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PHYSICAL AND *IN VIVO* ANTI HYPERTENSIVE ACTIVITY OF RED SPINACH (*Amaranthus cruentus)* FOAM MAT DRYING

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Abstrak

Selama lima tahun terakhir, hipertensi di Indonesia mengalami peningkatan. Penggunaan nutraseutikal seperti bayam merah (BM), yang kaya akan antosianin, dapat membantu menurunkan tekanan darah. Penelitian ini bertujuan mengevaluasi sifat fisik dan aktivitas antihipertensi dari produk foam mat drying (FMD) BM secara in vivo. Produk FMD BM dibuat dengan mencampurkan 100 g BM dengan 100 ml air, ditambahkan 6% Tween 80 dan 15% maltodekstrin, kemudian dikeringkan dalam oven pada suhu 45°C. Granul yang dihasilkan diayak menggunakan ayakan 60 mesh, lalu diuji kualitas fisik dan aktivitas in vivo menggunakan tikus Wistar yang diberi larutan NaCl 2% selama 14 hari untuk memodelkan hipertensi. Tikus dibagi menjadi beberapa kelompok: kontrol positif (KP; Captopril 5 mg), kontrol negatif (KN; 1% CMC Sodium), dan tiga kelompok perlakuan (C1-C3) yang diberikan FMDBM dosis 0,5%, 1%, dan 1,5%. Data kualitatif dianalisis secara deskriptif dan data kuantitatif dianalisis menggunakan ANOVA. Granul FMDBM menunjukkan parameter fisik yang baik, termasuk laju aliran, sudut diam, pH, dan kelarutan. Dalam uji aktivitas antihipertensi, C3 menunjukkan penurunan tekanan darah tertinggi (37,31±1,12%) namun masih berbeda signifikan dari KP (41,79±2,75%). Hasil ini berkorelasi dengan kandungan antosianin dalam FMDBM, menunjukkan bahwa FMDBM dapat menjadi produk nutraseutikal yang efektif dan terbukti secara saintifik.

Kata kunci: *bayam merah, foam mat drying, antihipertensi, nutrasetikal*

Abstract

Over the past five years, hypertension in Indonesia has increased. The use of nutraceuticals such as red spinach (BM), which is rich in anthocyanins, can help lower blood pressure. This study aims to evaluate the physical properties and antihypertensive activity of BM foam mat drying (FMD) products in vivo. FMD BM products were prepared by mixing 100 g of BM with 100 ml of water, adding 6% Tween 80 and 15% maltodextrin, then dried in an oven at 45°C. The resulting granules were sieved using a 60 mesh sieve, then tested for physical quality and in vivo activity using Wistar rats fed 2% NaCl solution for 14 days to model hypertension. The rats were divided into several groups: positive control (KP; Captopril 5 mg), negative control (KN; 1% CMC Sodium), and three treatment groups (C1-C3) given FMDBM doses of 0.5%, 1%, and 1.5%. Qualitative data were analyzed descriptively and quantitative data were analyzed using ANOVA. The FMDBM granules showed good physical parameters, including flow rate, angle of repose, pH, and solubility. In the antihypertensive activity test, C3 showed the highest blood pressure reduction (37.31±1.12%) but was still significantly different from KP (41.79±2.75%). These results correlated with the anthocyanin content in FMDBM, suggesting that FMDBM could be an effective and scientifically proven nutraceutical product.

Keywords: *red spinach; foam mat drying; anti-hypertensive; nutraceutical*

1. INTRODUCTION

According to data from Riskesdas (2018), 34.1% of people in Indonesia aged 18 and more had high blood pressure. This means that there are an estimated 63,309,620 people with high blood pressure in Indonesia (Riskesdas, 2018). The current data on deaths due to hypertension has reached 427,218, with the majority of hypertension patients undetected (Tumundo

et al., 2021). As many as 32.3–49.5% of patients diagnosed with hypertension do not regularly take medication, and 44% of patients are unaware that they have been diagnosed with hypertension (Mura & Hilmi, 2023). It is necessary to increase public awareness and patient compliance in the prevention and treatment of hypertension, particularly among adult and elderly patients (Alkhusari et al., 2023). This can be pursued by using functional beverages or foods in the form of nutraceuticals.

