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# ANALYSIS OF BIOACTIVE COMPOUNDS POTENTIAL IN ETHANOL EXTRACT OF WATERMELONS (*Citrullus lanatus*) MESOCARP

*Analisis Potensi Senyawa Bioaktif pada Ekstrak Etanol Mesokarp Semangka (Citrullus lanatus)*

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***ABSTRAK***

*Semangka (Citrullus lanatus) merupakan buah tropis yang banyak dibudidayakan dan dikonsumsi di Indonesia. Namun, konsumsi masyarakat umumnya terbatas pada bagian daging buah, sedangkan mesokarp (lapisan putih antara kulit dan daging buah) sering kali dibuang sebagai limbah. Kondisi ini turut menyumbang peningkatan limbah organik dari sektor hortikultura yang belum dimanfaatkan secara optimal. Selain itu, mesokarp semangka diketahui mengandung senyawa bioaktif seperti flavonoid, fenolik, dan alkaloid yang memiliki aktivitas antioksidan, antiinflamasi, dan antidiabetik. Meskipun potensinya telah banyak dilaporkan, namun pemanfaatannya secara optimal dalam pengembangan agen terapi alami masih terbatas. Penelitian ini bertujuan untuk mengeksplorasi kandungan senyawa bioaktif dari ekstrak etanol mesokarp semangka dengan dua konsentrasi pelarut berbeda, yaitu etanol 70% dan etanol 96%, menggunakan metode maserasi. Desain penelitian yang digunakan berupa eksperimental laboratorik. Simplisia mesokarp semangka diekstraksi, kemudian dianalisis kadar total flavonoid, fenolik, dan alkaloid menggunakan metode spektrofotometri UV-Vis. Hasil menunjukkan rendemen pada etanol 70% sebesar 51.7%, lebih tinggi dibandingkan etanol 96% sebesar 44.65%. Kandungan flavonoid dan alkaloid lebih tinggi ditemukan pada ekstrak etanol 70% (masing-masing 4,01% dan 1438,03 µg/g), sementara kandungan fenolik lebih tinggi ditemukan pada etanol 96% (5,92%). Penelitian ini mengindikasikan bahwa pemilihan konsentrasi pelarut yang tepat sangat menentukan keberhasilan ekstraksi senyawa bioaktif dari mesokarp semangka, sehingga berpotensi dimanfaatkan sebagai bahan dasar dalam pengembangan agen antioksidan alami.*

***Kaca kunci:*** *Citrullus lanatus, ekstraksi, etanol 70%, etanol 96%, mesokarp semangka, senyawa bioaktif*

**ABSTRACT**

Watermelon (*Citrullus lanatus*) is a tropical fruit that is widely cultivated and consumed in Indonesia. However, consumption by the general public is limited to the flesh of the fruit, while the mesocarp (the white layer between the skin and the flesh) is often discarded as waste. This situation contributes to an increase in organic waste from the horticultural sector that has not been optimally utilised. Additionally, watermelon mesocarp is known to contain bioactive compounds such as flavonoids, phenolics, and alkaloids, which exhibit antioxidant, anti-inflammatory, and antidiabetic activities. Although its potential has been widely reported, its optimal utilisation in the development of natural therapeutic agents remains limited. This study aimed to explore the content of bioactive compounds from ethanol extracts of watermelon mesocarp with two different solvent concentrations, specifically 70% ethanol and 96% ethanol, using the maceration method. The research design used is an experimental laboratory study. Watermelon mesocarp simplicia was extracted, then analyzed for total flavonoids, phenolics, and alkaloids using the UV-Vis spectrophotometric method. The results showed that the yield



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of 70% ethanol was 51.7% higher than 96% ethanol of 44.65%. Higher flavonoid and alkaloid content was found in 70% ethanol extract (4.01% and 1438.03 µg/g, respectively), while higher phenolic content was found in 96% ethanol (5.92%). This study indicates that the selection of the right solvent concentration greatly determines the success of the extraction of bioactive compounds from watermelon mesocarp, so it has the potential to be utilized as a basic material in the development of natural antioxidant agents.

