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Islamic Pharmaceutical Education and Prediction of Shogaol from Jahe Hijau (*Zingiber officinale var. viridis*) for MMP9 Expression Inhibitor

Fendy Prasetyawan
*Prodi Pendikan Profesi Apoteker, Fakultas Ilmu Kesehatan, Universitas Kadiri
Email: fendy.pra@gmail.com

Yuneka Saristiana
**Prodi Pendikan Profesi Apoteker, Fakultas Ilmu Kesehatan, Universitas Kadiri
Email: yunekasaristiana@gmail.com

Ratna Mildawati
***Prodi Farmasi, STIKes Ganesha Husada Kediri
Email: ratnamildawati@gmail.com

Mujtahid Bin Abd Kadir
****Prodi Farmasi, Fakultas Kedokteran dan Ilmu Kesehatan, Universitas Muhammadiyah Makasar
Email: mujtahid@gmail.com

Novyananda Salmasfattah
*****Prodi Pendikan Profesi Apoteker, Fakultas Ilmu Kesehatan, Universitas Kadiri
Email: salmasfattah@gmail.com

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Abstract

Zingiber officinale var. viridis, commonly known as green ginger, contains various bioactive compounds, one of the most prominent being shogaol. This study aimed to investigate the potential of shogaol as an inhibitor of Matrix Metalloproteinase-9 (MMP9) expression using an in silico prediction method. The SMILES structure of shogaol was retrieved from PubChem and analyzed using the WAY2DRUG/Pass Online platform. The result revealed a high probability of activity (Pa = 0.863) for MMP9 expression inhibition, suggesting its therapeutic relevance in managing inflammation and cancer progression. Furthermore, this research integrates the principles of Islamic Pharmaceutical Education by emphasizing the use of halal, natural compounds, and ethical scientific inquiry. The findings support the potential role of shogaol as a natural, faith-compatible therapeutic candidate and encourage further exploration in both pharmaceutical research and Islamic-based health education.

Keywords: Shogaol, Green Ginger (Zingiber officinale var. viridis), MMP9 Inhibitor

INTRODUCTION

Pharmaceutical education within the context of Islam emphasizes the integration of modern scientific knowledge with Islamic values, aiming to produce professionals who are not only technically proficient but also possess a deep ethical and spiritual awareness (Muslikh, F. A., 2023). This approach encourages the exploration and utilization of natural resources that are both halal and thayyib, including traditional medicinal plants which align with Islamic principles (Kawiji, K., 2024). One such medicinal plant with notable potential is green ginger (*Zingiber officinale var. viridis*). Renowned for its diverse bioactive compounds, such as gingerol, shogaol, and zingerone, green ginger offers numerous health benefits. Shogaol, in particular, has garnered significant attention in pharmacological studies due to its pronounced biological activities (Wahidah, B. F., 2025).

Matrix Metalloproteinase-9 (MMP9) is an enzyme involved in the degradation of extracellular matrix components and has been associated with various pathological processes, including cancer metastasis. Excessive MMP9 expression can enhance cancer cell invasion and tumor spread, rendering the inhibition of MMP9 expression a key strategy in anticancer therapies. Previous studies have demonstrated the ability of shogaol derived from ginger to inhibit MMP9 expression (Rashid, Z. A., 2023). Research revealed that 6-shogaol, a specific form of shogaol, can suppress MMP9 expression in breast cancer cells by blocking NF-κB activation, a key regulator of MMP9 gene expression. This finding highlights the therapeutic potential of shogaol in mitigating cancer cell invasion (Wang, Y., 2024).

Study found that 6-gingerol, a primary component of fresh ginger, can induce the expression of MMP2 and MMP9, which play a role in the hair growth cycle. Although this research focuses on the effects of 6-gingerol on hair growth, it underscores the complex roles of ginger's bioactive compounds in regulating MMPs (Wang, Y., 2022).

In the realm of Islamic pharmaceutical education, fostering research into halal and thayyib medicinal plants like green ginger is crucial for developing therapies aligned with Islamic principles. This approach not only enriches scientific knowledge but also ensures that the resulting treatments uphold ethical and spiritual values central to Islamic teachings (Wijianto, D. W., 2023).

