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Porang (*Amorphophallus oncophyllus*) flour macerated with *Strobilanthes crispus* reduced the blood glucose levels of streptozotocin-induced diabetic rats

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Short title: Porang (*Amorphophallus oncophyllus*) with *Strobilanthes crispus* reduced blood glucose level

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Abstract

BACKGROUND: Diabetes mellitus (DM) is a group of metabolic diseases indicated by hyperglycemia. Dietary regulation represents a viable means of controlling blood glucose levels. Porang (*Amorphophallus oncophyllus*) is a local tuber that has a low glycemic index due to its high glucomannan content. In combination with *Strobilanthes crispus* (SC), which is rich in antioxidants, porang flour could be a promising treatment approach for DM.

OBJECTIVES: This study aimed to determine the effect of porang flour macerated with SC on the blood glucose levels of diabetic rats.

METHODS: Thirty-five Wistar (*Rattus norvegicus*) rats were divided into five groups on the basis of their diets: normal/negative control (NC) group (non-diabetic, standard AIN-93 diet), positive control (PC) group (streptozotocin [STZ]-induced diabetic), glibenclamide (GB) group (STZ-induced diabetic, medicated with GB 100 mg/200 g body weight [BW]), porang (NP) group (modified AIN-93 diet, fiber substituted with 11% porang flour [equal to 1.1 g/200 g BW]), and SC-macerated porang (SP) group (modified AIN-93 diet, fiber substituted with 11% porang flour macerated with SC [equal to 1.1 g/200 g BW]). The rats' food intakes, stools, and BWs were recorded throughout the study, while their blood glucose levels were measured before the induction of DM, three days after the induction of DM, and at the end of the study (14-day treatment period). The data were statistically analyzed using a one-way analysis of variance (ANOVA) combined with Duncan's multiple range test.

RESULTS: The rats' feed intakes during the 14-day treatment period were almost the same, which influenced their BWs. After the induction of DM, the rats' BWs appeared to decrease, albeit not to a statistically significant extent. This weight loss may have been better controlled in the treatment groups because the glucomannan content of the porang led to an improvement in the rats' glucose metabolism, especially in the NP and SP groups. The rats' stools appeared normal in consistency and moisture, and it was confirmed that there were no diarrhea incidents. The glucomannan content also decreased the blood glucose levels in the NP and SP groups. The SP group showed the best results in terms of decreased glucose levels due to the addition of SC as a source of antioxidants.

CONCLUSION: Porang exerted an antidiabetic effect that was comparable with the effect of glibenclamide (a commercial drug). In combination with SC, it provided a high level of antioxidants. Porang should be further studied to optimize its antidiabetic potency and potential for use as a functional food or nutraceutical.

Keywords: *Diabetes mellitus, blood glucose, Amorphophallus oncophyllus, Strobilanthes crispus, porang*

Introduction

Diabetes mellitus (DM) is a group of metabolic diseases associated with insulin function or secretion disorder and indicated by hyperglycemia (1,2). The negative impact of DM is known to result in comorbidities such as multiple secondary micro- and macro-vascular complications and neuropathic disorders (3). If DM is not taken seriously, it may lead to a significant decrease in quality of life as well as an increase in health-related costs.

In addition to the use of hypoglycemic drugs, dietary regulation represents a means by which patients can control their blood glucose levels. A diet that is rich in foods that have a low glycemic index can have a positive effect in terms of lowering blood glucose levels (4). Porang (*Amorphophallus oncophyllus*) is a kind of konjac tuber that is widely cultivated in Indonesia. It has a low glycemic index (5) due to its high glucomannan content. Various studies concerning the health effects (6,7) and applications of porang have been conducted (8–14), although the use of raw porang flour remains rare due to the limited availability of calcium-oxalate-free flour.

Porang flour macerated with *Strobilanthes crispus* (SC has previously been studied with regard to its safety (15) and low calcium oxalate content (16). The SC content of porang, which is rich in flavonoid and phenolic acid (17), has shown potential in relation to the treatment of DM. However, its potency has not yet been adequately studied. The aim of the present study was to determine the effect of porang flour macerated with SC on the blood glucose levels of diabetic rats.

Methods

Plant material

The porang tubers used in this study were obtained from a farmer in Madiun, East Java. The tubers were cleaned of sand, sliced, and dried. They were then ground and sifted through a 40-mesh sieve to make powder/flour. Next, the flour was macerated with SC, as described in Patent Application No. S00202006668 (16).

