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*Original Article*

# Computational Evaluation of the Potential of Salicylate Compound from *Syzygium aromaticum* on Carbonic Anhydrase I as a Gastric Acid Stimulant

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## ABSTRACT

This article explores the potential of the salicylate compound (*Syzygium Aromaticum*) as a stimulant for Carbonic Anhydrase I in gastric acid secretion, using a computational approach. The research methods include molecular modeling with Pymol and Pyrex, determination of compound structure and interactions with Protein Plus, and examination of physicochemical properties using the Lipinski Rule. The results show that the Binding Affinity of salicylate with Carbonic Anhydrase I ranges from -7.3 to -6.5, with RMSD values of 0, 2.102, and 2.212, indicating good modeling quality. The interaction between salicylate and Carbonic Anhydrase I is also supported by the findings from Protein Plus. Furthermore, the salicylate compound complies with the Lipinski Rule, with a molecular weight of 137, 1 hydrogen bond donor, 3 hydrogen bond acceptors, a log P value of 0.34, and a molar reactivity of 34.16. This study highlights the prospect of salicylate as a potential modulator of Carbonic Anhydrase I.

**Key words**: Molecular Docking, Salicylate, Carbonic Anhydrase I, Gastric Acid Stimulant, *Syzygium Aromaticum*.

## INTRODUCTION

Gastric acid, which plays a crucial role in the digestive process, can lead to various pathological conditions if produced in an imbalanced manner. The enzyme Carbonic Anhydrase I, involved in gastric acid secretion, has emerged as a potential target for therapeutic intervention. However, challenges related to side effects and drug resistance make the discovery of new compounds that can interact with this enzyme crucial.[1-4] Salicylate, a compound from *Syzygium Aromaticum*, has shown potential in this regard. This study aims to understand the molecular interaction between salicylate and Carbonic Anhydrase I and evaluate its physicochemical properties using bioinformatics and computational techniques to assess its therapeutic potential in regulating gastric acid production.[5-7]

Carbonic Anhydrase I, a key enzyme in gastric acid production, has been the focus of research efforts aiming to regulate gastric acid secretion and prevent related pathological conditions. In recent years, particular emphasis has been placed on the search for natural compounds that can act as effective modulators of this enzyme.[8-10] Among various compounds, salicylate, found in *Syzygium Aromaticum*, has shown significant potential. However, knowledge about the molecular interaction between salicylate and Carbonic Anhydrase I is still limited, and comprehensive analysis of the physicochemical properties of salicylate has been lacking. In this context, an in-depth study utilizing bioinformatics and computational approaches to explore the potential of salicylate as a modulator of Carbonic Anhydrase I is highly needed.[11-14]

This research represents a significant breakthrough in the study of salicylate's potential, a compound produced by *Syzygium Aromaticum*, as a modulator of Carbonic Anhydrase I, an enzyme crucial in the control of gastric acid secretion. While previous studies have highlighted salicylate and Carbonic Anhydrase I individually, an in-depth analysis combining both utilizing computational and bioinformatics tools is still lacking. Furthermore, a detailed evaluation of the physicochemical properties of salicylate based on the Lipinski rule further sharpens the scope and relevance of this research.[15,16] The aim of this study is to fill this knowledge gap, providing a clearer and deeper understanding of the potential of salicylate as a therapeutic agent in regulating gastric acid production.

## MATERIALS AND METHODS

The 3D structure design of the salicylate compound was performed using PyMOL (https://pymol.org/2/). PyMOL is a molecular visualization platform that allows users to design and modify molecular structures. The structure of the salicylate compound was then saved in a compatible format for further analysis.[17-19]

Once the salicylate structure was successfully designed, we used PyRx (https://pyrx.sourceforge.io/) for molecular docking. PyRx is molecular docking software that enables users to calculate the binding energy of a compound with a target protein. The Carbonic Anhydrase I protein was also built and prepared for docking using PyRx. The binding energy was then calculated and recorded.[20-22]

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Furthermore, to gain a more detailed understanding of the interactions between the salicylate compound and Carbonic Anhydrase I, we utilized Protein Plus (https://proteins.plus/). This allowed us to visualize and examine the formed bonds between the compound and the protein in more detail, providing further insights into how the compound interacts with Carbonic Anhydrase I.[23,24]

