Biological Activity Investigation of Phytocomponents in Mangosteen (*Garcinia mangostana L.*): *In Silico Study*

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Abstract

Indonesia has abundant medicinal plants, which have been historically used by the population in treating diseases for generations. Traditional Indonesian medicine and the medicinal plants used could lead to the discovery of novel drugs. The mangosteen or *Garcinia mangostana* L. is a well-known medicinal plant that has been used to treat various diseases worldwide. The pharmacological activities and phytochemical composition of the whole plant of mangosteen have been investigated and identified by scientists in recent decades. Therefore, this study aims to generate the prediction of the biological activity of phytocompotents in mangosteen. In this study, we extracted 18 phyocomponents of mangosteen from PubChem, an open chemistry database at the National Institutes of Health (NIH), USA. Then, we predicted the pharmacokinetic properties and druglike nature of the phytocomponents using the SwissADME web server, Swiss Institute of Bioinformatics, Swiss. Furthermore, PASS (Prediction of Activity Spectra for Substances) web resource has been employed as a strong potential tool to predict the biological activity. In summary, we revealed the biological activity of 18 phytocomponents of the mangosteen. However, further trials, such as in vitro and in vivo evaluation, are needed to prove the validity of these findings.

Keywords: Biological activity, *Garcinia mangostana* L., *in silico*.

Introduction

Indonesia has rich sources of natural medicines and traditional medicine preparations that have been used by most of the population for generations[1,2,3]. A direct advantage of traditional medicine formulations to the community is the ease of obtaining them[4]. The demand for plants used as traditional medicine formulations by the community is also increasing because plant-derived medicines have proven to be healthier and do not cause as many side effects as those derived from chemicals. However, a problem with traditional medicine formulations is the lack of adequate knowledge and information about the various types of plants commonly used as ingredients and their methods of use[5,6].

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Garcinia mangostana L. or mangosteen appertain to the family of Clusiaceae and genus *Garcinia*[7]. *Garcinia* is a large genus that consists of around 400 species originated from Malay Peninsula, East India, and Southeast Asia, including Indonesia. Moreover, based on the morphological and cytological studies, it can be suggested that the mangosteen is originated from Southeast Asia[8]. As a matter of fact, mangosteen is a plant as traditional medicine for hundreds of years worldwide[9].

Furthermore, mangosteen contains bioactive compounds such as xanthones, terpenes, anthocyanins, tannins, phenols, and some vitamins[10,11]. In fact, mangosteen's pericarp has many important benefits for health[12,13,14]. The main compounds in the content of mangosteen's pericarp are xanthones[15]; such as alpha-mangostin[16], gamma-mangostin[3,17], 8-deoxygartanin, garcinone E, mangostanol[18], beta-mangostin[19], tovophyllin A and B[20],

mangostenin[21], and mangostenones C, D, and E[22]. The main xanthone derivative is alpha-mangostin, this compound has a variety of pharmacological activities such as antidiabetic[23,24], antioxidants, and anti-inflammatory[12,13,14,25]. Therefore, this study aims to generate the prediction of the biological activity of phytocompotents in mangosteen.

Materials and Methods

Data retrieval

We extracted 18 phyocomponents of mangosteen from PubChem, an open chemistry database at the National Institutes of Health (NIH), USA (Table 1). We revealed the Canonical SMILES of the 18 phytocomponents and submitted them to the SwissADME web server for further analysis.

Table 1. Phytocomponents of the mangosteen revealed from the PubChem database.

No	Compounds	Formula	Molecular Weight
1	Alpha-mangostin	$C_{24}H_{26}O_6$	410.46 g/mol
2	Beta-mangostin	$C_{25}H_{28}O_6$	424.49 g/mol
3	Gamma-mangostin	$C_{23}H_{24}O_6$	396.43 g/mol
4	Gartanin	$C_{23}H_{24}O_6$	396.43 g/mol
5	Garcinone A	$C_{23}H_{24}O_5$	380.43 g/mol
6	Garcinone B	$C_{23}H_{22}O_6$	394.42 g/mol
7	Garcinone C	$C_{23}H_{26}O_7$	414.45 g/mol
8	Garcinone D	$C_{24}H_{28}O_7$	428.47 g/mol
9	Garcinone E	$C_{28}H_{32}O_6$	464.55 g/mol
10	1-Isomangostin	$C_{24}H_{26}O_6$	410.46 g/mol
11	9-Hydroxycalabaxanthone	$C_{24}H_{24}O_6$	408.44 g/mol
12	3-Isomangostin	$C_{24}H_{26}O_6$	410.46 g/mol
13	6-Deoxy-gamma-mangostin	$C_{23}H_{24}O_5$	380.43 g/mol
14	BR-xanthone A	$C_{23}H_{24}O_6$	396.43 g/mol
15	BR-xanthone B	$C_{14}H_{10}O_6$	274.23 g/mol
16	Garcimangosone A	$C_{28}H_{28}O_6$	460.52 g/mol
17	1-Isomangostin hydrate	$C_{24}H_{28}O_7$	428.47 g/mol
18	Calabaxanthone	$C_{24}H_{24}O_5$	392.44 g/mol

