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Research Article

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The Effect of 15% Ocimum Basilicum L. on Lymphocyte Following Tooth Extractionin Diabetes Mellitus Wistar Rats

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Abstract

Background: *Diabetes mellitus (DM) is a condition of hyperglycemia caused by abnormalities in insulin secretion, insulin action, or both. The International Diabetes Federation (IDF) notes that the prevalence of DM in the age range 75 - 79 years was calculated at 19.9% in 2019 and is anticipated to increase to 20.4% and 20.5% in 2030 and 2045. Around 75% of DM patients suffering from periodontitis and patients with DM are known to have a higher prevalence of periodontal disease than those without DM. Hyperglycemia can trigger increased production of AGEs which can inhibit the wound healing process in diabetes. Ocimum basilicum L. contains phytochemical substances, especially flavonoids, steroids, alkaloids, tannins and saponins which play a role in reducing the number of lymphocyte cells and inhibiting the production of AGEs.*

Method: *This study used a true experimental laboratory with a posttest only control group design. Tooth extraction was performed on rats that had been induced by alloxan and given different treatments to each group. Each group received 15% Ocimum basilicum L. extract gel, CMC-Na gel, and hyaluronic acid gel. Histopathological preparations were then observed for the number of lymphocyte cells on days 1, 3, and 5.*

Results: *The average number of lymphocyte cells in the group given 15% Ocimum basilicum L.*

Conclusion: *15% Ocimum basilicum L. extract gel had an effect on reducing the number of lymphocyte cells on each day of observation when compared to the negative control group with the lowest mean number of lymphocyte cells in the treatment group on day 5 are 16.67 cells, this means that basil leaf extract gel 15% Ocimum basilicum L. extract gel has an effect in reducing the number of lymphocyte cells in the post-tooth extraction in inflammatory phase of wistar rats (Rattus norvegicus) with type 2 diabetes mellitus.*

Keywords: Ocimum Basilicum l., Diabetes Mellitus, Tooth Extraction, Lymphocyte Cell

Introduction

High blood sugar levels or hyperglycemia caused by abnormalities in insulin secretion, insulin action, or both are characteristic of the metabolic disease known as diabetes mellitus [1].

In Indonesia, the results of the 2013-2018 Basic Health Research stated that there were significant results in the prevalence of diabetes mellitus sufferers around 1.5% [4]. In 2019, the International Diabetes Federation (IDF) reported that the prevalence of diabetes was 9.65% in men and 9% in women [2].

IDF notes that the prevalence of diabetes mellitus in the age range 75 - 79 years was calculated at 19.9% in 2019 and is anticipated to increase to 20.4% and 20.5% in 2030 and 2045 [3].

Hyperglycemia or high blood sugar can trigger increased production of Advanced Glycation End Products (AGEs), which are non-enzymatic products of macromolecular glycation. Based on research made by (2018) people with diabetes mellitus are estimated to lose teeth at a higher rate than the general population [4]. This shows that there is a procedure for tooth extraction for diabetes mellitus sufferers. If the patient has type 2 diabetes mel-

litus, the gums may take longer to heal after tooth extraction and are more susceptible to infection because blood sugar levels are consistently above the normal range. Anti-inflammatory agents are needed to speed up the wound healing process [5].

One of the plants that has anti-inflammatory properties which has been proven to speed up wound healing is basil leaves. Basil leaves can be used as a wound medicine because this plant contains phytochemical substances, especially flavonoids, steroids, alkaloids, tannins and saponins [6, 7].

The anti-inflammatory activity of flavonoids is created by inhibiting cyclooxygenase and lipoxygenase, which in turn reduces the number of inflammatory cells that migrate to the wound area so that the inflammatory reaction tends to run quickly and the quality of proliferation through transforming growth factor β (TGF-β) is not hampered [37].

Based on research conducted by in a study with white mice, using a gel made from basil leaf extract was proven to speed up the healing process [8]. Gel extract treatment with a concentration of 15% was proven to be more effective than concentrations of 5% and 10% in this study. Wistar rats were used as experimental animals in this research because wistar rats have similar physiological systems to humans and can reproduce and have a fast response.

The various impacts of the elements of basil leaves made the author interested in understanding the effect of administering 15% basil leaf extract gel on the number of lymphocyte cells in the post-tooth extraction inflammatory phase of wistar rats (Rattus norvegicus) with type 2 diabetes mellitus [9].

