Synergism test on date seeds (*Phoenix dactylifera* l.) And peanut shells (*Arachis hypogea* l.) Extract on antioxidant activity

Galuh Anjani Garnisaputri[1], Intan Kurnia Putri[2]*, Melania Perwitasari[3], Dede Dwi Nathalia[4]

[1,2,3,4] Department of Pharmacy, Sekolah Tinggi Ilmu Kesehatan Mitra Keluarga, Bekasi, Indonesia.
*Correspondence author : intan.kurnia.p@stikesmitrakeluarga.ac.id

Abstract

Free radicals can cause body tissue damage and cancer. Several compounds that can overcome tissue damage in the body are called antioxidant compounds. Antioxidant compounds can be found in various plants, such as dates and peanuts. The purpose of this study was to evaluate the antioxidant activity contained in date seeds and peanut skin as well as the synergistic effect of the combination of date seed extract and peanut shell extract. The samples used were ethanolic extract of date palm seeds and peanut shells by maceration extraction method. The Ferric Reducing Antioxidant Power (FRAP) method with UV-Vis spectrophotometry was applied to evaluate the antioxidant activity. The results of the phytochemical screening showed that the ethanol extract of date palm seeds and the ethanol extract of peanut shells contained flavonoid compounds characterized by a change in color to orange and phenolic compounds indicated by a change in color to black. The results of antioxidant activity using the FRAP method were 130.370% for date seed extract and 170.353% for peanut shell extract. Combining the ethanolic extract of date palm seeds and the ethanol extract of peanut shells obtained a percentage difference value of 78.575%. Peanut shell extract has higher antioxidant activity than date seed extract, and combining the two has a synergistic effect.

Keywords: Antioxidant activity; Cancer; Date seeds; FRAP; Peanut skin; Synergism

Introduction

Based on data from *the World Health Organization* (2022), there were a total of 396.914 cases of cancer in Indonesia and a total of 234.511 deaths. Deaths from cancer are expected to continue to increase to more than 13.1 million in 2030 (Ministry of Health, 2019). *Cancer* is a malignant tumor characterized by abnormal growth of body cells. The types of cancer most commonly found in patients in hospitals are breast cancer (28.7%) and cervical cancer (12.8%) (Ministry of Health of the Republic of Indonesia, 2018). One of the causes of cancer is free radicals, which attack cells in the human body and cause tissue damage. Compounds that are useful in helping overcome tissue damage caused by free radicals are antioxidants (Alghiffari, 2021).

Antioxidants are helpful in preventing cancer cells and work by capturing free radicals, so they can inhibit the proliferation of cancer cells and become anticancer agents. Antioxidant compounds can be obtained from synthetic compounds or natural compounds. Currently, people prefer to use traditional medicine because it is believed to have milder side effects than synthetic drugs. Indonesia has many types of plants that have potential as natural antioxidants, one of which is dates and peanuts (Santoso *et al.*, 2022).

Dates (*Phoenix dactylifera* L.) is a plant that can be used as a medicinal plants. Dates have been shown to have antioxidant, antimicrobial, and anti-inflammatory activity. The functional effects of dates are not only limited to the fruit but also to the seeds. In traditional medicine, date seeds treat various ailments, including cancer, digestive disorders, diarrhea, liver disorders, diabetes, and lung infections (Bouhlali *et al*., 2021). The antioxidant properties contained in date seeds can function to fight oxidative stress caused by free radicals. These date seeds are usually just waste and require further efforts to utilize them (Huang *et al*., 2020).

Peanuts (*Arachis hypogea* L.) have the same benefits as date seeds, namely that they can treat cancer and liver disorders (Fadly *et al.*, 2022). In addition, peanuts are widely known for their high content of phenolic compounds with antioxidant activity that is concentrated in the skin and has health effects on the human body (Lima & Alencar, 2022). So far, using peanuts is still limited to processing the seeds. In contrast, the use of peanut shells has not been maximized and is only considered waste, usually only for animal feed and fertilizer. It turns out that peanut skin contains a lot of flavonoids, and the most considerable flavonoid content is luteolin (Ichsani, 2021). Vrianty *et al*. (2019) stated that luteolin is an anti-inflammatory, antioxidant, and anticancer. Therefore, further efforts are needed to make peanut shells a helpful material.

