Potency Evaluation of Temulawak Through Physicochemical, Pharmacokinetics, Druglikeness, Water Solubility, Tox Prediction For KUB Chickens

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Abstract.

Temulawak is one of the spices in Indonesia that is useful as a phytobiotic. Phytobiotics are beneficial for livestock in maintaining health, namely maintaining immunity, especially in chickens. One type of chicken that is widely cultivated in Indonesia is the KUB chicken to increase its productivity. This study aims to identify the potential compounds found in temulawak (Curcuma Xanthorrhiza). The research methods included literature studies and ADMET testing. The most abundant compound in temulawak was β-Curcumene with a molecular weight of 204.35 g/ml, a hydrogen bond donor count of 0, a hydrogen bond acceptor count of 0, and a TPSA value of 0.00 Å2 . The β-Curcumene compound is not classified as an inhibitor of CYP1A2, CYP2C19, CYP2D6, CYP3A4. β-Curcumene has drug-like properties according to the rules of Lipinski, Ghose, Veber, Egan but does not have drug-like properties according to Muegge's rules. The log S ESOL value of -4.93 is in the moderate solubility category, the log S SILICOS – IT value of -3.55 is good solubility, and the log S Ali value of -6.27 is in the poor solubility category. β-Curcumene has toxic compounds that are active and affect BBB-barrier performance by 97%, ecotoxicity target by 64%, estrogen hormone performance by 75%, and drug metabolism performance by 65%.

Keywords: *β-Curcumene; ADMET; Curcuma Xanthorrhiza and Temulawak.*

I. INTRODUCTION

Phytobiotics are useful for antibacterial, healing, disease prevention, and boosting the immune system. The use of phytobiotics can replace the function of synthetic antibiotics, such as for improvement in growth, health, and productivity in livestock. Phytobiotics can be used in humans and livestock through herbal ingredients, one of which is temulawak. (Yusuf et al., 2023). Animal productivity is an important parameter because it is related to growth. Animal productivity measured through weight gain, FCR, body size, and the amount of meat, eggs, and milk produced. These indicators were influenced by various factors, such as improving livestock nutrition, maintaining livestock hygiene and health, including the administration of natural phytobiotics as feed additives for livestock, and minimizing the use of synthetic antibiotics in feed. The use of phytobiotics did not have a negative impact on livestock production and health and did not cause resistance to microorganisms. Traditional medicine contains many natural ingredients that are widely used in Indonesia, originating from plants of the Zingiberaceae family, and such as temulawak (Curcuma xanthorrhiza Roxb) (Praceka et al., 2022). Temulawak is classified as a medicinal plant and has active ingredients. (Sinabariba et al., 2024). Temulawak contains phytochemical compounds such as Tricyclene, α-Pinene, Camphene, Sabinene, β-Pinene, β-Myrcene, α-Phellandrene, α-Terpinene, p-Cymene, Limonene, β-Ocimene, γ-Terpinene, α-Terpinolene, Eucalyptol / 1,8-cineole, Sabinene hydrate, Linalool, Camphor, Isoborneol, Borneol, Terpinen-4-ol, α-Terpineol, 9-Eiemene, α-Cubebene, Copaene, 7 epi-Sesquithujene, Sesquithujene, cis-α-Bergamotene, Caryophyllene, γ -Elemene, β-Farnesene, α-Curcumene, β-Curcumene, β-Sesquiphellandrene, Germacrene B, Curzerene, cis-Sesquisabinene hydrate, β-elemenone, Isospathulenol, β-Bisabolol, Germacrone, Curcuphenol, Xanthorrhizol (Septama et al., 2022).

Previous studies have stated that temulawak could increase and to increase the body weight of native chickens (Prastowo et al., 2020). Temulawak is useful for reducing abdominal fat in broiler chickens (Sahara et al., 2025). Temulawak has an impact on the feed consumption of laying hens (Junita et al., 2024). Egg

