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Research Article

# In-silico Analysis Potential Of *Curcuma zedoaria* As A Candidate For Degenerative Disease Therapy

**Fitria Dwi Damayanti[1], Risma Ayu Setiawan[1], Tri Luthfiana Maretha[1], Trikxy Viori Andhani[1], Faiznanda Awwaluddin[1], Resi Puguh Prihantono[1] , Ahmad Shobrun Jamil[1,*]**

[1] Pharmacy Study Program, Faculty of Health Sciences, University of Muhammadiyah Malang

[*] *Corresponding author: shobrun@umm.ac.id*

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**Abstract:** Indonesia has a high and diverse biodiversity, particularly in plant species. There are numerous advantages to using various plants that grow in Indonesia. Indonesia is also known for its abundance of spices and other natural resources. Rapid research is required in the use of this plant in order for bio-based products to be widely accepted. Using in-silico predictions by utilizing meta data provided by several credible sites is one of the important rapid methods in analyzing the benefits of the chemical content of *Curcuma zedoaria* (Temu putih). The goal of this in-silico analysis-based study is to gain an understanding of the pharmacology of a plant known as potency simplicia *Curcuma zedoaria*. Analyzing metadata from various sources is the research method. Prediction of absorption, distribution, metabolism, and excretion (ADME) was obtained from http://www.swissadme.ch/. The prediction of target proteins for phytochemical compounds of *Curcuma zedoaria* is available at http://www.swisstargetprediction.ch/, while the construction of active protein networks and interactions after induction of compounds contained in *Curcuma zedoaria* rhizome is available at https://string-db.org. According to the in-silico analysis performed with some of the software mentioned above, the rhizome of *Curcuma zedoaria* (Temu Putih) contains 71 active compounds, 64 of which are highly bioavailable. According to in-silico research, *Curcuma zedoaria* (Temu Putih) contains curcumin compounds (diarylheptanoid) and its derivatives have antioxidant activity, which functions to prevent stress from physiological stimulation that can increase the number of leukocytes.

**Keywords**: Biodiesel In-silico, Prediction, Curcuma zedoaria. Anxiety Disorders

## Introduction

Indonesia is known for its abundance of spices and other natural resources, as well as its diverse biodiversity. With a high level of biodiversity, it can be used as a medicinal plant, becoming the primary ingredient in the production of herbs and herbal medicines. Medicinal plants are widely used by the general public because they have low side effects when compared to chemical drugs and help to reduce the use of chemical drugs. Turmeric plants (*Zingiberaceae*) are one of the medicinal plants commonly used in traditional Indonesian herbs [1].

Temu Putih (*Curcuma zedoaria*) is a spice in the Curcuma genus that is related to Intersection manga (*Curcuma manga*) and Intersection ireng (*Curcuma xanthoriza*) [2]. This plant can grow up to 1.5 m in height, has leaves that can reach 80 cm in length, and the leaves in the middle are purple [3,4]. Curcumin compounds (diarylheptanoid) in Temu putih rhizome plant and its derivatives have antioxidant effectiveness in preventing stress from physiological stimulation that can increase the number of leukocytes [4]. Other compounds in this plant, namely essential oils, aid in the digestive process by stimulating nervous system secretion, resulting in the production of digestive enzymes such as pepsin, trypsin, lipase, and amylase, which are secreted into the stomach and small intestine to increase nutrient metabolism [4].

According to data from the Ministry of Health of Indonesia in 2007, there were 450 million people who had to live with mental disorders, and 11.6 percent of adult individuals (aged 18 years and over) to the elderly experienced emotional disorders, such as anxiety and depression [6]. Basic Health Research on adult Indonesians shows an increase in emotional disorders, by 6% in 2013 and 9.8 percent in 2018, with headaches, sleep problems, decreased appetite, and fatigue being the most common symptoms [7]. This is an in-silico predictive study that makes use of meta data from a number of credible websites. *Curcuma zedoaria* (Temu putih) chemical compound content was obtained from the website http://www.knapsackfamily.com/. The website http://www.swissadme.ch/ provided absorption, distribution, metabolism, and excretion (ADME) predictions [8, 9]. The classification of metabolites found in *Curcuma zedoaria* is described on the website http://www.swissadme.ch/ [8]. used to predict the target protein of Temu putih rhizome phytochemical compounds on the page http://www.swisstargetprediction.ch/ [10, 11]. The activated protein network construction and its interactions following the induction of *Curcuma zedoaria* compounds were obtained from the https://string-db.org page.