Material and Method

The research design used is laboratory experimental research (true experimental laboratories). Posttest only control group design is used as a research design by making observations or measurements after treatment and the results will be compared with the control group. The type of sample used was 27 wistar rats which had been induced with alloxan monohydrate 150 mg/kg BW which were grouped into 3 groups, namely negative control (Kn) using CMC-Na, positive control (Kp) using hyaluronic acid 0.2%, and the treatment group (P) used 15% Ocimum basilicum L [10]. extract gel which was adjusted to the sample euthanasia period, on days 1, 3 and 5 after tooth extraction. Each sample of the wistar rat incisor tooth socket and the surrounding tissue and bone after extraction were taken, then a histological preparation was made for further study. The variable that will be observed for data collection is the development of histological wound healing by identifying the number of lymphocyte cells. Using a binocular microscope with 400x magnification, the number of lymphocyte cells was counted with the aim of identifying the healing center in the histological preparation and then the number of lymphocyte cells was counted.

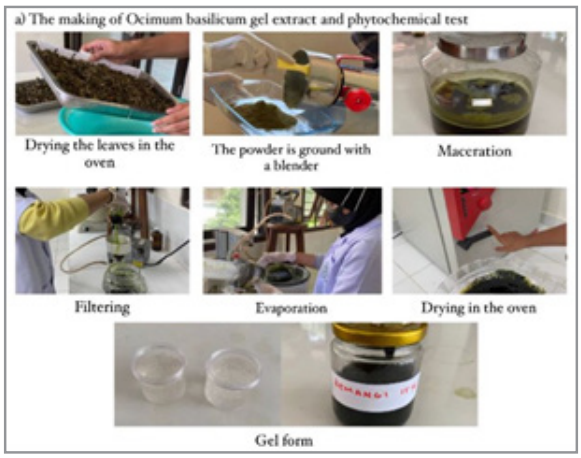

Figure 1: The Making of 15% Ocimum basilicum L. Extract Gel.

Figure 2: Treatment Process on Experimental Animals.

Result

Table 1: The Average Number of Lymphocyte Cells

Group	Observation	Mean	Deviation Standard	Number of Sample
Positive Control	1 day	50.00	5.000	3
	3 days	36.67	2.887	3
	5 days	25.00	5.000	3
Negative Control	1 day	83.33	16.073	3
	3 days	116.67	7.638	3
	5 days	121.67	12.583	3
Treatment	1 day	38.33	7.638	3
	3 days	21.67	7.638	3
	5 days	16.67	2.887	3

Based on the results of this study, the mean number of lymphocyte cells in the positive control group on days 1, 3 and 5 was 50.00 ± 5,000; 36.67±2.887; and 25.00±5,000 cells. The mean result of the number of lymphocytes in the negative control group on days 1, 3 and 5 was 83.33 ± 16,073; 116.67±7.638; and 121.67±12,583 cells. In the treatment group, the mean number of lymphocytes on days 1, 3 and 5 was 38.33 ± 7,638; 21.67±7.638; and 16.67 ± 2,887 cells.

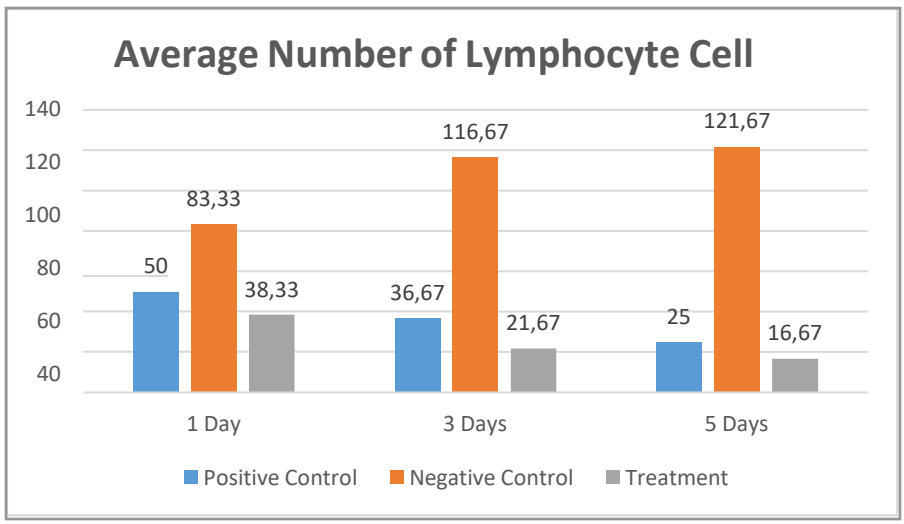

Figure 3: Mean Comparison of Lymphocyte Cells

Based on the Shapiro-Wilk normality test (Table 2), each group shows a significance value of p>0.05 so it can be said that all data samples are normally distributed.

