Differences in Blood Glucose Levels of Rats (*Rattus norvegicus*) Given Sugar Cane Juice and Cyclamate Solution as a Sweetener

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ABSTRACT

Background: Artificial sweeteners can cause glucose intolerance, which is a condition where the glucose in the blood is abnormal. Purpose: This research was conducted to determine the difference in blood glucose levels of mice as experimental animals that were given sugarcane juice as a natural sweetener and cyclamate solution as an artificial sweetener. **Methods:** The research method applied was laboratory experimental followed by checking blood glucose levels using a GCU easy touch glucometer and the data analysis method used was descriptive analysis. **Results:** the average blood sugar before treatment was P0 (control) 110 mg/dl, P1 (test animals given sugarcane juice solution) 63 mg/dl, P2 (test animals given sodium cyclamate solution) 69.5 mg/dl. Then, the average blood sugar after treatment was, P0 (control) 77.5 mg/dl, P1 (test animals given sugar cane juice) 81.5 mg/dl, P2 (test animals given cyclamate solution) 101.5 mg/dl etc. From this data, it was obtained that the level of glucose in the blood decreased by an average of 32.5 for P0. Then, there was an increase in blood glucose levels with an average of 18.5 for P1. In addition, there was an increase in blood glucose levels with an average of 32 for P2. Blood sugar levels in the treatments given cyclamate and sugar cane juice both experienced an insignificant increase in blood sugar, but within two weeks the average increase in blood sugar was highest in the treatment given cyclamate. **Conclusion:** There are differences in blood glucose levels of mice as experimental animals given sugarcane juice as a natural sweetener and cyclamate solution as an artificial sweetener.

Keywords: glucose, sugar cane, cyclamate

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INTRODUCTION

Sugar is a source of carbohydrates that are used as sweeteners. People often use sugar as an ingredient to add sweetness to the food and drinks they consume. Sodium cyclamate is an artificial sweetener that can be distributed freely. Excessive use of sodium cyclamate sweetener as an additive in food and drinks can trigger the growth of diseases such as cancer.

An individual's blood sugar levels can experience an increase in what is called hyperglycemia. Uncontrolled blood sugar levels can cause diabetes mellitus (Pratama *et al.*, 2018). Artificial sweeteners can cause glucose intolerance. Glucose intolerance can be defined as a condition where the glucose in the blood is abnormal. Several studies that have been conducted have found that there is the potential that consumption of low-calorie artificial sweeteners can cause an increase in blood glucose (Setiady, 2019).

This research was carried out to determine the difference in blood glucose levels of rats (Rattus norvegicus) given sugar cane juice and cyclamate solution as a sweetener using a glucose check unit.

The theoretical benefit of the results of this research is expected to provide scientific information regarding differences in blood glucose levels of rats (Rattus norvegicus) given sugar cane juice and cyclamate solution as a sweetener using a glucose check unit. Meanwhile, it is hoped that the practical benefits of the results of this research can be a source of information regarding sweeteners that make blood glucose levels not too high.

METHODS

Study design

The design of this research used laboratory experimental researchs followed by checking blood glucose levels using the GCU easy touch glucometer. The data analysis method used descriptive analysis. The samples were divided into three research groups with one control group and two treatment groups.

Samples

The research samples were obtained from the veterinary clinical pathology laboratory in the amount of six animals using random sampling samples of Wistar rats which were divided into three research groups with one control group and two treatment groups.

Animal treatment

A physical examination is carried out, including weight measurement. After that, the samples were divided into each group with each group consisting of 2 mice. Mice were acclimatized for 4 days so they could adapt to the laboratory environment. Ad libitum feeding and drinking. On the last day of acclimatization, the mice's blood glucose levels will be checked using GCU. There were 3 groups in this study which were divided into control group, group P1 sugarcane solution, and group P2 cyclamate solution. In the control group, mice will only be fed pellets and drink distilled water. In test group P1, mice were given 15 ml of sugar cane juice according to the average drinking needs of mice. Sugar cane juice is dispensed every day and given food pellets and drinking distilled water. Test group P2, mice were given 13.58 mg of cyclamate solution dissolved in 15 ml of siphoned water every day and given pellet food and drinking distilled water.

