves extract (*Psidium guajava)* are free from lumps.

The process continues by dissolving maltodextrin and gelatine with guava leaves extract (*Psidium guajava*). The ratio of maltodextrin to gelatine is 2:1, the amount of maltodextrin and gelatin mixture is 10% of the extract (10 grams) and the amount of guava leaves extract (*Psidium guajava)* is 100 ml. After that, dissolve the mixture for approximately 30 minutes until the solution is mixed. The mixed maltodextrin, gelatin, and guava leaves extract solution is poured into a petri dish with a thickness of 3 mm. Followed by drying at 50°C until the solution dries and is sieved and filtered using a 40-mesh sieve until it becomes a fine powder which will be put into capsules.

The resulting microencapsulation was then subjected to phytochemical testing and determination of flavonoid levels at the Basic Sciences Laboratory, Faculty of Agriculture, Warmadewa University, Denpasar. Apart from that, encapsulation morphology tests were also carried out using SEM (Scanning Electron Microscope at the MERO Foundation Chemistry Laboratory.

Data Processing Methods

The data obtained from the test results are quantitative data through a series of in-silico computational processes. First, the researchers determined the structure of compounds used in tuberculosis treatment using PubChem software. Second, the active potential of the compounds contained in *Psidium guajava* with ideal conditions (Potential active (Pa) > 0.1) was

predicted through Way2Drug software. The third process is target protein analysis by several software (PharmMapper, SuperPred, and Swiss Target Prediction) with the largest percentage role in tuberculosis therapy. Fourth, after selecting a protein that plays the biggest role, the target protein will be modelled in 3 dimensions through Swiss-Model software. Furthermore, researchers validated the structure of the compound using ERRAT graphic processing by Saves Webserver 6.0. Fifth, stereochemical properties of target protein were evaluated through the Ramachandran plot by Saves Webserver 6.0. Sixth, carried out molecular docking between ligand and macromolecule using PyRx and visualized with PyMol. Seventh, the docking results are converted in a two-dimensional form to determine the interactions between the amino acids and their residues through the ProteinPlus webserver. Eighth, Swiss-ADME webserver is used to analyze drug similarity, pharmacochemical, and physicochemical. Last step is Toxicity test of drug candidates for tuberculosis therapy using ProTox software.

RESULTS AND DISCUSSION

Phytochemical Tests

From the phytochemical tests that we have carried out, we obtained data indicating that the encapsulation of *Psidium guajava* leaves contains polyphenolic substances with the majority being positive value (+), including flavonoid

Numbers	Parameters	Results
1	Alkaloids	-
2	Flavonoids	+
3	Tannin	+
4	Phenol	+
5	Steroids	-
6	Terpenoids	-
7	Saponin	+

Figure 1. Table Results of microencapsulated phytochemical tests on guava leaves

From the test results in Basic Sciences Laboratory, Faculty of Agriculture, Warmadewa University, Denpasar obtained flavonoid content in microencapsulation amounting to 201,513 mg/100mg QE.

One of the derivatives of flavonoid compounds is chalcone which is found in guava leaves extract (*Psidium guajava*). This compound has functions as antibacterial, anti-inflammatory, and antioxidant [9].

SEM Test Results

From the SEM tests that we have carried out, we obtained an average length of 115.442 μm where this result corresponds to the ideal size of microencapsulation particles which range is 5-5000 μm [10].

Below is the image from the SEM Test with 50x magnification (cropped).

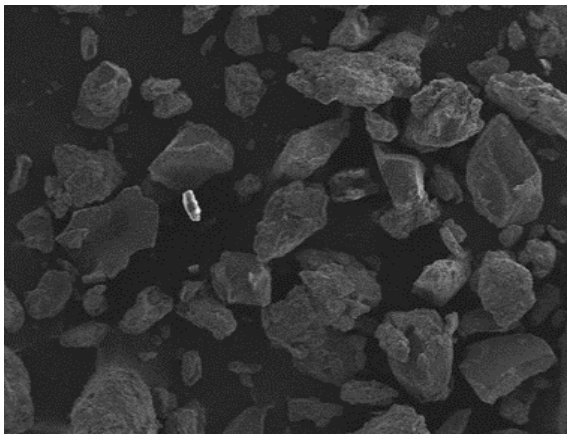


Figure 2. Visualization of microencapsulation of guava leaves extract

Morphological visualization of the encapsulation of guava leaf extract can be seen in Figure 3 below.