The findings of the study can give an overview of the potential of *Curcuma zedoaria*, which contains secondary metabolites of terpenoid compounds, particularly sesquiterpenoids and monoterpenoids. In this study, three compounds are used to create new drugs that can be used to treat anxiety disorders. The findings of this study are also expected to inspire other researchers to conduct a thorough investigation into the potential of native Indonesian plants as sources of raw materials for herbal medicines.

## Materials and Methods

### Materials

In this study, the in-silico method was used via computerized analysis. Knapsack family (http://www.knapsackfamily.com/), pubchem (https://pubchem.ncbi.nlm.nih.gov), swissADME (http://www.swissadme.ch/), swiss target (http://www.swisstargetprediction.ch/), and string db (https://string-db.org) are some of the servers used for this research.

### Phytochemical Data Warehouse and Phytochemical Data Unification

The data source used to determine the chemical content of *Curcuma zedoaria* is the warehouse page of the Knapsacfamily Database which opened on July 15, 2022 with the page http://www.knapsackfamily.com/. The data is obtained by entering the scientific name of the plant in the search engine section and selecting the menu "knapsack keyword search". The results are copied into an Excel worksheet. Furthermore, the data is unified by completing the identity of the compounds including canonical smiles by entering one by one the names of the compounds contained in the *Curcuma zedoaria* in the data warehouse https://pubchem.ncbi.nlm.nih.gov on July 16, 2022. The result of this unification is a list of names compounds in *Curcuma zedoaria* , compound code, synonyms, canonical smiles and other supporting data

### Prediction of the Absorption, Distribution, Metabolism and Excretion (ADME) of Compounds in Temu Putih Rhizoma.

The website http://www.swissadme.ch/ was used to predict the ADME compounds found in Temu putih rhizome. The canonical smile of the compound *Curcuma zedoaria* was obtained from https://pubchem.ncbi.nlm.nih.gov/ and incorporated in the previous step, in the menu provided http://www.swissadme.ch/. Canonical smiles entry is done directly for all compounds with the order of entry canonical smiles and followed by the eleven character code compounds that we created ourselves in the previous unification table. Then click the "run" menu and the results of the ADME analysis will appear.

### Prediction of the relationship between *Curcuma zedoaria* and cell proteins

The STRING database, available at https://stringdb.org, aims to collect, evaluate, and integrate all existing protein-protein interaction information sources in the database, as well as to supplement it

with computational predictions. The goal is to present a complete and objective picture of the network of cell-cell protein interactions, including both direct (physical) and indirect (functional) interactions between these proteins [12]. Proteins from the http://www.swisstargetprediction.ch/ database appear in many variations of the protein menu in the STRING data. The program will then process and generate network configurations of proteins involved in the induction of Temu Putih compounds in cells.

## Results and Discussions

Three approaches can be used in exploratory research to determine the activity of compounds in plants. The first is an in vitro test, followed by an in vivo test, and finally by an in-silico test. The in-silico test has scientific validity, is relatively new, and has high accuracy [13].

Temu Putih rhizome compounds, which initially contained 71 compounds, were reduced to 64 compounds because they were selected during the Swissdme application on the web at http://www.swissadme.ch is used to forecast the pharmacokinetics of the body's substances. In order to find canonical SMILES for compounds that are significantly anticipated to have pharmacodynamic activity, go to https://pubchem.ncbi.nlm.nih.gov, copy the canonical SMILES, and then visit the SwissADME webpage at http://www.swissadme.ch. Paste SMILES are employed in the right column to present a list of SMILES. Press the Run button, then wait for the a moment. Results from SwissADME are provided; select Show the cooked egg, then let the boiled egg be seen. Our group only selects the compound that is inside the boiled egg circle. The compound outside of the boiling egg circle is subsequently deleted from the Excel data. Then, the data for compounds with excellent is seen in Excel. The data in Excel is then analyzed for substances with strong bioavailability and solubility, while those are noted and colored red as indicate that.

