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The Effect of Giving D-Galactose as an Aging Inducer on Body Weight, Glucose Levels and Interleukin-6 Levels in Wistar Rats

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Abstract. *Aging is a complex biological process characterized by a decline in physiological functions and an increased susceptibility to chronic diseases. D-galactose, although a naturally occurring monosaccharide, can induce aging when administered in high doses by increasing oxidative stress and inflammation, as indicated by elevated levels of reactive oxygen species (ROS) and interleukin-6 (IL-6). This study aimed to analyze the changes in body weight, blood glucose levels, and IL-6 levels in Wistar rats following D-galactose administration, with the goal of gaining insights into aging mechanisms and exploring potential therapeutic targets for age-related diseases. This was an experimental study using a pre- and post-test design, involving 20 male Wistar rats divided into two groups: a treatment group that received 150 mg/kgBW of D-galactose and a control group that received 0.9% NaCl, both for a duration of six weeks. The study was conducted at the PSPD Research Laboratory, Faculty of Medicine and Health Sciences, UIN Alauddin Makassar, from August to October 2024. Body weight, fasting blood glucose, and serum IL-6 levels were measured weekly using ELISA and a glucometer. Variables analyzed included body weight, glucose levels, and IL-6 levels, with controlled variables such as age, sex, strain, feed, water, and housing conditions. Data were analyzed using an independent t-test with a significance level of $p < 0.05$. Although changes were observed in all variables, the administration of D-galactose did not result in statistically significant differences in body weight or blood glucose levels between the treatment and control groups. These findings suggest that the aging process induced by D-galactose may involve more complex mechanisms and require further investigation to fully understand its effects and implications for human health.*

Keywords: *D-Galactose, Aging, Body Weight, Glucose, Interleukin, Wistar Rats*

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INTRODUCTION

Aging is a complex and universal biological process, characterized by progressive decline in physiological functions and increased susceptibility to various chronic diseases (Wu et al., 2015). In an effort to understand the mechanisms of aging and develop effective interventions, animal models have been widely used to mimic the human aging process. One method that is often used is the induction of aging using D-Galactose, a simple sugar known to accelerate the aging process through increased oxidative stress and inflammation (Gama et al., 2021; Azman & Zakaria, 2019). D-Galactose is a monosaccharide that in normal physiological amounts is not toxic. However, chronic high-dose administration in laboratory animals has been shown to cause signs of aging that resemble natural aging (Hsieh et al., 2009). D-Galactose increases the production of reactive oxygen species (ROS), which in turn causes oxidative damage to cellular

macromolecules such as DNA, proteins, and lipids. According to Hirano (2021), this condition triggers an inflammatory response characterized by increased levels of pro-inflammatory cytokines such as interleukin-6 (IL-6). Therefore, D-Galactose is often used as an aging-inducing agent in biomedical research to study the molecular and physiological aspects of aging (Guo et al., 2020).

Changes in body weight can provide an indication of the general health and metabolic balance of mice (Hoevenaars et al., 2013). In aging, unintended weight loss is often observed, which can be attributed to a decrease in muscle mass and body fat (Petersen & Smith, 2016; Liguori et al., 2018; Fatemi et al., 2018). Blood glucose levels are an important indicator of metabolic health. Glucose dysregulation is common in aging, which can increase the risk of type 2 diabetes and other metabolic diseases. Increased blood glucose levels in mice induced by aging with D-Galactose may reflect insulin resistance and metabolic dysfunction (Gama et al., 2021; Fatemi et al., 2018; Rusu et al., 2020). Align with research from Bachmann et al., (2020) IL-6 is a pro-inflammatory cytokine that increases during the aging process. Increased IL-6 levels are associated with chronic inflammation known as "inflammaging," a low-grade, long-lasting inflammatory state that contributes to various age-related diseases. Therefore, measuring IL-6 levels may provide insight into the level of systemic inflammation in mice induced by aging (Narazaki & Kishimoto, 2018; Tanaka & Kishimoto, 2012).

By understanding how D-Galactose affects these changes in body weight, glucose levels, and IL-6 levels, we can gain deeper insight into the aging process and develop strategies to reduce the negative impacts of aging on human health. This research has great potential to contribute to the development of medical science in Indonesia, especially in facing the challenges of an aging population.