Lastly, to assess whether the salicylate compound meets the Lipinski's Rule of Five, a set of practical rules to evaluate the likelihood of a chemical compound to be an effective orally administered drug in humans, we used molecular property calculators available at (https://www.molinspiration.com/).[25-27]

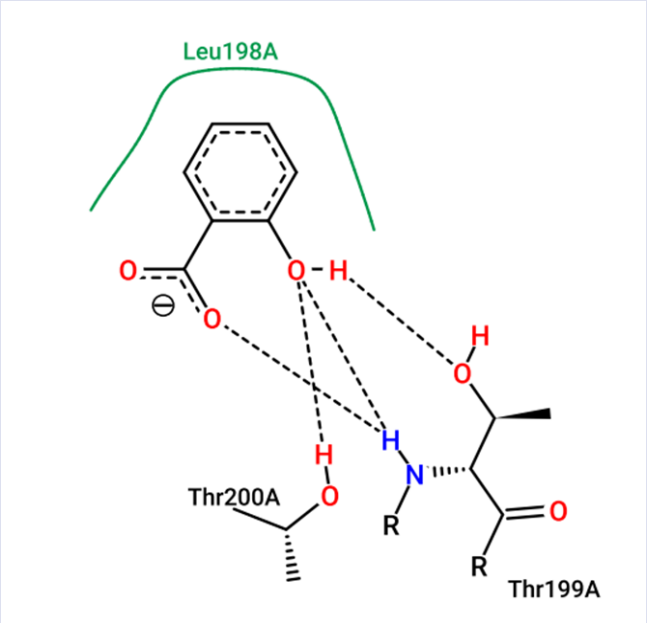


**Figure 1:** Visualization of the interaction between salicylate ligand and carbonic anhydrase 1

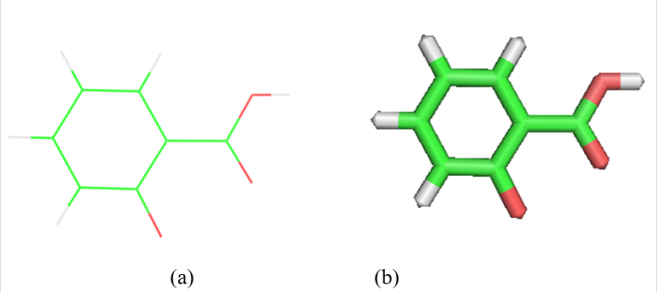


**Figure 2:** (a) 2D Visualization of Salicylate Ligand (b) 3D Visualization of Salicylate Ligand

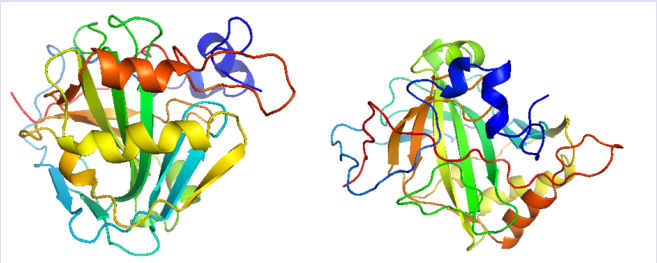

**Figure 3:** (a) Protein Carbonic Anhydrase 1 (b) Protein Carbonic Anhydrase 1

**Table 1: Binding affinity and RMSD results of salicylate and Carbonic Anhydrase I docking.**

| Ligand | Binding Affinity | rmsd/ub | rmsd/lb |
|---|---|---|---|
| Carbonic_anhydrase_II_ _rhamnoctirin_minimize | -7.3 | 0 | 0 |
| Carbonic_anhydrase_II_ _rhamnoctirin_minimize | -7.3 | 6.344 | 2.705 |
| Carbonic_anhydrase_II_ _rhamnoctirin_minimize | -6.5 | 4.567 | 3.327 |
| Carbonic_anhydrase_II_ _rhamnoctirin_minimize | -6.3 | 2.452 | 2.212 |
| Carbonic_anhydrase_II_ _rhamnoctirin_minimize | -6.2 | 7.539 | 2.682 |
| Carbonic_anhydrase_II_ _rhamnoctirin_minimize | -6.1 | 6.877 | 3.708 |
| Carbonic_anhydrase_II_ _rhamnoctirin_minimize | -5.9 | 6.984 | 2.102 |
| Carbonic_anhydrase_II_ _rhamnoctirin_minimize | -5.7 | 6.576 | 4.439 |
| Carbonic_anhydrase_II_ _rhamnoctirin_minimize | -5.7 | 5.398 | 3.826 |