### The Results of Swissadme

We selected compounds from the Swissadme results that met the following criteria: good bioavailability (from table 1, the darker the color, the better the bioavail ability), results lipinski 0, and the last with synthetic accessibility results higher than 4.5

**Table 1.** the research results of a Swiss Adme (http://www.swissadme.ch) analysis of Temu Putih rhizome compounds

| Molecule | MW | TPSA | Ali Solubil | Ali Solubil | Ali Class | Silicos-IT class | log Kp (cm/s) | Lipinski #violations | Bioavailability Score | Synthetic Accessibility |
|---|---|---|---|---|---|---|---|---|---|---|
| Curcarabranol A | 252.35 | 54.37 | 1.39 | 0.0055 | Soluble | Soluble | -6.77 | 0 | 0.55 | 3.39 |
| Curcarabranol B | 252.35 | 54.37 | 1.39 | 0.0055 | Soluble | Soluble | -6.77 | 0 | 0.55 | 3.39 |
| Isozedoarondiol | 252.35 | 57.53 | 0.96 | 0.0038 | Soluble | Soluble | -6.7 | 0 | 0.55 | 4.13 |
| (1S,4S,5S,10R)-zedoarondiol | 252.35 | 57.53 | 0.96 | 0.0038 | Soluble | Soluble | -6.7 | 0 | 0.55 | 4.13 |
| Wenyujinin R | 252.35 | 57.53 | 0.96 | 0.0038 | Soluble | Soluble | -6.7 | 0 | 0.55 | 4.13 |
| Oxycurcumenol | 250.33 | 49.83 | 2.97 | 0.0119 | Very solul | Soluble | -6.92 | 0 | 0.55 | 4.91 |
| Aerugidiol | 250.33 | 57.53 | 2.15 | 0.00857 | Soluble | Soluble | -6.93 | 0 | 0.55 | 4.26 |
| 12-hydroxycurcumenol | 250.33 | 49.69 | 5.98 | 0.0239 | Very solul | Soluble | -7.12 | 0 | 0.55 | 5.86 |
| Curcumenol-9,10-epoxide | 250.33 | 41.99 | 1.79 | 0.00716 | Soluble | Soluble | -6.66 | 0 | 0.55 | 5.45 |
| Curcumenolactone A | 248.32 | 43.37 | 2.27 | 0.00914 | Soluble | Soluble | -6.74 | 0 | 0.55 | 4.11 |
| Curcumenolactone B | 248.32 | 43.37 | 2.27 | 0.00914 | Soluble | Soluble | -6.74 | 0 | 0.55 | 4.11 |

### The Results of Swisstarget and String db

Swissadme selected 11 compounds and then searched the website for protein targets (http://www.swisstargetprediction.ch/). Only one of the 11 compounds examined did not have a protein target because when the compound canonical smile of 12-hydroxycurcumenol was entered into the Swisstarget web, it said "There was no similar activity discovered. There will be no target." There were

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no similar cases in the reference. One excel sheet was collected from ten compounds with protein targets, copied, and pasted in string web db (https://string-db.org/) before clicking "search."

