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# Predictive Pharmacological Activity of Galangal Rhizome (*Alpinia galanga* (L.) Willd.) Through in Silico Analysis as an Effort to Accelerate The Research of Indonesian Medicinal Plants

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**Abstract**

*Indonesia has high biodiversity, especially plant species. There are many benefits that can be Obtained from various plants that grow in Indonesia, one of which is as a health supplement or medicinal raw material. Fast researches are important in the use of these plants so that bio-based products can be widely accepted. One of the important fast methods in analysing the benefits of plant chemical compounds is the in-silico prediction utilizing metadata spread over various pages providing scientific data about plants, their chemical compound content and biological activity. This study was focused on predictively observing the biological activity of the compounds in the rhizome of Alpinia galanga. The research method is by analysing metadata from various sources. Data on the content of chemical compounds can be accessed through the page https://phytochem.nal.usda.gov/, classification of metabolite compounds contained in plants using http://classyfire.wishartlab.com/, prediction of absorption, distribution, metabolism and excretion (ADME) uses http://www.swissadme.ch/, to determine the relationship between plant compounds and body proteins, http://www.swisstargetprediction.ch/ and prediction of cellular mechanisms seen through https://string-db.org. Based on in silico analysis by utilizing some of the above software, it can be seen that the rhizome of the Alpinia galangal plant has 80 active compounds, 47 have high bioavailability and 9 compounds with tight cell proteins. Based on in silico exploration, it is also known that A. galangal has potential as an antioxidant, antimicrobial, anti-cancer and various other pharmacological activities.*

## 1. INTRODUCTION

Indonesia is known as a country with the third largest biodiversity in the world (Murray et al., 2015). As an archipelago located in the tropics, Indonesia has many endemic plant species that have various potentials. One of the important things in the abundance of plants that should be utilized optimally is in the health aspect, such as ingredients for health supplements and raw materials for medicines. In order to accelerate the research of traditional medicines in Indonesia, of course, requires a fast, easy and scientific method in predicting the biological and pharmacological activity of Indonesian plants. This acceleration can support in vitro, in vivo, pre-clinical and clinical trials so as to produce high quality natural medicines originating from Indonesia.

Galangal is one of the traditional plants used traditionally by the Indonesian people as a cooking spice and traditional medicine (Widyowati and Agil, 2018). This plant is known to contain many metabolite compounds that have pharmacological activity in the body. In this study, a predictive exploration of the activity of compounds in *A. galanga* will be carried out. Using the in-silico analysis method. In silico analysis is a computational method with a fairly accurate meta-data base. An in-silico approach that helps select plant materials or natural products with the possibility of strong biological activity. This approach can also provide insight into the rationalization of the biological activity of natural products. In-silico simulations can be used to demonstrate the ligand-binding properties of proteins for various molecular structures (Atanasov et al., 2015)

This research is a predictive in-silico study using meta data provided by several credible sites. The content of the chemical compound *Alpinia galanga* (Galangal) was obtained from the page https://phytochem.nal.usda.gov/ (Jankun et al., 2016; klipzewska et al., 2018), The prediction of absorption, distribution, metabolism and excretion (ADME) obtained from the page http://www.swissadme.ch/ (Daina et al., 2017; Ferreira & Andricopulo, 2019). The classification of metabolite compounds contained in *A. galanga* refers to the page http://classyfire.wishartlab.com/ (Djoumbou et al., 2016; Wishart et al., 2018). Prediction of target protein for phytochemical compounds *A. galanga* is used on the http://www.swisstargetprediction.ch/ page (Daina et al., 2019; Zhou et al., 2019). The activated protein network construction and interaction after the induction of compounds contained in *A. galanga* rhizomes were obtained from the https://string-db.org page.

The results of this study are expected to provide an overview of the pharmacological potential of *A. galanga*. The study results are also expected to stimulate other researchers to conduct a comprehensive study of the pharmacological potential of various native Indonesian plants so that their use can be maximized as a source of medicinal raw materials.

