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The Effect of Trehalose Sugar on Insulin Resistance in Old Rats by Assessing HOMA-IR (Homeostasis Model Assessment-Insulin Resistance)

Pengaruh Gula Trehalosa terhadap Resistensi Insulin pada Tikus Tua dengan Penilaian HOMA-IR (Homeostasis Model Assessment-Resistensi Insulin)

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ABSTRACT

Background: Insulin resistance is a condition in which insulin cannot take up glucose, increasing blood glucose. Elderly people are more exposed to insulin resistance, requiring dietary interventions that extend longevity. Trehalose, a naturally occurring sugar, showed potentially reduce insulin resistance which can be measured using the HOMA-IR (Homeostasis Model Assessment-Insulin Resistance) index.

Objectives: This study aimed to assess HOMA-IR levels as a parameter of insulin resistance in old rats after giving trehalose sugar.

Methods: Experimental research with 28 male Wistar rats (*Rattus norvegicus*) was separated into 4 groups, the control group of young rats (Group A), the control group of old rats (Group B), a group of old rats that were given 2% Trehalose solution (Group C), and a group of old rats that given 2% sucrose solution (Group D) that observed for 8 weeks.

Results: The results showed differences in HOMA-IR levels ($p < 0.001$) between old and young subjects. The intervention in Group C was optimal in reducing levels of HOMA-IR ($p < 0.001$) by 18.2% compared with the old control, while Group D increased levels of HOMA-IR by 14.3% ($p < 0.001$) compared with the old control. The age of the subjects with HOMA-IR level is positively correlated ($p < 0.001$; $r = 0.721$) and the weight of subjects with the HOMA-IR level is also positively correlated ($p < 0.001$; $r = 0.698$), indicating that the older and the greater weight of subject resulting in the bigger of HOMA-IR value.

Conclusion: Trehalose is effective in reducing HOMA-IR levels as a parameter of insulin resistance in old rats.

ABSTRAK

Latar Belakang: Resistensi insulin merupakan keadaan dimana insulin tidak mampu untuk mengambil dan memanfaatkan glukosa didalam tubuh sehingga kadar glukosa darah meningkat. Individu lanjut usia beresiko tinggi mengalami resistensi insulin sehingga diperlukan intervensi diet yang dapat meningkatkan harapan hidup. Trehalosa sebagai gula alami diketahui memiliki potensi dalam menurunkan resistensi insulin yang dapat diukur menggunakan indeks HOMA-IR.

Tujuan: Tujuan dilakukannya penelitian ini adalah untuk menilai kadar HOMA-IR sebagai indikator terhadap resistensi insulin pada tikus tua setelah pemberian gula trehalosa.

Metode: Penelitian eksperimental menggunakan hewan coba yaitu tikus putih jantan jenis Wistar (*Rattus norvegicus*) sebanyak 28 ekor, yang kemudian dibagi menjadi 4 kelompok yaitu kelompok kontrol tikus muda (Kelompok A), kelompok kontrol tikus tua (Kelompok B), kelompok tikus tua yang diberikan larutan Trehalosa 2% (Kelompok C), dan kelompok tikus tua yang diberikan larutan Sukrosa 2% (Kelompok D) kemudian diamati selama 8 minggu.

Hasil: Hasil dari penelitian menunjukkan bahwa ada perbedaan kadar HOMA-IR ($p < 0.001$) antara subyek yang tua dengan muda, dimana usia berbanding lurus dengan HOMA-IR. Intervensi pada Kelompok C optimal dalam menurunkan kadar HOMA-

IR ($p < 0,001$) sebanyak 18,1% dibandingkan dengan kontrol tua, sedangkan Kelompok D meningkat kadar HOMA-IR 14,3% ($p < 0,001$) dibandingkan kontrol tua. Usia subyek dengan kadar HOMA-IR menunjukkan korelasi positif ($p < 0,001$; $r = 0,721$) dan berat badan subyek dengan kadar HOMA-IR juga menunjukkan korelasi positif ($p < 0,001$; $r = 0,698$), sehingga semakin besar usia dan berat badan subyek maka semakin besar nilai HOMA-IR.

Kesimpulan: Trehalosa efektif dalam menurunkan kadar HOMA-IR sebagai indikator terhadap resistensi insulin pada tikus tua.

