



TESTING OF KAEMPFEROL CONTENT IN ETHANOL EXTRACT OF MELINJO SEEDS (*GNETUM GNEMON L.*) AND BAJAKAH ROOT (*SPATHBOLOBUS LITTORALIS*) USING THE IN SILICO METHOD AS A CANDIDATE FOR LUNG CANCER DRUG

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Abstract

This research is about testing the antiviral activity of compounds contained in Melinjo seed (*Gnetum gnemon L.*) and Bajakah root (*Spathbolobus littoralis*) as an anti lung cancer drugs candidate using the in silico method. The purpose of this study was to determine the antiviral activity and interactions of the bioactive component that used in this study is kaempferol which has an anti cancer effect. The result of the Docking of the kaempferol compound and protein migration inhibitory factor machropages that do not have water or are clean. Bajakah root and melinjo seed contain kaempferol compound which are able to prevent or cure cancer, especially in lung cancer patients. Kaempferol compound has antioxidant potential that works to counteract free radicals in the body, making it very suitable for use as a candidate for lung cancer drugs.

Article History

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Key Words

Melinjo seed, Bajakah root, Etanol extract, Antioxidant, Kaempferol, In Silico Method

Introduction

Lung cancer also known as bronchogenic carcinoma is a malignant lung tumor that originates from the airways or bronchial epithelium which is characterized by damaged cells which then grows into tumor which then spreads across the lung causing the lung functions to deteriorate. Malignancy is one of the leading causes of cancer and accounts for 2,206.771 (11.4%) out of 19,292.789 cases worldwide (Data Source Globocon 2020. Graph Production Global Cancer Observatory, <http://gco.iarc.fr/>).

Lung cancer is classified as one of the leading causes of death and accounts for 1.8 million deaths worldwide. In Indonesia, lung cancer is the cancer with the third-highest number of sufferers. One of the efforts to reduce mortality from cancer is by developing anti-cancer drugs derived from plants (HARI KANKER SEDUNIA, www.suryahusadha.com).

Cigarette smoke (tobacco) is the main cause for lung cancer and contains 63 types of carcinogenic (Indonesian Lung Doctors Association, 2003: 2). These cancer-causing chemicals plays a key role in developing lung cancer. Some other causes of lung cancer are radiation and air pollution. Nutrition and genetics have also shown to play a key role (Albert & Samet, 2003 : 21).

There are several types of treatments performed on cancer patients depending on the stage of cancer, such as radiotherapy or chemotherapy. Chemotherapy is used more widely and is treated using drugs or certain chemical compounds which aims to kill or minimise the proliferation of cancer cells (Lesnussa, 2012). However, chemotherapy treatment is very



expensive and not affordable for many people, therefore the use of traditional medicines derived from plants has long been known and practiced by several countries in various continents such as in Asia and Africa as an alternative method.

Making Melinjo Seed and bajakah root extract :

Melinjo seed and Bajakah root powder of 300 grams was extracted by maceration method for 6 days with 96% ethanol sample ratio of 1:10 while occasionally stirring. By means of 300 grams of melinjo seed and bajakah root powder macerated with 96% ethanol as much as 2250 ml for 3x24 hours, then filtered using filter paper and vacuum flask assistance, the filtrate is collected in Erlenmeyer (filtrate I). The residue obtained was soaked again with 750 ml of 96% ethanol for 3x24 hours. Then the results of the soak were filtered again and obtained filtrate II. After that, filtrate I and filtrate II were put together and evaporated using a rotary evaporator at a temperature of 55 degrees Celsius until no more pearl condensation occurred in the condenser so that a thick extract was obtained.

One of the most important medicinal plants that can be used are Bajakah Roots and Melinjo Seeds. Based on scientific research, it was concluded that Bajakah root contains many phytochemical cell compounds that act as anti-cancer. Where for tannins and flavonoids, these compounds play a role by releasing hydroxyl compounds where they will bind to cancer compounds, thereby inhibiting the process of cancer (Budi, 2019). While the main components of Melinjo seeds are stilbenoids, stilbenoid bioactivity such as anti-inflammatory, neuroprotective, anti-cancer, antimicrobial, and antidiabetic effects (Mattoo et al, 2020).

With continuous changes to the environment and lifestyle, it is necessary to extract new molecules that have the potential to be used for disease prevention and for discovering new drugs that may be critical to cancer survival. Ultrasonication is a method that can be used, as it utilizes mechanical waves to break bonds or functional groups in materials. The smallest particles can be obtained with this technique.