Table 2: Normality Test Results.

Group	Days		Shapiro-Wilk	
		Statistic	Sig.	df
Positive Control	1	1.000	1.000	3
	3	1.000	1.000	3
	5	1.000	1.000	3
Negative Control	1	0.871	0.298	3
	3	0.964	0.637	3
	5	0.871	0.298	3
Treatment	1	0.964	0.637	3
	3	0.964	0.637	3
	5	1.000	1.000	3

Analysis using the One-Way ANOVA test was carried out on data that was normally and homogeneously distributed. For data based on treatment groups, each group was tested with One Way ANOVA because it is normally distributed and homogeneous, data is said to be significant if (p<0.05).

Table 3: Homogenity Test Results Based on Each Group

Group	Levene Statistic	p
Positive Control	0,211	0,816
Negative Control	1,161	0,375
Treatment	1,333	0,332

The p value for each group is based on Table 3, namely the positive control group is 0.816, the negative control group is 0.375, and the treatment group is 0.332. Based on the results of the analysis, it was found that the positive control, negative control and treatment groups had homogeneous data (p>0.05).

Table 4: Homogenity Test Results Based on Euthanasia Days.

Group	Levene Statistic	p
Day 1	3,525	0,097
Day 3	1,333	0,332
Day 5	2,340	0,177

The p value for each group is based on Table 4, namely euthanasia on the 1st, 3rd and 5th day respectively, are 0.097; 0.332; 0.177. Based on the results of this analysis, it was found that each group showed a significance value ($p>0.05$), so it could be said that all data samples were homogeneous.

Table 5: One-Way ANOVA Test Result Based on Control and Treatment Groups

Group	Sum of Squares	df	F	Sig.
	120173.630	8	51.172	0.000

The observational data analyzed using the One-Way ANOVA test showed that the infiltration number of lymphocyte cells in all groups had significant differences ($p<0.05$).

Discussion

This study chose a gel dosage form with topical application on rat tooth sockets after extraction. The gel preparation was chosen because it has several advantages, such as cooling, does not cause scars, is easy to spread evenly when applied, provides good absorption, and is easy to use.

The research results obtained were that there was a significant decrease in the average number of lymphocyte cells in the treatment group compared to the positive and negative control groups. The negative control group had a higher average number of lymphocytes than the treatment group. The highest number of lymphocyte cells in the negative control group occurred on day 5, with 121.67 cells, while the lowest number of lymphocyte cells occurred in the treatment group on day 5, amounting to 16.67 cells. Lymphocyte cells decrease over time due to the wound healing process which is characterized by a decrease in inflammatory cells [11]. The negative control group using placebo gel did not experience a decrease in lymphocyte cells because the CMC-Na gel did not contain active compounds, so it did not cause significant changes to the lymphocyte infiltration pattern.

Hyperglycemia or metabolic disorders characterized by decreased insulin production, is a characteristic feature of type 2 diabetes mellitus [12].

Hemostasis, inflammation, proliferation, and remodelling are steps in wound healing that can be disrupted due to diabetes mellitus. Hyperglycemia induces the production of Reactive Oxygen Species (ROS) by mitochondria which causes diabetes complications. Oxidative stress caused by hyperglycemia can be prevented if glycemic control is good. In the early stages of type 2 diabetes mellitus, there is an association between hyperglycemia, increased oxidative stress, and excessive formation of AGEs. As the disease progresses, persistent protein glycation occurs with mitochondrial DNA damage and may result in a cascade of events leading to synergy between oxidative stress and AGEs. The effects of this metabolic imbalance activate the inflammatory process through binding to AGEs or ROS receptors which can change the composition and structure of the extracellular matrix. When it comes to tooth extraction, diabetic patients may face additional challenges due to post-operative problems such as prolonged bleeding and slow wound healing. The most common symptom is increasing periodontitis due to hyperglycemia which can alter the migration and phagocytic activity of mononuclear and polymorphonuclear (PMN) cells.