The ADI of cyclamate is 0-11 mg/kg for humans. BSA-CF Human/Rat for human 50 kg, rat 200g = 0.162

$$AED = \frac{\frac{11 mg}{kgBB}}{0,162} = \frac{67,9 mg}{kgBB}$$

AED = HED : BSA-CF

Cyclamate dose for rats weighing 200g (x):

$$\frac{67,9 \ mg}{x} = \frac{1000 \ g}{200 \ g}$$
$$1000x = 13580$$
$$x = 13,58 \ mg$$

Mice were fasted for approximately 12 hours. Rats that have been handled with a towel. Prepare the glucose check unit and install the strip. Clean the rat's tail using an alcohol swab. Puncturing with a needle and syringe until the blood comes out and it is felt that it is sufficient to check the strip. The strip that has been installed on the glucose check unit is touched to the blood until a sound is heard. Wait a moment and note the results that appear on the glucose check unit.

Data analysis

The data obtained will be analyzed using descriptive analysis, which is a form of statistics that describes or depicts the data that has been obtained as it is without intending to make conclusions that apply to the general public in the form of graphic tables and narratives.

RESULT AND DISCUSSION Rat Blood Glucose Level Profile

The data in this research comes from data obtained when providing

treatment to experimental animals. There were 6 experimental animals divided into 3 groups as differentiating treatments, namely group P0 as control, P1 as rats given sugar cane juice, P2 as rats given sodium cyclamate. Each treatment group contained 2 experimental animals. The experimental animals were acclimatized for 4 days and then blood sugar levels were measured. After that, treatment was given for 14 days and blood sugar levels were measured again.

Table 1. Fasting blood sugar (GDP) and cholesterol levels in white mice after administration of the extract

Treatment	Blood Sugar Pre	Blood Sugar Post	Increased Blood
	Treatment (mg/dl)	Treatment (mg/dl)	Sugar (mg/dl)
P0	110	77,5	-32,5
P1	63	81,5	18,5
P2	69,5	101,5	32



Figure 1. Profile of rat blood glucose levels before and after treatment.

Treatment	Body Weight Pre Treatment (gram)	Body Weight Post Treatment (gram)	Weight loss (gram)
P0	82,5	76	6,5
P1	69,5	63	6,5
P2	81	76,5	4,5

Table 2. Rat body weight before and after treatment



Figure 2. Body weight profile of mice before and after treatment.

From the data in table 1, there was an increase in blood glucose levels with an average of 18.5 for P1 (test animals were given sugarcane juice solution). In addition, there was an increase in blood glucose levels with an average of 32 for P2 (test animals were given sodium cyclamate solution). However, a decrease in blood glucose levels was obtained with an average of 32.5 for P0 (control).

Based on research from Setvadi, et al, it was stated that the cyclamate treatment group showed a significant increase in fasting blood glucose. However, the results of our study showed an increase in blood glucose levels in the cyclamate treatment which showed the highest average, but the increase was not significant. This is because the highest increase in blood sugar levels in experimental animals P2 (1) to 112 mg/dl after this treatment does not exceed normal blood sugar levels in experimental animals, namely 50 - 135 mg/dl. The results of this study are in line with research conducted by Wasudevan, et al. If the use of the artificial sweetener sodium cyclamate does not cause an increase in blood sugar that exceeds normal limits. making it safe for diabetes sufferers and

for controlling excessive sugar levels. Of course, this use must be within certain limits and must be supervised by a doctor or health expert.

In the group treated with sugarcane juice there was an increase in blood sugar levels with an average of 18.5. This still does not have a significant increase because blood sugar levels do not exceed the normal sugar levels of experimental animals. There is an increase in blood sugar levels because the substances contained in sugar cane juice are carbohydrates, sucrose, iron, calcium, antioxidants, glucose, sugar and calories, vitamins and minerals (Sulistivanto, et al., 2021). The glucose and sucrose content affects blood sugar levels in experimental animals. However, the results of blood glucose levels did not increase significantly or did not exceed the increase from treatment with sodium cvclamate.

Then, in the control group there was a decrease in blood sugar levels by 32.5 mg/dl due to confounding factors that influenced the research results. The confounding factor in question is sampling mice that have different blood sugar levels. In the control group, samples of mice were found that had high initial blood sugar levels. So that in the control group who were not given any treatment, there was a decrease in blood sugar levels during treatment. Apart from that, because mice don't like the food they are given, they eat little, this can be seen from the amount of leftover food given.

Rat Body Weight Profile

Based on our research in the data in table 2, the sugarcane juice treatment group and the control group experienced greater weight loss than the sodium cyclamate treatment group, around 6.5 grams, while the sodium cyclamate treatment group was around 4.5 grams. The large weight loss, especially in the control group and the sugarcane juice treatment group, could be influenced by several confounding factors. Meanwhile, weight loss in the sodium cyclamate treatment group experienced lower weight loss than the others due to the influence of confounding factors, but according to Wasudevan et al, sodium cyclamate is safe for obese sufferers because it does not cause weight gain. This made it possible for the weight loss in the sodium cyclamate treatment group to not be too large.

