

TESTING OF ANTIOXIDANT CONTENT IN ETHANOL EXTRACT OF MENGKUDU FRUITS (*MORINDA CITRIFOLIA L.*) USING THE IN SILICO METHOD AS A CANDIDATE FOR BREAST CANCER DRUG

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Submitted 13 April 2025

Accepted 16 April 2025

Published 17 April 2025

ABSTRACT

This research examines the antiviral activity of compounds contained in Mengkudu Fruits or Noni Fruit (*Morinda Citrifolia L.*) as potential anti-breast cancer drugs using the in silico method. The purpose of this study was to determine the antiviral activity and interactions of the bioactive component, which is an antioxidant with an anti-cancer effect. The result of the Docking of the Flavonoid compound and protein migration inhibitory factor, machropages that do not have water or are clean. Mengkudu fruit, or Noni Fruit, contains flavonoid compounds that are able to prevent or cure cancer, especially in breast cancer patients. Flavonoid compound has antioxidant potential that works to counteract free radicals in the body, making them very suitable for use as a Candidate for breast cancer drugs.

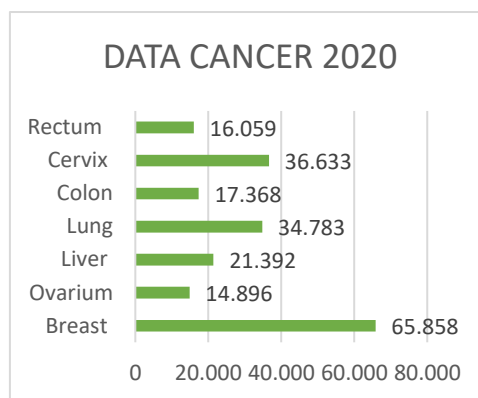
Keywords: *Breast cancer, In Silico, Morinda Citrifolia L*

1. INTRODUCTION

Cancer is a disease that develops as a result of aberrant bodily activity. Cancer is a serious, non-communicable disease that often manifests as a mass that grows over time and affects bodily structures and cells. Breast cancer is one of the many forms of cancer. Breast cancer, as its name implies, affects the chest region. The fast and uncontrollably growing cell proliferation that results from the cells that make up breast tissue losing their normal function might cause this cancer.

Medical authorities from various countries are still researching ways to treat breast cancer patients. Breast cancer is the most common cancer among women in the world. This is due to the fact that breast cancer is the most common malignancy in women throughout the world. This is because breast cancer is the most common cancer that attacks women throughout the world. Throughout the country, breast cancer has caused almost 500,000 deaths, with the characteristics of male patients being 0.6 per 1000 population and women being 2.2 per 1000 population (Health Research and Development Agency, 2013). It has been recorded that there are more than 11,511 cases of breast cancer in Indonesia. According to the World Health Organization (WHO), there was an increase of 12.7 million cases of cancer in Indonesia from 2008 to 2012.

Based on Globocan data obtained in 2020, new cases of cancer in Indonesia reached a total of 396,914 cases, and the number of new cases of breast cancer reached 68,858 cases (16,6%). It is estimated that the number of cancer deaths reaches more than 22,000 cases. Cancer in Indonesia reached a total of 396,914 cases, and the number of new cases of breast cancer reached 68,858 cases (16,6%). It is estimated that the number of cancer deaths reaches more than 22,000 cases.



The high rate of increase in breast cancer in Indonesia is due to a lack of knowledge and the inability to access treatment. Treatment for breast cancer is currently limited to chemotherapy, and there is still no drug that can eliminate cancer in the breast. This is because breast cancer is a disease whose main cause has not yet been found, but several researchers state that breast cancer is a cancer that arises from genetic factors or can be known as multifactorial. Chemotherapy is a modern treatment technique that can be used to treat breast cancer. Chemotherapy is carried out by means of regular check-ups and regular medication that is given by the hospital. Apart from chemotherapy, around 28% of sufferers believe in traditional treatment, and 7% of sufferers consume herbal medicine. Herbal medicines are medicines made from plants, including stems, fruit, roots, and leaves. One of the plants that can be used as a herbal medicine for cancer is the noni fruit. Noni fruit, or *Morinda citrifolia* L, has anticancer and antioxidant effects that are good for use as a cancer medicine. Research results from the American Association for Cancer Research state that noni fruit has anticancer and antitumor effects. Noni fruit has several good natural compounds, namely alkaloids, flavonoids, terpenoids, and tannins. Apart from that, noni fruit has been used to treat diseases using herbal medicine techniques for a long time, such as diabetes, high blood pressure, blood vessel problems, and many more. Since noni fruit is known to contain ingredients that can treat breast cancer, this study used a variety of techniques, including in silico testing, phytochemical testing, alkaloid and terpenoid testing, and PSA (Particle Size Analyzer) testing, to determine how the ingredients in noni can alleviate the pain of breast cancer patients.