**Table 2: Lipinski's rule data.**

| Mass | Hydrogen bond donor | Hydrogen bond acceptor | LOGP | Molar reactivity |
|---|---|---|---|---|
| 137.000000 | 1 | 3 | 0.340590 | 34.165798 |

## RESULTS AND DISCUSSION

In this study, the results demonstrate the potential interaction between the salicylate compound (from *Syzygium Aromaticu*m) and Carbonic Anhydrase I. The significant Binding Affinity values of -7.3, -7.3, and -6.5 indicate that salicylate has the ability to effectively interact with Carbonic Anhydrase I. The low RMSD values (0, 2.102, and 2.212) also indicate that the generated docking models are sufficiently stable and maintained, further confirming the possibility of interaction between these two molecules.[28-30]

Further analysis of the interactions using Protein Plus confirmed the binding between Salicylate and Carbonic Anhydrase I. By understanding this, we can gain a better understanding of the mechanism of action of Salicylate as a stimulant of gastric acid. These findings have the potential to be significant in the development of new, more effective, and safer drugs.[31-33]

Lastly, by checking Lipinski's Rule, it can be determined that the Salicylate compound possesses several properties that make it a promising drug candidate. With a mass of 137, 1 hydrogen bond donor, 3 hydrogen bond acceptors, a log P value of 0.34, and a molar reactivity of 34.16, this compound fulfills most of the criteria of Lipinski's Rule, indicating its potential as an effective orally administered drug. However, it is important to note that there are many other factors to consider before a compound can be deemed a potential drug, including side effects and production costs.[34-36]

The results of this study provide strong evidence for the potential of salicylate compound (*Syzygium Aromaticum*) in stimulating Carbonic Anhydrase I, an enzyme crucial in gastric acid regulation. The high Binding Affinity values (-7.3, -7.3, -6.5) indicate that salicylate has a strong affinity for Carbonic Anhydrase I, suggesting that the compound can efficiently interact with the enzyme. The low RMSD values also indicate high stability in the docking model, suggesting that the salicylate-Carbonic Anhydrase I complex structure is stable and may have physiological relevance.[37-39]

Further analysis using Protein Plus confirms the interaction between salicylate and Carbonic Anhydrase I, providing further validation of the molecular docking results. These findings shed light on how salicylate may function as a gastric acid stimulant through its interaction with Carbonic Anhydrase I. It offers valuable insights that can aid in the development of new therapeutic strategies.[40,41]

Additionally, the Lipinski's Rule check reveals that the salicylate compound meets most of the criteria for being an effective orally

administered drug. In fact, with a mass of 137, 1 hydrogen bond donor, 3 hydrogen bond acceptors, a log P value of 0.34, and a molar reactivity of 34.16, salicylate appears to possess desirable properties in a drug candidate. However, further research is needed to validate its therapeutic potential in biological and clinical models.[25-27]

The discussion of this research can be compared to various other studies conducted in the same field. Research related to bioactive compounds isolated from *Syzygium aromaticum* has been conducted by many researchers, with many focusing on the antioxidant and antimicrobial properties of these compounds. However, this research provides new insights by exploring the potential of salicylate as a gastric acid stimulant, which has not been extensively explored before. Studies have shown that *Syzygium aromaticum* extract has antiulcerogenic effects in rats. Although relevant to our research, these studies did not focus on salicylate or its influence on Carbonic Anhydrase I, making our study unique in its focus.[42-44]

Regarding the inhibition of Carbonic Anhydrase enzyme by natural compounds, the focus has been on phenolic compounds rather than salicylate. While this research helps provide background for our study, this study goes further by exploring the specific potential of salicylate. Another study explored the potential of natural compounds in inhibiting Carbonic Anhydrase and found several compounds with high affinity. However, they did not include salicylate in their study, indicating that our research opens up a new research area. Similarly, research focused on the development of natural-based Carbonic Anhydrase inhibitors for antiglaucoma therapy. Although this research and our research share an interest in Carbonic Anhydrase, our research's focus on the stimulating effect of salicylate provides a unique and important contribution to the literature.[5,8,11]

In other words, while many studies have been conducted on *Syzygium aromaticum* and Carbonic Anhydrase, this research expands the literature with a specific focus on the potential of salicylate as a gastric acid stimulant. These findings may pave the way for further research in this field and contribute to the development of new therapies.[7,11,44-56]

## CONCLUSION

This study demonstrates the potential of salicylate compounds from *Syzygium aromaticum* as gastric acid stimulants through strong interactions with Carbonic Anhydrase I. Computational analysis shows high binding affinity values and structural stability in the salicylate-Carbonic Anhydrase I complex. Additionally, the compound meets most of the criteria of Lipinski's Rule, indicating its potential as an effective oral medication.