Methods

In this study using the descriptive with design of research is pre-experimental. This research was carried out at the chemical laboratory of STIKes Mitra Keluarga in January – March 2023. The materials used were date palm seeds (phoenix dactylifera) type of Sukari, Peanut shells (Arachis hypogaea L.), 70% ethanol, 2,4,6-tripyridylstriazine (TPTZ) (Sigma), $FeCl_3$ (ferric chloride)(Brataco),and Vitamin C (L-Ascorbic Acid) (Sangon Biotech), Mg (Magnesium)

(Merck), HCl (hydrochloric acid), DMSO (Dymethyl sulfoxide), H_2SO_4 (Acetic acid), CH_3COONa (Sodium acetate), $FeSO_4$ (Brataco) and used several tools, namely test tubes, trays, test tube racks, plastic wrap, 60-80 mesh sieve, aluminum foil, knife, tissue, measuring cup,beaker glass,Spatula, Porcelain cup, Filter paper, Glass funnel, Stirring rod, Drop pipette, Vial bottle, Glass cuvette, Micropipette, Analytical balance, Microtip,Rotary evaporator(IKA), Oven, Vortex Mixer, UV-Vis Spectrophotometer (thermo).

Plant determination test

The dates seed and peanut shells used were subjected to a determination test at the National Research and Innovation Agency (BRIN), Bogor.

Preparation of Sample Extract

Date seeds are dried for 2 hours in an oven at 60°C. Furthermore, the date palm seeds are mashed using a blender until a fine powder is obtained. The fine powder of the date seeds was weighed as much as 250 grams (Siregar et al., 2018). Then maceration extraction was carried out soaked in 500 mL 70% ethanol. The yield was filtered using filter paper to separate the filtrate from the residue. The filtrate is concentrated usingrotary evaporatorsat 60°C at a speed of 90 rpm to obtain the ethanol extract of date palm seeds (Nazilah, 2019).

Peanuts were dried in an oven at 60°C for 3 days. After drying, the peanut shell simplicia is ground using a blender to make it into powder. Then the peanut shell powder was sieved using a 60 mesh sieve to obtain a fine peanut shell powder (Fadly *et al.*, 2022). Then maceration extraction was carried out by soaking peanut shell powder in 2 L of 70% ethanol and leaving it for 3 days. The juice is filtered and the residue is squeezed. The residue was re-macerated with the same solvent and left for 2 days. Then separate the filtrate and evaporate itrotary evaporatorsat a temperature of 60°C to obtain a thick ethanol extract of peanut shells (Kursia *et al.*, 2020).

Determination of Extract Water Content

The water content of the extract was tested using a moisturizer analysis tool by weighing 1 gram of extract of date palm seeds and peanut shells into a device that has been set at 105°C for 30 minutes (Susanto, 2021).

Phytochemical Screening

Phytochemical screening includes Flavonoid and phenol test. Flavonoid test on date seed extract and peanut shell extract was carried out by evaporating the extract until dry and then adding 2-3 drops of ethanol. After that, 0.2 gram of Mg powder and a few drops of 5M HCl were added. If a red, orange or purple color is formed, then there are flavonoid compounds (Ichsani, 2021). Phenol test on date seed extract and peanut shell extract was carried out by mixing the extract with 3-4 drops of 1% $FeCl_3$. The presence of phenol compounds can be seen from the formation of a blackish green color (Azizah & Widya Wati, 2018).

Preparation of Acetate Buffer

Acetate buffer with a pH of 3.6 was prepared from 0.155 grams of sodium acetate (CH_3COONa) added with 0.8 mL of concentrated acetic acid and dissolved with distilled water to exactly 50 mL in a measuring flask.

Preparation of 2,4,6-trippyridyl-striazine (TPTZ) Solution

TPTZ was weighed as 30 mg, dissolved in 40 mmol/L HCl to exactly 10 mL. A solution of 40 mmol/L HCl was prepared by dissolving 0.1656 mL of concentrated HCl in 50 mL of distilled water.

Preparation of FeCl3.6H2O Solution

FeCl3.6H2O was weighed as much as 0.27 grams, dissolved in distilled water in a measuring flask to exactly 50 mL.

Preparation of FRAP Reagent

FRAP reagent is prepared by mixing 25 mL of acetate buffer; 2.5 mL TPTZ solution; 2.5 mL FeCl3.6H2O solution. Then add distilled water to exactly 100 mL in the measuring flask.