Experimental animals

The present study was conducted in accordance with the requirements of the Health Research Ethics Committee of Universitas Alma Ata (reference no. KE/AA/VI/273/EC/2017). Thirty-five Wistar (*Rattus norvegicus*) rats that were eight weeks of age and had body weights of 121–159 g were used in this study. The rats were divided into five groups on the basis of their diets. Each control group was fed with a standard AIN-93 diet (18): NC group (normal/negative control, non-diabetic), PC group (positive control, streptozotocin [STZ]-induced diabetic), and GB group (STZ-induced diabetic, medicated with glibenclamide 100 mg/200 g bodyweight [BW]). The two treatment groups were fed with a modified AIN-93 diet in which the fiber was substituted with 11% (equal to 1.1 g/200 g BW) porang (NP group) or SC-macerated porang (SP group). The rats were individually housed in wire cages at an ambient temperature with a 12 hour light-dark cycle. Their food intakes, stools, and BWs were recorded throughout the study, while their blood glucose levels were measured before the

induction of DM, three days after the induction of DM, and at the end of the study (14-day treatment period).

Induction of diabetes, blood preparation, and biochemical analysis

The intraperitoneal injection of nicotinamide (110 mg/kg BW) was performed prior to the induction of DM with 8 mg/200 g BW of STZ. The rats were categorized as diabetic when their blood glucose level was more than 126 mg/dL (1). The blood glucose levels were determined from plasma samples by means of the GOD-PAP (glucose oxidase–peroxidase aminoantypirin) enzymatic method. The plasma was prepared via the centrifugation of blood samples (at 400 rpm for 15 minutes) that had been drawn from the vena retro-orbital sinus using the microcapillary technique.

Statistical analysis

All data were presented as the mean ± standard deviation (SD). A one-way analysis of variance (ANOVA) combined with Duncan's multiple range test (DMRT) at $p < 0.05$ was used to compare the data among the groups. A paired T-test analysis was also used to compare the data from before and after the treatment. All the analyses were performed using Statistical Package for the Social Sciences (SPSS) software (version 16.0; SPSS Inc., Chicago, USA).

Results and Discussions

Feed intake, body weight of rat, and observation of stools

Feed intake of rats during 14 d of treatment periods could be seen in Table 1. The amount of intake was almost the same every day with the mean value recorded in the range of 6.18-9.59 g/dL. Among the groups, NC showed the lowest amount of feed intake and was statistically different from others ($p<0.05$). It may be due to NC rats' behavior that looked more active than other groups. It caused some feeds were fallen or be mixed in the drinking water, so that could not be weighed. The feed intake of NC was also statistically different with PC ($p<0.05$). It indicated that the inducement of diabetes influenced the feed intake or rat's appetite.

Feed intake relates to the body weight of rats. The body weight of rats during the study could be seen in Table 1. During 14 d of treatment, the bodyweight of rats seemed down, but not statistically different ($p>0.05$). This weight loss value increased after STZ induction that may be caused by insufficient insulin. It leads to an inability of glucose to be used as energy, therefore the availability in the body was provided by fat catabolism. If it was happened continuously can lose body weight (19,20,21). However, the body weight in treatment groups (GB, NP, and SP) could be controlled by increasing the insulin sensitivity resulting in the improvement of glucose metabolism (22) for GB groups or by the role of glucomannan as fiber in NP and SP groups that fulfilled the intestine and decrease the feed intake (6,23). It may also decrease postprandial glucose and improve insulin sensitivity (24,25). The previous study has also been studied for the potency of porang glucomannan as a prebiotic that increased short-chain fatty acid (SCFA) in the colon (6) leading to the improvement of glucose and lipid metabolism (23,26) and resulting in controlling of body weight (24).

The inability of body weight to increase in this study was also confirmed by the observation of stools that could be seen in Table 1, especially to know whether there was diarrhea or other disorder in gastrointestinal. The data showed that stools in all groups were in normal moisture and consistency. It meant that there was no diarrhea, instead there were also no difficulties in defecating process. The previous study proved that glucomannan absorbed much water and influenced the dry and wet stool weight, the defecation frequency, and colonic flora in stool (27). The porang consumption and its combination with SC did not affect the gastrointestinal response.