METHODS

A pre-test and post-test control group analysis through true experimental design assessed health changes in Wistar rats due to D-galactose aging inducer. The series of laboratory tests took place at the PSPD Research Laboratory located in the Faculty of Medicine and Health Sciences that functions as part of Universitas Islam Negeri Alauddin Makassar from August through October 2024. Eighteen male Wistar rats (Rattus norvegicus) were chosen through the inclusion criteria meeting requirements for being active and healthy with weights within 200 to 250 grams and ages at 6 to 8 months. The studied population met these particular criteria which aimed to standardize baseline physiological parameters to eliminate possible confounders. Race placement occurred randomly for a total of 18 male Wistar rats between two equal groups which contained nine rats each. The simple lottery method served as the randomization method to prevent selection bias. The control participants received everyday intraperitoneal 0.9% NaCl solution administrations that functioned as the biological reference point. Each day the treatment group received intraperitoneal D-galactose injections with 150 mg/kg of body weight administered for six weeks straight. The investigative team selected D-galactose as a research substance because of its proven ability to generate aging symptoms by increasing oxidative stress and inflammation in rodents thereby making it an effective method for simulating accelerated aging. All animals were allowed to adapt to laboratory conditions through seven days of constant monitoring before the experimental interventions began to protect against environmental stress leading to experimental errors.

The experimental rats lived alone in standard plastic cages in controlled environmental conditions that included temperatures between 22–25°C as well as 50–60% humidity and a 12-hour light-dark sequence throughout the study duration. The subjects received standard laboratory feed and they could consume water at their discretion. Rats were kept in individual cages for two reasons: first to minimize social stress while second to maintain precise measurements of each rat's physiological data. The measurement of body weight occurred weekly at the same time of day by using a calibrated digital scale providing 0.01 gram precision. A standardized time schedule was used to measure body weight both as a control for biological

diurnal variations and to track metabolic changes during the study duration. The collected body weight data acted as a comprehensive measurement to track metabolic and health conditions especially when studying the effects of aging induction.

The assessment of fasting blood glucose levels required blood collection from the distal tail vein through capillary sampling after a 12-hour overnight fasting period. Researchers measured these variables when the study began in Week 0 and after the study duration at Week 6. A validated glucometer determined blood glucose measurements while giving immediate accurate results. The researchers chose this measure to identify any metabolic imbalances that accompany age-related biological changes including insulin resistance. The researchers examined systemic inflammation through the measurement of interleukin-6 (IL-6) because it served as a biomarker of inflammatory responses. Blood extraction occurred through the medial canthus of the aged rats by using a capillary pipette to reduce their distress and obtain sufficient serum volume. A physician extracted 3 milliliters of blood from study participants during their initial and final phases. The specimen clotted at room temperature for 15–30 minutes while waiting for centrifugation at 1000 rpm for 10 minutes to obtain the serum fraction.

The research team obtained and stored the supernatant at −20°C to wait for examination. The Rat Interleukin-6 (IL-6) ELISA Kit allowed testing of derived serum samples according to manufacturer's recommended procedures to measure IL-6 levels. The ELISA plate reader used 620 nm wavelength to measure IL-6 concentration in the serums through optical density readings. The researchers chose this cytokine because it functions crucially during inflammation and it demonstrates proven relations with aging processes along with diseases associated with older age. The gathered quantitative information about body weight together with fasting glucose levels and IL-6 concentrations received statistical treatment using an independent t-test to establish mean value differences between control and treatment group measurements. The statistical analysis required a significance level of $p < 0.05$ to validate differences between groups. A data evaluation assessed whether D-galactose treatment results in detectable changes to metabolic and inflammatory markers connected with aging (Duan et al., 2017).

RESULT AND DISCUSSION

This study is an experimental study with a Pre and Post-test pattern conducted on August 1 - September 19, 2024, which is divided into 2 stages, namely the adaptation stage for 7 days, and the treatment stage for 42 days (6 weeks). Maintenance of experimental animals and blood sampling for blood glucose and blood serum were carried out at the Research Laboratory of the Medical Education Study Program, Faculty of Medicine and Health Sciences, UIN Alauddin Makassar, while the IL-6 examination was carried out at the HUMRC Laboratory Research Unit/Hasanuddin University Teaching Hospital.