## 2. MATERIALS and METHODS

### Phytochemical Data Warehouse and Phytochemical Data Unification

The data source used to determine the chemical content of Alpinia galanga is the warehouse page of the Dr Duke Phytochemical Database with the page https://phytochem.nal.usda.gov/ (Jankun et al., 2016; Bantalzewska et al., 2018). The data is obtained by entering the scientific name of the plant in the search menu and selecting the menu (p) which means phytochemicals in the Latin name search list. The search results are then specified by looking for chemical content in the rhizome by selecting the rhizome menu on the advanced search menu. The results obtained are then downloaded in the form of 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 *A. galanga* rhizome in the data warehouse https://pubchem.ncbi.nlm.nih.gov/, the result of this unification is a list of names compounds

in *A. galanga*l rhizome, compound code, synonyms, canonical smiles and other supporting data.

**Prediction of the absorption, distribution, metabolism and excretion (ADME) of compounds in Rhizoma Alpinia galanga.**

Prediction of ADME compounds contained in *A. galanga*'s rhizome was carried out using http://www.swissadme.ch/ (Daina et al., 2017). Canonical smiles of *A. galanga* compound were obtained from the page https://pubchem.ncbi.nlm.nih.gov/ and unified in the previous stage, in an entry 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 A. galanga and cell proteins**

Prediction of the relationship of plant compounds with cell proteins is used http://www.swisstargetprediction.ch/ (Daina et al., 2019). Canonical smiles data are entered one by one. Every single compound will give rise to several candidate protein relations with strong, medium to weak probability. The strong probability shows that the protein relationship with the compound is high, meaning that the cellular activity involving the protein is high after the induction of the *A. galanga* compound.

**Prediction of tissue protein**

The STRING database on the https://string-db.org page aims to collect, assess and integrate all sources of information on protein-protein interactions that exist in the database and to complement it with computational predictions. The aim is to show a comprehensive and objective picture of the network of cell protein-cell relationships, including direct (physical) and indirect (functional) interactions between these proteins (Szklarczyk et al., 2019). Proteins that have been recorded through the database http://www.swisstargetprediction.ch/ are included in the multiple protein menu in the STRING data. Then the program will process and generate network configurations between proteins associated with the induction of *A. galanga* compounds in cells.

## 3. RESULTS

In exploratory research, to determine the activity of compounds in plants and to test their pharmacological properties, three approaches can be used. The first is the in vitro test, the second is the in vivo test and the third is the in silico test. In silico tests have both scientific strength and are quite new and have good accuracy (Wen et al., 2016). In this research, an exploratory study of the pharmacological potential of *A. galanga* rhizoma in humans was carried out.

The first thing to do in this study is to find data on the content of chemical compounds in *A. galanga*'s rhizome. The results of data mining from the https://phytochem.nal.usda.gov/ rhizoma Alpinia galanga are known to contain 80 compounds. Of the 80 compounds, 42 were known to have pharmacological activity. Of the 80 types of compounds contained in *A. galanga*'s rhizome, the terpenoids and flavonoids are dominated by compounds. There are several types of vitamins such as thiamine and riboflavin. There are also proimer metabolites such as protein, carbohydrates and lipids.

To be successful as a drug, a strong molecule must meet its target at the appropriate concentration in the body and remain in the bioactive state long enough to cause predictable biological events. Drug production includes evaluation of absorption, delivery, metabolism and excretion (ADME). The prediction results of ADME (Absorption,

Distribution, Metabolism and Excretion) through http://www.swissadme.ch/ show that 47 compounds have high bioavailability of the 80 identified compounds. This bioavaliability by the SWISSADME application is determined by several physicochemical parameters that refer to the effectiveness of compounds that have drug-likenes potential, such as: lipophilicity, size, polarity, solubility, flexibility and saturation (Daina et al., 2017).

Based on the test results of the active compound *A. galanga* and target protein using http://www.swisstargetprediction.ch/, it is known that there are eight compounds that have very strong interactions with cell proteins, namely Ethynyl Estradiol, Acetyleugenol, Palmitic Acid, Galanal A, Galanal B, Galangin, Galangin 3-Methyl Ether, Kaempferid, and Nicotinic Acid. Ethynyl estradiol is known to have anti-depressant activity (Vega Rivera et al., 2016) and has proliferative activity in cells (Sastradinata et al., 2019).