Table 1: Feed intake, body weight, and stool character of rats during 14 d of treatment periods

Groups	Feed intake (g)	Stools character		Body weight (g)		
		Water content (%)	Consistency	Before intervention	After intervention	Δ.K
NC	6.18±0.8[a]	39.40 ±2.2[a]	Slightly hard	133.2±7.3	130.4±13.0	-2.8[a]
PC	9.56±1.1[b]	76.20 ± 5.3 [a]	Soft	134.4±11.8	123.4±13.8	-11.0[a]
GB	9.59±1.9[b]	71.40 ± 3.0[a]	Soft	141.2±9.9	133.0±10.3	-8.2[a]
NP	9.64±0.6[b]	78.80 ± 5.1[a]	Soft	150.0±6.0	142.6±27.6	-7.4[a]
SP	8.84±1.8[b]	70.20 ± 2.8[a]	Soft	138.8±13.4	132.80±4.1	-6.0[a]

*Different superscript letter in the same columns indicated significantly different result ($p<0.05$). NC group (normal/negative control, non-diabetic, AIN-93 diets), PC group (positive control, streptozotocin (STZ)-induced diabetic, AIN-93 diets), GB group (STZ-induced diabetic, AIN-93 diets, medicated with glibenclamide), NP group (STZ-induced diabetic, AIN-93 modified diets with 11% porang flour), SP group (STZ-induced diabetic, AIN-93 modified diets with 11% SC-macerated porang flour).

Blood glucose levels

Table 2 showed that the initial blood glucose levels were in the range of 50-135 mg/dL. It meant that all intervention groups were normal. The measurement of initial blood glucose levels of rats aimed to ensure that the rats were in normal condition. After being induced with STZ, blood glucose levels in diabetic groups increased in the range value between 217-244 mg/dL. The rats with blood glucose levels more than 126 mg/dL were included in diabetic groups (1). STZ induced diabetes by damaging β-cells through the production of radicals NO that may block the Fe-containing enzymes and the breakdown of secondary radicals caused peroxide of lipids, reduced antioxidant, and led to DNA damage (28, 29).

The intervention of commercial drug (GB group) and porang flour (NP and SP) significantly decreased blood glucose levels ($p<0.05$), although they were still above 126 mg/dL, especially for NP and SP (Table 2). GB worked by stimulating the insulin secretion in the pancreas gland through sensitizing of β-cells allowing glucose-induced changes in the synthesis and release of insulin (22). NP and SP worked as the fiber that has high water absorption and is very viscous (6) that may decrease food absorption in the small intestine and decrease postprandial glucose and insulin secretion leads to the improvement of insulin sensitivity (24,25). This was also confirmed by the histopathological study of the pancreas that showed the maintaining of pancreatic structure in diabetic rats treated by konjac glucomannan (24).

This study also presented that SP groups had a similar antihyperglycemic ability with GB. The role of fiber in porang was strengthened by the existence of SC. SC is the source of flavonoids and phenolic acids that possessed antidiabetic activity in diabetic rats (17). SC was also useful in decreasing calcium oxalate in porang and had no acute toxicity result (15) which allows its use as a functional food.

Table 2: Blood glucose levels of rats in various treatment during 14 days of treatment

Groups	Blood glucose levels (mg/dL)			
	Before STZ induction	After STZ induction	After intervention	ΔK
NC	69.6 ± 0.9[b]	67.17±1.4	67.4±2.0	0.67[a]
PC	66.7 ± 1.1[a]	244.4±7.4	215.7±6.1	1.26[a]
GB	70.4 ± 2.2[b]	217.40±7.8	121.8±5.3	-96.0[b]
NP	68.3±1.1[ab]	217.4±9.2	156.8±4.3	-62.9[c]
SP	68.7±1.9[ab]	224.5±7.3	133.2±1.9	-91.3[b]

* Different superscript letter in the same coloumn indicated significantly different result ($p<0.05$). ΔK showed the different value between 0 d and 14 d using T-test. NC group (normal/negative control, non-diabetic, AIN-93 diets), PC group (positive control, streptozotocin (STZ)-induced diabetic, AIN-93 diets), GB group (STZ-induced diabetic, AIN-93 diets, medicated with glibenclamide), NP group (STZ-induced diabetic, AIN-93 modified diets with 11% porang flour), SP group (STZ-induced diabetic, AIN-93 modified diets with 11% SC-macerated porang flour).

