International Journal of Research and Review
[Indexed, Peer-Reviewed Journal]
Volume 12; Issue: 6; June 2025
Website: www.ijrrjournal.com
Research Paper *E-ISSN: 2349-9788; P-ISSN: 2454-2237*

In Silico Evaluation of Drug-Likeness and ADME Properties of *Parkia timoriana* Phytochemicals for Potential Therapeutic Applications

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DOI: https://doi.org/10.52403/ijrr.20250648

ABSTRACT

Parkia timoriana, known locally as "Kedawung", has long been used in traditional medicine and is recognized for potential therapeutic effects. This study aimed to evaluate the pharmacokinetic profiles and target interactions of three dominant seed-derived compounds—Oleic Acid, 1H-Imidazole, 2- (diethoxy methyl), and Methyl Stearate—through in silico approaches. Canonical SMILES data were retrieved from PubChem and analyzed using Swiss ADME and Swiss Target Prediction. All three compounds exhibited favorable molecular weights and TPSA values within the optimal range for passive absorption. 1H-imidazole showed the best overall profile, including blood–brain barrier permeability, low skin penetration, and no CYP450 inhibition. BOILED-Egg modeling and bioavailability scores further confirmed its high drug-likeness potential. Target prediction revealed Oleic Acid and Methyl Stearate interacted predominantly with fatty acid-binding proteins, indicating potential in metabolic disorders. While 1H-imidazole was predicted to interact with carbonic anhydrase isoforms, especially CA9, associated with cancer metabolism. These findings highlight the pharmacological relevance of *P. timoriana* metabolites and support further development of these compounds as drug candidates.

Keywords: *Parkia timoriana*, Swiss ADME, Swiss Target Prediction, therapeutic, drug candidates

INTRODUCTION

Parkia timoriana is a leguminous tree belonging to the Fabaceae family found abundant in Indonesia, and commonly referred to as 'Kedawung' by the local community. It was a popular folkloric ethnomedicinal treatments for colic and cholera. The seed especially, has been used as an insecticide, antibacterial, treatment for stomach disorders and regulating liver function [1].

Several studies had reported that *P.timoriana* seeds had high antioxidant properties because it contained alkaloids, saponins, tannins, flavonoids, and triterpenoids [2]. It also reported had antibacterial properties against some pathogenic bacteria; *Bacillus pumilus, Bacillus subtillis, Escherichia coli* and *Pseudomonas aeruginosa* [3]. Moreover, it also exhibited antidiabetic activity by inhibiting α-amylase and α-glucosidase which are crucial enzymes involved in carbohydrate digestion [2]. Collectively, the reported studies suggest that *Parkia timoriana* holds strong potential as a source

of bioactive compounds for future drug development, particularly in the areas of anti-inflammatory, anticancer, and antidiabetic therapies.

Nevertheless, studies focusing on the pharmacological considerations required for drug development, such as pharmacokinetics, molecular targets, and therapeutic specificity, remain limited for *Parkia timoriana*. Ralte *et al.* [3] had reported the presence of various bioactive compounds in different parts of the plant, including the leaves, stems, flowers, pods, and seeds. Their findings were further supported by molecular docking analyses against BCL-2, a key regulator of apoptosis, and COX-2, an enzyme involved in inflammation, both of which were used to explore the potential anticancer and anti-inflammatory activities of the plant-derived compounds. However, dedicated investigations that comprehensively evaluate the therapeutic potential of *P. timoriana*'s metabolites as future drug candidates are still scarce.

The need for comprehensive preclinical drug-likeness evaluation, particularly studies that assess the pharmacokinetic suitability of plant-derived compounds, is critical before *Parkia timoriana* can be further explored as a viable source for commercial drug development. Such studies typically involve is in silico ADME profiling, which predicts a compound's Absorption, Distribution, Metabolism, and Excretion properties. The Absorption evaluates oral drug administration to enter the bloodstream that influenced by physicochemical properties such as membrane permeability, transporter specificity, and metabolic enzyme interactions. The term Distribution refers to the process by which a drug is transported throughout the body especially entering cell membrane, affected by blood flow, protein binding, and membrane permeability. While Metabolism involves the chemical breakdown of the drug, mainly in the gut or liver, which can reduce its bioavailability. Drug excretion is refer to the elimination of the drug or its metabolites via urine or feces, essential for preventing accumulation and determining dosing schedules [4].

