**Sargassum polycystum** juice alleviates the syndrome on the type 2 diabetic rats

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**Abstract.** Weight loss, polyphagia, polyuria, and polydipsia appear frequently on type 2 diabetics. This syndrome can be corrected by hypoglycemic agents where it can source from synthetic and natural compounds. *Sargassum polycystum* contains many bioactive compounds that contribute probably to improve this syndrome. Juicing is one of techniques to separate quickly and easily the bioactive solution from their matrices. This study aimed to evaluate *S. polycystum* juice for the improvement of type 2 diabetic rat syndrome. This study was conducted at the Pharmacology Laboratory, Faculty of Medicine, Universitas Brawijaya. There were seven groups in this study: negative control, negative control + 1 mL juice, diabetes control, diabetes + drug, diabetic rats + 0.5 mL juice, diabetic rats + 1 mL juice, and diabetic rats + 1.5 mL juice. This study used metformin as an oral hypoglycemic drug. Observations of changes in blood glucose and improvement of diabetes syndrome were carried out at the end of the study. The diabetic rats showed hyperglycemia and diabetes syndrome, while administration of *S. polycystum* juice in diabetic rats improved blood sugar levels and diabetes syndrome, but these results were not as optimal as oral hypoglycemic drugs. This study concluded that administration of *S. polycystum* juice could reduce hyperglycemia and improve diabetes syndrome in type 2 diabetic rats.

1. **Introduction**

Polyphagia, polydipsia, polyuria, and decreasing body weight are syndromes that appears in diabetics. Diabetes mellitus is a metabolic disorder characterized by hyperglycemia. Hyperglycemia in people with type 2 diabetes mellitus occurs as a result of insulin resistance. Insulin levels in people with DM 2 are enough, but the number of receptors on the cells has decreased. It makes it difficult for glucose to enter the cell until the cells lack glucose deficiency and, ultimately, hyperglycemia [1][1].

*Sargassum polycystum* is a brown seaweed that is known to contain several bioactive compounds. The bioactive it contains have blood-glucose-lowering activity [2][3][2-4], especially in improving glucose homeostasis [5].

Juicing is one of techniques to obtain the bioactive solution. Juice is a liquid obtained by separating ingredients from matrices plant by pressing. [6]. This study proposed to evaluate the *S. polycystum* juice in improving diabetes syndromes in type 2 diabetic rats.

2. **Methodology**

Glucometer from GlucoDr. AGM-2100) was used to measure blood glucose. *S. polycystum* was obtained from the island of Talango, Sumenep district, Madura. Normal male *Rattus norvegicus* 2-3
months old was induced into a type 2 diabetes model after being treated with a high-fat diet and then injected with streptozotocin. Thirty-five rats weighing about 200 g that were acclimatized and modelled into type 2 diabetes were given food and drink ad libitum. This research group, namely: (1) negative control, (2) negative control + 1 mL juice, (3) DM2, (4) DM2 + metformin, (5) DM 2 + 0.5 mL juice, (6) DM2 + 1 mL juice, and (7) DM2 + 1.5 mL juice. Blood glucose and diabetes syndrome in each group were performed at the end of the study [7]. The data obtained between groups were analyzed for diversity with one-way analysis, where the confidence interval used was 5%.

3. Result and discussion

3.1. Blood glucose
Changes in blood glucose content between treatments were carried out to determine whether there was an improvement in blood glucose levels due to treatment. Table 1 shows the difference in blood glucose levels of experimental animals due to treatment.

Table 1 blood glucose and diabetic syndromes on control and type 2 diabetic rats administered with S. polycystum juice

| Groups                     | Blood glucose (mg dl⁻²) | Body weight (g) | Polyuria (mL) | Polyphagia (g) | Polydipsia (mL) |
|----------------------------|-------------------------|-----------------|---------------|---------------|----------------|
| (-) control                | 122.6±3.65ᵃ             | 213.1±3.29ᶠ     | 11.3±0.45ᵃ    | 11.4±0.42ᵃ    | 13.3±0.45ᵃ     |
| (-) control + 1.0 mL juice | 118.8±2.59ᵃ             | 210.9±7.07ᶠᵉ    | 11.7±0.35ᵃ    | 10.7±0.45ᵃ    | 12.3±0.45ᵃ     |
| DM                        | 341.8±4.60ᶠ             | 174.7±5.9ᵃ      | 32.2±1.15ᶠ    | 22.3±0.42ᶠ    | 46.8±0.84ᶠ     |
| DM + metformin             | 142.2±2.77ᵇ             | 203.6±5.7ᵈᵉ     | 18.3±0.45ᵇ    | 12.6±0.42ᵇ    | 19.1±1.20ᵇ     |
| DM + 0.5 mL juice         | 289.0±7.58ᵉ             | 184.7±3.03ᵇ     | 29.6±0.89ᶜ    | 18.3±0.74ᶜ    | 41.2±0.79ᶜ     |
| DM + 1.0 mL juice         | 204.0±5.24ᵈ             | 192.8±3.27ᶜ     | 24.0±0.79ᵈ    | 15.8±0.45ᵈ    | 33.5±1.15ᵈ     |
| DM + 1.5 mL juice         | 173.2±3.77ᶜ             | 198.9±5.34ᵉᵈ    | 21.4±0.42ᵉ    | 13.6±0.41ᵉ    | 22.6±0.89ᵉ     |