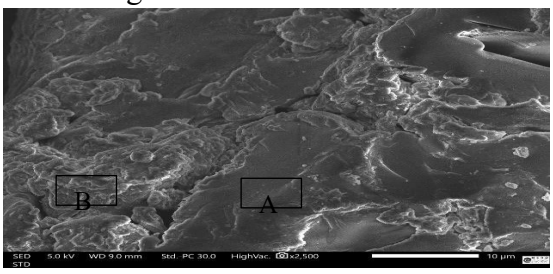


Figure 3. (A) Smooth microencapsulation surface morphology areas; (B) Areas of rough microencapsulation surface morphology

Figure 3 shows that there are smooth and rough surfaces on the microencapsulation of guava leaves extract. Results of Scanning Electron Microscope shows that guava leaves extract was successfully encapsulated in the maltodextrin-gelatine coating well.

Structural Formula

Structure of the active compounds in *Psidium guajava* leaves was obtained through PubChem website The resulting output structure is a conversion of the molecular formula of the compound which is adjusted again using the Canonical SMILES (Simplified Molecular Input Line Entry System).

Chalcone has a molecular formula C15H12O. With the result of Canonical SMILES C1=CC=C(C=C1)C=CC(=O) C2=CC=CC=C2. Therefore, the output structure of the compound obtained is.

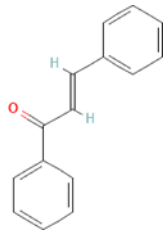


Figure 4. Chalcone structure

Potency of Active Compounds

This analysis used the website 'Way2drug'. This website is a spectrum analyzer of the biological activity of a chemical compound that uses the PASS (Prediction of Activity Spectra for Substances) software base for predictions of various types of biological activity based on the structure of organic compounds. The output that will show in this analysis is a table listing activities that can be produced by chemical compounds, with details of Pa (activation potential) and Pi (inactivation potential). The main indicator of the activity of a compound is when Pa>Pi Biological activity in chalcone compounds that have an important role in tuberculosis therapy including antioxidants, anti-inflammatory, antibacterial and membrane permeability inhibitor.

The Following table is Pa and Pi results from each biological activity of chalcone compounds based on PASS analysis.

Determining Protein Targets

Activity	Pa	Pi
Membrane permeability inhibitor	0.695	0.041
Anti-inflammatory	0.676	0.019
Antioxidants	0.421	0.010

Figure 5. Table PASS Analysis Results

The determination of the target protein required three stages of intensive analysis through several softwares. The results of the three analyzes will then be compared simultaneously to create a 'Protein Mapping', in which the mapping results are the elimination of several target proteins that do play a role in tuberculosis therapy.

First, we used PhamMapper software, it is a server designed to identify candidate protein targets through newly discovered molecules contained in drugs, natural products, or other compounds with unidentified binding targets, with a pharmacophore mapping approach.

Second, we used Swiss-Target software, it is a server that analyzes the prediction of the most likely macromolecular target of a small molecule, which is assumed to be bioactive. In this analysis, the researcher narrows the species object down to Homo sapiens only.

Third, we used SuperPred software, it is a prediction server for ATC codes and compound targets. The Anatomical Therapeutic Chemical (ATC) classification system is used for the classification of drugs published by WHO. This classification is based on the therapeutic and chemical characteristics of a drug.

The following is a table of results from some of the target protein predictions.+

The following results show some of target protein predictions. To decide

which will be used as target protein, the data from PharmMapper, Swiss- Target and

Target	Common names	Uniprot ID	ChEMBL ID	Target Class
Nitric oxide synthase, inducible (by homology)	NOS2	P35228	CHEMBL 4481	Oxidoreductase
MAP kinase p38 alpha	MAPK14	Q16539	CHEMBL 260	Oxidoreductase
Monoamine oxidase B	MAOB	P27338	CHEMBL 2039	Enzymes
Monoamine oxidase A	MAOA	P21397	CHEMBL 1951	Enzymes
Epidermal growth factor receptor erbB1	EGFR	P00533	CHEMBL 203	Kinase

Figure 6. Table List of Target Proteins in Chalcone

SuperPred will go through String-DB to create the 'Protein Mapping' to show the interaction between many of possible protein predictions and to eliminate the target protein that do not play role in tuberculosis theraphy. In String-DB software, all of the protein predictions will be inputed to show the interactions between the proteins, in this step we also choose the tuberculosis KEGG Pathways to narrow down the possibilities. The following image is showing multiple proteins that are involved in tuberculosis treatment. Red circle indicates protein that involved in tuberculosis KEGG Pathways.