Overview of Experimental Animals

The experimental animals used in this study were male rats of the Rattus Novergicus strain Wistar (Murwani & Muliartha, 2006). The sample size of the experimental animals for the study was 18 rats. The body weight of the rats was 200-250 grams with an age of 6-8 months and the rats were in good health and had never been used in research. The experimental animals were then divided into 2 groups, each consisting of 9 male white rats. Each group was placed in a different cage and had the same environmental factors (temperature and humidity) so that external factors that could interfere with the research results could be minimized.

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Table 1. Characteristics of Male White Rats of Wistar Strain

	Group	
	K	**P**
N	9	9
Treatment	NaCl 0,9%	D-Galaktosa
Age (months)	± 6-8 month	± 6-8 month
Gender	Male	Male
Initial Body Weight (gr)	223,56±4,47	228,44±4,45
Initial Blood Glucose Levels (gr/dl)	95,22±5,44	92,56±2,25
Description: K (control group); P (treatment group)		

Treatment was given to each group, namely the control group (K) which received 0.9% NaCl and the treatment group (P) which received 150 mg/kgBW D-galactose for 6 weeks. The weight of the mice was measured once a week. The experimental animals were acclimatized for 7 days before treatment. The samples were adapted to their new home, by providing food and drink (Andrianto et al., 2021). This treatment was the same for all mice. Each mouse was placed in a single cage so that the experimental animals were not stressed. Blood sampling from mice for blood glucose and IL-6 examination was carried out twice, namely at the end of acclimatization (week 0) or before being given treatment (pre-treatment), and at the end of treatment (post-treatment) in the 6th week, where blood samples were obtained from experimental animals by piercing the medial canthus area and collecting them using a capillary pipette.

The blood collected as much as 3 cc was then placed in a vacutainer. Blood was left in the vacutainer for 15-30 minutes at room temperature to allow coagulation and sedimentation to occur. After that, centrifugation was used to separate blood from serum by rotating at a speed of 1000 rpm for 10 minutes. The supernatant was then collected and stored in a freezer at a temperature of 200C. The serum that was successfully collected was measured for IL-6 concentration using an ELISA kit at a wavelength of 620 nm using an ELISA reader. This study has been tested for ethics, so that the procedures carried out are in accordance with ethical procedures in experimental animals (Intan & Khariri, 2020). The results of the average body weight in old male white mice can be seen in the graph below:

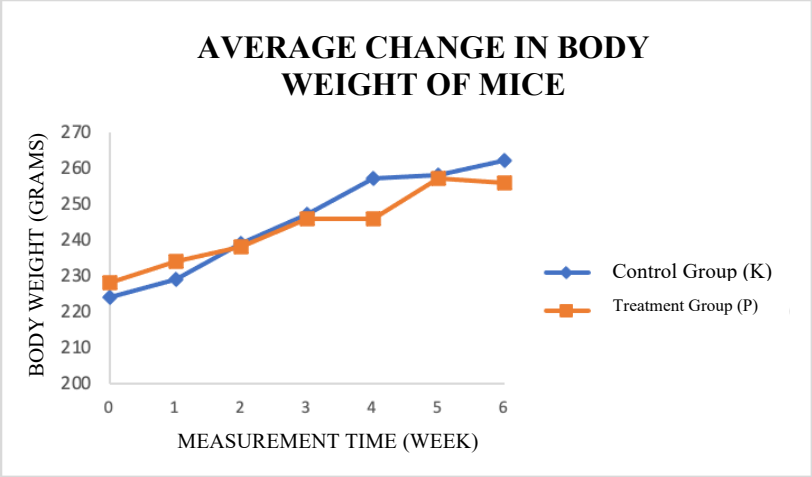

Figure 1. Data on Changes in Body Weight of Mice in Each Group

The graph above shows changes in body weight of male white mice during treatment, with measurements every week for 6 weeks. In the control group (K) there was an increase in body weight during treatment, while in the treatment group (P) there was a decrease in body weight.