**Keywords:** *Bioactive compounds. Citrullus lanatus, Ethanol 70%, Ethanol 96%, Extraction, Watermelon mesocarp*

## INTRODUCTION

Watermelon (*Citrullus lanatus*) is a tropical fruit that is widely cultivated in Indonesia. It belongs to the *Cucurbitaceae* family along with pumpkins and melons. The availability of watermelon in Indonesia is relatively abundant considering that this plant is able to grow optimally at various altitudes and in accordance with tropical climatic conditions, but it will grow and develop well in the lowlands with temperatures of 23-28°C [1]. Watermelon has several parts, starting from the exocarp, mesocarp, and endocarp. The white layer in watermelon that is between the skin and pulp is called the mesocarp [2]. However, public consumption is generally limited to the flesh of the fruit, while the mesocarp tends not to be utilized and is discarded as waste [3].

Previous studies reported that watermelon mesocarp contains bioactive compounds such as flavonoids, phenolics, and alkaloids [4]. Bioactive compounds are chemical components that naturally occur in plant and animal tissues and have biological potential that is beneficial to human health. Research on bioactive compounds has been carried out in the context of developing supplements and drugs that aim to improve human health and for alternatives to the limitations of existing drugs [5], [6], [7]. The content of bioactive compounds in watermelon mesocarp is indicated as a potential source of antioxidants and antidiabetic and anti-inflammatory agents and to prevent and treat diseases, especially those caused by free radicals [8], [9], [10], [11].

Various extraction techniques have developed, ranging from the use of simple tools to the use of modern tools. Extraction is the process of separating chemical compounds from plant or animal tissues with the help of appropriate solvents [12]. There are several extraction methods, one of which is maceration. Maceration is one of the extraction methods that is often used because it is suitable and good for industrial and small-scale. This method relies on the solubility principle, where the solvent is selected based on its ability to dissolve the target compound from other complex mixtures. Generally, the starting material used in extraction is simplicial, which is a natural material that has been dried [13].

The choice of solvent plays a crucial role in determining the success of the extraction process, especially in maintaining the stability and functional activity of the extracted compounds [14]. The effectiveness of extraction and the composition of bioactive compounds are strongly influenced by the type and volume of solvent used. The solubility principle is the basis for solvent selection, where polar compounds dissolve more easily in polar solvents, while non-polar compounds tend to dissolve in non-polar solvents [15]. One solvent that is often used for the extraction of bioactive compounds is ethanol [16].

Ethanol is one of the most commonly used polar solvents in the extraction of bioactive compounds from natural materials. Its high polarity and ability to penetrate cell membranes make it effective in accelerating the diffusion process of active compounds from plant tissues into the solvent [17]. The extraction processes using ethanol are usually carried out through the soaking method, in which the extracted material is immersed in ethanol with a certain concentration at a predetermined temperature and time. In this process, the active compounds found in the natural material matrix will be dissolved into the solvent medium step by step [18].

Several studies have shown that variations in solvent concentration, such as 70% and 96% ethanol, can affect the yield of the extract produced [19]. Another study reported that differences in solvent concentration affect the yield of red dragon fruit peel extract. The use of



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70% ethanol yielded the highest extraction yield of 10%, while the use of 96% ethanol resulted in a lower yield of 8% [20]. Meanwhile, another study stated that there were differences in the content of secondary metabolites in rose apple leaf extract. Extracts obtained using ethanol solvents with concentrations of 70% and 96% contain secondary metabolites such as flavonoids, tannins, and steroids [21].

Based on the previous discussion, it is known that variations in solvent concentration can affect the yield and content of bioactive compounds in plant materials. However, to date, there have been no reports examining the effect of solvent concentration differences on the yield and bioactive compound content of watermelon mesocarp. Therefore, this study was conducted to investigate the effect of using 70% and 96% ethanol on the yield and bioactive compound content produced from watermelon mesocarp. Given the limited research related to the effect of ethanol concentration on the composition and activity of bioactive compounds from watermelon mesocarp, the results of this study are expected to provide a scientific basis for the utilization of fruit waste as a source of natural ingredients for the development of functional foods and phytopharmaceutical products.