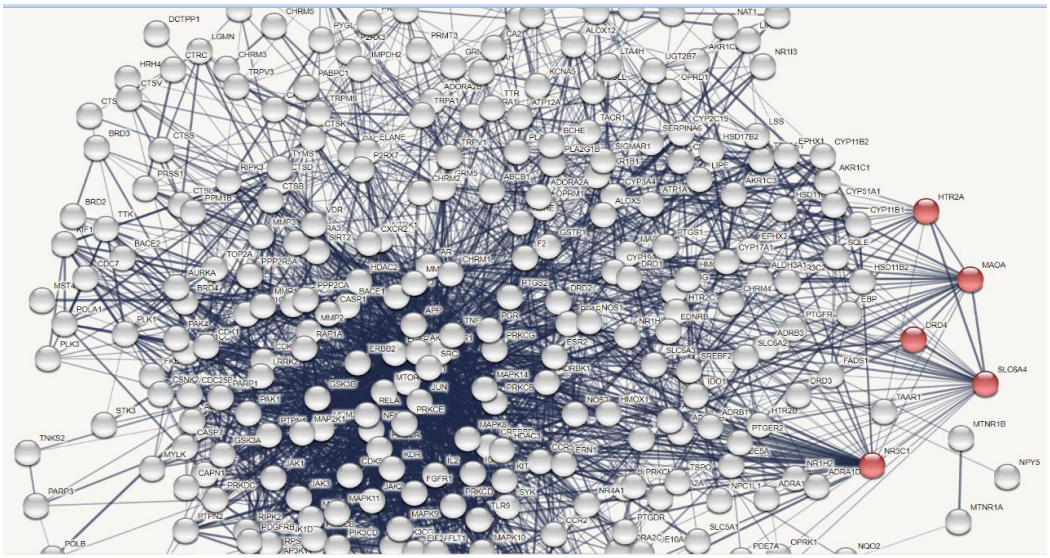


**Figure 1.** An example of the results of the analysis with String-DB (https://string-db.org) looks at the cell protein network that responds to the cucumadiol and (+)-germacrone-4,5 compound in *Curcuma zedoaria*.

Our team discovered these 5 proteins by first visiting the analysis part and then the illness list section using the db string data. There are many ailments that this simplicia can treat, but we chose to focus on anxiety problems for this study. The five proteins are HTR2A (binding ligand causes conformational changes that trigger signaling via guanine nucleotide-binding protein (G protein)), MAOA (catalyzes oxidative deamination of b-aminobutyric acid), and NR3C1 (Has the lowest transcriptional activation activity of all the isoforms made by alternative initiation and has transcriptional repression activity) (D4 dopamine receptor; Belongs to the G-protein plus receptor 1 family.)(**Table 2**).

**Table 2.** the connection between compounds and proteins

| No | Senyawa | Protein |
|---|---|---|
| 1. | Cucumadiol | NR3C1<br>SLC6A4<br>DRD4 |
| 2. | (+)-germacrone-4,5 | HTR2A<br>DRD4<br>NR3C1 |
| 3. | Curcumenol-9,10-epoxide | MAOA |

Secondary metabolites of terpenoid compounds, particularly sesquiterpenoids and monoterpenoids, are found in Temu putih (*Curcuma zedoaria Rosc*.).Temu Putih which is effective as an antineoplastic against cancer cells because it contains curcuminoids and flavonoids that can be obtained from ethanol extract, can aid in the healing process of cancer. Curcuma zedoaria ethanol extract, which has anticancer activity against Hela cells. Curcumin obtained from the ethanol extract of the rhizome of Curcuma zedoaria can trigger sit c by stimulating the occurrence of reactive oxygen and releasing membrane potentials in the mitochondria due to the activation of caspase 3, which causes apoptosis[14].

Curcuminoids (*Diarylheptanoids*) and other chemical compounds found in white ginger rhizome include essential oils, zingiberen, cineol, polysaccharides, and other groups. *Curcumin*, *Demethoxycurcumin*, and *Bisdemethoxycurcumin* are examples of known *Curcuminoids. Epicurzerenone, Kurdion*, and *Zedoaron* are all present in the volatile Temu putih oil (1-1.5%). *Curcuma zedoaria* contains essential oils as its constituents. The active ingredients in the Temu putih plant have been shown to be anti-cancer and antioxidants[15].

## Conclusion

Based on in-silico analysis performed with some of the software mentioned above, the Temu Putih rhizome plant contains 71 active compounds, 64 of which are highly bioavailable. This analysis also revealed that the two compounds found in Temu Putih rhizome could be used to develop a new drug for anxiety disorders. Relative to in-silico studies, *Curcuma zedoaria* has the potential to treat cancer, diabetes, ischemia, hypertension, skin diseases, and other diseases.

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