Docking application for food tenacity protection

B N Kholila¹, D N Martono² and T E B Soesilo²

¹Magister Programe of Environmental Science, School of Environmental Science, University of Indonesia, Salemba, Indonesia.
²School of Environmental Science, University of Indonesia, Salemba, Indonesia
*Corresponding author e-mail: nowo2003@yahoo.com

Abstract. Sustainable agriculture is based on the concept of organic agriculture. However, the sustainability of agriculture system depends on the system and the people. Therefore, the human knowledge on concerning the sustainable environment is the main contribution towards achieving food security. One of the systems that could be utilized for the preservation of food security is through ‘in silico’ approach with docking application. The production under organic agriculture is more resilient against threat, it is also more stable thus the food security and the environmental condition could be preserved. This research aims to recommend computerized technology (docking) as a supporting device with a function to view the effectivity of the natural basic materials on the creation of biopesticide. Therefore, the utilization of docking application for the creation of biopesticide is able to contribute to the alleviation of environment quality degradation in order to preserve food security as well as to enhance the knowledge on agricultural behavior. The result found in this research is the computerized analysis outcome for the past four years using docking application that has obtained the value Ki converted as IC₅₀ and the value of LC₅₀ so that it could find its effectivity and toxicity.

1. Introduction

The increasing population becomes one of the causes of land use change such as agricultural lands. Empirically, paddy field area is an area that is most vulnerable towards land use change from agricultural land [1]. Records in BPS in 2017 stated that the reduced paddy fields has caused a decrease in production or harvest from 29,245 tons to 4,054 tons [2]. The increasing population is line with the number of food production required to be supplied, but the fact is that the land use change still continues. This has force the agricultural actors to be able to intensively farm thus initiating the efforts to minimize the yield loss due to plant pest organisms by utilizing pesticides [3].

Pesticide is chemical mixture that is bioactive, but produce many contamination and residual effects on soil, land ecosystem as well as waters. [4]. Therefore, the indecent use of pesticides will cause serious threat. A country’s food security target is achieved when the food security is at a regional or national level, especially in household or individual level is achieved [5]. The fulfillment of food domestic food security must be encouraged with new innovation to obtain sustainable quality and quantity standards. The continuity of agricultural system depends on the current system and the people. Therefore, the basic knowledge affecting the behavior to choose and the right implementation of pesticides or a switch to an environmental-friendly pesticide/ biopesticide to create sustainable agriculture.

Sustainable agriculture is based on the concept of organic agriculture with the principle of ecosystem sustainability, production result as well as safe products [6]. Organic agriculture is defined as an agriculture that does not include synthesis elements [7]. One of them is by utilizing biopesticide that is
effective for agriculture pest control without causing any damage to the ecological chain or worsen the environmental pollution [8], thus the ecosystem cycle could continue to be sustainable in order to fulfill the food security with superior products.

*In silico* approach is one of the alternatives to actualize organic agriculture capable to achieve sustainability that is efficient in terms energy, time and cost in terms of the creation of biopesticide. *In silico* performed through molecular docking is one of the modelling approaches to predict ligand affinity towards protein targets [9]. The function of molecular docking consists of the conformation from the ligand and the protein (position/pose) that might occur to the protein binding pockets. Generally, molecular docking performs a position search with a pattern of flexible ligand and rigid protein that furthermore on every position is assessed based on the form and characteristics thus finding the most appropriate position.

Molecular docking has been widely used for drug discovery as well as its development by utilizing the research algorithm components and algorithm that creates the complex probability between protein and ligands thus the ligand binding affinity could be measured [10]. Studies about insect hormones have been considered important due to the ability to be used in the insecticides and pesticides, these hormones become the base of the molecular docking as the macromolecule or protein. In the context of biopesticides, ligand is based from compounds found in plants. Therefore, a series of phyto—pesticides formula preparation with the cost and time spent as well as the remainder of the formulation which are wasted could be controlled.

This research aims to show that docking application could contribute to support food security and sustainable agriculture with the knowledge of Ki value converted into IC\textsubscript{50} and LC\textsubscript{50} values obtained through computerized interaction of molecular docking shown in the last four years of research. Not only the food security, but also in terms of environment, contamination could be maintained due to the accurate result of the molecular docking containing compounds from an environmental-friendly material. Therefore, agriculture based on sustainable agriculture with the implementation of ecological principles in the design and management of agricultural ecosystem [11] would reach a high level of environmental performance and productivity [12].

2. Materials and Methods
This research uses methods of literature study about docking application utilized to show the interaction occurring between the ligands and macromolecules. The chosen result is a research conducted for the last four years determined as the limitation. The chosen interaction is a specific interaction for the utilization of docking application supporting the agricultural activities that show an interaction and inhibitor value produced through molecular docking.