## METHODS

This study used an experimental laboratory design. The research sample was ethanol extract of watermelon mesocarp (*Citrullus lanatus),* with the variables studied being total alkaloids, total phenolics, and total flavonoids to evaluate the influence of solvent concentration on the levels of these bioactive compounds. This research was conducted at Laboratorium Penelitian dan Pengujian Terpadu (LPPT) of Gadjah Mada University in March 2025.

### A. Research Materials and Equipment

The materials used were watermelon mesocarp (*Citrullus lanatus*), 70% ethanol, 96% ethanol, 2N and 4N Hydrogen Chloride, sodium nitrite, aluminium chloride, sodium hydroxide, distilled water, gallic acid, folin-ciocalteu, sodium carbonate, chloroform, 0.1N NaOH, Bromocresol Green, phosphate buffer, magnetic stirrer, water bath, autoclave, glass cuvette, spectrophotometer, rotary evaporator, incubator cabinet dryer, oven, test tubes, dropper pipettes, measuring cups, filter paper, jars, analytical balance, and a flouring machine.

### B. Procedure

#### 1. Sample Preparation

Watermelon fruits were obtained from farmers in Mojosari Village, Puger District, Jember Regency, East Java. The samples used were selected purposively based on optimal ripeness and fresh, intact fruit condition, free from physical damage or contamination. The process preparing simplicia includes separating 85 kg of watermelon flesh from the outer skin and white skin. Following this, 31.6 kg of watermelon mesocarp was cut into small pieces with a thickness of approximately 1 cm. The pieces were then dried using a cabinet dryer at 45°C. The samples were then pulverized using a milling machine to produce fine powder or simplified after drying.

#### 2. Extraction

The extraction of watermelon (*Citrullus lanatus*) mesocarp was carried out using the maceration method, in which the sample was soaked in ethanol as the solvent. The obtained simplicia was weighed and subsequently immersed in 70% and 96% ethanol for 3 × 24 hours. Following the separation and filtering of the sediment and filtrate, two more maceration cycles lasting 2 x 24 hours each were conducted. The resulting filtrate was concentrated using a rotary evaporator at a temperature of 40°C with a rotation speed of 100 rpm until the solvent evaporated completely, to obtain a concentrated crude extract. [11].

#### 3. Total flavonoid

Total flavonoid content was measured using the UV-Visible spectrophotometry method with two repetitions. A precisely weighed portion of watermelon mesocarp extract of 50 mg was used for analysis. Then, 0.3 mL of 5% sodium nitrite ($NaNO_2$) solution was added, and


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the mixture was incubated at room temperature for 5 min. Next, 0.6 mL of 10% aluminum chloride ($AlCl_3$) solution and 2 mL of 1 M sodium hydroxide (NaOH) were added sequentially. The resulting mixture was then diluted with distilled water to a final volume of 10 mL using a volumetric flask. The solution was transferred into a cuvette, and the absorbance was measured at a wavelength of 510 nm using a UV-Vis spectrophotometer [22].

**4. Total Alkaloids**

The quantification of total alkaloids was conducted using the UV-Vis spectrophotometric method with two repetitions. Approximately 50 mg of the sample was weighed and mixed with 5 mL of 2N hydrochloric acid, followed by thorough shaking. The resulting solution was washed three times with 10 mL of chloroform using a separatory funnel, and the chloroform phase was discarded. The aqueous phase was then neutralized with 5 mL of 0.1N sodium hydroxide. Subsequently, 5 mL of bromocresol green (BCG) solution and 5 mL of phosphate buffer were added. The mixture was extracted with 5 mL of chloroform and stirred using a magnetic stirrer at 500 rpm for 15 minutes. This extraction step with chloroform was repeated two additional times. The chloroform layers were then collected, evaporated under a stream of nitrogen gas, and the residue was reconstituted in chloroform to a final volume of 5 mL. Absorbance was measured at a wavelength of 470 nm using a UV-Vis spectrophotometer [23].