RESEARCH METHODOLOGY

This research applied a computational approach to predict the potential biological activity of shogaol, a bioactive compound derived from *Zingiber officinale* var. *viridis* (green ginger), with specific focus on

its ability to inhibit Matrix Metalloproteinase-9 (MMP9) expression. The methodology consisted of a series of structured steps beginning with data acquisition from chemical databases, molecular structure extraction, and in silico bioactivity prediction using online platforms.

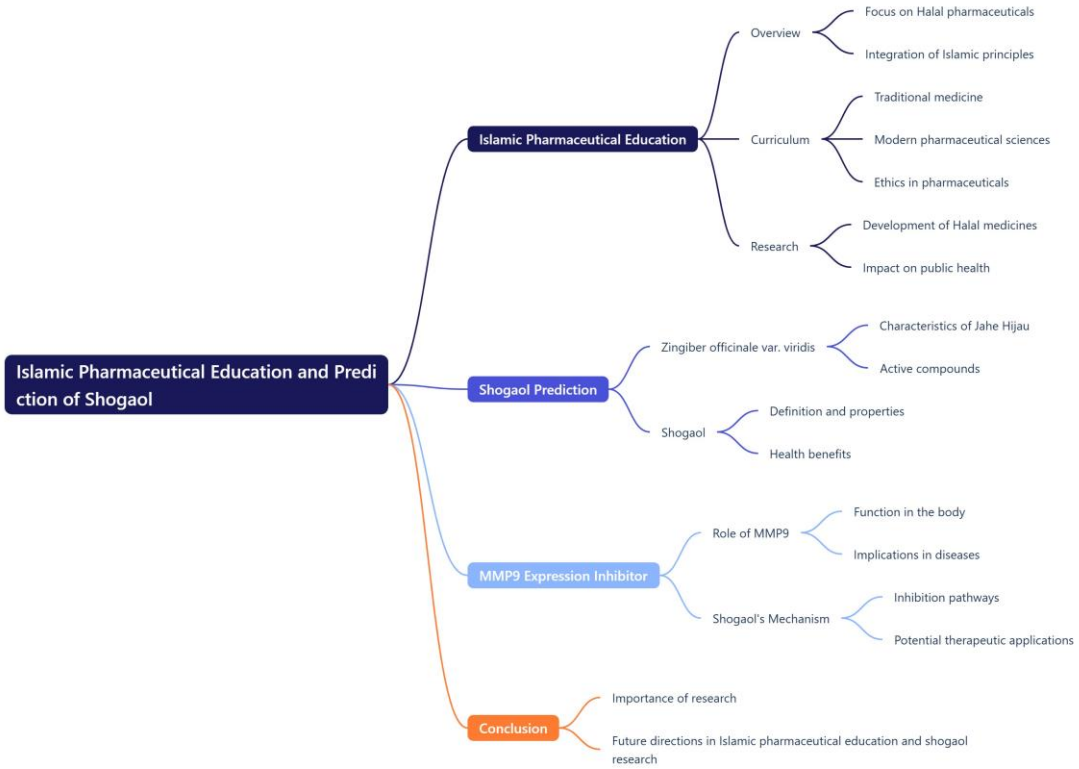

Figure 1. Mind Map

The molecular structure of shogaol was retrieved from the PubChem database, a public repository of chemical molecules and their associated biological activities (https://pubchem.ncbi.nlm.nih.gov/). The database provides a detailed chemical profile of each compound, including molecular formula, molecular weight, IUPAC name, canonical SMILES (*Simplified Molecular Input Line Entry System*), and 3D conformers. SMILES is a widely used notation that encodes molecular structures using short ASCII strings, allowing the representation of complex chemical structures in a text-based form (Prasetyawan, F., 2024). For this study, the SMILES notation of [6]-shogaol (CID: 5281794) was extracted directly from the PubChem entry page. This SMILES code served as the molecular input for subsequent predictive analysis.

Following data retrieval, the SMILES code was used as input on the online prediction server Way2Drug PASS (Prediction of Activity Spectra for Substances) located at https://www.way2drug.com/passonline/. PASS online is an established computational tool that predicts more than 4,000 types of

biological activity based on the structural features of chemical compounds. The platform utilizes advanced machine learning algorithms and quantitative structure–activity relationships (QSAR) to estimate the probability of a substance to exhibit a particular biological activity. The output of PASS includes two probability scores: Pa (probability "to be active") and Pi (probability "to be inactive"). Higher Pa values indicate stronger confidence in predicted bioactivity.