METHOD AND EXPERIMENTAL DETAILS

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rotary evaporator at a temperature of 55 degrees Celsius until no more pearl condensation occurred in the condenser so that a thick extract was obtained.

Phytochemical Test

A. Flavonoid

A total of 0.5 grams of simplisia powder was added to 10 ml of hot water, boiled for 10 minutes and filtered in hot conditions, into 5 ml of filtrate added 0.1 gram of magnesium powder and 1 ml of concentrated hydrochloric acid and 2 ml of amyl alcohol, shaken and allowed to separate, Flavonoids are positive if red, yellow and orange colors occur in the amyl alcohol layer (Depkes RI, 1989).

B. Saponin

A total of 0.5 grams of simplisia powder is put into a test tube, 10 ml of hot water is added, cooled and then shaken for 10 seconds, if a stable foam is formed for not less than 10 minutes and does not disappear with the addition of 1 drop of 2 N hydrochloric acid, it shows the presence of saponins (Ministry of Health of the Republic of Indonesia, 1989).

C. Tannins

A total of 0.5 grams of simplisia powder is filtered with 10 ml of distilled water, the filtrate is diluted with water until colorless. 2 ml of solution is taken and 1-2 drops of 1% iron (III) chloride reagent are added. If a green, blue or blackish color occurs, it indicates the presence of tannin (Harborne, 1987).

D. Terpenoid

Acetic acid anidrat 2 ml was added to 1 ml of melinjo seed extract then 2 ml of concentrated sulfuric acid was added. The presence of terpenoids is indicated by a color change from violet to blue or green (Sumiyati, 2014).

In Silico Test

In silico is a research method that utilizes computational technology and databases for drug development research. The development of anticancer compounds through in silico studies is very useful as initial information so that the development of cancer drugs is not trial and error.

Research Results and Discussion

A. Research process

The manufacture of the melinjo seed and bajakah root extract was done through several stages. After obtaining high quality Bajakah and Melinjo, it went through the



crushing and blending process, which was then weighed. The crushed Bajakah and Melinjo then went through maceration method using 96% ethanol with a ratio of 1:5 (1-part Melinjo, Bajakah & 5 parts ethanol). This was then left for 4 days and stirred in between every 2 days. After 4 days, it was filtered using a 100-mesh filter paper. The results of filtering evaporated for the remaining extract.



Picture 1.1 Destruction process, Weighing process, Maceration process



Picture 2.1 Ultrasonication process and PSA

The manufacture went through several stages. The good quality Bajakah roots and Melinjo seeds were identified and acquired through careful selection process. The roots were cut into small pieces and grinded using a suitable grinder. The Melinjo seeds were first extracted by peeling the Melinjo fruit and then seeds were dried under the sun, which was the grinded by either mashing or grinding using a grinder. Once both have been finely ground correctly, they were mixed and packed into tea bags. The correct way to consume them is to simply use the tea bags to brew regular tea using hot water. The Bajakah roots are also made



in capsules this making consumption of these very easy and productive and can be incorporated into a daily routine without any need for drastic adaptation for consumers which makes this product even more viable and accessible.



Picture 3.1 Product : tea process

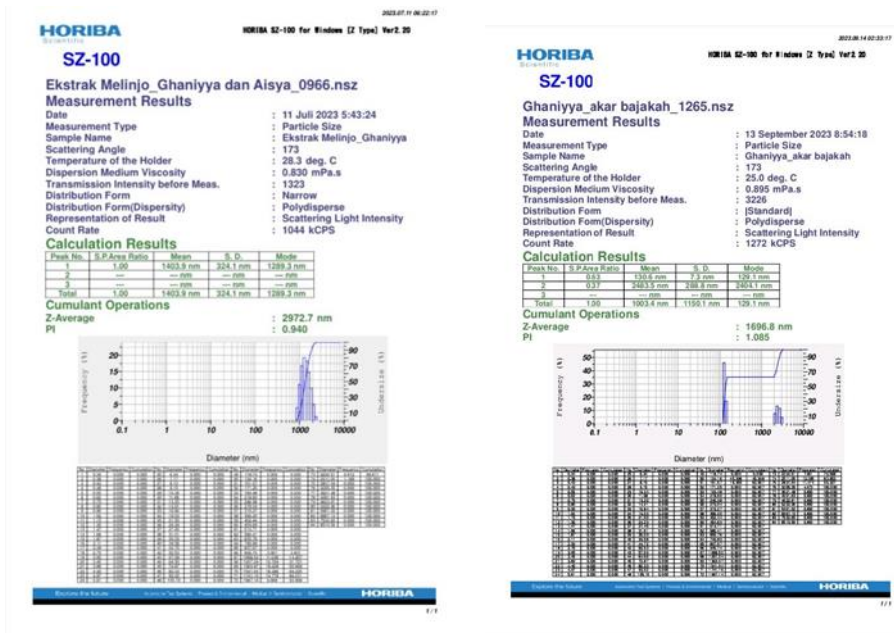


RESULT

PSA and Phytochemical test results at UNNES Semarang. The tests yield pretty good and good results following the results of the tests we have tested in the laboraturium.



