Research Article

The Effect of Cyclamate, Stevia, and Sugar on Blood Glucose Levels in White Rats (*Rattus norvegicus*)

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Abstract

Background: Artificial sweeteners are often used in everyday life because they are relatively cheap and in small amounts can provide many times the sweetness of granulated sugar. The use of artificial sweeteners in the long term can cause various health problems. Therefore, this study aims to determine blood glucose levels given several sweetener solutions so that people are more selective in choosing sweeteners in everyday life.

Method: This type of research is true experimental using posttest-only control group design method. This study used three treatments on white rats (Rattus norvegicus) Wistar strain, namely cyclamate, stevia, and granulated sugar with a dose of 10mg/kgBW for 2 weeks. The data were analyzed using the Saphiro-Wilk test, Kruskal-Wallis test, and Mann-Whitney test.

Results: The results showed that the average blood glucose given cyclamate was 128.33, stevia was 84.43, and sugar was 86.13. While the results of the normality test showed $p > 0.05$ with a value of 0.107 for cyclamate, 0.126 for stevia, and 0.365 for granulated sugar. The results of the homogeneity test showed $p < 0.05$ with a value of 0.002 and the Kruskal-Wallis test showed $p < 0.05$ with a value of 0.003.

Conclusion: there was a significant difference and in the stevia group against the control group and the sugar group against the control group showed $p > 0.05$ with a value of 0.536 and 0.121, which means there is no significant difference.

Keywords: cyclamate, stevia, sugar, blood glucose levels

INTRODUCTION

The choice of sweetener in everyday life greatly affects the pattern of life. Unhealthy lifestyles, such as never controlling daily intake, consuming sweet drinks, alcoholic beverages, soft drinks, coffee, and sweet tea. [1] There are so many cheap sweeteners, however, that can cause various health problems, for example, artificial sweeteners. The effect of artificial sweeteners on the body can cause various problems such as inhibiting the activity of several liver enzymes, damaging liver cells, impaired glucose tolerance, kidney damage, heart problems, etc. [2] An example of an artificial sweetener is cyclamate.

Cyclamate is an artificial sweetener in the form of an odorless white crystalline powder and can add thirty times the sweetness of sucrose. [3]

Not only artificial sweeteners can cause health problems, other sweeteners such as sugar can also cause health problems such as increased blood glucose levels which eventually become hyperglycemia and lead to Diabetes Mellitus.

Some sweeteners do cause health problems, but stevia is different. Stevia is a natural sweetener derived from the leaves of Stevia Rebaudiana Bertonii which contain steviol so that it can provide a sweet taste. [4] Stevia in high doses can provide insulinotropic, antidiabetic, and antihypertensive effects. [5]

METHODS

1. Study Design

The type of research used in this study is true experimental which aims to determine the effect of cyclamate, stevia, and granulated sugar on blood glucose levels in male Wistar white rats (Rattus norvegicus) using the post test-only control group design method.

2. Population and Sample

The number of samples used in this study was 8 individuals per group. So the number of samples required for this study were 32 individuals. Rattus norvegicus will be grouped into 4 groups, namely K, P1, P2, P3. Group K (unsweetened), group P1 (given 10mg/kgBW granulated sugar solution), P2 group (given 10mg/kgBW cyclamate solution), P3 group (given stevia solution 10mg/kgBW). The sweetener solution will be given orally once a day for 14 days.

3. Study Instruments

The materials used in this study were cyclamate, stevia, granulated sugar, aquades, materials for the maintenance of Rattus norvegicus (rat food and mineral water in plastic bottles), materials for administering

sweetener solutions (3cc and 5cc syringes and 8Fr rat sonde). Tools for measuring blood glucose (GES brand glucometer strips and strips and alcohol swabs), tools for the treatment of experimental animals (rat cages 25 x 15 x 10 cm, water bottles, and scales).

RESULT

After administering a solution of cyclamate, stevia, and sugar for 14 days, then on the 14th day blood glucose levels will be measured which can be seen in table 1 below:

Table 1. Blood Glucose Level Calculation Results Data

Group	Average glucose	Standard deviation
K	86,13	9,538
P1	99,86	16,965
P2	128,33	10,203
P3	84,43	4,650

Description:
K : Untreated group
P1 : The treatment group of white rats given granulated sugar at 10mg/KgBW dose
P2 : The treatment group of white rats was given cyclamate at 10mg/KgBW dose
P3 : The treatment group of white rats was given stevia at 10mg/KgBW dose

From table 1 the group that has the highest average blood glucose is group P2 which is given a cyclamate solution with the value of 128.33 and the group that has the lowest average blood glucose is the P3 group which is given stevia solution with a value of 84.43.