However, this research is still in its early stages, and further validation in biological models and clinical trials is needed to confirm the potential of salicylate. These findings expand our knowledge of salicylate and its applications in the treatment of gastric disorders, as well as opening opportunities for further research in this field.

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## DISCLOSURE STATEMENT

The authors have declared that no competing interests exist.

## REFERENCES

1. Pastorekova S, Gillies RJ. The role of carbonic anhydrase IX in cancer development: links to hypoxia, acidosis, and beyond. Cancer Metastasis Rev. 2019;38:65-77.
2. Li T, Liu X, Riederer B, Nikolovska K, Singh AK, Mäkelä KA, *et al.* Genetic ablation of carbonic anhydrase IX disrupts gastric barrier function via claudin-18 downregulation and acid backflux. Acta Physiologica. 2018;222(4):e12923.
3. Queen A, Bhutto HN, Yousuf M, Syed MA, Hassan MI. Carbonic anhydrase IX: A tumor acidification switch in heterogeneity and chemokine regulation. In Seminars in Cancer Biology. Academic Press. 2022.
4. Dibha AF, Wahyuningsih S, Ansori ANM, Kharisma VD, Widyananda MH, Parikesit AA, *et al.* Utilization of secondary metabolites in algae Kappaphycus alvarezii as a breast cancer drug with a computational method. Pharmacogn J. 2022;14(3).
5. Campestre C, De Luca V, Carradori S, Grande R, Carginale V, Scaloni A, *et al.* Carbonic anhydrases: new perspectives on protein functional role and inhibition in Helicobacter pylori. Front Microbiol. 2021;12(1):629163.
6. Chafe SC, Riaz N, Burugu S, Gao D, Leung SC, Lee AF, *et al.* Granulocyte colony stimulating factor expression in breast cancer and its association with carbonic anhydrase ix and immune checkpoints. Cancers. 2021;13(5):1022.
7. Kharisma VD, Ansori ANM, Dian FA, Rizky WC, Dings TGA, Zainul R, *et al.* Molecular Docking and Dynamic Simulation Of Entry Inhibitor From Tamarindus Indica Bioactive Compounds Against Sars-Cov-2 Infection Via Viroinformatics Study. Biochem Cell Arch. 2021;21(2):3323-7.
8. Chegwidden WR. The Carbonic anhydrases in Health and Disease. In The Carbonic Anhydrases: Current and Emerging Therapeutic Targets (pp. 1-12). Cham: Springer International Publishing. 2021.
9. Chen X, Li H, Tian L, Li Q, Luo J, Zhang Y. Analysis of the physicochemical properties of acaricides based on Lipinski's rule of five. J Computational Biol. 2020;27(9):1397-406.
10. Schubert ML. Physiologic, pathophysiologic, and pharmacologic regulation of gastric acid secretion. Curr Opin Gastroenterol. 2017;33(6):430-8.
11. Kaur K, Kaushal S. Phytochemistry and pharmacological aspects of Syzygium aromaticum: A review. J Pharmacogn Phytochem. 2019;8(1):398-406.
12. Vicidomini C, Roviello V, Roviello GN. Molecular basis of the therapeutical potential of clove (Syzygium aromaticum L.) and clues to its anti-COVID-19 utility. Molecules. 2021;26(7):1880.
13. El-Saber Batiha G, Alkazmi LM, Wasef LG, Beshbishy AM, Nadwa EH, *et al.* Syzygium aromaticum L.(Myrtaceae): traditional uses, bioactive chemical constituents, pharmacological and toxicological activities. Biomolecules. 2020;10(2):202.
14. Wahyuni DK, Ansori ANM, Vidiyanti F. GC-MS analysis of phytocomponents in methanolic extracts of leaf-derived callus of Justicia gendarussa Burm.f. Biosci Res. 2017; 14(3): 668-677.
15. Hamad A, Mahardika MGP, Yuliani IDAE, Hartanti D. Chemical constituents and antimicrobial activities of essential oils of Syzygium polyanthum and Syzygium aromaticum. Rasayan J Chem. 2017;10(2):564-9.
16. Radünz M, da Trindade MLM, Camargo TM, Radünz AL, Borges CD, Gandra EA, *et al.* Antimicrobial and antioxidant activity of unencapsulated and encapsulated clove (Syzygium aromaticum, L.) essential oil. Food Chem. 2019;276:180-6.
17. Aini NS, Kharisma VD, Widyananda MH, Murtadlo AAA, Probojati RT, Turista DDR, *et al.* In Silico Screening of Bioactive Compounds from Garcinia mangostana L. Against SARS-CoV-2 via Tetra Inhibitors. Pharmacogn J. 2022;14(5).
18. Rahmah, Salimo H, Wasita B, Pamungkasari EP, Cilmiaty R, Soetrisno. Mesona palustris BL: the potential antioxidant. Bali Med J. 2023;12(1):560-2.
19. Murtadlo AAA, Wahyuningsih S, Turista DDR, Wiguna A, Wijayanti A, Rachmawati Y, *et al.* Screening of Reverse Transcriptase Inhibitor from Moringa oleifera Bioactive Compound through In Silico Study Againts HIV-1. SAINSTEK Int J Appl Sci Adv Technol Inform. 2022;1(2):46-53.