When it comes to tooth extraction, diabetic patients may face additional challenges due to post-operative problems such as prolonged bleeding and slow wound healing. The most common symptom is increasing periodontitis due to hyperglycemia which can alter the migration and phagocytic activity of mononuclear and polymorphonuclear (PMN) cells.

Long-term hyperglycemia impairs the ability of leukocytes to phagocytose, making the body more susceptible to infection and inflammation (both of which cause an increase in leukocyte counts). This decrease will trigger chronic hyperglycemia and cause subclinical inflammation in diabetes mellitus sufferers.

The inflammatory phase is a normal process when the body experiences injury. As a result of this injury, the body will respond in the form of inflammation, one of which is an increase in leukocyte cell types. The leukocyte cells that play an important role in the inflammatory process are lymphocyte cells. The increase in lymphocyte cells cannot continue, so the number of lymphocytes must be reduced so that the inflammatory process is not prolonged and the healing process can occur quickly. The inflammatory process is characterized by an increase in leukocyte cells, meaning that the number of lymphocytes also increases, however if the number of lymphocytes is too low then the body is unable to phagocytize antigens or fight the source of infection so efforts are needed to maintain an adequate number of lymphocytes if injury occurs to the body [13].

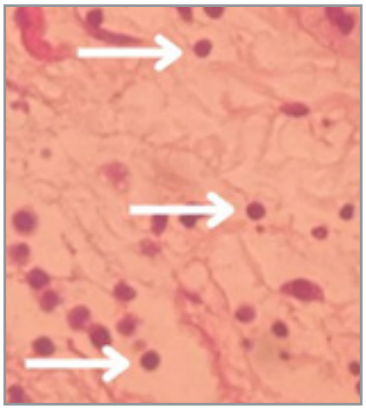

Figure 3: Histological Appearance of Lymphocyte Cells.

Basil leaf extract gel was used in this study to determine the effect on the number of lymphocyte cells in type 2 diabetes mellitus. This is because basil leaves have the main anti-inflammatory, antioxidant and anti-microbial abilities that plays a role in reducing inflammatory cells. Research says that basil leaves contain metabolite compounds such as alkaloids, flavonoids, steroids, tannins and saponins [14].

According to research conducted by which tested the effectiveness of on the legs of rats with edema, it showed that the conjugation of β - cyclodextrin in basil leaves could inhibit the number of lymphocytes, leukocytes, granulocytes and monocytes that were indicating the effectiveness of complex regulation of leukocytes during acute inflammatory responses. The research also said that flavonoids are the highest anti-inflammatory agents in basil leaves. The anti-inflammatory effect of basil leaf extract is induced by adipocyte cells through TNF suppression.

Basil leaf extract with high concentrations is said to be able to reduce the number of leukocyte cells and significantly increase anti-inflammatory and anti-oxidant parameters. This research proves that the ability of basil leaf extract to reduce the expression of inflammatory cytokines is induced by IL-1β, IL-6, TNF-α, and also suppresses NF-κB. According to [15]. the role of flavonoids as anti-inflammatory agents is by reducing the number of leukocytes and being able to reduce complement activity, so that it can reduce leukocyte adhesion to the endothelium which results in a reduction in the inflammatory process.

This research is supported by research conducted by which states that the anti-inflammatory activity of flavonoids is created by inhibiting cyclooxygenase and lipoxygenase, which in turn reduces the number of inflammatory cells that migrate to the wound area so that the inflammatory reaction tends to run smoothly, fast and quality proliferation through TGF-β is not hampered [16].

Based on this research, it can be seen that basil leaf extract gel 15% has an effect in reducing the number of lymphocyte cells in the inflammatory phase after tooth extraction of Wistar rats with type 2 diabetes mellitus. It can be seen that there is significance of the decrease in the number of lymphocyte cells in the treatment group compared to the negative control group at each observation time [17-40].

Conclusion

Based on the research results, it can be concluded that administration of 15% basil leaf extract gel had an effect on reducing the number of lymphocyte cells on each day of observation when compared to the negative control group with the lowest mean number of lymphocyte cells in the treatment group on day 5 a total of 16.67 cells, which means that 15% basil leaf extract gel has an effect in reducing the number of lymphocyte cells in the post- tooth extraction inflammatory phase of Wistar rats with type 2 diabetes mellitus [41-53].

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