Table 2. Data Normality Test

	Shapiro-Wilk		
Group	**Statistic**	**df**	**Sig.**
Control	0,964	6	0,851
Sugar	0,899	6	0,365
Cyclamate	0,830	6	0,107
Stevia	0,838	6	0,126

From table 2 the normality test shows p> 0.05 with a control value of 0.851, granulated sugar of 0,365, cyclamate of 0.107, and stevia of 0.126.

Table 3. Homogeneity Test

Group	Levene Statistics	Df1	Df2	Sig.
Blood Glucose	6.682	3	24	0,002

From table 3 the homogeneity test shows a significance value of 0.002 which means it is not homogeneous because $p < 0.05$.

Table 4. Kruskal-Wallis Test

Kruskal-Wallis H	df	Asymp. Sig.
14.144	3	0,003

From table 4 the Kruskal-Wallis test shows a significance value of 0.003 which means there is a significant difference because $p < 0.05$.

Table 5. Mann-Whitney Test

Group	Sig.
Control towards sugar	0,121
Control towards cyclamate	0,001
Controls towards stevia	0,536

From table 5, the Mann Whitney test shows a significant difference between the control group and the cyclamate group with a significance value of 0.001.

DISCUSSION

The results of the administration of cyclamate solution in Experimental animals showed a high increase in blood glucose with an average of 128.33. This is due to a decrease in Akkermansia muciniphila bacteria due to the provision of low-calorie artificial sweeteners. These bacteria are able to reduce lipopolysaccharide and increase the thickness of mucus which can make up the cell surface of gram-negative bacteria. Lipopolysaccharide then binds to Toll-like receptor-4 (TLR-4) on macrophages to produce inflammatory mediators and this inflammation can result in pancreatic b cell damage which will eventually lead to insulin resistance which ultimately results in increased blood glucose levels. [2] A previous study conducted by Setiady (2019) using a cyclamate dose of 13.58 mg/kgBW can cause an increase in blood glucose compared to the control group. The results of the two studies show that cyclamate can increase blood glucose levels so that cyclamate should not be used in daily life because according to Setiady (2019) use within a period of 5 weeks, cyclamate can cause glucose intolerance through digestive tract dysbiosis resulting in insulin resistance. Research conducted by Tiara (2018) shows that cyclamate can cause kidney health problems as indicated by the presence of edema in the glomerulus due to pro-

tein deposits. Setiady (2019) and Tiara (2019) research shows that cyclamate can cause various health problems with short-term use. [6]

The results of giving stevia solution to experimental animals showed a decrease in blood glucose by an average of 84.4. This is because stevia leaves contain stevioside which can stimulate insulin secretion in pancreatic b cells so that it can repair damage to pancreatic b cells which can have a more severe insulin-lowering effect if not repaired. Previous research conducted by Pradini (2017) using a dose of 75 mg/kgBW showed that stevia can reduce blood glucose levels. The results of both studies show that stevia can lower blood glucose levels so that stevia can be used as a sweetener in everyday life. It is still not known whether the use of stevia in the long term is safe, however, according to previous research conducted by Raini (2011) and according to previous research conducted by Guru (2019), stevia leaves are safe, not mutagenic, and do not provide any effect and efficacy. at low doses (3mg/kg/day) but stevia has no antioxidants. The use of high doses of stevia has an insulinotropic, antidiabetic, and antihypertensive effect. Research by Pradini (2017), Raini (2011), and Guru (2019) shows that stevia does not cause various health problems, so stevia can be used as a sweetener in everyday life and even used as a sweetener to replace granulated sugar. [7],[8]

The results of giving a solution of granulated sugar to experimental animals showed an increase in blood glucose levels by an average of 99.8. This is because fructose infusion can induce hepatic insulin resistance. It should be noted that sugar dissolved in water is very easy to assimilate, therefore sugar dissolved in water will cause an increase in blood glucose levels more quickly. [9] Previous research conducted by Novrian (2020) using a dose of 30 mg/dl can increase blood glucose levels. From the results of the two studies, it shows that sugar can increase blood glucose levels, therefore granulated sugar should not be used often in everyday life because it can cause an increase in blood glucose which will eventually cause hyperglycemia and lead to diabetes mellitus. [10]