Pharmacokinetics and drug-likeness predictions

In the present study, we predicted the pharmacokinetic properties and druglike nature of the phytocomponents using the SwissADME web server, Swiss Institute of Bioinformatics, Swiss. We identified gastrointestinal absorption prediction for the oral drug probability according to the white of the BOILED-Egg[26] and Lipinski parameter for the drug-likeness prediction implemented from Lipinski *et al*. (2001)[27].

Biological activity prediction

We employed PASS (Prediction of Activity Spectra for Substances) web resource as a strong potential tool to predict the biological activity. This web resource estimates the predicted activity spectrum of a compound as probable activity (Pa) and probable inactivity (Pi) as described by Goel *et al*. (2011)[28] and we used Pa>0.3.

Results and Discussion

We successfully revealed pharmacokinetics, drug-likeness, biological activity predictions of the various phytocomponents from *Garcinia mangostana* L. All phytocomponents predicted as high in pharmacokinetics prediction (gastrointestinal absorption), except Garcinone E. In addition, all phytocomponents predicted fulfill all Lipinski rule-of-five. Furthermore, 18 phytocomponents of *Garcinia mangostana* L. predicted as antioxidant, anti-inflammatory, and antineoplastic activity.

In addition, phytochemical screening, based on ethnomedicinal data, is considered as an effective approach for the discovery of new therapeutic agents. The major bioactive secondary metabolites of mangosteen are xanthone derivatives[1,4]. The major constituents from the xanthone fraction in mangosteen were found to be α-mangostin and γ-mangostin[4,14]. More than 60 other xanthones are isolated from its different plant parts of including 3-isomangostin, β-mangostin, gartanin, mangostanin, 1-isomangostin, garcinone B, 9-hydroxycalabaxanthone, mangostanol, mangostinone demethylcalabaxanthone, 8-deoxygartanin, and garcinone D[1]. The majority of investigations are focused on the extraction and structure elucidation of xanthones from the pericarp of mangosteen[14]. Recently, the presence of these compounds in the stem, seed, and heartwood was reported by many authors[9,11,19,20,23,24,25].

On the other hand, bioinformatics provides more efficient target discovery and validation approaches, thus help to ensure that more drug candidates are successful during the approval process and making it more cost-effective[26]. Notably, the work of Lipinski *et al*. analyzed orally active constituents to describe physicochemical ranges for high probability opportunities to be an oral drug. This called rule-of-five delineated the relationship between pharmacokinetics and physicochemical parameters. Lipinski rule-of-five helps in distinguishing between drug-like and non-drug like molecules. It predicts a high probability of success or failure due to drug-likeness for molecules complying with 2 or more of the following rules, such as molecular mass less than 500 Dalton, high lipophilicity, less than 5 hydrogen bond donors, less than 10 hydrogen bond acceptors, molar refractivity should be between 40-130[27].

In this study, an attempt has been made to investigate a more extensive pharmacological appearance of phytoconstituents by application of PASS web resources. The proposed in silico method extends further to generate novel bioactivities of selected phytochemical leads, related side-effects, and their mechanisms. In addition, the recent version of PASS predicts approximately 3750 pharmacological activities, specific toxicities, biochemical mechanisms of action, and metabolic terms on the basis of the structural formula of drug-like substances with average fidelity ~95%. This might be further validated in vitro as well as in vivo trials[28]. In line with this, the present study revealed the use of PASS for exploring the hidden pharmacological potential of the various phytocomponents from the mangosteen.

Conclusion

In summary, we revealed the biological activity of 18 phytocomponents of the mangosteen. However, further trials, such as *in vitro* and *in vivo* evaluation, are needed to prove the validity of these findings.

Conflict of Interest: The authors declare that they have no conflict of interest.

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Ethical Approval: No ethical approval needed.

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