Kata Kunci: Trehalosa, HOMA-IR, Resistensi Insulin, Penuaan.

INTRODUCTION

In the elderly, accumulation of senescent cells and increased levels of visceral fat can lead to elevated blood levels of pro-inflammatory cytokines and impaired insulin signaling¹. The elderly are more susceptible to impaired glucose tolerance. If left untreated, it can develop insulin resistance, which can eventually result in type 2 diabetes mellitus. Diabetes affects over 90% of persons as they age, about 50% of people with type 2 diabetes are over 60 year².

Insulin resistance may play an important role in the development of DM, particularly type 2 diabetes. Fink³ (1983) discovered that two-hour plasma glucose levels on the Oral Glucose Tolerance Test (OGTT) average increased by 5.3 mg/day. Meanwhile, fasting plasma glucose (FPG) levels have grown on an average of 1 mg/dl every ten years³.

Older people are more likely to have insulin resistance⁴ a result of neurohormonal changes, particularly IGF-1 (insulin-like growth factor-1) and DHEAS plasma (*Dehydroepiandrosterone plasma*), which result in decreased glucose uptake due to decreased insulin receptor sensitivity and action⁴. In addition, there was also a decrease in leptin and HMW Adiponectin levels, which play a role in glucose homeostasis and energy balance⁵. The dietary intervention has been shown to increase health and life expectancy in the elderly.

Trehalose is a sugar that occurs naturally in plants and insect⁶ and is composed of two glucose molecules. In rats fed a high-fat diet (HFD), trehalose has been demonstrated to help avoid the development of the metabolic syndrome and improve insulin resistance⁶.

The research found that administrated obese rats with trehalose reduced insulin resistance by decreasing adipocyte hypertrophy and boosting serum HMW adiponectin⁷. Another study also showed daily consumption of 10 grams of trehalose can enhance glucose tolerance as measured by the Oral Glucose Tolerance Test (OGTT)⁸.

To our knowledge, no research has been done to see how trehalose affects insulin resistance in the elderly population using HOMA-IR levels as a marker of insulin resistance.

The study's findings are likely to serve as a guide for choosing a balanced diet for elderly individuals to reduce the negative effects of insulin resistance associated with aging. If trehalose is effective at reducing insulin resistance, it can be used to create a variety of health products or foods. Thus, this study aimed to figure out the HOMA-IR levels as an indicator of insulin resistance in elderly rats following trehalose sugar delivery.

METHODS

Male Wistar (*Rattus norvegicus*) rats aged 3-4 months for young rats and 12-18 months for old rats were used in this research⁹. The experimental rats were obtained from Breeder rats Makassar, South Sulawesi. All of the animal experiments were conducted at the Entomology Laboratory of the Faculty of Medicine, Hasanuddin University Makassar. The sample comprised 28 rats which split into four groups, each including seven rats ($n = 7$).

The Federer formula was used to determine the¹⁰ of the rat sample to be used in this study¹⁰, which is¹¹ follows: $(t-1)(n-1) \geq 15$; where t is the number of treatment groups and n is the number of samples per group. According to the formula, the optimal sample size is 7 rats/group. Thus, the total sample size was 28 rats were allocated to one of the four groups at random.

Preparation of experimental animals

For one week, the cage was adapted/acclimatized. Male Wistar rats were fed a standard diet/feed and provided with adequate water, as well as having their body weight monitored daily. The standard diet was Van Der Vour standard diet that contains 20% protein, 7% fat, 15-20% fiber, and 1% calcium and 0.8% phosphorus. To maintain a stable environment, the cages were cleaned daily; the Wistar rats were housed in a room with adequate air circulation and sustained at a standard room temperature ($28 \pm 2^\circ\text{C}$) with a humidity of $50\% \pm 10\%$, and the room lights were set to a 12-hour dark cycle, and 12 hours of illumination.