Picture 1.2 Phytochemical Result

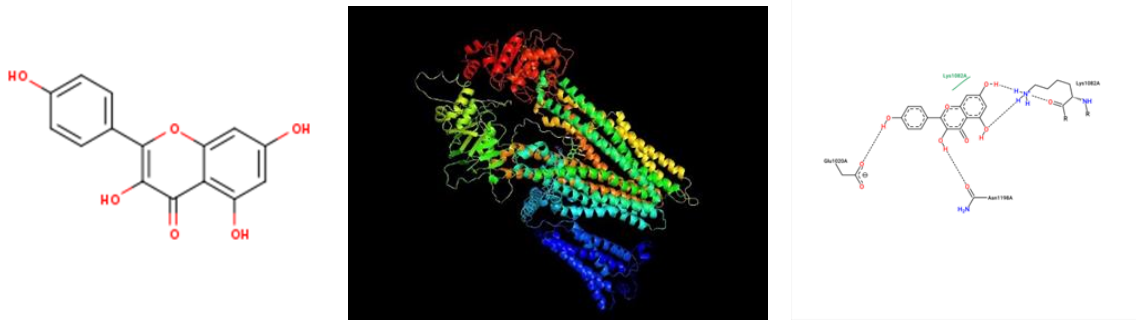


Picture 2.2 PSA Result



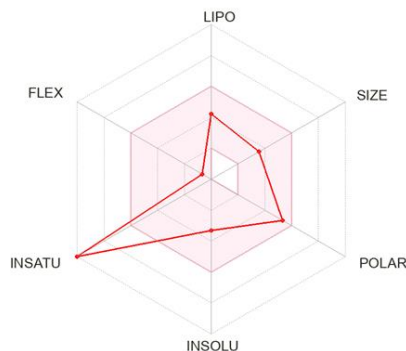
IN SILICO TEST

The bioactive component that we used in this study is kaempferol which has an anti-cancer effect as can be seen in the 2D image



Picture 2.3 Chemical structure of kaempferol, 3D picture of Kaempferol, 2D diagram of interaction between ligand and target protein

The figure below shows the results of the docking of the kaempferol compound and protein migration inhibitory factor machropages that do not have water or are clean.



Picture 2.4 Radar bioavailability of kaempferol

In the bioavailability radar of Kaempferol, it is explained that this compound can be said to be good and suitable for use as a drug candidate because it is in the pink area which is seen in the red dots and lines.

DISCUSSION

From the data we obtained, Bajakah root and Melinjo seeds contain kaempferol compounds which are able to prevent or cure cancer, especially in patients with lung cancer. In the kaempferol compound, it has antioxidant potential that works to counteract free radicals in the body, making it very suitable for use as a candidate for lung cancer drugs.



CONCLUSION

1. The results of phytochemical tests that have been carried out obtained compounds from the flavonoid, kaempferol, and terpenoid groups.
2. Melinjo seed and bajakah root extract has high antioxidant and kaempferol effectiveness, which are useful for reducing the risk of lung cancer.
3. We have observed that the melinjo seed and bajakah root fractions exhibited antioxidant activity. Melinjo seed and bajakah root are more potent as anticancer. *Gnetum gnemon* L and *Spatholobus littoralis* can be considered as a potential source of anticancer agents. However, more research is needed to determine as mechanism of action.
4. Traditional therapies such as chemotherapy and radiation are associated with substantial side effects. Therefore, it is very important to develop new approaches that have fewer side effects and are safer. *In silico* research has demonstrated the use of food-based flavonoids in cancer prevention and therapy. *In silico* it is feasible to be synthesized and further developed as an anti-lung cancer drug candidate.

Therefore, future research directions could potentially expand the use of food-based flavonoids as potent and effective methods of cancer prevention therapy.

5. From the result of the PSA test, the particle size is around 1.400 nm or 1.4 micro meters. The particle size is quite large but the distribution is even or it can be called homogeneous, because the “peak” of the test result only show one size

REKOMENDATION

It has been proven that the Bajakah roots and Melinjo seeds can prevent lung cancer and its safe to we use it, so it is necessary to develop this research.



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