The disturbing factors in question include non-uniform sampling of mice, mice experience stress when they are given treatment so that the mice experience a decrease in their appetite for eating and drinking and there is human error that occurs on the first day when the wrong treatment is given so that the mice test animals experience stress. Apart from that, the health condition of each mouse is unknown. such as the normal condition of the insulin hormone. So that when the condition of the rat's insulin hormone is still normal, the increase in the rat's blood sugar level will not exceed normal levels.

CONCLUSION

There was an increase in blood glucose levels in the sodium cyclamate treatment group by 32 mg/dl, while the increase in blood glucose levels was 18.5 mg.dl. So, from the results of our research, comparing blood sugar levels in the cyclamate treatment with sugar cane juice, there was an insignificant increase in blood sugar, but within 2 weeks the highest average increase occurred in the treatment using sodium cyclamate. Apart from that, there was a decrease in body weight in all treatment groups due to confounding factors, namely non-uniform sample selection, unknown health conditions of experimental animals and human error in providing treatment so that the mice experienced stress and decreased appetite for eating and drinking.

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Author Contribution

V.A.K, M.V.K, I.Z, and, A.J.S conceptualization, R.A and A.A.P.H contributed to the animal study, R.A.V analyzed data and N.P.A draft preparation, Z.F.H writing review and editing.

Competing Interest

The authors declare that there are no competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Ethical Approval

All trials were examined and approved by the Faculty of Veterinary

Medicine at Airlangga University's Ethical Approval Committee assessed this work, and it was given ethical approval under No. 1.KEH.081.06.2023.

Data Availability

The article includes data that was used to support the study's conclusions.

REFERENCES

- Agung, B., W. Handang & M. Mirandy, P.S. 2013. Peningkatan kualitas post thawing spermatozoa epididimis sapi dengan suplementasi catechin sebagai antioksidan pada pengencer semen. J Ilmu Ternak 13:34-36.
- Ansar, NAzaruddin and Aziz, A.D., 2019. Pengaruh suhu dan lama penyimpanan terhadap perubahan pH dan warna nira aren (Arengga pinnata Merr) setelah penyadapan. Teknik Pertanian LAmpung, pp.97-106.
- Cahyadi, W, 2008, Analisa Dan Aspek Kesehatan Bahan Tambahan Pangan, Edisi Kedua, Bumi Aksara, Jakarta
- Casu, R.E., Grof, C.P.L., Rae, A.L., McIntyre, C.L., Dimmock, C.M. & Manners, J.M.(2003). Identification of a novel sugar transporter homologue strongly expressed in maturing stem vascular tissues of sugarcane by expressed sequence tag and micro array analysis. Plant Mol. Biol. 10,1-16.
- Chattopadhyay, S., Raychaudhuri, U., & Chakraborty, R. (2014). Nonnutritive sweeteners-a review. J Food Sci Technol, 51(4), 611-621.
- Devitria, R., & Sepryani, H. (2018).
 Identifikasi Natrium Siklamat pada Minuman Sirup yang dijual di Lima SD Kecamatan Sukajadi Pekanbaru. Klinikal Sains: Jurnal Analis Kesehatan, 6(1), 1-7.

- Dewi, S.R., Izza, N., Agustiningrum, D.a., Indriani, D.W., Sugiarto,Y., Mahawani, D.M and Yulianingsih, R., 2014. Pengaruh suhu pemasakan Nira dan Kecepatan pengadukan terhadap kualitas gula merah tebu. Jurnal teknologi Pertanian, 15(3), pp.149-158
- Dharma Audi Samsuri, Samsuri, Anak Agung Sagung Kendran. 2020. Kadar Glukosa Darah Tikus Putih (Rattus norvegicus) yang Diberikan Ragi Tape. 9(4):531-539. Fakultas Kedokteran Hewan, Universitas Udayana.
- Elsevier. 2016. Artificial sweeteners. Meyler's Side Effects of Drugs (Sixteenth Edition). 713-716.
- Erwinda, M. D. dan Wahono Hadi Susanto. 2014. Pengaruh pH Nira Tebu (Saccharum offinarum) dan Konsentrasi Penambahan Kapur Terhadap Kualitas Gula Merah. Jurnal Pangan dan Agroindustri Vol.2 No.3 p.54-64. Universitas Brawijaya, Malang.
- Fontaine, D. 2019. 5 Common **Ouestions for Diabetic** Models. https://www.jax.org/news-andinsigh ts/jaxblog/2019/september/5-commonquestions-for-diabetic-models#:~: text=For%20%27healthy%27%2C % 20non%2D,a%204%20%E2%80% 93%206%20hour%20fast [7

November 2023].