The majority of nutraceuticals currently circulating are imported products (Indonesia Halal Lifestyle Center, 2021). This affects the price of nutraceuticals, making them more expensive compared to herbal medicine. It is crucial to develop natural ingredient products into affordable and contemporary beverages. One of the strategies to increase the use of Indonesian natural ingredients in modern products is through the sanctification and modification of natural ingredients into nutraceutical products (Siswanto, 2012). Red spinach serves as a natural resource for utilization. This plant can be found in various places in Indonesia at a relatively low price (Rangkuti et al., 2017).

Research has shown that red spinach (RS) ethanol extract has antioxidant activity (Pratiwi, 2019). Red spinach extract has the potential to lower blood pressure and blood sugar levels in test animals by 47% induced by cigarette smoke (Suryanita et al., 2022). Red spinach ethanol extract contains anthocyanin, which are color pigments that are unstable to light, air, and high temperatures (Nasrullah et al., 2021).

One of the efforts to preserve the anthocyanin color pigment is through the formation of foam mat drying (FMD). The FMD results of red spinach proved to have an antioxidant capacity of 63% (Arifin et al., 2024). The color of the sample did not show significant difference between FMD and lyophilization (Indah et al., 2020). The FMD process is more efficient compared to the extraction process, which is time-consuming, costly, generates waste that is difficult to process when using ethanol solvent, has a low yield, and results in higher product selling prices (Kurniasari et al., 2019) Previous research has shown that foam mat drying produces granules with excellent color (Asiah et al., 2012).

Research on the in vivo antihypertensive effectiveness of foam mat drying red spinach granules is required based on the description above in order to generate scientifically validated nutraceutical granules for supplementary therapy. This research intends to assess the physical characteristics and antihypertensive effects of BM foam mat drying (FMD) products through in vivo experiments.

2. RESEARCH METHOD

The tools used in this research are an oven (Memmert), blender (Philips), mixer (Miyako), moisture content, CODA non-invasive blood pressure (Kent-Scientific), oral syringe, blunt 5 ml, and glassware (Pyrex), pH meter (Hanna), and analytical balance (OHAUS).

The materials used in this study are red spinach plants obtained from spinach farms in Sumowono, Bandungan, Central Java. Other materials used (technical grade) include Tween 80, maltodextrin, and distilled water. The modeling material for the test animals is NaCl (2% in an aqueous solvent).

Determination of red spinach plants: The morphological state of the plant was matched with identification keys found in literature to be sure of the species of the simplicia used in this research. The organism was recognized from its physical form (morphology) and visible traits. Plant determination was carried out at STIFAR Semarang.

Production of Red Spinach (RS) foam mat drying (FMD): The RS leaves were picked, washed, and left to dry to remove the water. The RS leaves were mixed with water in a 1:1 ratio (100 g of red spinach to 100 ml of water) and then blended for 2 minutes. The blended red spinach leaves were taken and mixed with a foaming agent of Tween 80 (6%), and stirred for 8 minutes. Then, 15% maltodextrin was added to the mixture and stirred for 3 minutes. The red spinach mixture was placed in a baking tray lined with 1 mm thick aluminum foil and dried using an oven at 45°C for 60 minutes.

Weight data were taken every 30 minutes until it stabilized (Kurniasari et al., 2020).

Quality control of RS FMD:

a. Organoleptic Test (Lachman et al., 1994): Visual inspection of the product's color, shape, taste, and smell conducts organoleptic tests.
b. Loss on Drying (LOD) Test (Ministry of Health Indonesia, 1995): The testing was conducted using 2 g of granules with a moisture content analyzer. The LOD of the granules is considered acceptable if it is less than 10%.
c. Flow rate and angle of repose test (Zats et al, 1996): As much as 10 grams of granules are placed into a fixed cylinder with a support until full. The bottom cover is opened, and the time for the granules to flow and the cone to form is measured. The angle of repose (α) is calculated based on tan α, which is the ratio of the height of the cone (cm) to the radius of the cone (cm). The value of the granule diameter angle ranges from 25° to 45° and meets the requirements for excellent flow properties. A good granule flow time is less than 10 seconds.
d. pH test: The pH test was conducted by Voight et al. (1984). As much as 5 grams (1 sachet) of the product is dissolved in 250 mL of water. The solution is tested for pH using a pH meter. The recommended pH is 5-7.
e. Solubility time test (Puspitasari and Suharsanti, 2022): As much as 5 grams (1 sachet of the product) is dissolved in 250 mL of water and stirred until completely dissolved with no sediment. The dissolution time is counted from the moment the product is poured into the water until the granules are completely dissolved and there are no residues.