This research incorporates Lipinski's Rule of Five to support the ADME profiling, focusing on molecular weight, lipophilicity, and hydrogen bonding properties. According to Lipinski *et al.* [5], a compound is more likely to exhibit favorable oral bioavailability if it meets the following criteria: molecular weight of 500 Daltons or less, LogP (octanol–water partition coefficient) of 5 or less, no more than 5 hydrogen bond donors (e.g., –OH, –NH groups), and no more than 10 hydrogen bond acceptors (e.g., oxygen or nitrogen atoms). Compounds that violate more than one of these rules are generally considered to have poor absorption or permeability. These physicochemical thresholds act as a preliminary filter in drug discovery, enabling the identification of compounds with suitable pharmacokinetic profiles before advancing to more resource-intensive stages.

In addition, several other pharmacokinetic parameters are essential for assessing the drug-likeness of *Parkia timoriana* phytoconstituents. These include gastrointestinal (GI) absorption, blood–brain barrier (BBB) permeability, and water solubility, which provide insights into a compound's oral bioavailability and systemic distribution. The bioavailability score and BOILED-Egg model further assist in visualizing and quantifying the pharmacokinetic behavior of compounds. Together, these in silico predictions offer a comprehensive evaluation framework for identifying promising drug candidates from natural sources [6]. Conducting such standardised evaluations by in silico analysis is essential to identify metabolite candidates from *P. timoriana* that not only show biological activity, but also possess suitable pharmacokinetic profiles for further development as safe and effective therapeutic agents.

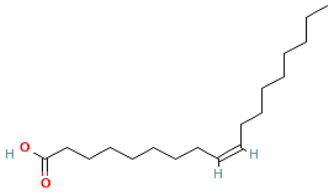
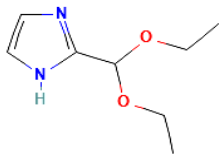
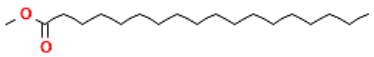
MATERIALS & METHODS

1. **Bioactive Compound Screening**
   Bioactive compounds of of *Parkia timoriana* seeds were reported by Ralte *et al.* [3] using GC-MS analysis. There were 20 phytochemical compounds were identified in the methanolic extract of *Parkia timoriana* seeds. Among these, three representative compounds—Oleic Acid, 1H-imidazole, 2-(diethoxymethyl), and Methyl stearate—were selected for further analysis. The selection was based on their relatively high abundance (as indicated by peak area percentage), structural diversity, and pharmacological relevance, allowing them to serve as representative candidates for subsequent pharmacokinetic and target prediction studies.
2. **Retrieval of SMILES Data**
   The canonical SMILES (Simplified Molecular Input Line Entry System) for each compound were retrieved from the PubChem database (https://pubchem.ncbi.nlm.nih.gov) for data input in Swiss ADME prediction tool.
3. **ADME Prediction using Swiss ADME**
   The obtained SMILES strings were input into the Swiss ADME tool (http://www.swissadme.ch/) developed by the Swiss Institute of Bioinformatics. This web tool was used to predict various pharmacokinetic parameters including physicochemical properties (e.g., TPSA, LogP), gastrointestinal (GI) absorption, blood–brain barrier (BBB) permeability, and bioavailability score. The "BOILED-Egg" model was also used to visualize passive GI absorption and brain penetration probability [6].
4. **Target Prediction using Swiss Target Prediction**
   The same SMILES data were then submitted to the Swiss Target Prediction platform (http://www.swisstargetprediction.ch/). The analysis was performed for *Homo sapiens* as the target organism. The tool uses 2D and 3D molecular similarity comparisons with known ligands. The output includes a list and pie chart classification of predicted protein targets, categorized into families such as enzymes, GPCRs, or transporters. The predicted targets for each compound were then analyzed to identify the most dominant interaction class and further analyzed by consulting relevant literature to assess their pharmacological significance.