**5. Total phenolic**

The total phenolic content was determined using the UV-Vis spectrophotometric metodh with two repetitions. A 50 mg portion of the sample was accurately weighed and mixed with 0.5 mL of Folin-Ciocalteu reagent and 5 mL of distilled water. The mixture was left to react at room temperature for 10 minutes. Subsequently, 1.5 mL of 20% sodium carbonate solution was added. The final volume was adjusted to 10 mL with distilled water using a volumetric flask, and the solution was transferred into a cuvette. Absorbance was measured at a wavelength of 760 nm using a spectrophotometer [24].

## RESULT

### 1. Extraction Watermelon Mesocarp (*Citrullus lanatus*)

The maceration method was used in the preparation of watermelon mesocarp extract with 70% ethanol and 96% ethanol. The yield is obtained from the ratio between the extract obtained and the weight of the simplicia used and is presented in Table 1.

**Table 1. Yield of Watermelon Mesocarp (*Citrullus lanatus*)**

| Solvent Concentration | Weight of simplicia (gram) | Weight Extract (gram) | Yield |
|---|---|---|---|
| 70% Ethanol | 1000 | 517 | 51.7 |
| 96% Ethanol | 580 | 259 | 44.65 |

### 2. Bioactive Compound Content (total phenolics, total alkaloids, and total flavonoids)

The variation of ethanol solvent concentration is known to affect the content of bioactive compounds extracted from the mesocarp of red watermelon (*Citrullus lanatus*). Analysis of the total content of flavonoids, alkaloids, and phenolics was carried out to assess the effectiveness of each solvent concentration in extracting these bioactive components. The results of measuring the content of bioactive compounds using the spectrophotometric UV-Vis method are presented in Table 2.

**Table 2. Bioactive Compound Content of Ethanol Extract of Watermelon Mesocarp (*Citrullus lanatus*)**

| Parameters | Unit | 70% Ethanol | 96% Ethanol | Methods |
|---|---|---|---|---|
| Total Flavonoid | % (b/b) | 0.40 | 0.08 | UV-Vis Spectrophotometric |
| Total Alkaloid | µg/g | 1438.03 | 120.48 | UV-Vis Spectrophotometric |
| Total Phenolic | % (b/b) | 0.40 | 5.92 | UV-vis Spectrophotometric |


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## DISCUSSION

This study employed the maceration method to extract compounds from watermelon mesocarp (*Citrullus lanatus*) using two different ethanol concentrations (70% and 96%). The extraction process was systematically designed to align the solubility properties of the target compounds with the polarity of the selected solvents. The strategic use of solvents aimed to extract a broad range of bioactive compounds including non-polar, semi-polar, and polar molecules, in order to produce a more comprehensive and representative extract. Ethanol is widely recognized as a safe and effective solvent for extracting phenolics, flavonoids, and alkaloids due to its balanced polarity and applicability across various plant materials [3].

The extraction results showed significant yield differences between the two solvents. The extract using 70% ethanol produced a yield of 51.7%, while 96% ethanol produced a yield of 44.65%. The percentage shows that 70% ethanol is effective in extracting compounds from watermelon mesocarp (*Citrullus lanatus*) [25]. Previous research conducted by Amin *et al*. [11] reported that watermelon mesocarp extract dissolved using 70% ethanol produced a yield of 34%; this shows good extraction ability. However, it should be noted that the yield also depends on the amount of simplicia used and the extraction method applied, which may vary across studies [26].

Ethanol solvent of 70% concentration is known to have an optimal ratio between water and ethanol, which makes it ideal in extracting compounds from plant parts such as skin, roots, and seeds [27]. The higher the ethanol concentration, the lower the solvent's polarity [25]. The solvent 70% ethanol, as a semipolar solvent, is able to dissolve polar compounds such as alkaloids and flavonoids, and semi-polar compounds such as some phenolics. This characteristic helps explain the superior extraction yield and compound recovery observed with 70% ethanol in this study. In addition, 70% ethanol also has the advantage of preventing the growth of microorganisms during the soaking process [9], [28], [29].