Conclusions

This study concluded that porang had antidiabetic capacity. This capacity was forced by the presence of SC and proved the comparable result with the glibenclamide as a commercial drug. Further study is needed in the optimalization of doses to improve the antidiabetic capacity and probability uses as functional food or nutraceuticals.

Acknowledgements

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RESULTS: The rats' feed intakes during the 14-day treatment period were almost the same, which influenced their BWs. After the induction of DM, the rats' BWs appeared to decrease, albeit not to a statistically significant extent. This weight loss may have been better controlled in the treatment groups because the glucomannan content of the porang led to an improvement in the rats' glucose metabolism, especially in the NP and SP groups. The rats' stools appeared normal in consistency and moisture, and it was confirmed that there were no diarrhea incidents. The glucomannan content also decreased the blood glucose levels in the NP and SP groups. The SP group showed the best results in terms of decreased glucose levels due to the addition of SC as a source of antioxidants.
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Introduction

Diabetes mellitus (DM) is a group of metabolic diseases associated with insulin function or secretion disorder and indicated by hyperglycemia (1,2). The negative impact of DM is known to result in comorbidities such as multiple secondary micro- and macro-vascular complications and neuropathic disorders (3). If DM is not taken seriously, it may lead to a significant decrease in quality of life as well as an increase in health-related costs.

In addition to the use of hypoglycemic drugs, dietary regulation represents a means by which patients can control their blood glucose levels. A diet that is rich in foods that have a low glycemic index can have a positive effect in terms of lowering blood glucose levels (4). Porang (*Amorphophallus oncophyllus*) is a kind of konjac tuber that is widely cultivated in Indonesia. It has a low glycemic index (5) due to its high glucomannan content. Various studies concerning the health effects (6,7) and applications of porang have been conducted (8–14), although the use of raw porang flour remains rare due to the limited availability of calcium-oxalate-free flour.

Porang flour macerated with *Strobilanthes crispus* (SC) has previously been studied with regard to its safety (15) and low calcium oxalate content (16). The SC content of porang, which is rich in flavonoid and phenolic acid (17), has shown potential in relation to the treatment of DM. However, its potency has not yet been adequately studied. The aim of the present study was to determine the effect of porang flour macerated with SC on the blood glucose levels of diabetic rats.

Methods

Plant material

~~Porang~~ The porang tubers used in this study were ~~was~~ obtained from ~~the~~ a farmer in Madiun, East Java. The tubers ~~was~~ were cleaned ~~from the~~of sand, sliced, and dried. ~~It was~~They were then ground and sifted through a ~~40~~ 40-mesh sieve to make powder/flour. ~~The~~ Next, the flour was macerated with SC, as described in Patent Application No. S00202006668 (16).

Commented [.2]: Was more than one tuber used in the study?

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Experimental animals

The present study was conducted in accordance with the requirements of the Health Research Ethics Committee of Universitas Alma Ata (reference no. KE/AA/VI/273/EC/2017). Thirty-five Wistar (*Rattus norvegicus*) rats that were eight weeks of age and had body weights of 121–159 g were used in this study. The rats were divided into five groups on the basis of their diets. Each control group was fed with a standard AIN-93 diet (18): NC group (normal/negative control, non-diabetic), PC group (positive control, streptozotocin [STZ]-induced diabetic), and GB group (STZ-induced diabetic, medicated with glibenclamide 100 mg/200 g bodyweight [BW]). The two treatment groups were fed with a modified AIN-93 diet in which the fiber was substituted with 11% (equal to 1.1 g/200 g BW) porang (NP group) or SC-macerated porang (SP group). The rats were individually housed in wire cages at an ambient temperature with a 12 hour light-dark cycle. Their food intakes, stools, and BWs were recorded throughout the study, while their blood glucose levels were measured before the

induction of DM, three days after the induction of DM, and at the end of the study (14-day treatment period).

Induction of diabetes, blood preparation, and biochemical analysis

The intraperitoneal injection of nicotinamide (110 mg/kg BW) was performed prior to the induction of DM with 8 mg/200 g BW of STZ. The rats were categorized as diabetic when their blood glucose level was more than 126 mg/dL (1). The blood glucose levels were determined from plasma samples by means of the GOD-PAP (glucose oxidase–peroxidase aminoantypirin) enzymatic method. The plasma was prepared via the centrifugation of blood samples (at 400 rpm for 15 minutes) that had been drawn from the vena retro-orbital sinus using the microcapillary technique.