Based on the image, the best protein target for chalcone is *Nitric oxide synthase, inducible* which has the common name NOS2 with the code UniProt P35228, so this compound is a target protein obtained from the conversion of chalcone.

Figure 7. KEGG Pathways of target proteins

Validation of Structures of Compounds

Validation structure of target protein was carried out using ERRAT graphic. ERRAT is a webserver to verify the protein structure determined by crystallography. Error values are plotted as a function of positions closing 9-residue window. Function error based on the interaction statistics of the non-bonded atoms in the protein structure listed. At this step, it requires the help of 'Saves Webserver version 6.0' so that the ERRAT graphical output can be calculated properly. 3D modeling of protein target *Nitric oxide synthase* (NOS2) which has been saved with the .pdb file type (specifically for protein) is processed using a C++ program, so the following results are obtained.

The figure above is an ERRAT graph which shows the overall quality factor of the NOS2 protein is 92.740% this

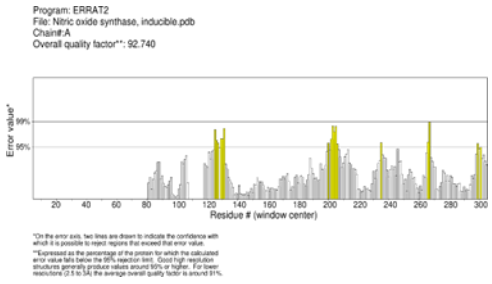


Figure 8. ERRAT graphic *Nitric oxide synthase*

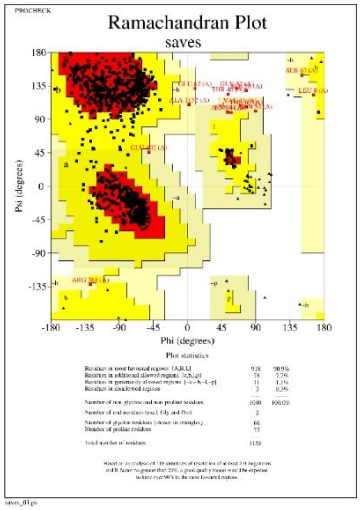
indicates a very high protein potential in terms of the possible error value of less than 5%.

Evaluation of Stereochemical Properties

Stereochemical properties evaluation of the model was carried out using a webserver namely 'Saves Webserver version 6.0' but with special software in the form of Procheck through analysis of

the 6 Ramachandran plot. The Ramachandran plot is a two-dimensional plot that depicts amino acid residues. Inside there is a corner phi as the X axis and psi as the Y axis. The combined output of the two angle references is used as a basis for assessing the stereochemical quality of a protein or enzyme model. The assessment is adjusted to the percentage of amino acid residues that are in the highly favored region (most favored regions) and prohibited areas (disallowed regions) of the Ramachandran plot.

Here is the result of the Ramachandran plot of protein *Nitric oxide synthase*, inducible.



The figure 9 shows a map of the distribution of amino acid residues from the *Nitric oxide synthase*, inducible protein.

Figure 9. Ramachandran plot of *Nitric oxidesynthase*

The distribution of the residue forms white to red areas. The white area is the disallowed region, while the red area is the most favored region. It is known that there is 90.9% deposit in the most favored region and 0.3% deposit in the disallowed region. This shows that the protein model used is of good quality.

Molecular Docking

Molecular docking is computational simulation using genetic-based methods that can be used to show the patterns of interaction between two molecules, natural compounds or ligands and receptors or proteins by attaching a small molecule (ligand) to the active side of the receptor.

This analysis was done by 'PyMol' software to predict the interactions between alpha-helix with beta-sheet from the selected target protein. After getting the output from 'PyMol', the next step is docking using the 'PyRx' software. This software will minimize chalcone as a ligand, then the program will process the chalcone comparison using the Python module. Output from executing compiler will show a table of Binding affinity, RMSD lower bound, and RMSD upper bound. Here are the results of molecular docking among the active compounds of chalcone that have decreased with target proteins *Nitric oxide synthase*, inducible.

The lower binding affinity value indicates that the interaction between the ligand and the protein receptor is more stable. The RMSD value <2.0 indicates that the calculation is more accurate and

Ligand	Binding Affinity	RSMD Lower Bound	RSMD Upper Bound
NOS2_chalcone	-7.2	0.0	0.0
NOS2_chalcone	-7.0	1,533	2,237
NOS2_chalcone	-6.7	2.359	3.266

Figure 10. Table Results of Molecular Docking

the resulting error is less occurs, so that the molecular docking in this research was successful, as proven by the smallest binding affinity value, which is -7.2 and both RMSD values are 0.0.