2. METHOD AND DETAIL EXPERIMENTS

This research was done from October to November 2023. The first step of the investigation was to use research data or the living environment to identify an issue. Research on the properties of noni fruit, which can treat cancer in general and breast cancer in especially, has been prompted by the issue of breast illness that many Indonesians experience.

Noni fruit powder was extracted using the maceration method for 4 days with 96% ethanol of 1:5 (1 part noni fruit and 5 parts 96% ethanol) while stirring occasionally. By macerating noni fruit powder with 96% ethanol for 4x24 hours, then filtering using filter paper and the help of a vacuum flask, the filtrate is collected in an Erlenmeyer (filtrate I). The residue obtained was soaked again in 96% ethanol for 2x24 hours. Then the soaking results are filtered again, and filtrate II is obtained. After that, filtrate I and filtrate II are combined and evaporated using a rotary evaporator at a temperature of 55 degrees Celsius until there is no more condensation of pirut on the condenser, so that a thick extract is obtained.

Phytochemical tests were carried out by testing the content of alkaloids, flavonoids, steroids, terpenoids, saponins, and tannins in noni fruit extract.

Alkoids

4 grams of spoons were used for the alkaloid testing process. After extracting the sample until it is smooth, add enough chloroform to make it smooth once more. After that, filter the mixture into a test tube, add 10 drops of 2N sulfuric acid to the filtrate, and add 10 milliliters each of ammonia and chloroform. After that, give the filter a few regular shakes and let it settle until a layer starts to develop. A test tube is filled with the upper layer. Utilizing Dragendroff and Mayer reagents, observe flavonoids. If a white precipitate occurs, the extract will be positive for Mayer alkaloids; if an orange-red precipitate forms, it will be positive for Dragendroff alkaloids.

Flavonoids

First, put the ethanol-macerated noni fruit extract into a test tube. After adding 10 milliliters of boiling water, boil for ten minutes, then filter while still hot. After filtering, mix 5 ml of the filtrate with 0.1 gram of magnesium powder, 1 ml of hydrochloric acid, and 2 ml of amyl alcohol. If the noni fruit extract alters the red, yellow, and orange colors present in the amyl alcohol layer, it will be positive for flavonoids.

Steroids

Take a 2 ml sample of noni fruit extract that has been certified with ethanol, and then give each 3 drops of concentrated HCL and 1 drop of concentrated. H_2SO_4 . If there is a green color change, the extract contains positive steroid compounds (Septianingsih, 2013).

Tannins

After macerating a sample of Noni fruit with ethanol for about five minutes, heat it. Next, add around two to three drops of 1% $FeCl_3$. A shift in hue to a blue or purple color indicates the presence of tannin chemicals in the sample (Marlinda dkk, 2012).

Saponins

A test tube containing 2 milliliters of the sample was filled with 10 milliliters of distilled water and agitated for around 30 seconds. The sample includes saponin components if, after 30 seconds, a stable foam forms.

Terpenoids

Take 2 ml of extract that has been macerated with ethanol. Give each extract 3 drops of concentrated HCL and 1 drop of concentrated. H_2SO_4 . The extract contains positive terpenoids if there is a red-purple color change in the reaction.

PSA (Particle Size Analyzer) is a laboratory tool used to determine the characteristics of particles in a sample being tested. PSA in research is used to determine particle size so that it can be used as a capsule medicinal product.

In Silico is a research method used to develop a drug. The data **produced** in this test is computational data, where we utilize technology to reduce the nature of trial and error in the drug development process.