The influence of solvent polarity is clearly reflected in the differences in bioactive compound content shown in Table 2. The content of bioactive compounds contained in Table 2, obtained from extraction with 70% ethanol solvent, is flavonoids 0.40% (b/b), alkaloids 1438.03 µg/g, and phenolics 0.40% (b/b), while 96% ethanol solvent is flavonoids 0.08% (b/b), alkaloids 120.48 µg/g, and phenolics 5.92% (b/b). From these data, it shows that the test results obtained for flavonoid content in ethanol extract of watermelon mesocarp (*Citrullus lanatus*) showed a higher value in 70% ethanol solvent at 0.40% (b/b) (equivalent to 4.01 mg QE/g), compared to 96% ethanol at 0.08% (b/b) (equivalent to 0.79 mg QE/g). These results indicate that flavonoids are more soluble in solvents with medium polarity. A study mentioned that flavonoid which are generally polar in nature, can be extracted more optimally using semi-polar solvents such as 70% ethanol, which has a combination of ethanol and water with medium polarity [30]. Conversely, 96% ethanol, which contains minimal amounts of water, exhibits lower polarity and is therefore classified as a semi-polar solvent with low polarity, making it less effective in extracting polar compounds [31]. The type of solvent has an important role in determining the amount of bioactive compounds that can get extracted because the effectiveness of the solvent is highly dependent on the suitability of its polarity with the target compounds to be extracted [14].

Flavonoid compounds are non-soluble compounds, so they dissolve more easily in 70% ethanol than in pure ethanol because 70% ethanol has higher polarity due to its water content [32]. Flavonoids are part of a class of phenolic compounds known to have high antioxidant activity that works by neutralizing unstable free radicals through a one-electron donation process to stop oxidative chain reactions. In addition, flavonoids can prevent the formation of free radicals by neutralizing or stabilizing reactive oxygen species (ROS) and eliminating oxidative species resulting from the metabolism of xenobiotic compounds. Flavonoids also work as anti-inflammatory agents by inhibiting inflammatory mediators and reducing oedema volume in the inflammatory process. This role is important in preventing cell damage due to oxidative stress and chronic inflammation [33].



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A similar pattern was observed in the alkaloid content, reinforcing the efficiency of 70% ethanol. Analysis of the alkaloid content showed that the extract with 70% ethanol contained 1438.03 µg/g of alkaloids, much higher than the 96% ethanol extract of 120.48 µg/g (Table 2). This supports the assumption that semi-soluble solvents such as 70% ethanol are more effective in dissolving alkaloid compounds, which are generally polar to semi-soluble in nature, making them more soluble in solvents that also have medium to high levels of polarity, such as 70% ethanol, which is a mixture of ethanol and water. In addition, the presence of water in the solvent also increases the diffusion of the solvent into plant tissue due to its highly hydrophilic nature, so alkaloid compounds are more easily diffused and dissolved in the solvent.

Alkaloids are bioactive compounds that are found in many types of plants. This compound is a chemical compound that has significant differences compared to other heterocyclic derivative compounds, as well as nitrogen-containing compounds, due to its unique structure and biological activity [34]. Alkaloids have an important role in regulating blood glucose levels in diabetes through various mechanisms, including increased insulin secretion and improved sensitivity to insulin. These compounds can stimulate pancreatic β-cells to produce more insulin, which in turn helps in controlling blood glucose levels more effectively [35]. Alkaloids are organic heterocyclic bases found in nature that are synthesized in plants through transamination reactions or amino acid biosynthesis pathways. Some of the biological activities/health benefits of alkaloids as reported in the literature include antihypertensive, antioxidant, anticholinergic, anti-inflammatory, antitumor, antimicrobial, antiviral, hypnoanalgesic, and antidepressant [36].

Other bioactive compounds found in the ethanol extract of watermelon mesocarp (*Citrullus lanatus*) are total phenolic compounds. In contrast, the total phenolic content was higher in the extract with 96% ethanol, which was 5.92% (b/b) (equivalent to 59.2 mg GAE/g), compared to 70% ethanol at 0.40% (b/b) (4.0 mg GAE/g). This difference may be due to the polarity of the solvent used. It was known in the previous study that 96% ethanol solvent has a more effective ability to extract more specific phenolic compounds compared to other solvents [26]. In addition, 96% ethanol solvent also more easily penetrated the sample cell wall to absorb more material compared to ethanol at lower concentrations [37]. Phenolic compounds have unstable properties that are easily degraded by various environmental factors such as light, pH, oxygen, temperature, and the existence of ions, which can further affect phenolic levels in each plant [38].