RESULT AND DISCUSSION

Three bioactive compounds isolated from *Parkia timoriana*—Oleic Acid, 1H-Imidazole-2-(diethoxy methyl), and Methyl Stearate—were subjected to in silico ADME profiling using the Swiss ADME tool [6]. Their molecular structure, formula, molecular weight are presented in the Table 1. The molecular weights of all three compounds are within the threshold for oral bioavailability (<500 Da), with 1H-Imidazole being the smallest (170.2 Da), followed by Oleic Acid (282.5 Da) and Methyl Stearate (298.5 Da). Structurally, Oleic Acid ($C_{18}H_{34}O_2$) is a long-chain monounsaturated fatty acid, while Methyl Stearate ($C_{19}H_{38}O_2$) is a saturated fatty acid methyl ester. Both possess lipophilic hydrocarbon chains that contribute to their high molecular weights and hydrophobic behavior. In contrast, 1H-imidazole, 2-(diethoxy methyl) ($C_8H_{14}N_2O_2$) is smaller heterocyclic compound containing polar functional groups, such as nitrogen and ether linkages, which are likely to enhance its water solubility (PubChem).

Table 1. Molecular Structures, Formulas, and Weights of Selected Compounds Identified from Parkia timoriana Seeds

Compound Name	Molecular Structure	Molecular Formula	Molecular Weight (g/mol)
Oleic Acid		$C_{18}H_{34}O_2$	282.5
1H-Imidazole, 2-(Diethoxy methyl)		$C_8H_{14}N_2O_2$	170.2
Methyl Stearate		$C_{19}H_{38}O_2$	298.5

Source: PubChem (https://PubChem.ncbi.nlm.nih .gov).

Moreover, the three compounds was analyzed using Lipinski's rule of five showed in Table 2. 1H-imidazole, 2-(diethoxy methyl) fully met all the criteria, while Oleic Acid and Methyl Stearate showed one violation due to excessive lipophilicity, with log PoW values of 5.65 and 6.24, respectively. These high values indicate strong hydrophobic characteristics, consistent with their long-chain lipid structures, though potentially limiting their aqueous solubility. In contrast, 1H-imidazole, 2-(diethoxy methyl) showed a much lower log PoW of 1.05, reflecting its polar, hydrophilic nature. However, a single violation of Lipinski's Rule does not necessarily preclude oral bioavailability or pharmacological effectiveness. As discussed by Roskoski [7], 30 of 74 FDA-approved protein kinase fail to fully comply with the Rule of Five. Despite such violations, these drugs remain clinically effective and orally bioavailable. Thus, while Lipinski's Rule serves as a valuable initial guideline, it should not be regarded as a definitive standard and must be interpreted flexibly based on the compound's mechanism of action.

The difference among the compounds was further reflected in their skin permeability (log Kp) values **(Table 2)** where 1H-Imidazole demonstrated the lowest permeability at –7.00, while Oleic Acid and Methyl Stearate displayed moderate values of –2.60 and –2.19, respectively. According to Daina *et al.* [6], the more negative log Kp value indicates lower skin permeability of the molecule. From the result, 1H-imidazole, 2-(diethoxy methyl) exhibits significantly lower skin permeability compared to the other two compounds. Oleic Acid and Methyl Stearate may permeate the skin more effectively than 1H-imidazole, 2-(diethoxy methyl), despite the latter's greater polarity.

Hydrogen bonding also plays a crucial role in drug discovery in determining the strength and specificity of interactions between a ligand and its biological target. Optimal hydrogen bonding can enhance binding affinity and pharmacokinetic properties of drug candidates. However, excessive hydrogen bonding potential may compromise membrane permeability and oral bioavailability [8]. Hydrogen bonding analysis **(Table 2)** showed that 1H-Imidazole, 2-(diethoxy methyl) had the

highest capacity, with 1 HBD and 3 HBA, followed by Oleic Acid with 1 HBD and 2 HBA. Methyl Stearate had the lowest, with 0 HBD and 2 HBA.