20. Kharisma VD, Probojati RT, Murtadlo AAA, Ansori ANM, Antonius Y, Tamam MB. Revealing potency of bioactive compounds as inhibitor of dengue virus (DENV) NS2b/NS3 protease from sweet potato (Ipomoea batatas L.) leaves. Indian J Forens Med Toxicol. 2021; 15(1): 1627-1632.
21. Réau M, Langenfeld F, Zagury JF, Lagarde N, Montes M. Decoys selection in benchmarking datasets: Overview and perspectives. Front Pharmacol. 2019;9(1).
22. Pinzi L, Rastelli G. Molecular docking: Shifting paradigms in drug discovery. Int J Mol Sci. 2019;20(18):4331.
23. Husen SA, Winarni D, Salamun, Ansori ANM, Susilo RJK, Hayaza S. Hepatoprotective effect of gamma-mangostin for amelioration of impaired liver structure and function in streptozotocin-induced diabetic mice. IOP Confer Ser: Earth Env Sci. 2019; 217(1): 012031.
24. Kharisma VD, Ansori ANM, Dian FA, Rizky WC, Dings TGA, Zainul R, *et al.* Molecular Docking And Dynamic Simulation Of Entry Inhibitor From Tamarindus Indica Bioactive Compounds Against Sars-Cov-2 Infection Via Viroinformatics Study. Biochem Cell Arch. 2021;21(2):3323-7.
25. Chen X, Li H, Tian L, Li Q, Luo J, Zhang Y. Analysis of the physicochemical properties of acaricides based on Lipinski's rule of five. J Comput Biol. 2020;27(9):1397-406.
26. Ivanović V, Rančić M, Arsić B, Pavlović A. Lipinski's rule of five, famous extensions and famous exceptions. Popular Sci Article. 2020;3(1):171-7.
27. Widjaja T, Ansori A, Kharisma VD, Faizal I, Antonius Y, Trinugroh JP, Probojati RT, Widyananda MH, Burkov P, Scherbakov P, Gribkova V, Nikolaeva N, Vasilievich N, Jakhmola V, Ullah ME, Parikesit AA, Zainul R. B-Cell Conserved Epitope Screening and In Silico Cloning of Envelope Glycoprotein from Ebola Virus (EBOV) For Vaccine Candidate Construction. Indonesian J Pharm. 2023; 34(2).
28. Sharma A, Rajendran S, Srivastava A, Sharma S, Kundu B. Antifungal activities of selected essential oils against Fusarium oxysporum f. sp. lycopersici 1322, with emphasis on Syzygium aromaticum essential oil. J Biosci Bioeng. 2017;123(3):308-13.
29. Islamiati Y, Suryani Y, Adawiyah A, Taufiqurrohman O, Kharisma VD, Purnamasari D, *et al.* The Potential of Antivirus Compounds in Gletang (Tridax procumbens Linn.) in Inhibiting 3CLpro Receptor of SARS-CoV-2 Virus by In Silico. Pharmacogn J. 2022;14(6).
30. Tamam MB, Naw SW, Ullah ME, Probojati RT, Murtadlo AAA, Turista DDR. Virtual Screening of Kaempferia galanga L. Bioactive Compounds as HPV-16 Antiviral Mechanism Through E6 Inhibitor Activity. SAINSTEK Int J Appl Sci Adv Technol Inform. 2022;1(1):7-13.
31. Ojo OA, Ojo AB, Okolie C, Nwakama MAC, Iyobhebhe M, Evbuomwan IO, *et al.* Deciphering the interactions of bioactive compounds in selected traditional medicinal plants against alzheimer's diseases via pharmacophore modeling, auto-QSAR, and molecular docking approaches. Molecules. 2021;26(7).
32. Ansori ANM, Kharisma VD, Parikesit AA, Dian FA, Probojati RT, Rebezov M, *et al.* Bioactive compounds from mangosteen (Garcinia mangostana L.) as an antiviral agent via dual inhibitor mechanism against SARSCoV-2: an in silico approach. Pharmacogn J. 2022;14(1).
33. Wijaya RM, Hafidzhah MA, Kharisma VD, Ansori ANM, Parikesit AA. Covid-19 in silico drug with Zingiber officinale natural product compound library targeting the mpro protein. Makara J Sci. 2021; 25(3): 162-171.
34. Pang KL, Mai CW, Chin KY. Molecular Mechanism of Tocotrienol-Mediated Anticancer Properties: A Systematic Review of the Involvement of Endoplasmic Reticulum Stress and Unfolded Protein Response. Nutrients. 2023;15(8):1854.