Preparation of 2% trehalose solutions

Based on the reference in previous studies, the concentration of trehalose used was 2% (using the formula $M/V \times 100\%$; where M is the mass of trehalose; and V is the volume of water/day that will dissolve the trehalose)¹¹. And the daily water intake for male Wistar rats > 12 months elderly is ± 40 ml/day⁹.

$$2\% = \frac{M}{V} \times 100\% \rightarrow 2\% = \frac{M}{40 \text{ ml}} \times 100\%$$
$$M = 0.8 \text{ gram}$$

According to the calculations, 0.8 grams of trehalose will be used, dissolved in 40 mL of distilled water, and autoclaved for ± 10 minutes to prevent contamination. The same applies to 2% sucrose used as a comparison in this study.

Preparation of 2% sucrose solutions

A concentration of 2% sucrose follows a concentration of 2% trehalose (using the formula $M/V \times$

100%; where M is the mass of sucrose; and V is the volume of water/day that will dissolve the sucrose). And the daily water intake for male Wistar rats > 12 months elderly is ±40 ml/day.

$$2\% = \frac{M}{V} \times 100\% \rightarrow 2\% = \frac{M}{40 \text{ ml}} \times 100\%$$

$$M = 0.8 \text{ gram}$$

According to the calculations, 0.8 grams of sucrose will be used, dissolved in 40 mL of distilled water, and autoclaved for ±10 minutes to prevent contamination.

Intervention

Group A is a control group of young rats that were only given a standard diet (up to 15-20 grams/day of Van Der Vour diet) and drank in moderation; Group B is a group of old rats that were only given standard diet (up to 25 grams/day of Van Der Vour diet) and drank moderately; Group C is a group of old rats that were given standard diet and a 2% trehalose solution placed in a rat's drinking bottle and Group D is a group of old rats that were given standard diet and a 2% sucrose solution placed in a rat's drinking bottle. This intervention lasted 8 weeks and was stopped at week 8 to collect serum samples.

Post Intervention (Sampling)

Before collecting the serum sampling, rats fasted for 12 hours before treatment¹². Three milliliters of blood were obtained from the anesthetized rats, intravenously in the tail of the rats, and then placed in a red vacutainer tube. The vacutainer tube containing the blood sample was then centrifuged for 20 minutes at 2500 rpm. Serum, top clear liquid, was collected and stored in an eppendorf tube. The sample is then stored in the freezer at -20°C.

HOMA-IR Level Examination

Biochemical examination of HOMA-IR levels was obtained from fasting insulin levels and Fasting Plasma Glucose (FPG). Fasting insulin levels have been tested in research labs HUM-RC of Rumah Sakit Pendidikan Universitas Hasanuddin (RSP-UH) using the Insulin Mouse ELISA KIT BT-LAB[®] with the Sandwich-ELISA principle expressed in mIU/L units. The FPG examination was carried out at the Pathology Laboratory of RSP-UH

Makassar using the hexokinase enzymatic method with the Clinical Chemistry Analyzer ABX Pentra 400 which was expressed in mg/dL units. Fasting insulin levels and FPG obtained will be used to measure HOMA-IR with the following formula:

$$\frac{\text{Fasting insulin} \left(\frac{\text{mIU}}{\text{L}}\right) \times \text{Fasting Plasma Glucose (mg/dL)}}{405}$$

The results in this study were analyzed using the SPSS version 25 for Windows. The one-way Anova and Kruskal-Wallis statistical data analysis tests were utilized, while the correlation test was performed using the Pearson and Spearman correlation tests. Each action conducted in this research has gained authorization to be used as a research sample and has been certified to fulfill the ethical requirements for conducting Health Research Ethics Commission (KEPK) FKUH - RSPTN UH - Dr. RSUP. Wahidin Sudirohusodo Makassar No: 172/UN4.6.4.5.31/PP36/2021.

RESULTS AND DISCUSSION

This study employed serum samples from White Rats (*Rattus norvegicus*) housed as experimental animals from March to May 2021. There were 28 samples that met the research criteria. The characteristics of the research subjects are presented in Table 1. This research subject was split into two groups based on their age, namely young rats aged 3-4 months and older rats aged 14-17 months with an average age of 12 months. The age range of 14-17 months in old rats was chosen based on the strain's maximum lifespan of up to 36 months. In humans, the aging process begins at 30 years old, whereas in rats, the aging process begins at 14 months. The examination's characteristics showed that the individuals' average body weight was 264 grams, with a minimum of 152 grams and a maximum of 368 grams. The laboratory tests on the subjects revealed that their average insulin level was 20.29 mIU/L, ranging from 4.18 mIU/L to 27.51 mIU/L, while their average Fasting Plasma Glucose (FPG) level was 100.89 mg/dL, ranging from 74 mg/dL to 129 mg/dL. The HOMA-IR index ranges from 0.78 – 8.68 and the median 5.79.