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Difference in Average Weight Change

Analysis of changes in the weight of experimental mice showed an increase in both groups, both the control group and the treatment group (Evans et al., 2014). The average change in weight of the pre-test (Week 0) and post-test (Week 6) in old male white rats of the Wistar strain in each group, the results can be seen in table 2 below:

Table 2. Average Change in Weight of Male White Rats of the Wistar Strain

Variable (time)	Group						*p-value**
	Control Group (K)			Treatment Group (P)			
	Min.	Max.	Mean±SD	Min.	Max.	Mean±SD	
Week 0	207	247	223,56±4,77	210	248	228,44±4,45	.465
Week 6	169	314	262,00±17,88	201	309	256,00±14,06	.795
Δ	38			28			

Description: Δ is the difference between the average value of weight change in Week 0 and Week 6

Source: Primary Data

At week 0, the average body weight of the control group was 223.56 grams with a range of 207 to 247 grams. Meanwhile, the treatment group had an average initial body weight of 228.44 grams with a range of 210 to 248 grams. The difference in initial body weight between the two groups was not statistically significant. After six weeks of treatment, there was an increase in body weight in both groups (Zelissen et al., 2005). The average body weight of the control group increased to 262.00 grams with a range of 169 to 314 grams, while the treatment group increased to 256.00 grams with a range of 201 to 309 grams. Although there was an increase in both groups, the results of the independent t-test showed that there was no statistically significant difference between the two groups (p = 0.795). This indicates that the administration of D-galactose at a dose of 150 mg/dl for six weeks did not have a significant effect on changes in body weight in model mice.

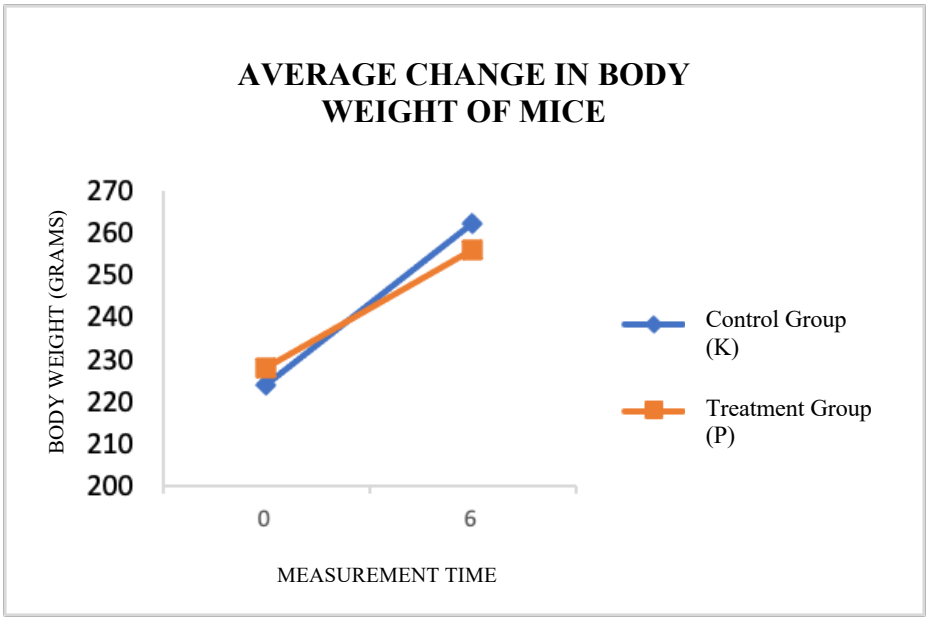

Figure 2. Average Change in Body Weight of Old Male White Rats of Wistar Strain

Data in Figure 2 shows that body weights of aged white male mice (K and P groups) rose as part of the analysis. The figure 2 demonstrates how body weight changed in Wistar rats who received treatment and those that served as controls during the six-week study duration. The data show body weight increase in both groups but the control participants gained more weight

as their mean increase reached 38.44 g while the treatment group recorded 28.44 g. The six-week period of D-galactose at 150 mg/kg body weight administration did not cause a weight change difference between the two groups according to statistical analysis ($p = 0.795$).

Current research data from this study separates from established reports showing D-galactose causes weight reduction through catabolic processes, muscle wasting or impaired metabolism (Azman & Zakaria, 2019; Petersen & Smith, 2016). The treatment span along with the drug dose level might have been insufficient to start either catabolic conditions or observable cachexia symptoms in the study subjects (Ferioli et al., 2018). Low concentrations of D-galactose treatment failed to produce statistically meaningful alterations in body weight amounts in C57BL/6J mice according to Wei et al. (2005). The observation of age-related body weight reduction in metabolically resistant Wistar rats might take an extended amount of time since these rodents have high metabolic resilience.