In vivo activity test of FMD nutraceutical from red spinach (Windriyati et al., 2019): This test has obtained ethical clearance from the Health Polytechnic of the Ministry of Health, Number 1358/EA/F.XXIII.38/2024. The test animals used in this study were 8 Wistar strain rats per group and given with 2% NaCl solution for 14 days (except for normal control). The rats were divided into:

a. Positive Control (PC): Test animals given captopril
b. Negative Control (NC): Test animals induced with a 2% NaCl solution for 14 days
c. K1: Test given 0.5% of RS FMD
d. K2: Test animals given 1% of RS FMD
e. K3: Test animals given 1.5% RS FMD

The test began with the determination of the dose based on the rat-to-human conversion factor. Blood pressure measurements were taken before, 24 hours after, and 72 hours after the test animals were induced. Blood pressure measurements were conducted 14 days after NaCl solution induction and 14 days after the administration of the RS FMD. All blood pressure measurements were conducted using the CODA instrument. The decrease in blood pressure was calculated for each rat and the average for each group.

Data Analysis: Qualitative and quantitative data were descriptively analyzed in the organoleptic test. The data from the in vivo experiments were analyzed using one-way ANOVA.

3. RESULT AND DISCUSSION

The result of plant determination according to identification number 026/EL-AFM/II/2023 sated that the plant used in this research was included in species of *Amarantus cruentus* with genus of Amaranthus. Figure 1 displays the physical appearance of the RSFMD.

The yield of the RSFMD was 92.43%. The FMD powder for red spinach is dark red with a characteristic spinach aroma. Compared to the extraction method that showed a reduction, the FMD process showed less reduction in yield obtained. This is related to the foaming process, where a foaming agent must be added to the red spinach powder. The evaporation method of extraction affects the yield of the extract because the solvent used is lost (Ibrahim et al., 2024; Rosyidah et al., 2022). The color of the RSFMD remained dark red which might show less oxidation due to the low temperature process (Akman et al., 2024). Compared to lyophillization from the previous research, the yield was 1.05% with the color were dark red and easily oxidized within 24 hours. The lyophillization process

needed special equipment and took a long process which resulted a yield below 20%.

Figure 1. The result of RSFMD

Table 1. The result of physical parameter test of RSFMD

Parameter*	FMD
pH	4,33 ± 0,55
Moisture Content (%)	1,22 ± 0,05
Granules flowability (seconds)	5,33 ± 0,12
Granules Solubility (seconds)	5,15 ± 0,11
Antioxidant Activity (% Inhibition)	75,81 ± 1,12

The results of the moisture content test meet the moisture content requirements for instant powdered drinks, which is a maximum of 3% (Nisfiyah et al., 2015). The results of the moisture content test obtained were less than 2%, thus meeting the moisture content requirement for powdered beverages, as explained in Indonesian National Standard, which has maximum moisture content in the range of 3.0–5.0% (Standar Nasional Indonesia, 2019). This is due to the heating process at a temperature of 45°C for 1.5 hours, which still considers the compounds present in FMD using low-temperature methods. The results align with previous FMD research, indicating that the final product should satisfy SNI requirements (Bustaman et al., 2022).

The results of the flow time test on FI, FII, and FIII meet the requirements. The flow rate of the granules is expressed in grams per second, so a good flow time test is between 4 and 10 seconds, whereas the results obtained for FI, FII, and FIII have an average of 6 seconds, which means they fall within the acceptable range. Maltodextrin's ability to absorb moisture quickly influences the solubility time (Eris et al., 2023).

The results of the solubility time test meet the requirements; the requirement for the natural drinking powder is 10 minutes. The solubility might be affected by the hydrophobic compound in the red spinach, which takes time to dissolve in water (Wiyono et al., 2024). The presence of Tween 80 may also affect the solubility. This occurs as a result of the hydrophilic nature of Tween 80. Because Tween 80 has a free hydroxyl group from oxyethylene, the bonding between it and water gets stronger as more Tween 80 is added (Risse & Drusch, 2024). Tween 80 has an HLB value of 15, which indicates that it has the potential to act as a foam-forming agent and has a likelihood of dissolving in water (Darmawati, 2019).