Table 1. Characteristics of research subjects based on age, body weight, laboratory and HOMA-IR

Variable	Minimal	Maximum	Median	Mean±SD
Age (months)	3	17	14	12±5.01
Body Weight (grams)	152	368	287.5	264±69.81
Laboratory				
Fasting Insulin (mIU/L)	4.18	27.51	24.90	20.29±8.92
Fasting Plasma Glucose (mg/dL)	74	129	99	100.89±14.05
HOMA-IR	0.78	8.68	5.79	5.16±2.49

The eight weeks intervention goal was to see if there was a difference in HOMA-IR levels between a control group given distilled water and a group of old white rats [31]. were given trehalose and sucrose. The HOMA-IR index was being used to evaluate insulin resistance in the subjects of this research because HOMA-IR is frequently used since it is a simple and valid method for determining insulin sensitivity by combining the fasting insulin index and fasting plasma glucose³⁴. The HOMA-IR value was

reached by combining the fasting insulin level (mIU/L) multiplied by the FPG level (mg/dL) and then dividing by 405. According to prior research with the same subject, the HOMA-IR cut-off value for experimental animal subjects Wistar rats was >3.9³². Table 2 shows the characteristics of research subjects by treatment group. These variables include average body weight, average fasting insulin levels, average FPG levels, and average HOMA-IR levels.

Table 2. Characteristics of research subjects based on treatment groups

Variable [Mean±SD]	Group				P*
	A: Young Control (n=7)	B: Old Control (n=7)	C: Trehalosa (n=7)	D: Sucrose (n=7)	
Age (months)	3.43±0.53*	14.71±1.11	14.43±1.13	15±1.11	0.001 ^a
Body Weight (grams)	164±7.87*	302±28.05	292±49.07	296±53.44	<0.001 ^b
Fasting Insulin (mIU/L)	5.32±1.36*	25.65±1.13	23.68±1.17*	26.48±0.85	<0.001 ^a
Fasting Plasma Glucose (mg/dL)	93.71±15.69*	103.57±9.40	91.71±5.22*	114.57±11.87*	0.03 ^b
HOMA-IR	1.23±0.32*	6.55±0.57*	5.36±0.37*	7.49±0.84*	<0.001 ^b

^a Kruskal-Wallis, ^b One-way Annona, * p<0.05 (significant compared to other groups)

To find out which group has a significant difference, a Post-Hoc test (Table 3) is carried out. Based on the Post-Hoc test for the variables of age and body weight, only group A had a significant difference (p<0.001) compared to the other groups because group A was a young rat with a wide different mean of age and weight compared to groups B, C, and D which were a group of old rats. In the fasting insulin variable, only group A (p<0.001) and group C (p<0.05) had a significant difference, while the fasting insulin levels in group B and group D did not have a significant difference. This

indicates that trehalose influences fasting insulin levels in old rats, while sucrose does not affect fasting insulin levels in treated old rats. In the FPG variable, group A (p<0.05), Group C (p<0.001), and Group D (p<0.001) had significant differences, indicating that both trehalose and sucrose effect on FPG levels in treated old rats. Finally, for the HOMA-IR variable, all groups, namely A (p<0.001), group B (p<0.05), group C (p<0.05), and group D (p<0.05) had significant differences, indicating that Trehalose and Sucrose affect HOMA-IR levels in treated old rats.