2.1. Article Analysis

Article analysis is performed based on these following categories: docking application, Ki value or IC\textsubscript{50}/LC\textsubscript{50} value, country of study, and agricultural supports. Those categories could contribute to comprehend the advancement of docking application in the agricultural sector from year by year. These data will give an overview that molecular docking approach could contribute in supporting food security with the knowledge of interaction obtained from ligands and macromolecules so as to increasing knowledge for the agriculture actors about environmental-friendly materials. Therefore, the system and the people occurring could support each other to support the creation of food security.

3. Result and Discussion
3.1. Result

Based on our method analysis and variable could create basic categories for the study on the utilization of the molecular docking as the agricultural activity support for the past four years. The study on molecular docking is related to the agricultural utilizing ligands and macromolecular that is in line with the agricultural problems. Ligands illustrate compound contained in the plants utilized as biopesticide and macromolecule materials or protein indicating plant-disturbing organisms or pests that are often detrimental to agricultural activities.

Table 1.1 Study of molecular docking in the sector of agriculture for the past four years

| Year | Reference | Country | Docking Application | Interaction | Result |
|------|-----------|---------|---------------------|-------------|--------|
| 2019 | Abdelgaleil et al. [13] | Egypt | Discovery Studio 3 software | Interaction between several monoterpenes ((1,8-cineole,(-) citronellal, limonene, α-pinene ,pulegone and 4-terpineol) indicating the high acaricidal activities by fumigant and the direct contact action on *Tetranychus urticae* Koch. | Pulegone has the highest toxicity level (LC$_{50}$=3,81 mg/L of air). Citronellal has the lowest fumigant toxicity with the value of LC$_{50}$=15,5 mg/L of air. Limonene has the highest value of inhibitors, namely IC$_{50}$ = 11,37 mg/L. |
| 2019 | Raghav, D., Susobhan M., & Krishnan [14] | India | Autodock 4.2 | The interaction occurring between Bovine Serum Albumin (BSA) and Karanjin has shown that Karanjin is bound closer. The interaction indicating that Karanjin has the lowest toxicity towards the human cervix cancer cells and L929 normal mouse fibroblast cells or in other words could hamper the cell growth of *B. subtilis* and *E. coli*. The pesticide works by way of hampering the proliferation of HeLa cells depending on the concentration of IC$_{50}$ value. IC$_{50}$ value that was obtained amounting to 0.22 mM. With the concentration of 5 mM could hamper 100% proliferation of HeLa cells producing acute cytotoxicity. |
| 2018 | Warsito et al. [15] | Indonesia | Autodock Tools | The optimization results conducted on the citronellal ligands from citronella oil, eugenol ligands from clove oil respectively are 2,18 mM and 1,14 mM. The interaction received from each ligands and macromolecules of 2DJC produced Ki amounting to 1.75 mM. From such Ki value, an insecticide formulation ratio of 4:1 was obtained |
3.2. Discussion

The food security of a country is achieved when the food security at a regional or national level especially in the household and individual level are met [5]. The food security has a strong correlation with the environmental condition and quality, meaning that the environment becomes one of the factors supporting food security. The environmental quality that could support food security is influenced by the system and people managing it. Hence, the human knowledge to preserve the environmental quality has a big role, in other words food security is closely related to knowledge. In addition to knowledge, in order to maintain food security requires new innovations that could immediately support food security. In silico approach becomes one of the alternatives that could be chosen to support food security. In silico approach uses the application docking that is used as a means for the knowledge of interaction occurring between the ligands and macromolecules [9]. This could aid determining binding value occurred between the ligands and macromolecules thus knowing the its potential toxicity. Literature study for the past four years was conducted as the limitation of study selection.

In the research for the past four years has shown a role of docking application to indicate the interaction occurring desired compounds. Despite of utilizing different software, but the results obtained is relatively showing results of binding energy as well as toxicity value of Ki value (Inhibition Constant), IC$_{50}$ (Inhibitory Concentration 50) as well as LC$_{50}$ (Lethal Concentration 50). Ki value is a value that shows the strength of the interaction between the ligands and macromolecules. This could be seen from the Ki value obtained from the docking result, where if the Ki value is smaller means the interaction...
occurring between the ligands and macromolecules is strong and only has a small inhibitor [16]. Ki value becomes the base to determine the IC₅₀ value which is a concentration that could hamper the interaction occurring amounting to 50%. In contrast to LC₅₀ that shows concentration causing death of 50% of the target organisms obtained from the calculation to determine the liveliness from a compound or extract in less than 24 hours [18]. This means by knowing the Ki value through molecular docking, the toxicity value could be discovered. The toxicity results through molecular docking proves the compound implementation as the potential for biopesticide [17].