weight in layer chickens can be increased through the adding of temulawak (Purwanti et al., 2023). The use of natural phytobiotics from temulawak (Curcuma Zanthorrhiza) could serve as a safe and sustainable alternative to synthetic antibiotics in KUB chickens. ADMET is useful for determining the effectiveness and therapeutic success of a drug (Hakiki et al., 2024). The physicochemical profile and toxicity properties of such as a compound are determined through ADMET testing. ADMET stands for Adsorption, Distribution, Metabolism, Excretion, and Toxicology (Izzaturahmi et al., 2023). The benefits of ADMET testing are such as identifying potentially toxic effects in compounds, reducing the potential for failure in drug development, and identifying drug interactions so that adverse effects can be minimized (Anastasya et al., 2023). With tox prediction, drug compounds that have toxic potential can be eliminated immediately at an early stage (Hajal and Meslamani, 2024). Native chickens have several advantages, such as good resistance to climate and ease of adaptation to dry land. One of the native chickens in Indonesia that has these advantages and is cultivated is the Balitnak Superior Native Chicken (KUB) (Laudengi et al 2025). The KUB chicken improvement is a process that involves the addition of temulawak as a phytobiotic. KUB chickens are widely raised to meet human demand for meat and eggs because of their superior growth and productivity, making them a popular choice for consumption in Indonesia and a valuable source of animal protein. Because of the importance of temulawak administration for KUB chickens, it is necessary to conduct tests to determine the potential compounds contained in temulawak, such as physicochemical content, pharmacokinetics, drug likeness, tox prediction, and water solubility. With these tests, it is hoped that the potential compounds contained in temulawak can be identified, thereby improving the health of KUB chickens.

II. MATERIALS AND METHODS

Materials

Microsoft Windows 11 operating system, 12th Gen Intel® Core™ i3 processor, 8 GB RAM. 1. Website http://www.swissadme.ch/index.php and website https://tox.charite.de. Compound β-Curcumene in Temulawak.

Methods

ADMET Testing

Physicochemical properties, pharmacokinetics, Druglikeness analysis, water solubility

1. A literature study of the compounds contained in temulawak (Curcuma Xanthorrhiza) based on research by Ibrahim et al., 2012; Septama, et al 2022) found that the most abundant compound was β-Curcumene.
2. Go online to the website https://pubchem.ncbi.nlm.nih.gov/ and type β-Curcumene in the search field to obtain the SMILE code.
3. Method for analyzing druglikeness, physicochemical properties, pharmacokinetics, and water solubility online via the website http://www.swissadme.ch/index.php

Toxicity Prediction Analysis

1. The analysis is conducted online via the website https://tox.charite.de/. Click the “Tox Prediction” menu, then enter the SMILE for the β-Curcumene compound in the Canonical Smiles field to obtain information on acute toxicity and binding to 16 toxicity targets
2. Select All and start tox prediction

Data Analysis

Physicochemical properties, pharmacokinetics, Druglikeness analysis, water solubility using http://www.swissadme.ch/index.php. Toxicity prediction analysis using website https://tox.charite.de/.

III. RESULT AND DISCUSSION

The pharmacokinetic profile needs to be known so that the presence of active substances in the body can be determined, particularly the pharmacological activity of new drugs (Bahi et al., 2020). The results of physicochemical observations on the β-Curcumene compound obtained a molecular weight of 204.35 g/ml, a hydrogen bond donor count of 0, a hydrogen bond acceptor count of 0, and is a class of drug that has good absorption. The benefit of Lipinski's rule is that it provides information about pharmacological activity and whether the compound can be active when given orally (Alfaridza et al., 2025). This is in accordance with

the five rules according to Lipinski et al (2001), which is a drug does not have good absorption if the hydrogen bond donor is more than 5, the hydrogen bond acceptor is 10, the molecular weight has a value of more than 500 daltons, and the log P value is greater than 5. The TPSA observation result for the β-Curcumene compound is 0.00 Å2, while according to Daina et al (2017), TPSA has an optimal value when it ranges from 20 to 130 Å2. Fadlan et al (2022) also said that TPSA, or Topological Surface Area, can affect molecular flexibility because it's related to rotatable bonds. Based on the observations and compared to the literature, we can conclude that the TPSA value of β-Curcumene has a less flexible molecule.

Pharmacokinetics Properties

The pharmacokinetic properties of β-Curcumene obtained from the research, based on the results of pharmacokinetic testing on β-Curcumene, it could be determined that it has a low GI with a skin permease value of -2.95 cm/s. Pharmacokinetics properties such as CYP1A2 inhibitor, CYP2C19 inhibitor, CYP2D6 inhibitor, CYP3A4 inhibitor were "No". Although CYP2C9 inhibitor was "Yes" on pharmacokinetics properties. The blood-brain barrier (BBB) cannot be crossed by β-Curcumene. According to Krihariyani et al (2020), an important indicator for drugs is their potential to cross the BBB, as this could reduce the negative effects or side effects of the drug, as well as its toxic properties. Additionally, it could influence the drug's pharmacological potential for the brain. The pharmacokinetic composition shows that β-Curcumene was not classified as an inhibitor of CYP1A2, CYP2C19, CYP2D6, or CYP3A4, which means that β-Curcumene had no effect on the metabolism of CYP1A2, CYP2C19, CYP2D6, or CYP3A4. However, β-Curcumene could act as an inhibitor and affect metabolism in CYP2C9. Based on the results of research by Hakiki et al., 2024, CYP2C9 was found to be abundant in the liver with the second highest expression level compared to other isoforms. The presence of compounds that were included as inhibitors affected the CYP2C9 metabolism process, which required a long time to remain in the body.