Visualization of Molecular Docking

Three-dimensional visualization that describes the interaction between the ligand and the target protein is obtained from 'PyMol' software. Meanwhile the two dimensional one is from 'ProteinPlus' webserver, it contains sub-software 'PoseView' to analyze the interaction lines between the results of molecular docking with amino acids and their residues.

Figure 11. Structure of *Nitric oxide synthase*

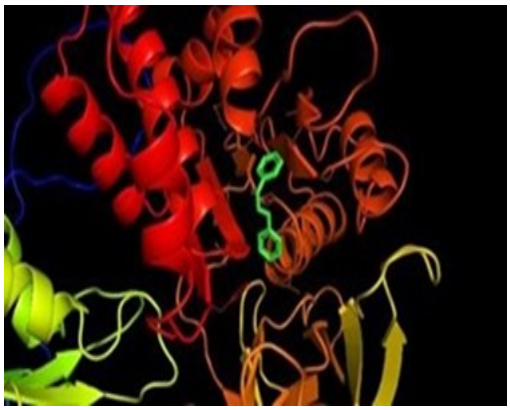


Figure 12. Visualization of ligands (Chalcone)

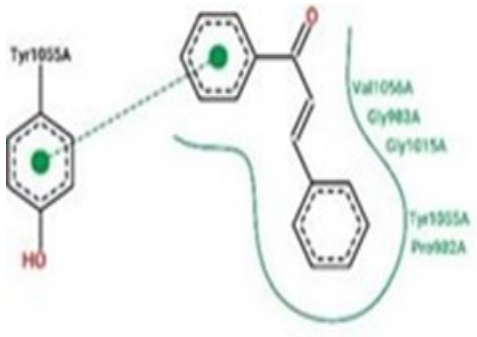


Figure 13. Two-dimensional visualization of molecular docking

From the interactions above, it can be seen that some of the amino acids formed include essential amino acids in the form of Valine (Val1056A), and conditionally non-essential amino acids in the form of Glycine (Gly983A and Gly1015A), Tyrosine (Tyr1055A) and Proline (Pro982A).

Analysis of Drug Similarity, Pharmacochemical, and Physicochemical

Evaluation of drug candidates is generally carried out through analysis of similarity properties with absorption profiles and similarity to drug (drug likeness), distribution, metabolism, and excretion (ADME). This analysis was performed with the 'Swiss-ADME' webserver where the output panel will list all the values in the ADME parameters. Graphic output (Bioavailability Radar) includes all molecules submitted in BOILED-Egg plots and executed with enhanced CADD tasks to estimate gastrointestinal uptake and global brain penetration, they are two main aspects of ADME affecting pharmacokinetics.

Aspect	Sub-aspect	Ideal Value
Physicochemical	Molecular weight	≤ 500
	Num. H-bond acceptors	≤ 10
	Num. H-bond donors	≤ 5
Lipophilicity	iLOGP	≤ 4.15

Figure 14. Table Lipinski Rules (Rule of Five)

Evaluation of drug-like properties is generally carried out according to the Lipinski rule (rule of five) where predictions of ADME can provide information regarding oral bioavailability, cell permease, metabolism, and elimination which are the pharmacokinetic and pharmacodynamic characteristics of a drug molecule. The table above is a detail of Lipinski's rules.

Results of Bioavailability Radar accompanied by a table sections one-panel-per-molecule output (Physicochemical Properties, Lipophilicity, Pharmacokinetics, 8 Drug Likeness and Medicinal Chemistry) of chalcone compounds:

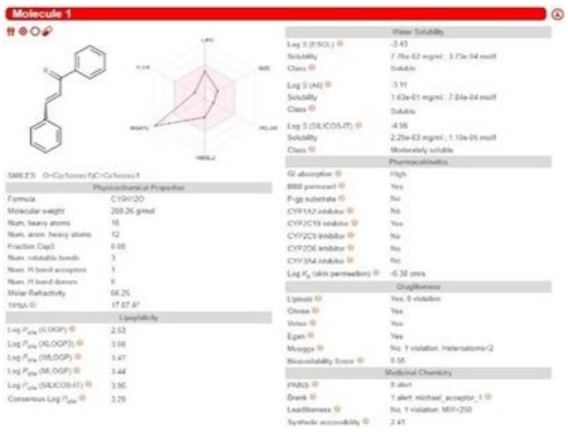


Figure 15. Section one-panel-per-molecule output

According to the Lipinski rule, the chalcone compound fulfills all the criteria. Molecular weight is 208.26 g/mol, Num. H -bond acceptors are worth 1, Num. H-bond donors are worth 0, and iLOGP is worth 2.53. Because the drug is in capsule form, there are several other criteria that must be met. In the Water Solubility aspect, all classes must show a 'Soluble' or easily soluble output. GI (Gastrointestinal) Absorption in Pharmacokinetics must show a 'High' output. Synthetic Accessibility in the Medicinal Chemistry close to number 1. The three specific criteria for oral drugs have been fully met starting from the output 'Soluble to moderately soluble' on Water Solubility, 'High' on GI (Gastrointestinal) Absorption, and a score of 2.41 on Synthetic accessibility.

From Figure 15, in the Drug likeness aspect, chalcone meets Lipinski, Ghoses, Veber, Egan, but does not meet Muegge's rules. The chalcone compound meets the Ghoses rule with the criteria for atomic number 20-70, molecular weight 160-480, refractivity 40-130, WLogP -0.4 to 5.6, Veber's rule with rotatable bonds criteria less than 10, TPSA value less than 140, Egan's rule with WLogP criteria less than 5.88, TPSA value less than 131.6. Apart from the drug likeness aspect, the pharmacokinetics aspect of cytochrome P450 isoforms (CYP1A2/CYP2C19/ CYP2C9/CYP2D6/CYP3A4) is a group of enzymes that are important in detoxification through xenobiotic oxidation. Chalcone does not act as a substrate or inhibitor of CYP1A2, CYP2C9, CYP2D6, CYP3A4 isoforms. So it does not affect metabolism and does not cause contraindications.

Toxicity Test of Drug Candidates

A toxicity test is needed to determine the level of toxic effect on the compounds contained in the drug preparation when taken orally. Toxicity prediction was obtained through analysis of the Protox-II webserver which is computer-based model adjusted for real data (in vitro or in vivo) to predict the toxic potential of the included compounds. The resulting output is a toxicity level prediction scheme such as oral toxicity (acute rodent toxicity), organ toxicity (hepatotoxicity), toxicological endpoints (such as mutagenicity, carcinogenicity, cytotoxicity, and immunotoxicity of B cell growth inhibition), toxicological pathways (AOPs) and toxicity targets (Novartis off-target) thereby providing insight into the possible molecular mechanisms behind such toxic responses.

The following is a schematic and detailed prediction of the toxicity of chalcone compounds in microcapsule drug candidates.

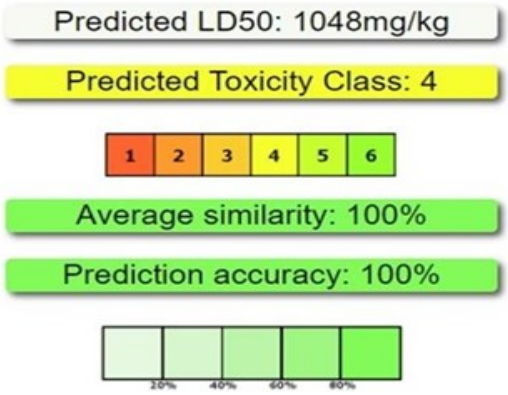


Figure 16. Results of LD50 and toxicity class

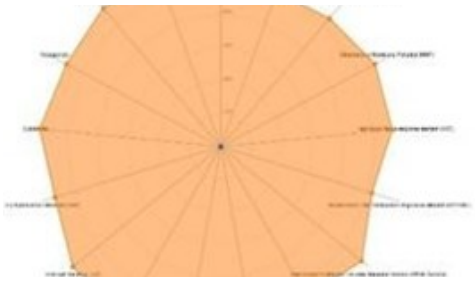


Figure 17. Scheme of the toxicity prediction from chalcone compounds

Classification	Target	Shorthand	Predictions
Organ toxicity	Hepatotoxicity	dili	Inactive
Toxicity end points	Carcinogenicity	carcino	Inactive
Toxicity end points	Immunotoxicity	immuno	Inactive
Toxicity end points	Mutagenicity	mutagen	Inactive
Toxicity end points	Cytotoxicity	cyto	Inactive

Figure 18. Table detailed table indicators of the toxicity prediction

The results of the analysis showed that a single drug dose (LD50) was at 1048 mg/ kg, which means that the toxicity level of the drug candidate is in class 4 (safe), but has a small potential to cause respiratory or skin sensitization. The 'Inactive' criterion is proven in the results of the analysis, meaning that the chalcone compound in the microcapsules capsules does not cause toxic side effects to the body when consumed orally.