Table 3. Post-Hoc Test based on treatment groups

Treatment Group	Treatment Group	P-Value				
		Age	Body Weight	Fasting Insulin	Fasting Plasma Glucose	HOMA-IR
Group A Young Control	Group B Old Control	<0.001*	<0.001*	<0.001*	0.374	<0.001*
	Group C Trehalose	<0.001*	<0.001*	<0.001*	0.987	<0.001*
	Group D Sucrose	<0.001*	<0.001*	<0.001*	0.010*	<0.001*
Group B Old Control	Group A Young Control	<0.001*	<0.001*	<0.001*	0.374	<0.001*
	Group C Trehalose	0.993	0.960	0.018*	0.224	0.003*
	Group D Sucrose	0.993	0.991	0.538	0.282	0.023*
Group C Trehalose	Group A Young Control	<0.001*	<0.001*	<0.001*	0.987	<0.001*
	Group B Old Control	0.993	0.960	0.018*	0.224	0.003*
	Group D Sucrose	0.951	0.997	0.001*	0.004*	<0.001*
Group D Sucrose	Group A Young Control	<0.001*	<0.001*	<0.001*	0.010*	<0.001*
	Group B Old Control	0.993	0.991	0.538	0.282	0.023*
	Group C Trehalose	0.951	0.997	0.001*	0.004*	<0.001*

* p<0.05 (significant compared to other groups)

Table 2 shows that there had been significant differences between the four treatment groups, both for age (p=0.001), body weight (p<0.001), fasting insulin levels (p<0.001), FPG levels (0.003), and HOMA-IR levels (p<0.001). The average HOMA-IR level was 1.23 in group A (control of young rats), 6.55 in group B (control of old rats), 5.36 in group C (old rats treated with 2% Trehalose), and 7.49 in group D (old rats treated with 2% sucrose). When these data are compared to the HOMA-IR

Index cut-off value, it is concluded that groups B, C, and D, which consist of old rats, have insulin resistance, whereas group A, which consists of young rats, is normal.

The old control group, Group B, had a 432% or 4 times increase in HOMA-IR levels when compared to the young control group (Group A). SPSS showed statistically significant results (p<0.001) or a substantial effect based on statistical data. This reveals that age has a big influence on the HOMA-IR and insulin resistance levels of research

subjects. These results are consistent with the statement that insulin resistance can develop with aging⁵. Aging is the most important contributor to decreased metabolism and health. Insulin resistance has been discovered and this is a regular occurrence in older people. In addition, aging is linked with increased levels of pro-inflammatory cytokines, which can affect the action of insulin¹⁶.

Insulin resistance seems to be a failure of the target tissue to react normally to insulin. When aging, insulin resistance and glucose intolerance might develop⁴. The mechanism of insulin resistance during aging is associated with several factors such as changes in the hormone IGF-1 (insulin-like growth factor-1), plasma DHEAS (plasma dehydroepiandrosterone) which result in decreased glucose uptake, receptor sensitivity, and insulin action³. Additionally, other factors such as decreased Leptin and HMW (High Molecular Weight) Adiponectin levels which are involved in glucose homeostasis, increased free fatty acid oxidation, all contribute to changes in body composition, most notably fat accumulation⁵.

This research indicated that the intervention group receiving 2% Trehalose (Group C) experienced an 18.1% decrease in HOMA-IR levels when compared to the old control group (Group B). SPSS showed significant results ($p < 0.001$) or a significant outcome based on statistical data. This shows that trehalose had a significant effect on insulin resistance reduction in the old rats used in this research. These results concur with a previous study on female rats aged 6 weeks, which demonstrated the reduction in insulin resistance and dyslipidemia following trehalose administration⁷. Another study demonstrates that trehalose can reduce insulin resistance in male mouse subjects through the restoration of mTOR phosphorylation and suppression of autophagy¹¹.

However, the levels of HOMA-IR in group C when compared with the results of group A (Control Young Rats) increased 335% or 3 times. This happened because the subjects used in group C were old rats, which were classified as having insulin resistance like the old control group (Group B). However, the increase of HOMA-IR levels in group C was still lower when compared to the increase of HOMA-IR levels in group B against group A. The results indicate that the consumption of trehalose in elderly/older subjects can reduce insulin resistance.

Another research showed that daily administration of trehalose can increase the number of adipocytes, in addition to a decrease in adipocyte

hypertrophy, and lower blood glucose⁸. Trehalose also protects against oxidative stress, one of which is Reactive Oxidative Species (ROS), and inhibits the inflammatory response induced by endotoxic shock in vivo and in vitro, making it a possibility to become a therapeutic agent for a variety of diseases related to oxidative stress and chronic inflammation¹⁷. Because trehalose's metabolism is similar to that of glucose, it can be efficiently hydrolyzed to glucose using the enzyme trehalase. Trehalase was already identified in the intestinal mucosa of humans and the majority of animals, as well as in the kidney, liver, and circulation¹³.