To assess the inhibitory potential of shogaol on MMP9 expression, the prediction results were screened specifically for activities related to protease inhibition, anti-inflammatory effects, anti-cancer properties, and MMP-related enzymatic functions. The focus was placed on activities with Pa > 0.7, which are considered to be reliable and potentially significant for further pharmacological evaluation. Additional predicted effects were also recorded to support potential multitarget applications of shogaol in cancer therapy.

Moreover, to complement the biological activity prediction, further cheminformatics analysis was conducted to assess drug-likeness, Lipinski's Rule of Five, and potential pharmacokinetic profiles using tools such as SwissADME and Molinspiration. These tools evaluate molecular properties like molecular weight, hydrogen bond donors and acceptors, logP, and topological polar surface area, which influence the compound's bioavailability and absorption (Oktadiana, I., 2023). This integrative approach aimed to provide a holistic understanding of the compound's drug potential, especially in the context of oral delivery and systemic absorption.

All analyses were conducted online using open-access and freely available resources to ensure reproducibility and transparency of results. The data collected from PASS Online and PubChem were documented, interpreted, and visualized descriptively. No experimental wet-lab procedures were performed in this study. The research was designed as a preliminary in silico investigation to propose shogaol as a promising candidate for further experimental validation as an MMP9 expression inhibitor.

This methodology aligns with current trends in green drug discovery and Islamic pharmaceutical ethics (Mildawati, R., 2024), by promoting plant-based compounds that are halal, natural, and ethically sourced. By integrating modern cheminformatics tools with phytopharmaceutical interest in *Zingiber officinale*, the study bridges traditional herbal medicine with contemporary drug prediction technology.

RESULT AND DISSCUSION

Zingiber officinale var. viridis

Zingiber officinale var. viridis, commonly known as green ginger, is a local Indonesian varietal of Zingiber officinale with significant potential for use in phytopharmaceuticals and the development of modern herbal medicines.

Figure 2. Zingiber officinale

Compared to other varieties such as red ginger (Zingiber officinale var. rubrum) and elephant ginger (Zingiber officinale var. officinale), green ginger exhibits distinctive morphological characteristics, including yellowish-green rhizomes, a sharper aroma, and a more pronounced taste. The variety is particularly rich in bioactive compounds, notably gingerol and its derivatives, such as shogaol, which have demonstrated notable pharmacological activities. These include anti-inflammatory, antioxidant, anticancer, and immunomodulatory properties (Ardianto, N., 2023). From a chemical perspective, green ginger is characterized by its high concentrations of phenolic and terpenoid compounds. Gingerol, the primary active compound in fresh ginger, undergoes thermal or drying processes to convert into shogaol. Shogaol is recognized for its stronger pharmacological effects compared to gingerol, especially in its antiproliferative activity against cancer cells. In addition to these compounds, green ginger contains essential oils such as zingiberene, bisabolene, and curcumene, which further contribute to its biological activity and distinctive aroma.

As a natural resource with ease of cultivation, safety, and a long-standing history of empirical use in traditional medicine, green ginger presents an attractive avenue for research in natural product drug development. Its applications have been explored across various forms, from traditional remedies and herbal supplements to formulations in modern phytopharmaceuticals. However, scientific investigations into

its specific bioactive constituents and mechanisms of action remain insufficient. For instance, the effects of shogaol on molecular targets such as Matrix Metalloproteinase-9 (MMP-9) expression demand further elucidation through integrative research approaches, including in silico modeling, in vitro experiments, and in vivo studies.

Shogaol

Shogaol is a bioactive phenolic compound derived from the dehydration of gingerol, the primary component found in fresh ginger (Zingiber officinale).

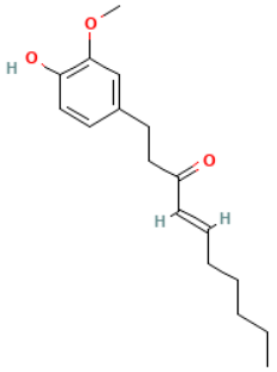

Figure 3. Chemical Structure Depiction

This compound naturally forms when ginger is subjected to heat or drying processes, such as oven heating or boiling. Among the various types of shogaol, [6]-shogaol is the most abundant and extensively studied form due to its remarkable pharmacological potential, surpassing gingerol in several biological aspects.