CONCLUSION

Based on the tests that have been carried out, it was concluded that the chalcone content in *Psidium guajava* leaves has potential as an alternative treatment for tuberculosis. Chalcone has potential as an antibacterial, anti-inflammatory, antioxidant and membrane permeability inhibitor properties with an active potential that is higher than its inactive potential. Chalcone with a single dose of the drug 1048 mg/kg is known to be feasible as a drug substance with proven feasibility in various pharmaceutical aspects and a low level of toxicity to the body. It means that, microcapsules based on guava (*Psidium guajava*) leaves extract have a relatively great potential when applied in tuberculosis therapy orally.

ACKNOWLEDGMENTS

First of all, we express our gratitude to God Almighty, for His blessings and grace that have enabled us to complete this research successfully. Secondly, we extend our heartfelt thanks to our parents. Without their support, motivation, and advice, this research would not have been successfully carried out. Thirdly, we express our deepest gratitude to our supervisor for the invaluable guidance and support in completing this research. Lastly, we would like to extend our sincere thanks to BSO Hermestha FK Undiksha, the Merofoundation Chemistry Laboratory, and the Basic Sciences Laboratory of the Faculty of Agriculture, Warmadewa University Denpasar. Without their assistance and guidance, this research would not have been completed.

REFERENCES

[1] P. D. d. I. K. K. R. Indonesia, “Infodatin Tuberkolosis 2018,” Kementrian Kesehatan Republik Indonesia, Jakarta, 2018.

[2] R. Adigun and R. Sing, "Tuberculosis," in *StatPearls*, StatPearls Publishing, 2023.

[3] A. N. Ramadiani and H. H. Rahmania, "SISTEM PAKAR PENDIAGNOSA PENYAKIT TUBERKULOSIS," *Jurnal Informatika Mulawarman,* vol. 12, no. 1, pp. 57-63, 2017.

[4] W. H. Organization, "Global tuberculosis report 2020," Global tuberculosis report 2020, Geneva, 2020.

[5] N. K. Suari Melinda, "Hubungan Kualitas Fisik Rumah dengan Kejadian TUBERCULOSISC Paru di Wilayah Kerja Puskesmas I Denpasar Selatan Tahun 2018," *Poltekkes Denpasar Repository,* pp. 12-13, 2018.

[6] R. C. L. D. G. B. M. Giovanni Sotgiu., "Tuberculosis Treatment and Drug Regimens," *Cold Spring Harb Perspect Med,* vol. V, no. 5, 2015.

[7] C. f. D. C. a. Prevention, "Adverse Events During Treatment of Tuberculosis," Centers for Disease Control and Prevention, [Online]. Available: https://www.cdc.gov/tuberculosis/topic/treatment/adverseevents.htm [Accessed 1 December 2024].

[8] D. H. J. Y. L. M. K. Z. Y. C. Yuanxin Qiu., "Kaempferol separated from Camellia oleifera meal by high-speed countercurrent chromatography for antibacterial application," European Food Research and Technology, no. 246, p. 2383–2397, 2020.

[9] W. Sepvianti and S. Kusumaningrum, "Synthesis And Antibacterial Activities Test Of Chalcone (E)-3-(4-(Dimethylamino)Phenyl)-1 Phenylprop-2-En-1-One Against Bacteria Contaminant Blood Products," *Journal of health,* vol. 8, p. 76, july 2021.

[10] W. Sepvianti and S. B. C. Kusumaningrum, "SINTESIS SENYAWA 4'-HIDROKSI-4-METOKSIKALKON DAN UJI AKTIVITAS ANTIBAKTERI TERHADAP BAKTERI," *PHARMA XPLORE – JURNAL SAINS DAN ILMU FARMASI,* vol. 7, no. 1, pp. 11-23, 2022.

[11] M. Lengyel, N. Kállai-Szabó, V. Antal, A. J. Laki and I. Antal, "Microparticles, microspheres, and microcapsules for advanced drug delivery," *Sci. Pharm,* vol. 87, no. 3, 2019.

[12] D. S. M. S. F. N. A. S. J. X. S. M. N. M. Kasi Pandima Devi., "Kaempferol and inflammation: From chemistry to medicine," *Pharmalogical Research,* vol. 99, pp. 1-10, 2015.