The pH test results obtained have an average pH of 4-5. The pH of red spinach requires an acidic pH to maintain the stability of anthocyanins as the active compound used (Khasanah et al., 2014).

The test results for antihypertensive drugs showed that C3 had the highest percentage of blood pressure reduction. This was significantly different from C1 and C2, and the CMC Na group. C1 and C2 only showed a significant difference compared to F3, captopril, and CMC Na. Captopril showed the highest decrease in blood pressure and significantly different to all groups. C3 might contain the highest anthocyanin so it gave the highest blood pressure reduction (Sun et al., 2020).

Based on the previous research, it was shown that the FMD of red spinach contains phenols and flavonoids (Luditasari et al., 2019). A qualitative study revealed that the FMD of red spinach has anthocyanin levels ranging from 10.45 to 0.15 per 100 grams (Arifin et al., 2024). This chemical reduces blood pressure by inhibiting angiotensin-converting enzyme, close to the mechanism of captopril.

Anthocyanins can maintain the flexibility of blood vessels, thereby preventing them from becoming rigid and preventing an increase in high blood pressure (Watson et al., 2015). Research has

shown that anthocyanins lower blood pressure and arterial stiffness, likely due to their ability to increase nitric oxide (NO) production (Horie et al., 2019). NO synthase inhibitors negate the impact of anthocyanins on endothelium-dependent vasodilation in both humans and rats (Aboonabi et al., 2015). Previous research demonstrated that the degree of vascular relaxation following blackcurrant supplementation, rich in anthocyanins, was associated with the overall quantity and concentration of anthocyanins rather than their antioxidant efficacy (Tabart et al., 2018). Anthocyanins improve endothelial function by suppressing the expression of endothelin-1 (Johnson et al., 2015).

The endothelial protective effects of ACYs are associated with their antioxidant activity. Researchers have already found that RSFMD can act as an antioxidant, as shown by the DPPH test with an IC50 value of 35.67 ± 1.87 (Arifin et al., 2024).

Table 2. In Vivo Antihypertensive Result of RSFMD

Treatment	Before induction		After 14 days of induction		After 14 days of treatment		Percentage of blood pressure reduction	
	Sistol	Diastol	Sistol	Diastol	Sistol	Diastol	Sistol	Diastol
C1	109.00 ± 2.92	81.60 ± 3.05	177.40 ± 3.21	141.00 ± 2.65	141.20 ± 2.59	123.80 ± 3.03	20.40 ± 1.48^{b,c,d}	12.15 ± 3.55^{b,c,d}
C2	110.00 ± 1.58	81.00 ± 2.92	178.40 ± 5.18	145.80 ± 4.49	135.00 ± 4.12	116.00 ± 5.87	24.25 ± 3.76^{b,c,d}	20.32 ± 5.82^{b,c,d}
C3	110.20 ± 2.86	82.60 ± 3.44	180.00 ± 2.92	140.00 ± 3.81	125.40 ± 3.58	87.80 ± 3.77	30.30 ± 3.02^{a,c,d}	37.31 ± 1.12^{a,c,d}
PC	108.60 ± 3.13	83.40 ± 3.36	183.00 ± 7.07	144.20 ± 9.15	111.20 ± 4.49	83.80 ± 3.83	39.17 ± 3.19^{a,b,d}	41.79 ± 2.75^{a,b,d}
NC	111.40 ± 2.61	82.60 ± 4.56	184.20 ± 4.82	147.80 ± 4.87	180.40 ± 6.53	140.20 ± 4.56	2.05 ± 1.42^{a,b,c}	5.11 ± 2.50^{a,b,c}

a=significantly different from F1& F2
b= significantly different from F3
c=significantly different from PC
d=significantly different from NC

4. CONCLUSION AND SUGGESTION

All RSFMD nutraceutical formulas meet the requirements as granules. RSFMD at a concentration of 1.5% has antihypertensive activity in vivo. It is suggested that FMDBM might be a viable and scientifically validated nutraceutical product.

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