* Superscript shows the difference between the treatments.

Table 1 shows that the glucose levels of groups A and B were not significantly different. The administration of S. polycystum juice in group B did not decrease blood glucose levels. Previous studies showed the same results [8]. It is possible because the dose is still below the dose of bioactivity [7].

Blood glucose levels on C were higher than on D (table 1). Metformin can lower blood sugar levels because this compound can increase glucose uptake by muscles and suppress glucokinase from producing hepatic glucose. Metformin is a biguanide compound that acts as a hypoglycemic agent by suppressing hepatic glucose production, increasing glucose uptake, and increasing glucose utilization by peripheral tissues [9].

Glucose levels at C were higher than those in F and G groups, while at E, it was no different (Table 1). It shows that the bioactive contained in the juice and its dosage can lower blood glucose levels. This bioactive in seaweed can inhibit the absorption of blood sugar in the small intestine and increase the uptake of glucose in the blood circulation. Previous studies have shown that polyphenols as bioactive can significantly reduce blood glucose levels of both mechanisms [5,10].

3.2. Body weight
Drastic weight loss is one of the markers of diabetes mellitus syndrome. The incidence of glycolysis may be high in the cells of the body of people with diabetes. Table 1 shows changes in body weight between the normal and the treatment groups administered with S. polycystum juice.

Body weights at A and B were not significantly different (Table 1). Normal rats about 2.5 months old weigh between 200 and 250 g [3]. This study showed that administration of S. polycystum juice did not affect weight gain. It is possible that the level of administration has not had an impact on metabolic
changes [7]. The presence of bioactive in Sargassum sp. in low doses does not affect the metabolism of nutrients so that it does not show any weight loss in experimental animals; even the administration of S. echinocarpum—methanol extract at a dose of 625 mg/kg BW has not given metabolic changes in test animals [7,11].

Group C was lighter than A (Table 1). It is possible because type 2 diabetes cannot use blood glucose as energy; therefore, it is done by utilizing other energy sources such as fat and protein to fulfil their energy. In order to fulfil ATP, fat from fat tissue hydrolyzed through beta-oxidation. This condition causes the body to lose weight. Previous studies have shown that rats with type 2 diabetes experience weight loss due to insulin resistance and do not enter the cells so that the use of glucose as an energy source in the body does not occur and eventually decreases [10].

Group D experienced weight gain as a result of metformin administration (Table 1). Metformin is a drug used for people with type 2 diabetes, and its use can lower blood sugar and loss weight [9].

Table 1 shows that the bodyweight of group C rats was lower than groups E, F, and G. Increasing the dose of Sargassum sp. body weight increased the body weight. The presence of polyphenols is thought to contribute to the increase in body weight of DM rats. Previous studies have shown that polyphenols can increase body weight because this bioactive can prevent the synthesis of new glucose and increase glucose uptake by body cells [7,8,11].

3.3. Polyuria
Diabetics will experience an increase in the frequency and volume of urine. During diabetes, the body experiences increased glycolysis, resulting in excess water production. Table 1 shows the profile of polyuria in normal and diabetic mice treated with S. polycystum juice. The urine volume in groups A and B was not significantly different (Table 1). It shows that the administration of S. polycystum juice does not provide a diuretic effect in normal individuals. A substance capable of increasing the rate of solution absorption and inhibiting the reabsorption of Na⁺ and Cl⁻, subsequently induces an increase in Na⁺ and water in the distal and proximal tubules and ultimately increases the volume of urine [11,12].

The urine volume of group C was higher than that of group A (Table 1). It indicated that group C had hyperglycemia and glucosuria, which increased osmotic pressure in the renal tubules and inhibited water reabsorption, causing polyuria. Very high urine volume in diabetics causes loss of various electrolytes, water, and glucose [11].

Urine volume decreased in group D because metformin decreased blood glucose levels (Table 1). This condition causes a decrease in cellular respiration to the production of H₂O. As a result, less urine is produced in the body [9].