## 4. DISCUSSION

Kaemferid is one of the compounds in *A. galanga*'s rhizome which has various pharmacological activities. Kaemferid is reported to be an anti-proliferation agent for cancer cells at least in the league cell line, namely Hela, HCC1954, SK-OV-3 (Nguyen et al., 2015). It was also reported that kaemferid has anti-adipogenic activity through inhibition of mitotic cell expansion, either by suppressing cell proliferation or by inducing apoptosis during the initial phase of differentiation (Kumkarnjana et al., 2019). Another study states that this compound can inhibit nerve tissue damage due to the attack of amyotrophic lateral sclerosis (ALS), ALS is a progressive nervous system disease that affects nerve cells in the brain and spinal cord, causing loss of muscle control (Srinivasan & Rajasekaran, 2018 ).

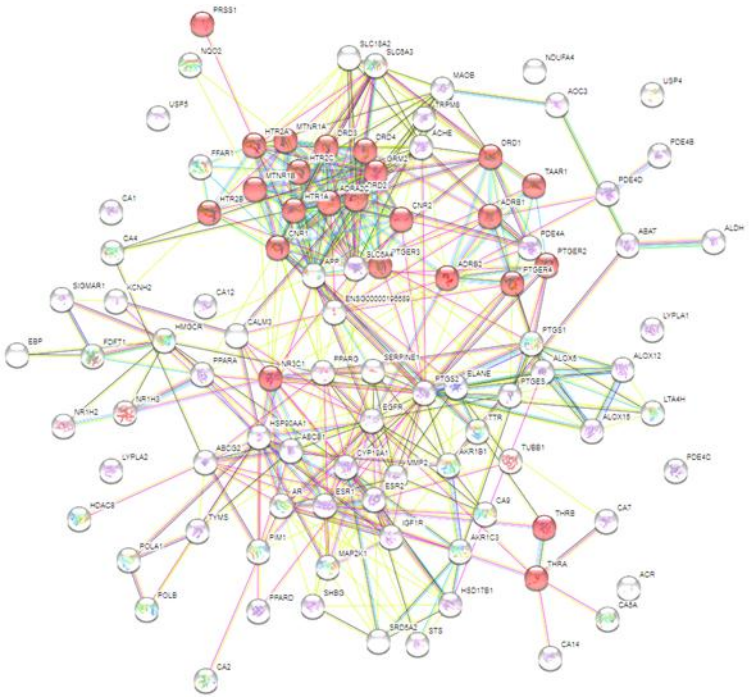

Figure 1. An example of the results of the analysis with String-DB (https://string-db.org) looks at the cell protein network that responds to the eugenol compound in *A. galanga*. The red dot is a protein neuroactive ligand-receptor interaction. Specifically describes the neuroactive protein-ligand relation pattern

The Acetyl Eugenol or eugenyl acetate in *A. galanga* has activity as an immuno-modulator. The mechanism of action is to stimulate. Eugenyl acetate has the same activity with eugenol in the aspect of being an immunomodulator, that is, it both suppresses the proliferation of B cells through T-cell independent pathways, the same as lipopolysaccharide, as well as T-cell dependent pathways. However, eugenol effectively stimulates T-cell proliferation more than eugenyl acetate via the same pathway as concanavalin (Saraphanchotiwitthaya et al., 2019). The components of essential oils (eugenol, -terpineol and -terpinene) have a bactericidal effect against gram-positive and gram-negative bacteria by disrupting their membrane systems. An important characteristic of their hydrophobicity, allows them to partition the lipids of bacterial cell membranes, disrupt cell structure and make them more permeable (Hachim & Shawi, 2016). One of the typical compounds of Alpinia galanga is galangin, this compound is included in the flavonoid group and has various pharmacological activities, including as an antioxidant, antimicrobial and anti-cancer cell proliferation (Dong et al., 2015; Eff & Rahayu, 2016; Huang et al., 2015).

## 5. CONCLUSION

Based on in silico analysis by utilizing some of the above software, it can be seen that the rhizome of the Alpinia galanga plant has 80 active compounds, 47 have high bioavailability and 9 compounds with tight cell proteins. Based on in silico exploration, it is also known that *A. galanga* has potential as an antioxidant, antimicrobial, anti-cancer and various other pharmacological activities.

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