Besides generating data related to Lipinski's Rule of Five, Swiss ADME also provides topological polar surface area (TPSA) values **(Table 2)**, which further support the evaluation of these three compounds transport properties. All three compounds had TPSA values within the optimal range for passive absorption (20–130 Å²). 1H-Imidazole exhibiting TPSA value of (47.14 Å²), Oleic Acid (37.30 Å²) and Methyl Stearate (26.30 Å²). According to *Ertl et al.* [9], TPSA values within this range are strongly correlated with oral drug absorption, indicating that the tested compounds may exhibit favorable passive transport across both intestinal and blood–brain barriers.

Additionally, all three compounds exhibited high gastrointestinal (GI) absorption **(Table 2)**, indicating good potential for oral administration. Only 1H-imidazole, 2-(diethoxy methyl) was predicted to cross the blood-brain barrier (BBB permeant), suggesting potential for Central Nervous System (CNS)-targeted applications, while the other two compounds are likely restricted to peripheral distribution. Importantly, 1H-imidazole, 2-(diethoxy methyl) showed no inhibition of major CYP450 enzymes, indicating a low risk of drug-drug interactions. In contrast, Methyl Stearate and Oleic Acid were predicted to inhibit CYP1A2, additionally Oleic Acid also affecting CYP2C9, suggesting caution in co-administration with drugs metabolized by these enzymes.

These pharmacokinetic properties can be visually interpreted using the BOILED-Egg model **(Figure 1)** introduced by Daina and Zoete [10], which graphically predicts passive GI absorption and BBB permeation based on TPSA and lipophilicity (WLOGP). In this model, compounds located within the white region (the "egg white") are predicted to have high probability of passive gastrointestinal absorption, ideal for oral administration. While those in the yellow region (the "yolk") are likely to cross the BBB via passive diffusion, suitable for central nervous system (CNS) drugs. In this study, 1H-imidazole, 2-(diethoxy methyl) is positioned within both the white and yellow zones, indicating promising oral bioavailability and BBB penetration. Oleic Acid and Methyl Stearate is located within the white region, suggesting good intestinal absorption but low CNS accessibility. Among the three, 1H-Imidazole shows the most balanced profile for systemic and CNS exposure.

Finally, the predicted oral bioavailability score summarizes key ADME properties, offering a concise indicator of a compound's suitability for oral administration in early drug evaluation. It estimates the likelihood that a compound achieves at least 10% oral bioavailability in rats [6]. Among the three, Oleic Acid showed the highest score (0.85), while 1H-Imidazole and Methyl Stearate each scored 0.55, indicating moderate oral bioavailability potential **(Table 2).**

Table 2. Predicted Physicochemical properties, pharmacokinetics, and drug-likeness of identified compounds according to Swiss ADME Analysis

	Oleic Acid	1H-Imidazole, 2-(Diethoxy methyl)	Methyl stearate
GI absorption	High	High	High
BBB permeant	No	yes	No
CYP1A2 inhibitor	Yes	No	Yes
CYP2C19 inhibitor	No	No	No
CYP2C9 inhibitor	Yes	No	No
CYP2D6 inhibitor	No	No	No
CYP3A4 inhibitor	No	No	No
Molecular weight	282.5	170.2	298.5
TPSA	37.30	47.14	26.30
Log Kp (cm/s)	–2.60	–7	–2.19

Log PoW	5.65	1.05	6.24
H- Bond Donor (HBD)	1	1	0
H- Bond Acceptor (HBA)	2	3	2
Lipinski's Rule Violation	1	0	1
Bioavailability Score	0.85	0.55	0.55