The degradation of trehalose to glucose, catalyzed by the enzyme trehalase into two glucose molecules and is an important process in many organisms. Trehalose degradation aims to restore cellular homeostasis following stress-induced overproduction of trehalose; or produce glucose to meet energy and/or carbon requirements. Interestingly, although mammals do not have a pathway for the biosynthesis of trehalose, they have trehalase in the intestine and kidney, which was previously known to be involved in the hydrolysis of ingested trehalose to glucose. The presence of trehalase in humans allows many further applications of trehalose and trehalose analogues¹⁸.

Meanwhile, the intervention group that received 2% sucrose (Group D) experienced an increase in HOMA-IR levels by up to 14.3% when compared to the old control group (Group B). SPSS showed significant results ($p < 0.001$) or a significant effect based on statistical data. This shows that sucrose administration to old rats can significantly increase insulin resistance. These results concur with a previous study that the metabolic profile shows an elevated risk of diabetes mellitus and cardiovascular disease in animals given sugar-sweetened drinks. Both sugar groups, namely 60% Sucrose and 50%/50% Fructose/Glucose, have Impaired Glucose Tolerance (IGT), which is a peripheral indication of insulin resistance¹⁹. Sucrose was employed as a comparison sugar in this study since it belongs to the disaccharide group, just like trehalose, another disaccharide sugar. Additionally, sucrose is frequently utilized in everyday life as a sweetener for food and beverages as granulated sugar. Most over the world, sucrose is used as the main sweetener. These findings suggest that sucrose consumption by elderly subjects may increase insulin resistance.