Weight increases in laboratory rodents occur naturally during aging since the male subjects in this research were 6–8 months old young adults. The weight gain in both groups might originate from normal metabolic development instead of showing no aging effects (Rose et al., 2023). The lack of weight changes in treated mice cannot confirm that D-galactose did not produce biological effects because weight measurements might not be suitable for detecting such changes under these study circumstances.

According to Pourhassan et al. (2013), Weight measurement does not reveal complete information about changes in body composition. The observed stability of body weight does not rule out the potential of D-galactose to promote sarcopenia alongside increased visceral fat levels when aging occurs naturally. Research would gain more depth if researchers included body composition assessments by either dual-energy X-ray absorptiometry (DEXA) or bioelectrical impedance analysis (BIA) to monitor refined physiological changes in future studies.

Natural and care environment conditions contribute to the evolutionary processes of degenerative changes (Wallace, 2005). The study used single housing for animals to eliminate social stress and achieve feed control and minimize experimental inconsistencies. The specific housing conditions might have established a less stressful environment because of which some adverse effects of D-galactose exposure were possibly minimized (Ross & Smith, 2020).

Developing a new interpretation of the aging process as multifaceted becomes possible by analyzing weight data together with the observed trends in glucose levels and IL-6 (pro-inflammatory cytokine). Weight measurements alone might fail to detect early aging phenomena or subtle changes because age-related deterioration processes often remain undetectable through large-scale indicators until the underlying molecular mechanisms advance beyond a certain point.

Difference in Average Blood Glucose Levels

Blood glucose level measurements at the beginning and end of the study showed a decreasing trend in both groups (Juvenile, 2008). At week 0, the average blood glucose level of the control group was 95.22 mg/dl with a range of 69 to 125 mg/dl. Meanwhile, the treatment group had an average initial blood glucose level of 92.56 mg/dl with a range of 76 to 106 mg/dl. The difference in initial blood glucose levels between the two groups was not statistically significant. The difference in the average blood glucose levels pre-test (Week 0), post-test (Week 6) in old male white rats of the Wistar strain in each group, the results can be seen in table 3 below:

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Table 3. Average Blood Glucose Levels of Male White Rats of Wistar Strain

Variable (time)	Group						*p-value**
	Control Group (K)			Treatment Group (P)			
	Min	Max	Mean±SD	Min	Max	Mean±SD	
week 0	69	125	95,22±5,44	76	106	92,56±3,71	.691
Week 6	82	87	84,44±0,66	75	95	87,22±2,25	.256
Δ	-10,78			-5,33			

Description: Δ is the difference between the average value of changes in blood glucose levels in Week 0 and Week 6

Source: Primary Data

After six weeks of treatment, the average blood glucose level of the control group decreased to 84.44 mg/dl with a range of 82 to 87 mg/dl, while the treatment group decreased to 87.22 mg/dl with a range of 75 to 95 mg/dl. Although there was a decrease in both groups, the results of the independent t-test showed that there was no statistically significant difference between the two groups (p = 0.256). This indicates that administration of D-galactose at a dose of 150 mg/dl for six weeks did not have a significant effect on changes in blood glucose levels in model mice.