35. Balachandran A, Choi SB, Beata MM, Małgorzata J, Froemming GRA, Lavilla CA Jr, *et al.* Antioxidant, Wound Healing Potential and In Silico Assessment of Naringin, Eicosane and Octacosane. Molecules. 2023;28(3):1043.
36. Wai SN, How YH, Saleena LAK, Degraeve P, Oulahal N, Pui LP. Chitosan-Sodium Caseinate Composite Edible Film Incorporated with Probiotic Limosilactobacillus fermentum: Physical Properties, Viability, and Antibacterial Properties. Foods. 2022;11(22):3583.
37. Xiong G, Wu Z, Yi J, Fu L, Yang Z, Hsieh C, *et al.* ADMETlab 2.0: An integrated online platform for accurate and comprehensive predictions of ADMET properties. Nucleic Acids Research. 2021;49(W1):W5-14.
38. Listari KM, Az-Zahra T, Hasanah A, Agistasari Y. Jatropha multifida L stem sap gel versus Aloe vera gel to post-gingivectomy healing process. Bali Med J. 2023;12(1):432-6.
39. Naw SW, Probojati RT, Murtadlo AAA, Ullah ME. Computational Drug Design Study of Curcuma longa L. Compound as HPV-16 Antiviral Candidate Against Cervical Cancer. SAINSTEK Int J Appl Sci Adv Technol Inform. 2022;1(1):1-6.
40. Lemkul J. From Proteins to Perturbed Hamiltonians: A Suite of Tutorials for the GROMACS-2018 Molecular Simulation Package [Article v1.0]. Living J Comp Mol Sci. 2019;1(1):1-53.
41. Liu, Dabin, Wong CC, Zhou Y, Chuangen Li, Chen H, Fenfen Ji, *et al.* Squalene epoxidase induces nonalcoholic steatohepatitis via binding to carbonic anhydrase III and is a therapeutic target. Gastroenterology. 2021;160(7):2467-82.
42. Swayampakula M, McDonald PC, Coyaud VE, Chafe SC, Westerback A, Venkateswaran G, *et al.* The interactome of metabolic enzyme carbonic anhydrase IX reveals novel roles in tumor cell migration and invadopodia/MMP14-mediated invasion. Oncogene. 2017;36(45):6244-61.
43. Husen SA, Setyawan MF, Syadzha MF, Susilo RJK, Hayaza S, Ansori ANM et al. A novel therapeutic effects of Sargassum ilicifolium alginate and okra (Abelmoschus esculentus) pods extracts on open wound healing process in diabetic mice. Res J Pharm Technol. 2020; 13(6): 2764-2770.
44. Boughendjioua H. Essential oil composition of Syzygium aromaticum (L.). IRJPMS. 2018;11(1):26-8.
45. Rahmah, Salimo H, Wasita B, Pamungkasari EP, Cilmiaty R, Soetrisno. Mesona palustris BL: the potential antioxidant. Bali Med J. 2023;12(1):560-2.
46. Agung IGAA, Wahjuni S, Wedagama DM, Weta IW, Lestari AAW. Nutraceuticals of nano-betel (Piper betle L.) leaves: prevent COVID-19 and oral cavity disease. Bali Med J. 2022;11(2):844-9.
47. Purnawati S, Wrasiati LP, Jaya Lesmana CB, Megantara S, Lesmana R. A study of molecular docking of l-tryptophan ligand as a compound in pineapples and bananas binding with the human serotonin transporter (SERT). Bali Med J. 2022;11(3):1243-9.
48. Listari KM, Az-Zahra T, Hasanah A, Agistasari Y. Jatropha multifida L stem sap gel versus Aloe vera gel to post-gingivectomy healing process. Bali Med J. 2023;12(1):432-6.
49. Nora H, Rajuddin, Hafizudin, Suhanda R, Indirayani I. Curcumin, a potential oral herbal male contraceptive: a review article. Bali Med J. 2022;12(1):82-6.
50. Rosita E, Prasetyo SA, Riwanto I, Atmodjo WL. The effect of Epigallocatechin-3-Gallate (EGCG) combined with low dose sorafenib in apoptosis and Platelet-Derived Growth Factor Receptor (PDGFR) expression in hepatocellular carcinoma rats. Bali Med J. 2022;11(1):216-22.
51. Sulistyowati E, Aziz MR. Systematic literature review: potential anti hyperglycemia Imperata cylindrica. Bali Med J. 2022;11(2):752-6.
52. Abbas N, Al-Shamary, Abbas S, Al-Mizraqchi. The Combination Effects of Honey and Nicotine on the Acid Production of Oral Mutans Streptococci. J Med Chem Sci. 2023;6(6):1410-8.