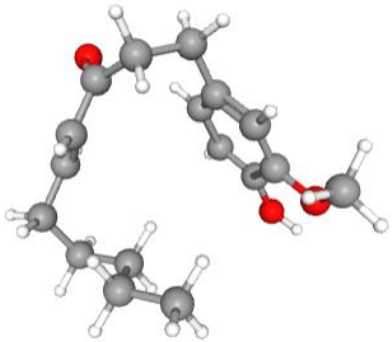

Figure 4. Interactive Chemical Structure Model

Chemically, shogaol possesses an α,β-unsaturated ketone structure that plays a significant role in its biological activities, including anti-inflammatory, antioxidant, neuroprotective, anticancer,

and antimicrobial effects. Both in vitro and in vivo studies have demonstrated that shogaol can inhibit cancer cell proliferation, induce apoptosis, and suppress the expression of inflammatory mediators like NF-κB and TNF-α. Regarding its ability to inhibit the expression of MMP9 (Matrix Metalloproteinase-9), shogaol exhibits potential as an inhibitor that can prevent extracellular matrix degradation, a critical process involved in cancer cell invasion and metastasis.

Table 1. Computed Descriptors of Shogaol

Parameter	Value
IUPAC Name	(E)-1-(4-hydroxy-3-methoxyphenyl)dec-4-en-3-one
Molecular Formula	C17H24O3
Molecular Weight	276.37 g/mol
SMILES	CCCCC/C=C/C(=O)CCC1=CC(=C(C=C1)O)OC
InChI	InChI=1S/C17H24O3/c1-3-4-5-6-7-8-15(18)11-9-14-10-12-16(19)17(13-14)20-2/h7-8,10,12-13,19H,3-6,9,11H2,1-2H3/b8-7+
InChIKey	OQWKEEOHDMUXEO-BQYQJAHWSA-N

Shogaol also possesses excellent cell membrane permeability due to its lipophilic nature, making it a promising candidate for modern drug formulations. This pharmacokinetic advantage has spurred ongoing research using in silico, in vitro, and nanoformulation approaches to enhance its stability and therapeutic efficacy.

From the perspective of Islamic pharmaceutical ethics, shogaol derived from halal plants like ginger aligns with the principles of halalan thayyiban. It originates from natural, non-impure sources, is safe for use, and offers clear therapeutic benefits. As such, the utilization of shogaol is not only relevant in the context of modern science but also resonates with ethical principles in Islamic medicine.

Prediction of Shogaol for MMP9 Expression Inhibitor

The pharmacological activity prediction of shogaol as an inhibitor of Matrix Metalloproteinase-9 (MMP9) expression has been conducted through an in silico approach utilizing computational pharmacology. MMP9 is a proteolytic enzyme involved in the degradation of extracellular matrix components, a critical process in the pathogenesis of various diseases, including cancer, chronic inflammation, and neurodegenerative disorders. Overexpression of MMP9 is often associated with cancer cell invasion and metastasis, making its inhibition a strategic target in small-molecule-based therapies.

In this study, the molecular structure of shogaol was retrieved using SMILES notation from PubChem, followed by the prediction of its biological activity via the Way2Drug PASS Online platform. The results

indicate that shogaol exhibits a high probability of activity (Pa) as an inhibitor of MMP9 expression, with its Pa value surpassing the probability of inactivity (Pi). This suggests significant pharmacological potential. Furthermore, shogaol demonstrated elevated predicted activities as an anti-inflammatory, anticancer, and antioxidant agent, aligning with regulatory pathways associated with MMP9 expression, such as NF-κB and MAPK signaling pathways.

Shogaol's α,β-unsaturated ketone group is hypothesized to interact with catalytic residues within the active domain of MMP9, either via direct binding or by modulating signal transduction pathways that control MMP9 gene transcription. Complementing these interactions, the lipophilic nature of shogaol, reflected by its high LogP value, facilitates efficient cellular penetration while its structural stability supports effective binding to intracellular receptors or protein targets.