PRODUCT PROCESS



1. Prepare the noni fruit to be used as tea, then wash it until clean.



2. After washing, cut the noni fruit into several small pieces.



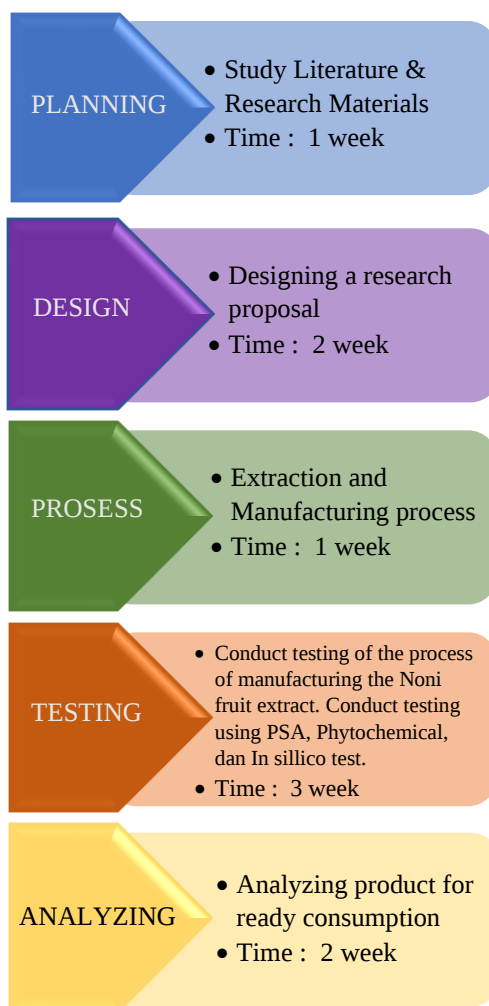
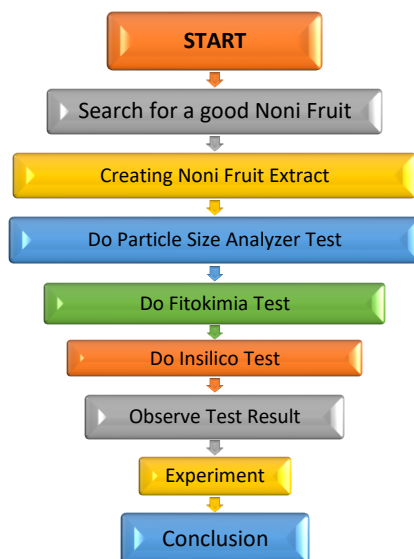
3. Place the noni fruit pieces in a baking dish, then dry the noni fruit under direct sunlight for approximately 3-4 days.



4. The dried noni fruit is mashed using a wooden mortar until the dry noni fruit becomes flaky



- Put the mashed noni fruit into a tea bag (1 tea bag contains 5 grams of noni powder). Brew noni tea with warm water, so the noni tea is ready to be consumed.

TIMELINE**RESEARCH AND DESIGN**

RESULT

Based on phytochemical and PSA tests carried out on Semarang State University (UNNES), below :



(Report of Phytochemical result test)

JURUSAN KIMIA FAKULTAS MIPA-UNNES
Gedung D-8 Kampus Sekeloa, Gunungpati, Semarang 50229
Telp. 024-8505035 Website: <http://www.kimia.unnes.ac.id>

SERTIFIKAT HASIL PENGUJIAN
Certificate Of Test Results

Nomor : 2023/10/30/13.40 Evap dan Fitokimia
Number :
Dibuat Untuk : Ghaniyya Putri Lusendra
Report for :
Jenis/ Nama Contoh : Mengkudu
Type/Name of Sample :
Parameter Uji : Evap dan Fitokimia
Parameters :
Tanggal Penerimaan Contoh : 30 October 2023
Sample receive on :
Tanggal Pengujian Contoh : 31 October 2023
Samples tested on :
Metode Uji : Evap dan Fitokimia
method :

Hasil Pengujian
Test Result

Parameter	Kandungan	Keterangan
Alkaloid Mayer	-	Positif apabila Terbentuk Endapan/Kabut Putih
Alkaloid Dragendroff	+	Positif apabila Terbentuk Endapan Jingga-Merah
Flavonoid	+	Positif apabila Terjadi Perubahan Warna Pink - merah
Steroid	-	Positif apabila Terjadi Perubahan Warna menjadi Hijau
Terpenoid	+	Positif apabila Terjadi Perubahan Warna merah - ungu
Saponin	-	Positif apabila Terbentuk Busa
Tanin	+	Positif apabila Terjadi Perubahan Warna biru-biru keunguan

Catatan/ Notes:
1. Hasil uji hanya berlaku untuk sampel yang diujikan/ The test results are only valid for the sample being tested
2. Dilarang menduplikasi laporan hasil uji tanpa izin resmi dari kepala laboratorium kimia/ It is illegal to duplicate the test results report without official permission from the head of the chemical laboratory