CONCLUSION

The results showed that there was an increase in blood glucose levels in treatment group 1 (sugar) and treatment 2 (cyclamate) with a dose of 10mg/kgBB, while treatment group 3 (stevia) showed a decrease in blood glucose levels so that of the three sweeteners, namely sugar, stevia, and

the sweetener cyclamate that does not raise blood glucose is stevia.

SUGGESTION

It is necessary to do further research with higher doses for sugar and stevia solution in white rats (Rattus norvegicus) to see if there is a significant difference with higher doses.

It is necessary to do further research with a longer time for sugar and stevia solution in white rats (Rattus norvegicus) to see the effect of a longer time on changes in blood glucose levels.

At the time of this study, many white rats (Rattus norvegicus) were too small and the number of samples and reserves was not large, so that in future studies more samples and reserves were needed.

This research requires a very large cost, more manpower, and looks difficult, however, the results of the study provide satisfaction for the researcher.

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REFERENCES

[1] Saryono, 2014. Pola Hidup Pasien Diabetes Melitus Tipe II Di RS PKU Muhammadiyah Gombong. *Jurnal Ilmiah Kesehatan Keperawatan.* *http://ejournal.stikesmuhgombong.ac.id/index.php/JIKK/article/view/133*

[2] Setiady, F. (2019). Pengaruh Kombinasi Pemanis Buatan Siklamat dan Sakarin Terhadap Kadar Glukosa Darah Dan Toleransi Glukosa. *Jurnal Mahasiswa PSPD FK Universitas Tanjungpura,* 5(1). https://jurnal.untan.ac.id/index.php/jfk/article/view/34954

[3] Huwaida, A. (2020). *Analisis Kadar Siklamat Dalam Sirup Secara Spektrofotometri UV-VIS.* Bogor: Institut Pertanian Bogor. https://ereport.ipb.ac.id/id/eprint/3075/1/J3L217174-01-Azzah%20Huwaida-cover.pdf

[4] Pathak, N. (2020). *Stevia.* WebMD. https://www.webmd.com/food-recipes/what-is-stevia

[5] Guru, A. O., 2019. Aktivitas Antioksidan Minuman Fungsional Campuran Daun Teh (Camellia sinesis L), Kayu Secang (Caesalpinia Sappan L), Dan

Daun Stevia (Stevia rebaudiana Bertonii M). *Repository Akademi Farmasi Putera Indonesia Malang*. http://repository.poltekkespim.ac.id/id/eprint/288/1/Angela%20Orpa%20Guru-Artikel%20Ilmiah.pdf

[6] Tiara, P., 2018. Pengaruh Natrium Siklamat Terhadap Histopatologi Ginjal Mencit (Mus musculus) Dan Sumbangsihnya Pada Materi Struktur Dan Fungsi Jaringan Hewan Di SMA/MA. Repository UIN Raden Fatah Palembang

[7] Pradini, S. A., 2017. Uji Efek Antidiabetik Kombinasi Ekstrak Etanol Daun Stevia (Stevia Rebaudiana Bert.) Dan Daun Sambiloto (Andrographis folium) Pada Tikus Jantan Galur Wistar Yang Diinduksi Aloksan. IJMS – Indonesian Journal On Medical Science, 4(2), pp. 177 - 182.

[8] Raini, M., 2011. Khasiat dan Keamanan Stevia Sebagai Pemanis Pengganti Gula. Media Litbang Kesehatan, 21(4), pp. 145-156.

[9] Amchra, F. Z. (2018). Effect of aspartame on human health: A comprehensive review. Journal of Medicinal Plants Studies , 6(1), 102-108

[10] Novrian, F. (2020). Perbandingan Peningkatan Kadar Glukosa Darah Puasa Sebelum Dan SesudahSesudah Pemberian Madu Hutan Dan Gula Pasir Mahasiswa Angkatan 2015 Fakultas Kedokteran Universitas Muhammadiyah Sumatera Utara. *Jurnal Ilmiah SIMANTEK, 4*(4), 146-152.