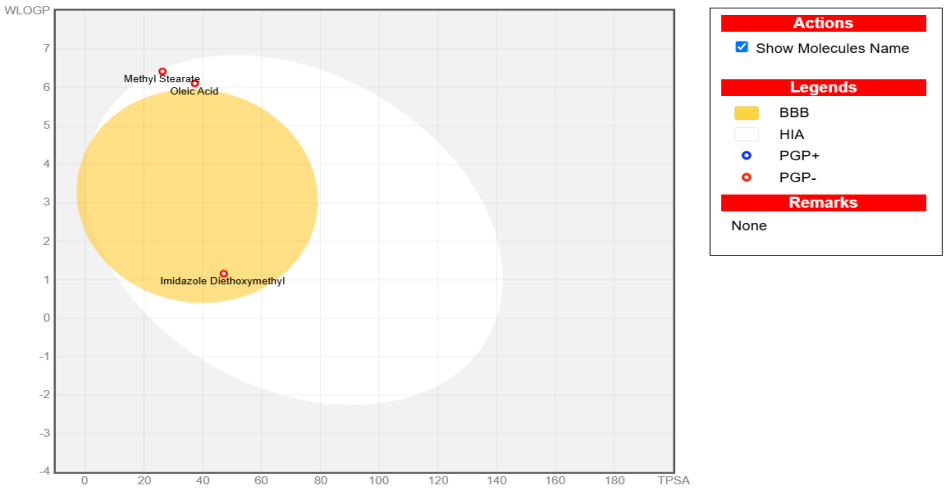


Figure 1. The BOILED-Egg model for oleic acid, methyl stearate, and 1H-imidazole, 2-(diethoxy methyl) illustrating passive gastrointestinal absorption (HIA) and blood–brain barrier (BBB) permeation. The white region represents high probability of HIA, while the yellow region (yolk) indicates potential for BBB penetration.

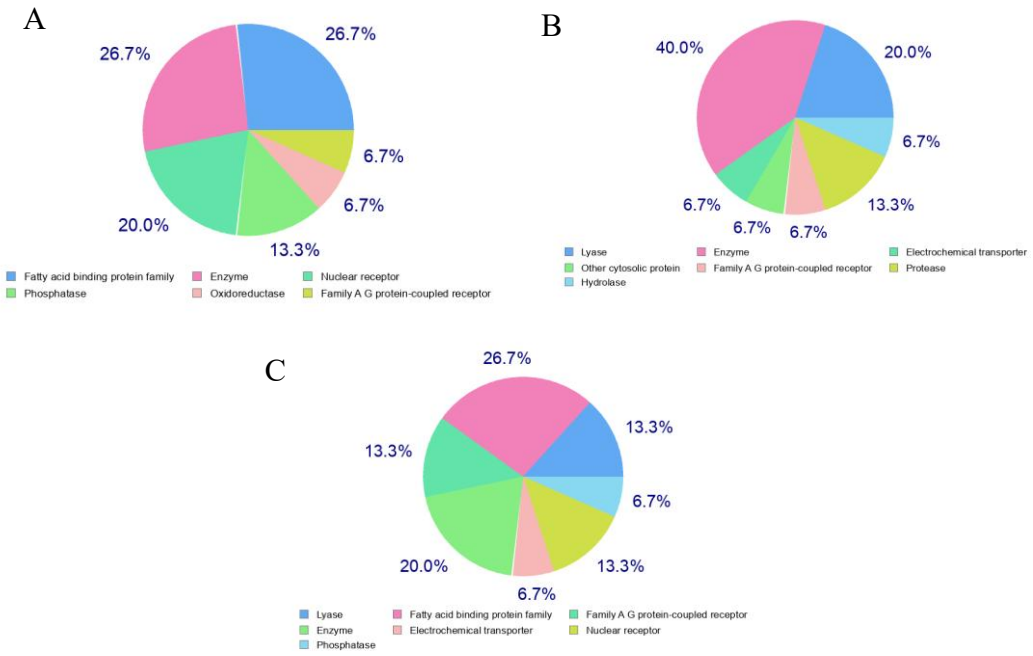


Figure 2. The Predicted target class distribution based on Swiss Target Prediction analysis for Homo sapiens. (A) Oleic acid; (B) 1H-imidazole, 2-(diethoxy methyl); (C) Methyl stearate. Each pie chart represents the top predicted target categories as a percentage of total predictions.