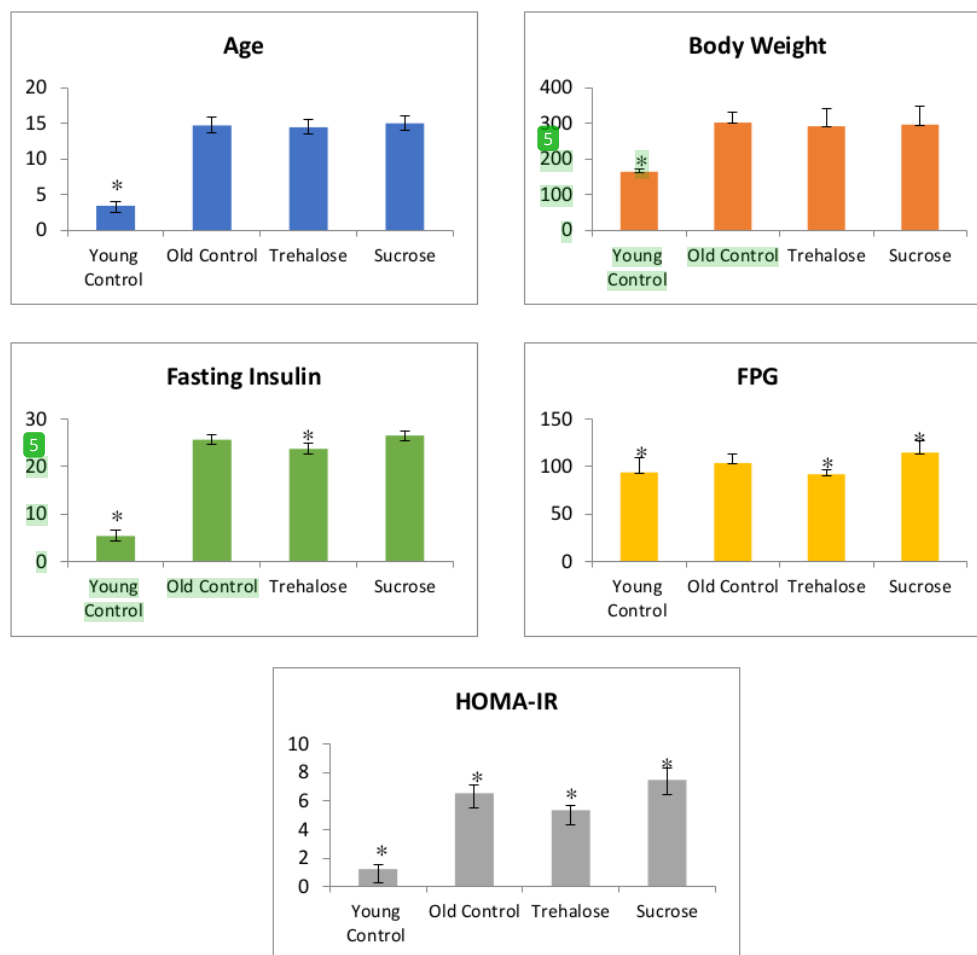


Figure 1. Graph of the characteristics of research subjects based on the treatment group
 *p<0.05 (significant compared to other groups), FPG = Fasting Plasma Glucose, HOMA-IR=Homeostasis Model Assessment-Insulin Resistance

Correlation tests were conducted on the variables: age and body weight of rats (No.1), age HOMA-IR levels of rats (No.2), and bodyweight and HOMA-IR levels of rats (No.3). Pearson's test was used to determine the correlation between the age and bodyweight of rats (No.1), and the results indicated a positive correlation between the subjects' age and body

weight, as shown in Table 4. The p-value (p< 0.001) shows that the data are correlated or related; a positive value indicates a positive correlation, showing that the elderly subject's, the greater the weight of the subject's value; and the Correlation Coefficient value of 0.889 show a perfect correlation (r=0.81 -1.00).

Table 4. Correlation test of age, body weight, and HOMA-IR levels

Correlation Test	Mean±SD	R	p
Age	12±5.01		
Rat Weight	264±69.81	0.889	<0.001 ^a
Age	12±5.01		
HOMA-IR	5.16±2.49	0.721	<0.001 ^b
Rat Weight	264±69.81		
HOMA-IR	5.16±2.49	0.698	<0.001 ^b

^a Pearson Correlation, ^bSpearman-rank Correlation, r = Correlation Coefficient

The correlation between rat age and HOMA-IR levels (No. 2) was determined using Spearman's test, which revealed a positive correlation between subject age and HOMA-IR levels with $p = 0.001$ and a Correlation Coefficient value = 0.721, as shown in Table 4. The value of $p < 0.001$ indicates that the data are correlated or related; a positive value indicates a positive correlation, showing that the elderly the subject, the greater the HOMA-IR level; and the value of Correlation Coefficient = 0.721 shows a strong relationship ($r = 0.51 - 0.75$). This supports the theory that insulin resistance can develop as a result of aging. Aging causes a progressive functional decline in molecular, cellular, tissue, and organismal. As organism ages, its susceptibility to disease and likelihood of mortality both rise.

Spearman's tests were performed to evaluate the relationship between rat body weight and HOMA-IR (No.3) levels. As shown in Table 4, there had been a positive correlation between body weight and HOMA-IR (No.3) levels with a $p < 0.001$ and a Correlation Coefficient value of 0.698. The p -value ($p < 0.001$) indicates that the data are correlated or related; a positive value suggests that the greater the subject's weight, the greater the HOMA-IR level; and the Correlation Coefficient = 0.698 indicates a strong relationship ($r = 0.51 - 0.75$). However, as shown in Figure 1, there was no significant difference in weight variables between the three groups ($p > 0.05$) for groups B, C, and D, which were old rat subjects. Significant differences were observed only in group A, which included young rats. These findings show the intervention with 2% trehalose or 2% sucrose had no significant effect on the bodyweight of old rats.

CONCLUSION

In conclusion, there were differences in HOMA-IR levels between old and young subjects, where age was directly proportional to HOMA-IR. There is a difference in HOMA-IR levels in the intervention group compared to the old control, where 2% sucrose increased HOMA-IR levels by 14.3% compared to the old control, while 2% Trehalose decreased HOMA-IR levels by 18.1% compared to old controls. Trehalose 2% and sucrose 2% did not have a significant effect on bodyweight of old rat subjects. Future studies are still necessary with humans as the subject of this research to figure out the effect of trehalose in HOMA-IR levels as an indicator of insulin resistance in the elderly.

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CONFLICT OF INTEREST DAN FUNDING DISCLOSURE

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