Semarang, 31 October 2023
Koordinator Laboratorium Kimia
FMP-UNNES

Mikhaela Nabidin, Ph.D.
NIP. 197905052005011002

We got several results. In The Phytochemical screening test obtained on November 6th, 2023, by macerating noni fruit extract, it was found that Dragendroff alkaloids, flavonoids, terpenoids, and tannins showed positive results. While Mayer's alkaloids, saponins, and steroids showed negative results. These four compounds have several functions for cancer as below:

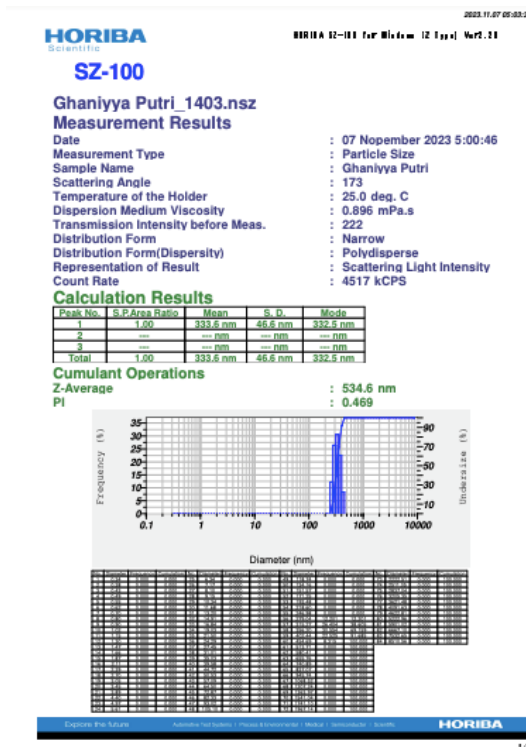
Dragendroff Alkeloid, as therapy, by triggering DNA damage, induces apoptosis, and acts as an anti-proliferative agent.

Flavonoids such as flavanone plays a good role in health, function as antioxidants, and can also ward off free radicals in the body.

Terpenoid as components that has the potential to act as antibacterials.

Tannin has several properties, such as an astringent, anti-diarrhea, antibacterial, and antioxidant (Venila,2020).

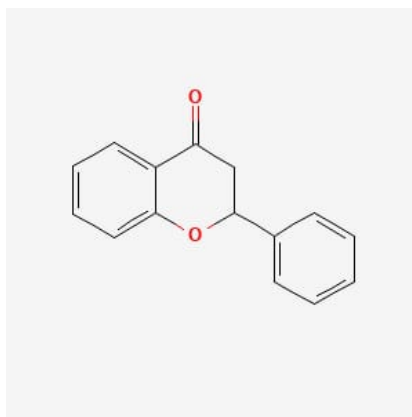
In this research, flavonoids will be used to treat breast cancer.



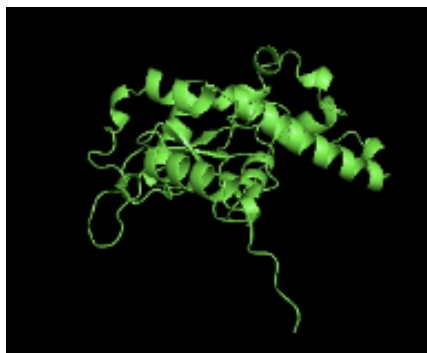
(Report of PSA result test)

On the PSA (*particle size analyzer*) test that was obtained on November 8th, 2023, it shows that the average particle size is 534,6 nm.

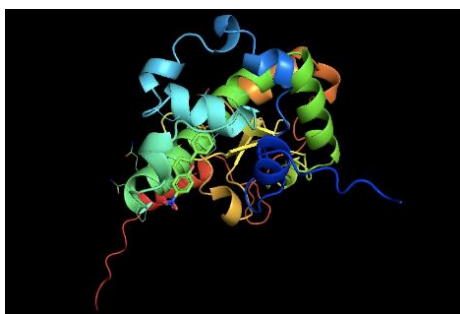
On the In Silico test, the bioactive components we used were Flavanones, which are derivatives of Flavonoid compounds, which have the ability to relieve cancer, especially breast cancer, which can be seen in the following chemical structure picture.