Statistical analysis

All data were presented as the mean ± standard deviation (SD). A one-way analysis of variance (ANOVA) combined with Duncan's multiple range test (DMRT) at $p < 0.05$ was used to compare the data among the groups. A paired T-test analysis was also used to compare the data from before and after the treatment. All the analyses were performed using Statistical Package for the Social Sciences (SPSS) software (version 16.0; SPSS Inc., Chicago, USA).

Results and Discussions

Feed intake, body weight of rat, and observation of stools

Feed intake of rats during 14 d of treatment periods could be seen in Table 1. The amount of intake was almost the same every day with the mean value recorded in the range of 6.18-9.59 g/dL. Among the groups, NC showed the lowest amount of feed intake and was statistically different from others ($p<0.05$). It may be due to NC rats' behavior that looked more active than other groups. It caused some feeds were fallen or be mixed in the drinking water, so that could not be weighed. The feed intake of NC was also statistically different with PC ($p<0.05$). It indicated that the inducement of diabetes influenced the feed intake or rat's appetite.

Feed intake relates to the body weight of rats. The body weight of rats during the study could be seen in Table 1. During 14 d of treatment, the bodyweight of rats seemed down, but not statistically different ($p>0.05$). This weight loss value increased after STZ induction that may be caused by insufficient insulin. It leads to an inability of glucose to be used as energy, therefore the availability in the body was provided by fat catabolism. If it was happened continuously can lose body weight (19,20,21). However, the body weight in treatment groups (GB, NP, and SP) could be controlled by increasing the insulin sensitivity resulting in the improvement of glucose metabolism (22) for GB groups or by the role of glucomannan as fiber in NP and SP groups that fulfilled the intestine and decrease the feed intake (6,23). It may also decrease postprandial glucose and improve insulin sensitivity (24,25). The previous study has also been studied for the potency of porang glucomannan as a prebiotic that increased short-chain fatty acid (SCFA) in the colon (6) leading to the improvement of glucose and lipid metabolism (23,26) and resulting in controlling of body weight (24).

The inability of body weight to increase in this study was also confirmed by the observation of stools that could be seen in Table 1, especially to know whether there was diarrhea or other disorder in gastrointestinal. The data showed that stools in all groups were in normal moisture and consistency. It meant that there was no diarrhea, instead there were also no difficulties in defecating process. The previous study proved that glucomannan absorbed much water and influenced the dry and wet stool weight, the defecation frequency, and colonic flora in stool (27). The porang consumption and its combination with SC did not affect the gastrointestinal response.

Blood glucose levels

Table 2 showed that the initial blood glucose levels were in the range of 50-135 mg/dL. It meant that all intervention groups were normal. The measurement of initial blood glucose levels of rats

aimed to ensure that the rats were in normal condition. After being induced with STZ, blood glucose levels in diabetic groups increased in the range value between 217-244 mg/dL. The rats with blood glucose levels more than 126 mg/dL were included in diabetic groups (1). STZ induced diabetes by damaging β-cells through the production of radicals NO that may block the Fe-containing enzymes and the breakdown of secondary radicals caused peroxide of lipids, reduced antioxidant, and led to DNA damage (28, 29).

The intervention of commercial drug (GB group) and porang flour (NP and SP) significantly decreased blood glucose levels ($p<0.05$), although they were still above 126 mg/dL, especially for NP and SP (Table 2). GB worked by stimulating the insulin secretion in the pancreas gland through sensitizing of β-cells allowing glucose-induced changes in the synthesis and release of insulin (22). NP and SP worked as the fiber that has high water absorption and is very viscous (6) that may decrease food absorption in the small intestine and decrease postprandial glucose and insulin secretion leads to the improvement of insulin sensitivity (24,25). This was also confirmed by the histopathological study of the pancreas that showed the maintaining of pancreatic structure in diabetic rats treated by konjac glucomannan (24).

This study also presented that SP groups had a similar antihyperglycemic ability with GB. The role of fiber in porang was strengthened by the existence of SC. SC is the source of flavonoids and phenolic acids that possessed antidiabetic activity in diabetic rats (17). SC was also useful in decreasing calcium oxalate in porang and had no acute toxicity result (15) which allows its use as a functional food.