Druglikeness

Druglikeness is such as the process of drug absorption and distribution related to orally given drugs, the criteria for which are based on Lipinski's Rule of Five (Syafrizayanti et al., 2023). Analysis of the characteristics of drugs affected by β-Curcumene showed that the content found in β-Curcumene based on the Lipinski, Ghos, Veber, and Egan rules was suitable but did not meet the suitability of Muegge's parameter rules. Research by Sardar (2023) stated that the bioavailability value with a good category was 0.55, so it can be concluded that the results of the study on the β-Curcumene compound with a bioavailability value of 0.55 were in the good category. Based on the rules of Lipinski, Ghose, Veber, and Egan for drug likeness analysis, the value is positive, namely Yes, which means that it has similarities with drugs, but according to Muegge's rule, the value is negative, namely No, which means that the β-Curcumene compound did not have similarities with drugs and therefore could not be used as a drug. The assessment of compatibility in drugs can be improved through computation, namely Muegge analysis. The drug category based on Muegge analysis can be outside the optimal limit if there was a "No" label on the molecule, which could be interpreted as the molecule having undesirable properties in terms of the efficacy and safety of oral drugs. However, this can be improved by 1) redesigning the molecule by arranging the structure according to specific objectives to achieve improvement in physicochemical properties, such as reduced molecular weight or increased solubility (Tian et al., 2015, Ritchie et al., 2011).

Water solubility

Absorption and effectiveness can affect solubility in drugs (Ferdiansyah et al., 2021). Drug solubility can affect the absorption of drugs in the gastrointestinal tract because drug solubility is a factor that impacts the absorption of drugs administered orally (Dara and Husni,2017). Based on ESOL observations, a log S value of -4.93 was obtained, which falls into the moderate solubility category, while SILICOS-IT was observed to have a log S value of -3.55, which falls into the good solubility category. However, Ali's observations showed a log S value of -6.27, which falls into the low solubility category. According to Staneva et al (2024), estimation using computational models required several methods in order to address tentative value differences.

Tox prediction

Medicines can have a damaging effect on organisms, which is called drug toxicity (Maulida et al., 2023). Toxicological assessment plays a role in identifying critical components of pharmacology, the environment, and chemical safety through the examination of harmful effects originating from chemicals, physical agents, and living organisms (Shao et al., 2024). The most common compound in temulawak (Curcuma Xanthorrhiza) is β-Curcumene, whose molecular structure was shown in Figure 1 .

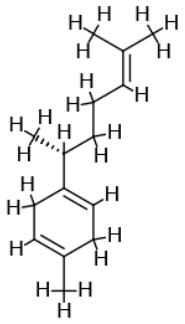

Fig 1. β-Curcumene Molecule

Computational methods for predicting toxicity have the advantage of determining toxic doses more quickly and minimizing the use of experimental animals. (Nursanti et al., 2023). Based on the results of the study, it was found that β-Curcumene contains toxic compounds about that were active or inactive. The toxic compounds in β-Curcumene that were active could affect the performance of the BBB barrier or the layer that protects the blood vessels in the brain by 97%. The toxic compounds with an ecotoxicity target of 64% and the β-Curcumene compounds that affected the estrogen receptor alpha (ER) target or affected estrogen hormone performance by 75%. β-Curcumene could affected the performance of Cytochrome CYP2C9, which is related to metabolic activities such as drug metabolism by 65%.

IV. CONCLUSION

The chemical composition found in temulawak is β-Curcumene. β-Curcumene in temulawak is compatible with drugs according to the Lipinski, Ghos, Veber, and Egan rules, which can be used as a phytobiotic in KUB chickens.

V. ACKNOWLEDGEMENT

This research was supported by funding from Banyuwangi State Polytechnic under the Internal Junior Lecturer Research scheme.

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