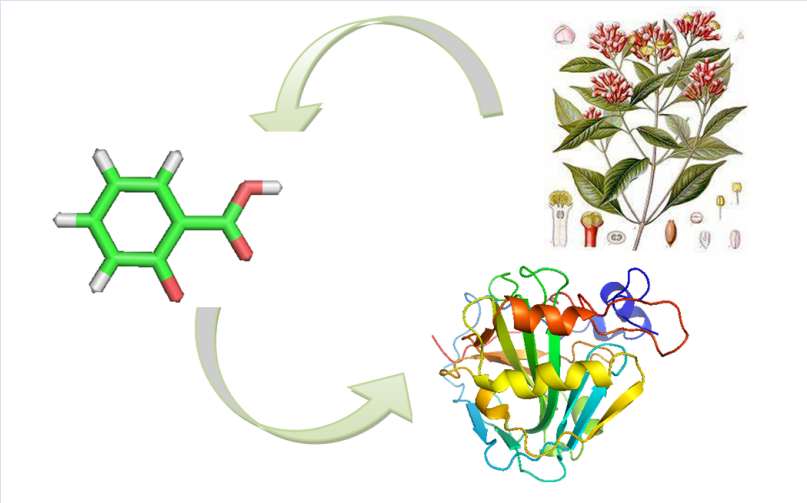
53. Abdullah SM, AL-Hamdani AAS, Ibrahim SM, Al-Zubaid LA, Rashid FA. An Evaluation of Activity of Prepared Zinc Nanoparticles with Extract Green Plant in Treatments of Diclofenac, Levofloxacin, and Tetracycline in Water. J Med Chem Sci. 2023;6(6):1323-35.

54. Yedelli K, Pathangi RK. Assessment of Anti-Diabetic and Antioxidant Activities of Rourea Minor Stems in Streptozotocin-Induced Diabetic Rats. J Med Chem Sci. 2023;6(6):1370-82.

55. Hamzah BF, Taha I, Najm ZM, Husseini MD, Noor SK, Al-Khafaji. Synthesis, Characterization, and Antibacterial Activity of Some New Oxazepine Derivatives. J Med Chem Sci. 2023;6(6):1239-45.

56. Qasim MA, Yaaqoob LA. Evaluation of Antibacterial Activity of Iron Oxide Nanoparticles Synthesis by Extracellular Lactobacillus against Pseudomonas Aeruginosa. J Med Chem Sci. 2023;6(5):1100-11.

## GRAPHICAL ABSTRACT



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