Preparation and Testing of $FeSO_4.7H_2O$ Standard Solution

A total of 50 mg of $FeSO_4.7H_2O$ was dissolved in 50 mL of distilled water in a volumetric flask until a concentration of 1000 µg/mL was obtained. In a measuring flask 10 mL is made concentration of 40 – 140 µg/mL. From each concentration, 100 µL was taken and then put into a volumetric flask and 3 mL of FRAP reagent was added. After that, it was incubated for 10 minutes at 37°C. The absorbance of each concentration was read using a UV-Vis spectrophotometer with the maximum wavelength.

Maximum Wavelength Determination

The maximum wavelength was obtained by measuring the absorbance of the $FeSO_4.7H_2O$ standard with the highest concentration (140 µg/mL). 100 µL of the solution was taken, then 3 mL of FRAP reagent was added, then read at every wavelength of 580-610 nm.

Determination of Antioxidant Activity Values

A total of 10 mg of date seed samples was dissolved in distilled water to 10 mL (1000 µg/mL) in a volumetric flask. Then take a volume of 1 mL and then put it in a 10mL volumetric flask and dilute it with distilled water up to the boundary mark, so that a concentration of 100 µg/mL is obtained. A total of 20 mg of peanut shell sample was dissolved in distilled water to 10 mL (2000 µg/mL) in a volumetric flask. From these concentrations, 100 µL of each was taken plus 3 mL of FRAP reagent in a volumetric flask. After that, it was incubated at 37°C for 10 minutes. Then read the absorbance using a UV-Vis spectrophotometer with the maximum wavelength. Antioxidant activity was obtained from absorbance data against FeSO4.7H2O standard series and stated to be equivalent to ppm Fe2+. The percentage of FRAP activity is calculated according to the formula (Widowati et al., 2022):

$$\text{FRAP activity (\%)} = (A/B) \times 100 \qquad (1)$$

A : control absorbance, B : sample absorbance

Synergism Test

The synergism test was carried out by mixing date seed extract (100 µg/mL) and peanut shell extract (2000 µg/mL) in a ratio of 100: 100, then determining the synergistic extract by calculating using the following formula (Skroza et al., 2022).

$$\text{Difference (\%)} = \left[\frac{ab\ x\ 100}{(Individual\ a + individual\ b) \div n}\right] - 100 \qquad (2)$$

Differences: Effects resulting from a mixture of extracts a and b, Combination ab: Antioxidant activity (Fe^{2+} levels) in the mixture of extracts a and b, Individual a / b: Antioxidant activity (Fe^{2+} levels) in extracts a / b, n: The number of compounds in the mixture.

Results and Discussions

The test was carried out at the National Research and Innovation Agency (BRIN). The purpose of the determination test is to prevent sample errors and guarantee the correct identification of plants based on their taxonomy (Nurulita et al., 2019). The test results stated that the date seeds used in this study were date seeds with the Latin name Phoenix dactyliferaL., family Arecaceae. Meanwhile, the test results for peanut shells used in this research have Latin names Arachis hypogaeaL., Fabaceae family.

The results of thick date seeds extract are presented in Figure and the results of the characteristics of date seed extract are presented in Table 1.

Figure 1. Extract of Dates Seeds

Table 1. Results of the Characteristics of Date Seed Extract

Specification	Description
%yield	12.6%
Color	Brownish black
Smell	Typical of dates

The results of thick peanut shell extract are presented in Figure 2 and the results of the characteristics of peanut shell extract are presented in Table 2.

Figure 2. Peanut Shells Extract

Table 2. Results of Characteristics of Peanut Shells Extract

Specification	Description
%yield (Maceration 1)	1.25%
%yield (Maceration 2)	0.9%
Color	Chocolate
Smell	Typical of Peanut

The results obtained for the water content of date seed extract and peanut shell extract can be seen in table 3.

Table 3. Extract Water Content Test Results

Samples	Replication	Water Content (%)	Mean ± SD
Seed Dates Extract	1	3.68	3.74 ± 0.10
	2	3.68	
	3	3.86	
Peanut Shells Extract	1	6.73	6.70 ± 0.06
	2	6.73	
	3	6.63	

Phytochemical screening was carried out to qualitatively determine the content of active compounds in plants contained in date seed extract and peanut shell extract (Kusmiati et al., 2018). Phytochemical screening in this study was carried out on the flavonoid and phenol compounds. The flavonoid test was carried out by mixing the extract with 0.2 grams of Mg powder and several drops of 5M HCl. Samples containing flavonoid compounds obtained a color change to red, orange, or purple (Ichsani, 2021). Then the phenol test was carried out using FeCl reagent31%. The presence of phenolic compounds was indicated by the formation of a black color (Azizah *et al*, 2018). The phytochemical screening results obtained for date seed extract and peanut shell extract can be seen in table 4.