Phenolic compounds are known to have a variety of biological activities, including antioxidant, anticancer, anti-inflammatory, and antimicrobial, and they play a role in protecting the body from heart disease and cell damage due to exposure to free radicals. As antioxidants, phenolic compounds function by reducing the level of ROS in the body [39]. Phenolic compounds act as antioxidants that are effective in inhibiting the oxidation process triggered by free radicals to protect cells and body tissues from oxidative damage. This process takes place through the inhibition of the initial (initiation) and advanced (propagation) stages of oxidative reactions, which overall contribute to fighting the damaging effects of free radicals [32]. Phenolic compounds of plant origin also have anti-diabetic effects through various mechanisms [40]. Not only that, phenolic compounds also inhibit the action of digestive enzymes such as α-glucosidase and α-amylase, which play a role in the process of breaking down carbohydrates into glucose. Thus, these compounds help slow down the absorption of glucose in the gut and control the postprandial spike in blood sugar levels [41].

One potential natural source of phenolic compounds and other bioactive constituents is the watermelon mesocarp. Based on previous research, watermelon mesocarp not only contains flavonoids, alkaloids, and phenolic compounds, but is also a rich source of citrulline, flavones, saponins, sterols, terpenoids, and other bioactive compounds that contribute to antioxidant activity and provide health-promoting effects [42]. Additionally, watermelon mesocarp is known to contain starch, non-starch polysaccharides, sugars, resistant starch, oligosaccharides, and pectin [43]. Pectin functions to reduce cholesterol levels in the blood


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[11]. Recent research shows that potassium levels in watermelon mesocarp are higher than those in watermelon flesh. Through analysis using atomic absorption spectrophotometry, it was found that potassium levels in watermelon mesocarp reached 286.47 mg/100 g, while in watermelon flesh, they were only 92.76 mg/100 g. This finding indicates the potential of watermelon rind as a better source of potassium than the flesh, which can provide additional benefits in supporting electrolyte balance and muscle function in the body [44].

Given the rich phytochemical profile of watermelon mesocarp including phenolic compounds with diverse biological activities. The extraction process plays a crucial role in ensuring that these compounds can be isolated effectively for further use. The difference in solvents in the extraction process significantly affects the total content of bioactive compounds produced, mainly due to the difference in polarity of each solvent, which determines the ability to dissolve certain compounds. Extraction efficiency not only depends on the type of solvent but is also influenced by the ratio of solvent to material, temperature, pressure, and extraction time, as well as the chemical and bioactive properties of the plant. Under uniform temperature and pressure conditions, the type of solvent and the characteristics of the plant's chemical compounds are the dominant factors that determine the success of extraction. The combination of these factors will affect the quality and quantity of bioactive compounds obtained. However, this study has limitations, namely that it has not analyzed several specific bioactive compounds such as quercetin, citrulline, and vitamin C due to limited facilities and reagents in the laboratory, so the interpretation of the results is still limited to the parameters analyzed.

## CONCLUSION

This study shows that solvent type affects the effectiveness of extracting bioactive compounds from watermelon mesocarp (*Citrullus lanatus*), which is influenced by the suitability of solvent polarity to the characteristics of the target compounds. Solvent 70% ethanol is more effective in extracting flavonoid and alkaloid compounds, while 96% ethanol is superior in extracting total phenolic compounds. This difference reflects the ability of each solvent to dissolve compounds based on their polarity. These compounds are known to have antioxidant, anti-inflammatory, and antidiabetic activities. The results of this study are expected to be used as a reference basis for the selection of extraction solvents to dissolve bioactive compounds in watermelon mesocarp. However, the limitations of laboratory facilities and reagents mean that analysis of some specific bioactive compounds cannot be carried out, so further, more comprehensive research is needed to expand understanding of the potential of red watermelon mesocarp extract as an antioxidant agent.

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