- Harlita. T. D., Rukmana, D. I., dan Nabillah. Z. (2023). Pengaruh Suhu Dan Waktu Penyeduhan Teh Kering Dalam Kemasan Terhadap Angka Kuman, Jurnal Sains Medisina, 1(3), 148–153.
- Hedrich HJ. 2006. Taxonomy and stock and strains. J Lab Rat 71-92.
- Lawrence, J. F. 2003. CYCLAMATES. Encyclopedia of Food Sciences and

Nutrition(Second Edition),AcademicPress. 1712-1714.

- Lia Melinda, Deny Kurniawan, Vita Pramaningsih. 2022. Identifikasi Pemanis Buatan (Siklamat) pada Penjual Minuman Es Teh Keliling di Sekolah Dasar Kelurahan Melayu Kecamatan Tenggarong. Environmental Occupational Health and Safety Journal. Vol.3 No.1.
- Malole, M. B. M. dan C. S. Pramono. 1989. Penggunaan Hewan-hewan Percobaan Laboratorium. Departemen Pendidikan dan Kebudayaan. Direktorat Jendral Pendidikan Tinggi Pusat Antar Universitas Bioteknologi. Institut Pertanian Bogor, Bogor.
- Natawijaya,D., Suhartonoand Undang, 2018. The analys of Sap Water Yleld and Palm Sugar Quality in Tasikmalaya District. Jurnal Agroforestri Indonesia 1(1)1, pp.57-64.
- Praja, Denny Indra. (2015). Zat Aditif Makanan: Manfaat dan Bahayanya. Garudhawaca.
- Pratama, O. W. P., Wuryanto, M. A., & Ginandjar, P. (2018). Gambaran Kadar Gula Darah Sewaktu Pada Penduduk Risiko Tinggi Diabetes Mellitus Tipe 2 Desa Ketawangrejo Kecamatan Grabag Kabupaten Purworejo. Global Health Science, 3(4), 287-293.
- Ramadhani, N., Herlina, H., & Utama, A. J. F. (2018). Penetapan Kadar Natrium Siklamat Pada Minuman Ringan Kemasan Dengan Menggunakan Metode Spektrofotometri UV. Jurnal Mandala Pharmacon Indonesia, 4(1), 7–12.
- Riswandi, M. D. 2022. Bagaimana Tebu Diolah Menjadi Gula Pasir di Pabrik PT RMI.https://home.rejosomanisind

o.c om/104/bagaimana-tebudiolah-menj adi-gula-pasir-dipabrik-pt-rmi [7 November 2023]

- S, C. S. ., Defanny, & Rakhmadi, F. A. (2020). Karakteristik Resistansi Air Teh Gula Alami dan Buatan. Prosiding Seminar Nasional Fisika Festival, 1, 32–35.
- Setiady, F. (2019). Pengaruh Konsumsi Kombinasi Pemanis Buatan Siklamat dan Sakarin terhadap Kadar Glukosa Darah dan Toleransi Glukosa. Jurnal Mahasiswa PSPD FK Universitas Tanjungpura, 5(1).
- Smith, J.B., & Mangkoewidjojo,S. (1998). Pemeliharaan, Pembiakan, dan Penggunaan Hewan Percobaan di Daerah Tropis.Tikus Laboratorium (Ratus norvegicus) : 37-57.Penerbit Universitas Indonesia
- Sugiyono. 2015. Metode Penelitian Kombinasi (Mix Methods). Bandung. Alfabeta.
- Sugiyono. 2016. Metode Penelitian Kuantitatif, Kualitatif, R&D. Bandung: IKAPI.
- Sulistiyanto, T. Q., Sinaga, S. M., & Suryanda, A. (2021). Pemahaman dan Perspektif Mahasiswa Mengenai Manfaat Air Tebu (Saccharum officinarum) dalam Prospek Kesehatan. Jurnal Pro-Life, 8(3), 199-204.
- Wasudevan, D.M, Sreekumari S dan Kannan Vaidyanthan. 2013. Textbook Of Biochemistry For Medical Student:seven edition. New Delhi: Jaypee Brother Medical Publisher.
- Winarno, F.G., 1992, Kimia Pangan dan Gizi, PT. Gramedia Pustaka Utama, Jakarta.
- Wolfensohn, S., dan Lloyd, M., 2013, Handbook of Laboratory Animal Management and Welfere, 4th ed., Wiley- Blackwell West Sussex,234.