The urine volume of group C was more than that of groups (E), (F), and (G) (Table 1). The presence of bioactive in the juice is thought to decrease blood glucose levels and urine volume production. Polyphenols can increase insulin sensitivity so that blood glucose entering cells increases. A decrease in the respiration process means a decrease in the production of H₂O so that the urine formed by the body is less volume [10,12].

3.4. Polyphagia
Polyphagia is an individual condition that becomes frequent and excessive to eat. Disturbances in carbohydrate metabolism cause these symptoms. The description of polyphagia in normal and diabetic rats treated with S. polycystum juice can be seen in table 1.

The level of consumption of groups A and B was not significantly different (table 1). The active substances in the juice show that it does not affect normal individuals. The bioactive levels contained in the juice may be still in doses that have not affected the physiological effects.

Table 1 shows that the level of consumption of group C is higher than that of group A. The body needs glucose intake during hyperglycemic times, but because there is no glucose in, it causes cells to lack energy. This condition causes excessive hunger, so this is correlated with increased food intake.
When hyperglycemic, the formation of blood glucose increases until the cells need an energy source [12]. Table 1 shows that the level of food consumption of D is close to normal. It is because metformin can increase glucose uptake so that the energy needs of cells can be met. Metformin can restore the ability of diabetic cells to absorb glucose results in the body's cells not experiencing a lack of energy.

The level of consumption of group C was higher than that of groups E, F, and G (Table 1). The bioactive and its dosage in juice can reduce the frequency of consumption. The polyphenols in the juice are due to their hypoglycemic activity. If glucose can enter the body and be converted into energy, then the energy needs in the cells will be fulfilled so that the stimulation of eating in the cells will be reduced [5].

3.5. Polydipsia
Diabetics also have a syndrome to drink with much frequency. It is the body's reaction to losing many fluids. Table 1 shows images of polydipsia in normal and diabetic mice treated with S. polycystum juice. Table 1 shows that the drinking volume of normal rats in groups A and B was not significantly different. The bioactive in S. polycystum juice did not show any hypoglycemic effect in the normal group. The consumption dose may be still below the dose that stimulates blood sugar intake [11].

The drinking volume of C was higher than that of A (Table 1). This condition indicates that DM rats have hyperglycemia. High blood sugar levels cause the body's osmotic pressure to change. The kidneys receive much water, which causes DM patients to urinate frequently. As a result, the body lacks water, become dehydrated and eventually increase the symptoms of thirst (polydipsia). Then the body feels thirsty and often wants to drink [5,11].

The use of metformin can reduce the drinking volume of DM rats (Table 1). It is possible because metformin can control blood glucose levels by increasing insulin sensitivity in cells and increasing the amount of glucose entering the body's cells [9].

The drinking volume of group C rats was more frequent than groups E, F, and G (Table 1). The presence of bioactive, especially phlorotannin in Sargassum juice, can lower blood glucose. This decrease results in the body not needing much water, so it does not become dehydrated; it correlates with a low drinking volume [11].

4. Conclusion
S. polycystum juice can reduce hyperglycemia and diabetes syndromes in the type 2 diabetic rats.

References
[1] American Diabetes Association 2015 Diab. Care 38 S1
[2] Muhamad F, Rahmi N, Asep A P 2015 Marine algae extracts: Processes, products, and applications (Wiley-VCH Verlag GmbH & Co. KGaA) p 381
[3] Muhamad F, Anies C 2018 Asian J. Pharm. Clin. Res. 11 337
[4] Nada I M, Muhamad F 2020 IOP Conference Series: Earth Envi. Sci. 493 (1), 012031
[5] Naheed A, Sara K S, Tahereh A 2017 Med. J. Islam Repub. Iran. 31 134
[6] Gilberto M, Francisco J B, Gustavo R V, Efigenia M, Gustavo A G, Emilio A, Sonia G. S 2015 J Food Func. 18 171
[7] Muhamad F 2021 IOP Conference Series: Earth Envi. Sci. 695 (1), 012050
[8] Priyanka M, Aparna K, Nancy P 2017 Biomed. Pharmacother. 90 268
[9] Meng X M, Ma X X, tian X L, Jiang Q, Wang L L, Shi R, Ding L, Pang S G 2017 Eur. Rev. Med. Pharm. Sci. 21 2232
[10] Narasimhanaidu K and Ponnaian S M P 2006 Basic Clin. Pharm Toxicol 98 97
[11] Muhamad F 2011 Disertasi Sekolah Pascasarjana Institut Pertanian Bogor
[12] Brian C, Jessie H, Kristina M, Mary G, ..., Michael M 2016 J. Nutr. Biochem. 31 150