Conclusions

This study concluded that porang had antidiabetic capacity. This capacity was forced by the presence of SC and proved the comparable result with the glibenclamide as a commercial drug. Further study is needed in the optimalization of doses to improve the antidiabetic capacity and probability uses as functional food or nutraceuticals.

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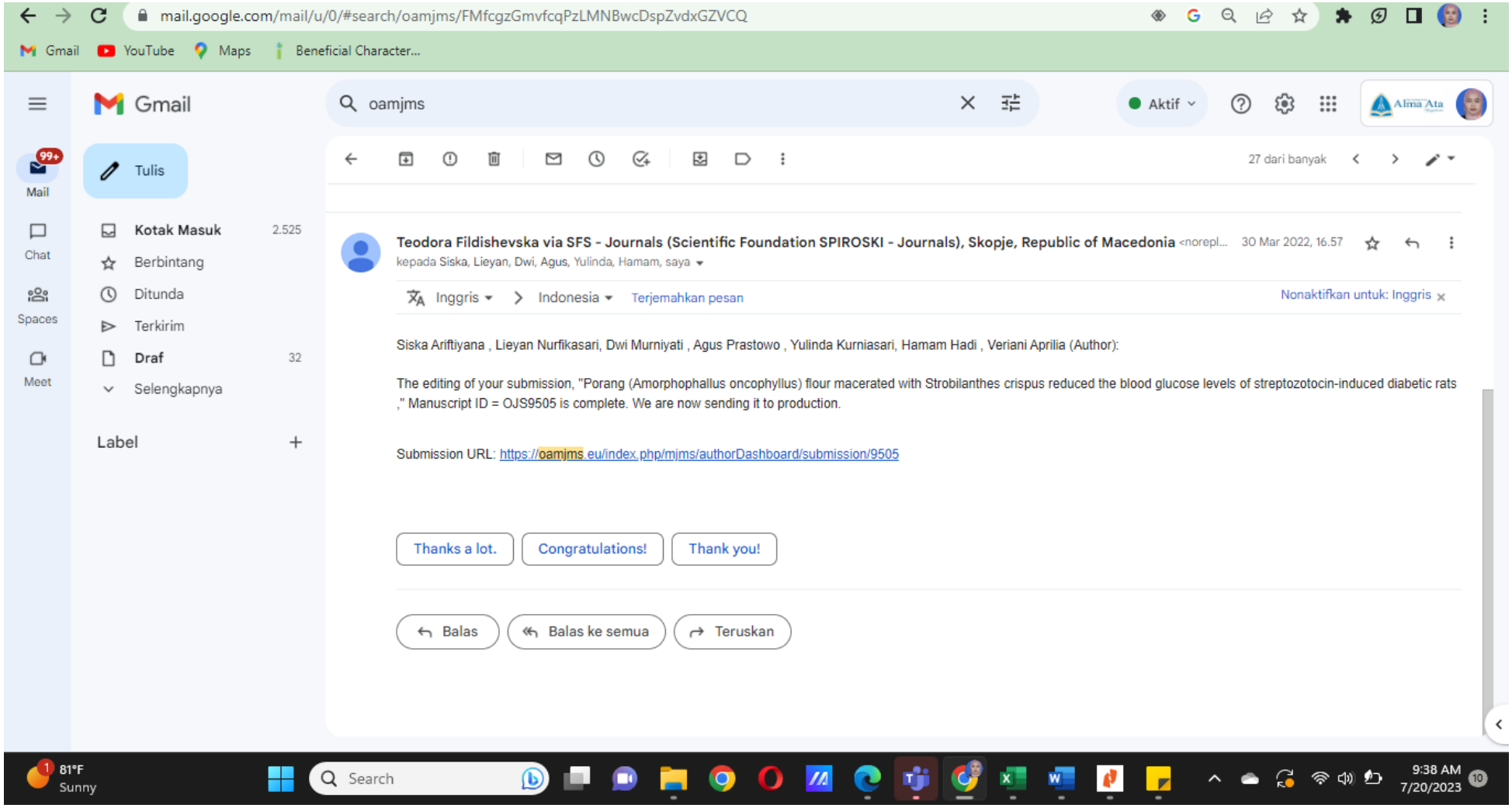

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