(Chemical structure of Flavanone)

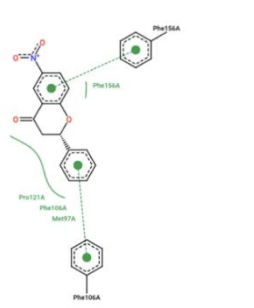


(3D structure of Protein Target)



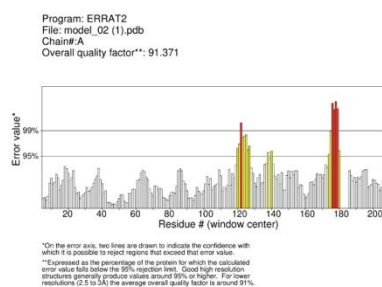
(3D picture Molecular Docking of Flavanone)

The result of the Docking of the Flavanone compound and protein migration inhibitory factor, machropages that do not have water or are clean.

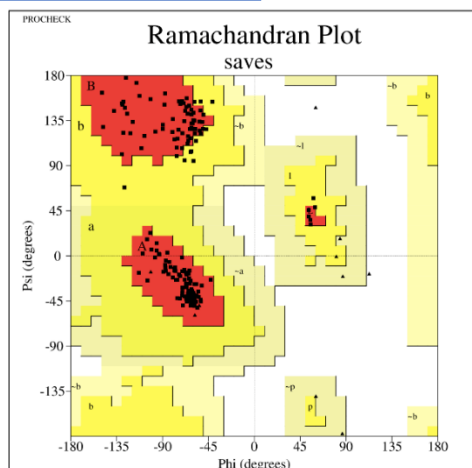


(Interaction between Ligand and Target Protein)

The bioactive component that we used in this study is flavanone, which has an anti-cancer effect, as can be seen in the 2D image. The interaction in the image shows that the flavanone ligand can be synthesized well with the target protein, and there are no obstacles.



(ERRAT Graphic)



(PROCHECK Ramachandran plot)



(Radar bioavailability of Flavanone)

In the bioavailability radar of Flavanone, it is explained that this compound can be said to be good and suitable as a drug candidate because most of it is in the pink area, which is seen in the red dots and lines. It means that Flavanone is a good compound because the pink area is radar safe on a compound.

Medicinal Chemistry	
PAINS	0 alert
Brenk	2 alerts: nitro_group, oxygen-nitrogen_single_bond
Leadlikeness	Yes
Synthetic accessibility	2.99

(Medical Chemistry of Flavanone)

Based on the Leadlikeness, it shows that Flavanone is a good compound to be used as a medicinal compound, and the synthetic accessibility shows that Flavanone has a value of 2.99, which means it tends to be easier to synthesize.

DISCUSSION

Based on the data we have obtained, Noni fruit extract contains Flavanones, which are Flavonoid derivatives with a content high enough to reduce cancer, especially breast cancer. The flavanone compounds contained in them are used as anticancer compounds and radical-

free antioxidants, which can relieve pain in cancer sufferers. Apart from that, synthetic bioactive compounds and drug content have good value and have more potential to become breast cancer drugs.

ACKNOWLEDGEMENT

We thank God Almighty for all His blessings so that this paper can be completed to completion. We do not forget to thank those who have contributed by providing support to us. We really hope that this research can increase readers' knowledge and experience. The writing team would like to thank Institut Teknologi Sepuluh November University, Surabaya, for providing us with the opportunity and support so that this research could run smoothly. In fact, we hope that this article can be put into practice by readers in their daily lives. We, as writers, feel that there are still many shortcomings in preparing this paper due to our limited knowledge and experience. For this reason, we really hope for constructive criticism and suggestions from readers for the perfection of this paper.

CONCLUSION

1. The results of the phytochemical tests carried out obtained compounds from the flavonoid group, dragendroff alkaloids, tannins, and terpenoids.
2. Noni fruit ethanol extract has high antioxidant effectiveness, so it is useful for reducing the risk of breast cancer.
3. In the research we conducted. We observed that (*Morinda citrifolia* L.) could be considered as a potential source of anticancer agents. However, further research is needed to find out the mechanism of action. The next suggestion for our team is to carry out in vivo & in vitro tests.
4. As more and more women seek natural therapies for general health, it is important to develop new approaches that have fewer side effects and are safer. In silico studies have 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-breast cancer drug candidate.
5. Therefore, future research directions have the potential to expand the use of food-based flavonoids as a potent and effective method of cancer prevention therapy.
6. From the PSA test results, the particle size is around 534.6 nm or 0.5346 micrometers. The particle size is very good because it is used as a nanoparticle technology, which is packaged in tea dosage forms, especially capsules. This product was created to make it easier for patients to take breast cancer medication, so it is hoped that it can relieve pain.

RECOMMENDATION

Noni fruit has been proven to be able to prevent breast cancer and is safe for us to use, so this research needs to be developed.

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