Table 4. Phytochemical Screening Results

	Flavonoid Test		Phenol Test	
Extract	**Before**	**After**	**Before**	**After**
Date Seeds	Yellow	(+) Orange	Yellow	(+) Black
Peanut Shells	Yellow	(+) Red	Yellow	(+) Black

Note : (+) = Compound detected, (-) = Compound not detected

Determine the maximum wavelength by reading the absorbance of FeSO standard standard$_4$.7H$_2$O with the highest concentration (140 µg/mL) in range 580 – 610 nm. The maximum wavelength obtained was 595 nm with an absorbance of 0.782. The maximum wavelength spectrum can be seen in Figure 3.

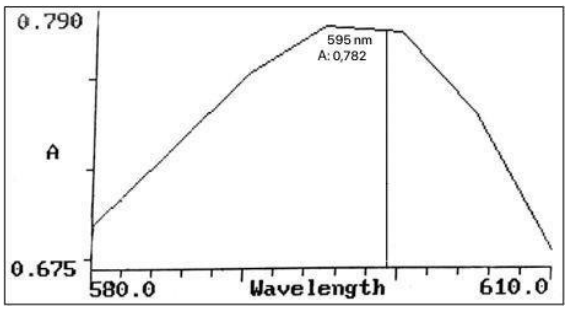

Figure 3. Maximum Wavelength Spectrum

The results of determining the standard curve absorbance were carried out in a series of solutions with a concentration of 50; 70 ; 100 ; 130 ; 140 µg/mL. The regression equation Y = 0.0032x + 0.1638 is obtained with a value of R^2 = 0.999, at a maximum wavelength of 595 nm, as shown in Figure 4. The standard curve concentration series absorbance table can be seen in table 5.

Table 5. Absorbance Data of FeSO$_4$.7H$_2$O Standard Curve

Concentration (µg/mL)	Absorbamce
50	0.328
70	0.384
100	0.482
130	0.585
140	0.611

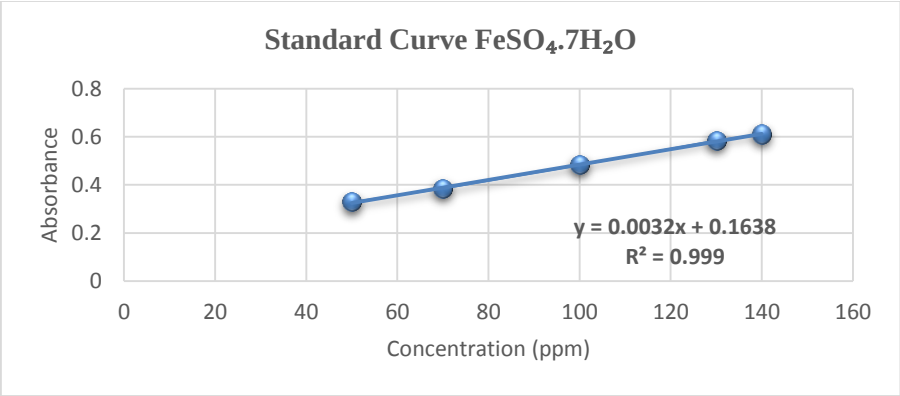

Figure 4. Standard Curve of FeSO$_4$.7H$_2$O

The control absorbance result was obtained at 0.611, while the sample absorbance was obtained by calculating the % FRAP activity to see how much antioxidant activity contained in date seed extract and peanut shell extract. The results of % FRAP Activity can be seen in table 6.

Table 6. FRAP Activity % Value

Formulas	Treatment		Fe^{2+} Rates (µg/mL)	Aktivity FRAP (%)	± SD
	Date Seeds Extract (%)	Peanut Shells Extract (%)			
F1	100	0	95,271	130,370	0,180
F2	60	40	100,062	126,240	0,313
F3	55	45	132,771	103,794	0,180

F4	50	50	107,771	120,118	0,180
F5	45	55	114,750	115,066	0,313
F6	40	60	80,375	145,131	0,313
F7	0	100	60,896	170,353	0,180

The synergism test was carried out in one step by mixing date seed extract and peanut shell extract in a ratio of 100:100. The synergism results of the two extracts can be seen in table 7.