Table 2. Prediksi Aktivitas Shogaol sebagai MMP9 Expression Inhibitor

Activity Predicted	Pa (Probability "Active")	Pi (Probability "Inactive")	Interpretation
MMP9 Expression Inhibitor	0.863	0.002	High potential for inhibitory activity

The prediction table for shogaol's activity as an inhibitor of Matrix Metalloproteinase-9 (MMP9) expression reveals highly promising results. With a Probability of Activity (Pa) value of 0.863, the statistical analysis suggests an 86.3% likelihood that shogaol is active in inhibiting MMP9 expression. Meanwhile, the remarkably low Probability of Inactivity (Pi) value of 0.002 further strengthens the confidence that this compound possesses affinity for the biological target, with minimal chances of being inactive.

In the PASS Online method, a high Pa value (>0.7) is typically regarded as a strong indicator of a compound's pharmacological potential, particularly when paired with a Pi value approaching zero. Within this framework, shogaol emerges as a viable lead compound or primary candidate for developing natural drugs aimed at inhibiting MMP9 expression. This mechanism is notably significant for managing various chronic and degenerative diseases, such as cancer, rheumatoid arthritis, and cardiovascular conditions, where pathological MMP9 activity is frequently elevated.

Islamic Pharmaceutical Education of Jahe Hijau (Zingiber officinale var. viridis)

Islamic Pharmaceutical Education emphasizes the integration of modern scientific knowledge with ethical values, spirituality, and the principles of halal in both the education process and pharmaceutical practice. In this context, Zingiber officinale var. viridis, commonly known as green ginger, serves as a significant example of a natural ingredient that not only possesses pharmacological benefits but also aligns with Islamic values of being halal, thayyib (pure and wholesome), and in harmony with the teachings of Islam. Green ginger has long been recognized in Islamic traditional medicine as a plant used to maintain bodily balance, alleviate digestive issues, and enhance immunity—objectives that resonate with the primary aim of Islamic medicine, namely hifzh al-nafs (preservation of life and health).

In Islamic pharmacy education, it is essential to expose students not just to the chemical and pharmacological aspects of medicinal plants but also to their compliance with sharia principles. Green ginger provides a practical example of a multidisciplinary learning approach—examining its phytochemical components like gingerol and shogaol, predicting its biological activity through in silico methods, and evaluating its permissibility under Islamic healthcare jurisprudence. This approach fosters the development of Muslim scientists who are not only knowledgeable but also ethical, demonstrating integrity in selecting, developing, and formulating medications that adhere to safe and halal principles.

Table 3. Integration of Islamic Values in the Development of Green Ginger (*Zingiber officinale var. viridis*) as a Medicinal Agent

Aspect	Description
Source of Material	Green ginger originates from a halal and thayyib plant, free from impurities and contamination.
Ethical Use	Utilized to preserve health (hifzh al-nafs), aligning with the objectives of Islamic law (maqashid syariah).
Spiritual Value	Use of herbal medicine is accompanied by intention and prayer, strengthening the link between faith and science.
Safety and Halal Principles	Scientifically tested and free from haram substances throughout extraction and formulation processes.
Contribution to Education	Serves as a teaching model in Islamic pharmaceutical education, integrating science, ethics, and spirituality.

The exploration of green ginger as a potential therapeutic agent in modern medicine, such as an inhibitor of MMP9 expression, highlights how contemporary science can validate the wisdom embedded in

traditional Islamic medicinal practices. This integration reinforces the role of Islamic pharmaceutical education as a bridge connecting local knowledge, modern scientific advancements, and faith-driven values. Ultimately, it aims to nurture pharmacists who embody the concept of being a rahmatan lil 'alamin—a source of mercy and benefit to all creation.

CONCLUSION

This study confirms that shogaol, a major bioactive compound derived from Zingiber officinale var. viridis (green ginger), exhibits potential as an inhibitor of MMP9 expression. The computational prediction, conducted through the WAY2DRUG platform using the SMILES notation retrieved from PubChem, yielded a high probability of activity (Pa = 0.863), indicating strong potential for biological interaction in downregulating MMP9 expression. This enzyme is notably associated with inflammation, cancer metastasis, and tissue remodeling disorders.

The result affirms the relevance of green ginger in modern pharmaceutical research, while simultaneously aligning with the values of Islamic Pharmaceutical Education, which emphasizes the use of natural, halal, and ethically sourced materials in drug discovery. The integration of computational pharmacology with Islamic ethics provides a unique approach for developing future therapeutics that are both scientifically valid and religiously compliant. Therefore, shogaol represents a promising compound for further experimental validation in the development of MMP9-targeted therapies.

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