A research in 2019 by Abdelgaleil et al. of the docking application utilizing the software of Discovery Studio 3 obtained LC₅₀ value from Pulegone amounting to 3.81 mg/L and LC₅₀ value from Citronellal, namely 15.5 mg/L on the interaction between several monoterpenes (1.8-cineole, citronellal, limonene, α-pinene, pulegone and 4-terpineol) showing the high acaricidal activity by fumigants and direct contact on Tetranychus urticae Koch. From the result of molecular docking conducted has shown that monoterpen Pulegone has a higher level of toxicity on Tetranychus urticae Koch than Citronellal[13]. This means to create biopesticide to eradicate Tetranychus urticae Koch (Red mites) requires natural raw materials containing Pulegone. In the same year as the research by Raghav, D., Susobhan M., & Krishnan, the docking application with the software of Autodock 4.2 is utilized to determine the interaction between Bovine Serum Albumin (BSA) and Karanjin and IC₅₀ value was obtained amounting to 0.22 mM that could hamper cell growth of B. subtilis and E. coli [14]. This shows that the inhibitor value produced was small thus the interaction between BSA and Karanjin is strong to hamper cell growth of B. subtilis and E. coli.

The utilization of docking application in 2018 by Warsito et al. and Kholila et al. in 2017 a result of molecular docking was obtained using the application Autodock Tools comprising Ki value which then is converted into LC₅₀ and IC₅₀ values. In the research of Warsito et al., Ki value was processed thus receiving ratio of biopesticide formulation from citronella oil and clove oil (4 : 1) thus receiving LC₅₀ value with a concentration of 0.05% (toxic contact) and 0.31% (leaf contact) [15]. This shows that the formulation produced has mortality value amounting to 50% only with the formula concentration of 0.05% and 0.31%. Whereas in the research of Kholila et al., the interaction on geraniol ligand, citronellal, citronellol (citronella oil), anethole and cineol (basil oil) through multiple docking based on the lowest Ki value, namely 2DJC macromolecule citronellal-anethole producing IC₅₀ value of 3.2 mM [16]. The lowest Ki value chosen for multiple docking was performed as the smaller the Ki value, the inhibitor value is also smaller, this means the interaction on ligands and macromolecule simulated has a strong interaction so that the toxicity value is also significant. In 2016 Gowrilakshmi, G. & M.S. Nalina S. Utilization the docking application of ArgusLab to observe the interaction of ligands lipase, amylase, protease and chitinase with protein Cytochrome b (H6TG75). The result obtained comprises of the minimum binding value (kcal/mol) amounting to -9.14 kcal/mol for Cytochrome b-Lipase; Cytochrome b-Amylase -8.12 kcal/mol: Cytochrome b-Protease -13.63 kcal/mol; Cytochrome b-Chitinase -12.27 kcal/mol [17]. The binding value produced shows that the interaction between the protein and ligands have caused cell degradation as well as bringing death to the insect pests.

Based on the research conducted for the past four years, utilizing docking application through in silico approach could determine the interaction between the ligands (compounds contained in the natural raw materials) and macromolecule (plant disturbing organisms) created in Ki or LC₅₀ value. The utilization of docking application proved to be effective to be used to support the manufacture of biopesticide formulation. This application will be more efficient as it does not need the preparation of a series of formulas. Therefore, the utilization of docking application also functions to reduce experimental waste to obtain the appropriate composition in the making of biopesticide.

Molecular docking application which is widely used for the past for years is Autodock Tools in several versions. Autodock Tools is a docking program with the technique of flexible docking and grid-based method for energy evaluation [19]. The process of application usage Autodock Tools has many steps but rendering with high quality results [16]. This application calculated intermolecular energy, internal energy as well as the output which later forms docking energy as well as binding energy [20]. This is to make the application Autodock Tools be used by many researchers to perform molecular
docking process. The use of molecular docking has been developed in several pharmaceutical field in development of new drug discovery and planning. The principle used in molecular docking, namely the placement of ligand interaction to the active side of the receptor which then is simulated based on the structural conformation and the nature of electrostatic [21].

**In silico** approach conducted to utilize the docking application could support the existence of food security through the accurate biopesticide modelling. Through this approach, the potential for the creation of organic agricultural is also higher due to the use of natural raw materials as biopesticide was proven in real terms with Ki value produced from the molecular docking process. On the other hand, with the knowledge of the appropriate toxicity value, this could be a trigger agricultural actors to be more interested or possibly switching to use environmental-friendly materials for agricultural activities. Therefore, the occurrence of environmental quality degradation will be smaller and the agricultural production could be maintained resulting in food security.

4. Conclusion

The food security threatened due to the agricultural land use change, especially the paddy fields being the matter that needs to be solved. **In silico** becomes one of the innovations to preserve food security. Docking application used for the past four years to know the conformity between the ligands and target protein (pests) in the agricultural activities is proved to have produced Ki, IC$_{50}$ as well as LC$_{50}$ values/50% toxicity value for agricultural problems. Molecular docking data results could be the knowledge base for the agricultural actors that support food security. Not only does this potentially could preserve food security, but also reduce environmental quality degradation so as to the creation of sustainability.

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