Table 7. Synergism Test Values

Formulas	Treatment		Fe^{2+} Rates (µg/mL)	Difference (%)	± SD
	Date Seeds Extract (%)	Peanut Shells Extract (%)			
F1	100	0	95,271	-	0,180
F7	0	100	60,896	-	0,180
F8	100	100	139,438	78,575	0,313

The first stage in this research was the determination test for date palm and peanut plants which was carried out at the Bogorines BRIN Herbarium, Cibinong. This determination test aims to ensure the correct identity of the plants to be used in research, as well as to avoid errors in sampling for phytochemical analysis. The results of the determination test that has been carried out can be obtained with certainty that the date palm used in this study is the correct species Phoenix dactyliferaL. from the family Arecaceae. Then the peanut plants used in this research are the correct species Arachis hypogaea L. from the family Fabaceae.

Sample preparation of date seed extract and peanut shells was carried out by dried in an oven at 60°C for 2 hours for date seeds and 3 days for peanut shells. The drying process aims to reduce the water content in the date seeds and peanut shells which can inhibit the separation process and prevent the growth of bacteria and fungi. This drying process uses a temperature not exceeding 60°C because temperatures that are too high can damage the physiological properties of grains and thermolabile active compounds and can cause oil to be trapped inside the seed shell (Riyadi, 2018). Sample extraction was carried out using the maceration method. Maceration is the process of soaking samples with suitable solvents at room temperature so as to reduce the risk of damage to secondary metabolites (Ichsani, 2021). This method is safer because it can protect thermolabile active compounds such as flavonoids and phenols (Nazilah, 2019). The maceration process was carried out by soaking the samples in 70% ethanol solvent for 2x24 hours for date palm kernels and 3x24 hours for peanut shells and then re-macerated for 2x24 hours. The 70% ethanol solvent was chosen because it is polar, has a polarity index of 4.3 and has low toxicity.

Characteristic checks carried out on each extract include shape, color and odor as well as % yield. In the extract of date seeds, 30.4 grams were obtained from 250 grams of date seed powder, so the % yield obtained was 12.16%. Riyadi (2018) states that date seed extract has a yield value of 4.929%. Yield value calculated to determine the amount of extract obtained in each gram of date seed powder. Whereas in the first extract of peanut shell used for the qualitative test, 2.5 grams were obtained from 200 grams of peanut shell powder, so the % yield obtained was 1.25%. The condensed extract of the two peanut shells used for the antioxidant activity test was obtained as much as 1.8 grams from 200 grams of peanut shell powder so that the % yield obtained was 0.9%. Ichsani (2021) states that the % yield obtained from peanut shell extract is 28.553%.

The extract obtained is then tested for water content using a tool moisture analyzer which aims to provide a minimum limit for the amount of water content in the extract, the higher the water content, the easier it is for fungi and mold to grow so that it can reduce the biological activity of the extract during the storage period. The results of determining the water content of extracts of date palm seeds and peanut shells after 3x replication were obtained at 3.74 ± 0.10% and 6.70 ± 0.06%. This result meets the requirements set by BPOM, namely water content ≤ 10% to minimize mold growth so as to produce good storage and extract quality (Hanif *et al*., 2019).

Phytochemical screening was carried out to qualitatively determine the content of active compounds in plants (Nazilah, 2019). The results show of the phytochemical test that the ethanol extract of the two samples contained secondary metabolites, namely flavonoids and phenols. This is because the ethanol solvent extraction process can increase the permeability of the simplex cell wall to attract components of polar and semipolar compounds (Fikayuniar *et al*., 2022). Phytochemical screening of date seed extract obtained the same results as previous studies. Bouhlali *et al*

(2020) stated that the ethanol extract of date seeds contains flavonoid and phenol compounds. This can be influenced by environmental conditions where grown, harvest time, storage conditions, geographical origin, light, temperature, fertilizer and soil type and method of extraction. Then, phytochemical screening of peanut shell extract also obtained the same results as previous research. Franyoto *et al* (2019) stated that the ethanol extract of peanut shells contains flavonoids, tannins, saponins, alkaloids and terpenoids. Annadira (2021) stated that the ethanol extract of peanut shells also contains phenol compounds.

Testing the antioxidant activity of date seed extract and peanut shell extract using the FRAP method requires several stages, such as determining the maximum wavelength, determining the standard curve, and determining the antioxidant activity value of the sample. Determination of the maximum wavelength is carried out to determine the wavelength with the highest absorption. Determination of the maximum wavelength was carried out by measuring the absorbance of a standard solution of $FeSO_4.7H_2O$ with the highest concentration (140 µg/mL) in the range 580 – 610 nm. This is because $FeSO_4.7H_2O$ provides absorption in the wavelength range 580 – 610 nm. The wavelength measurement using a UV-Vis spectrophotometer gives the highest absorption at a wavelength of 595 nm with an absorbance of 0.782. The results obtained are the same as Nurhayati's *et a*l., (2022) obtained a maximum wavelength of 595 nm.