In order to explore the therapeutic potential of the three phytochemicals, Swiss Target Prediction was utilized to identify their most probable protein targets based on molecular similarity. It is an in-silico tool predicts likely macromolecular targets of bioactive small molecules using a combination of 2D and 3D similarity comparisons with known

ligands [11]. The result **(Figure 2)** showed that Oleic Acid was predicted to interact predominantly with members of the fatty acid-binding protein (FABP) family, particularly FABP4 which plays a central role in fatty acid transport, lipolysis, insulin sensitivity, and inflammatory responses [12]. This interaction suggests that Oleic Acid derived from *Parkia timoriana* may serve as a promising candidate for drug development targeting inflammation-related conditions. Notably, FABP4 functions both as a biomarker and a therapeutic target, especially in the context of metabolic disorders, insulin resistance, atherosclerosis, and cardiovascular diseases [12].

Swiss Target Prediction analysis revealed that enzymes constituted the most prominent target class for 1H-imidazole, 2-(diethoxy methyl), accounting for 40% of the top predicted interactions **(Figure 2)**. However, this enzyme category is broad and does not specify exact enzyme types. Interestingly, the second most frequent class was lyases (20%), which several carbonic anhydrase (CA) isoforms were identified, including CA1, CA2, and CA9. CA2 is associated with physiological acid–base balance and is a known therapeutic target for renal and neurological disorders [13]. Meanwhile, CA9 is overexpressed in hypoxic tumors and promotes cancer cell survival in acidic environments. Therefore, inhibition of CA9 has been explored as a strategy for anticancer therapy [14]. The predicted interaction of the imidazole derivative with these isoforms suggests its potential application in targeting CA-related pathologies, including cancer and pH-associated diseases.

Swiss Target Prediction analysis for Methyl Stearate **(Figure 2)** revealed that the compound was predicted to interact primarily with members of the fatty acid-binding protein (FABP) family (26.7%), followed by enzymes (20%) and G protein-coupled receptors (GPCRs) (13.3%). This target profile is similar to Oleic Acid, which also showed predominant interaction with FABP family proteins. The similarity is likely due to the shared lipophilic structure of both compounds as fatty acid derivatives. Given this, the potential biological effects of Methyl Stearate may likewise be mediated through FABP-related lipid transport and metabolic pathways, rather than through specific enzyme inhibition mechanisms.

Among the three compounds, only Oleic Acid yielded high-confidence target predictions with probabilities of up to 1.0, suggesting strong structural similarity to known bioactive ligands. In contrast, the predicted targets for both 1H-imidazole, 2-(diethoxy methyl) and Methyl Stearate had interaction probabilities of 0.0, indicating that these results should be interpreted cautiously and serve primarily as preliminary insights rather than definitive biological predictions. Further molecular docking or experimental validation would be required to confirm their actual binding affinities.

CONCLUSION

This study demonstrates the pharmacokinetic and therapeutic potential of three bioactive compounds derived from *Parkia timoriana* seeds through in silico ADME profiling and target prediction. Among the tested compounds, 1H-imidazole, 2-(diethoxy methyl) exhibited the most favorable drug-likeness profile, including BBB permeability, low risk of CYP450 inhibition, and balanced physicochemical properties. Oleic Acid showed high oral bioavailability but was limited to peripheral targets, while Methyl Stearate displayed marginal absorption potential. Swiss Target Prediction analysis revealed Oleic Acid and Methyl Stearate shared similar lipid-associated target classes especially fatty acid-binding proteins. These interactions suggest potential therapeutic applications in managing metabolic disorders, such as obesity, insulin resistance, and cardiovascular diseases. Meanwhile, 1H-Imidazole potentially targets cancer-related carbonic anhydrase isoforms (CA9). These findings suggest that *P. timoriana* seed metabolites, particularly 1H-Imidazole,

warrant further investigation as promising candidates for drug development.

Declaration by Authors

Acknowledgement: None
Source of Funding: None
Conflict of Interest: No conflicts of interest declared.