Making a standard curve with a standard solution of $FeSO_4.7H_2O$ was carried out with 5 series of concentrations. The choice of concentration is based on the Lambert-Beer law which states the absorption requirement is 0.2 – 0.8 to avoid photometric errors (Asmorowati & Lindawati, 2019). The standard curve absorbance measurement was carried out by repeating the test 3 times with the aim of obtaining more accurate data. The results of determining the $FeSO_4.7H_2O$ standard curve which can be seen in Figure 5.10 show that the concentration is directly proportional to the absorbance value. The greater the concentration of the standard standard solution $FeSO_4.7H_2O$, the higher the absorbance value produced (Rahayu *et al.*, 2021). When measuring the absorbance, the regression equation $FeSO_4.7H_2O$ was obtained, namely $y = 0.0032x + 0.1638$, where y is the absorbance and x is the concentration of antioxidant activity. The linearity value results are shown by the coefficient of determination (R^2) value of 0.999, where the condition for acceptance of a good coefficient of determination is ≥ 0.997. This shows that there is a linear relationship between the concentration of the $FeSO_4.7H_2O$ standard standard solution and the absorbance value. Linearity can be said to be good if it meets the acceptance requirements (Gayatri, 2021).

Determination of the value of antioxidant activity in this study using the FRAP method (Ferric Reducing Antiozidant Power). The principle of this method is the ability of the compound antioxidants in reducing the Fe^{3+}-TPTZ compound to Fe^{2+}-TPTZ (Wulandari, 2021). The more Fe^{3+} concentration reduced by sample becomes Fe^{2+} then the antioxidant activity of the sample also increases big (Pebriana *et al.*, 2019).

Determination of antioxidant activity in the form of absorbance. The absorbance was obtained when measuring the maximum wavelength of the $FeSO_4.7H_2O$ standard solution. The standard solution was reacted with FRAP reagent and then incubated at 37°C for 10 minutes. The aim of incubation is so that the antioxidant reaction process with FRAP reagent achieves a perfect reaction and is not influenced by stability factors. Antioxidant stability can be affected by several factors, namely light, oxygen, and pH. The value of the sample antioxidant activity is expressed in % FRAP activity with Fe^{2+} levels (µg/mL) using standard $FeSO_4.7H_2O$. The value of the antioxidant activity was determined from the two extract samples in 7 mixing stages (F1 – F7), where F1 only contained date seed extract and F7 only contained skin extract. peanuts, while F2 – F6 contains a mixture of extracts based on a predetermined formula. The results showed that F7 contained the highest FRAP activity value of 170.353%, which means that when the FRAP reagent was reacted with peanut shell extract it had a very strong antioxidant activity compared to date seed extract in F1 of 130.370%. Then when the extracts started to be mixed as in F2 – F6, the one with the highest FRAP activity value was F6 where date palm seeds were 40% and peanut shells were 60% which was 145.131%. This is directly proportional to the results of the activity of the peanut shell extract itself.

In this study, single extracts of date palm seeds and peanut shells had antioxidant activity. The ability as an antioxidant of these two plant extracts can still be improved, one way is by combining the extracts between the two. This is known as the synergistic effect. The synergism effect is the effect of two or more combinations of different types of antioxidants that have a greater effect than the effect of the individual antioxidants separately (Septiana *et al.*, 2020). Apart from producing a synergistic effect, the combination of extracts can also produce additive or antagonistic effects. In this study, the combination of date seed extract with peanut shell extract produced a synergistic effect with a % difference value of 78.575. The percentage value of this difference is used to determine antioxidant potential, namely having a synergistic effect if the value is positive (% difference > 0) or antagonistic if the value is negative (% difference <0).

Conclusions

Based on the results of quantitative tests using the FRAP method, samples of date seed extract have antioxidant activity with % FRAP activity of 130.370%. Then, based on the results of quantitative tests using the FRAP method, samples of peanut shell extract have antioxidant activity with % FRAP activity of 170.353%. The results obtained from the combination of date seed extract and peanut shell extract have a synergistic effect on increasing antioxidant activity with a % difference value of 78.575 because the % difference result is > 1.

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