REFERENCES

1. Sumarni W, Sudarmin S, Sumarti SS, Kadarwati S. 2022. Indigenous knowledge of Indonesian traditional medicines in science teaching and learning using a science–technology–engineering–mathematics (STEM) approach. Volume ke-17. Springer Netherlands.
2. Suryanti V, Sariwati A, Sari F, Handayani DS, Risqi HD. 2022. Metabolite Bioactive Contents of Parkia timoriana (DC) Merr Seed Extracts in Different Solvent Polarities. HAYATI J Biosci. 29(5):681–694. doi:10.4308/hjb.29.5.681-694.
3. Ralte L, Khiangte L, Thangjam NM, Kumar A, Singh YT. 2022. GC–MS and molecular docking analyses of phytochemicals from the underutilized plant, Parkia timoriana revealed candidate anti-cancerous and anti-inflammatory agents. Sci Rep. 12(1):1–21. doi:10.1038/s41598-022-07320-2.
4. Vrbanac J, Slauter R. 2016. ADME in Drug Discovery. Second Edition. Elsevier Inc.
5. Lipinski, C. A., Lombardo, F., Dominy, B. W., & Feeney, P. J. (2001). Experimental and computational approaches to estimate solubility and permeability in drug discovery and development settings. Advanced Drug Delivery Reviews, 46(1–3), 3–26. https://doi.org/10.1016/S0169-409X(00)00129-0
6. Daina A, Michielin O, Zoete V. 2017. SwissADME: A free web tool to evaluate pharmacokinetics, drug-likeness and medicinal chemistry friendliness of small molecules. Sci Rep. 7(March):1–13. doi:10.1038/srep42717.
7. Roskoski R. 2023. Rule of five violations among the FDA-approved small molecule protein kinase inhibitors. Pharmacol Res. 191(April):106774. doi: 10.1016/j.phrs.2023.106774.
8. Labby, K. J., Senske, M., & Fierke, C. A. (2020). Contributions of hydrogen bonds to the function and specificity of protein–ligand interactions. Biochemistry, 59(7), 485–499. https://doi.org/10.1021/acs.biochem.9b00920.
9. Ertl P, Rohde B, Selzer P. 2000. Fast calculation of molecular polar surface area as a sum of fragment-based contributions and its application to the prediction of drug transport properties. J Med Chem. 43(20):3714–3717. doi:10.1021/jm000942e.
10. Daina A, Zoete V. 2016. A BOILED-Egg To Predict Gastrointestinal Absorption and Brain Penetration of Small Molecules. ChemMedChem. 1117–1121. doi:10.1002/cmdc.201600182.
11. Daina A, Michielin O, Zoete V. 2019. SwissTargetPrediction: updated data and new features for efficient prediction of protein targets of small molecules. Nucleic Acids Res. 47(W1):W357–W3664. doi:10.1093/nar/gkz382.
12. Furuhashi, M., Tuncman, G. Y., Gorgun, C. Z., Makowski, L., Atsumi, G., Vaillancourt, E., ... & Hotamisligil, G. S. (2007). Treatment of diabetes and atherosclerosis by inhibiting fatty-acid–binding protein aP2. Nature, 447(7147), 959–965. https://doi.org/10.1038/nature05844
13. Yan M, Cai L, Duan X, Tycksen ED, Rai MF. 2025. Carbonic anhydrase 2 is important for articular chondrocyte function and metabolic homeostasis. Bone. 190(June 2024):117313. doi: 10.1016/j.bone.2024.117313.
14. Pastorekova S, Gillies RJ. 2019. The role of carbonic anhydrase IX in cancer development: links to hypoxia, acidosis, and beyond. Cancer Metastasis Rev. 38(1–2):65–77. doi:10.1007/s10555-019-09799-0.

How to cite this article: Arina Amalia Putri, Nurina Tahta Afwi Maulina, Puspa Hening. In silico evaluation of drug-likeness and ADME properties of *Parkia timoriana* phytochemicals for potential therapeutic applications. *International Journal of Research and Review*. 2025; 12(6): 409-416. DOI: *https://doi.org/10.52403/ijrr.20250648*

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