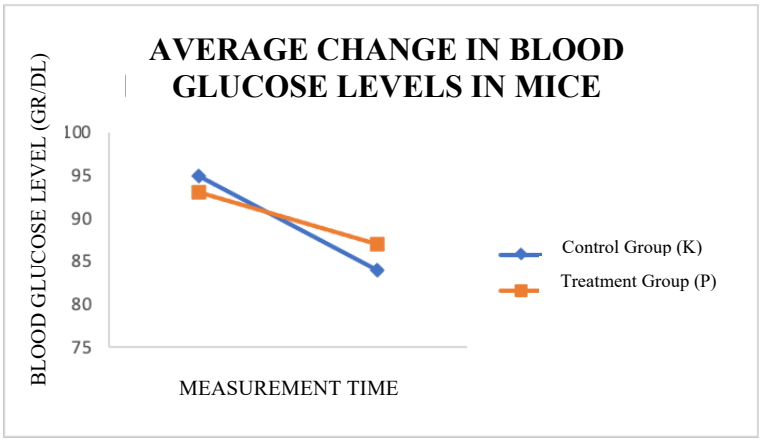

Figure 3. Average Change in Body Weight of Old Male White Rats of Wistar Strain

Blood glucose levels of old male white mice increased as shown in Figure 3 through comparison between the control group (K) and treatment group (P). During six weeks researchers assessed the average alterations in fasting blood glucose levels using Figure 3 between the treatment and control test groups. Between Week 0 and Week 6 both groups showed declining glucose levels yet the control group suffered a reduced glucose level of −10.78 mg/dL whereas the treatment group experienced less marked glucose decrease at −5.33 mg/dL. When D-galactose administration was analyzed with independent t-test both groups of animals failed to show statistically significant differences ($p > 0.05$) because the reviewed treatment dosage did not cause hyperglycemia or metabolic glucose disruption. The research results conflict with findings by Du et al. (2012) and Bo-Htay et al. (2020) who observed D-galactose aging produced insulin resistance and mitochondrial dysfunction and raised fasting glucose levels. The dissimilarities between outcomes can be linked to different experimental methods and animal strain traits (Råberg et al., 2007). The current research based its design on Wistar rats yet most previous investigations utilized Sprague-Dawley rats together with the C57BL/6J mouse strain that potentially displayed dissimilar responses to D-galactose.

During this study insulin signaling disruptions might have remained insufficient because of the 6-week treatment period coupled with the 150 mg/kgBW drug dose being moderate. The pancreatic insulin secretion during early stages of glucose regulation changes successfully

compensated the system to maintain homeostasis concerning glucose levels (Asmasary, 2022). The body operates through metabolic reserve capacity which allows it to handle initial mild stress without developing obvious pathological issues.

The analysis of glucose levels mainly depends on tail prick blood collection from capillaries to measure blood glucose (Eugster et al., 2007). Laboratory assessments of glucose which utilize rodent tail blood show higher variability compared to serum-based measurements while such measurements can be altered by hypoglycemia that results from sample collection stress. Investigating fasting insulin measurements alongside HOMA-IR values would provide better information about glucose-insulin changes in aging model tests.

Recommendations indicate that the trend of reduced glucose levels in the treatment group when compared to controls shows a potential for early metabolic effects although statistical significance was not present (Strasser et al., 2010). Continuous exposure to D-galactose at these study levels might lead to insulin resistance coupled with minor mitochondrial problems although these conditions may stays below the threshold for developing overt hyperglycemia. Rusu et al. (2020) together with Ross & Smith (2020) demonstrate that D-galactose-induced metabolic aging responses result in non-linear time- and dose-dependent patterns according to their research.

Evaluating the Physiological and Inflammatory Impact of D-Galactose-Induced Aging in Wistar Rats

A research examined how D-galactose affects male Wistar rats through measurements of their physical characteristics together with their blood glucose levels and interleukin-6 (IL-6) concentrations for creating an accelerated aging model. After six weeks of daily D-galactose intraperitoneal D-galactose treatment at 150 mg/kg body weight both body weight and blood glucose values remained statistically similar to measurements from the control group. Future studies must analyze IL-6 levels due to their significance in monitoring the inflammatory state from D-galactose aging although no statistical tests were shown in the results provided.

Studies by Azman & Zakaria (2019) showed D-galactose used to reduce body weight but this current study did not reveal substantial body weight changes. Body weight increased in similar ways between control and treatment groups within the present study context. The findings are in line with Wei et al., (2005) research which demonstrated that minimal changes in body weight occurred in C57BL/6J mice after receiving small doses of D-galactose. The weight gain seen between the treatment and control group could stem from either the natural development for the animals or body maintenance patterns rather than investigational factors (Heymsfield et al., 1999). The experimental design divergence along with the usage duration and feeding background elements between studies could explain why weight loss results from Du et al. (2012); Hao et al. (2014) contrasted with the findings of this study.

The study findings contradict previous research about D-galactose administration because fasting blood glucose levels decreased but failed to achieve statistical significance in both groups (Du et al., 2012; Bo-Htay et al., 2020). The anatomical differences among the animals probably result from the combination of sensitivities between strains and the lengths of administration timing and the natural metabolism of each animal. The metabolic reaction patterns between Sprague-Dawley rats differ from the response patterns of Wistar rats who took part in this research. The limited duration of six weeks along with moderate D-galactose administration probably did not create lasting metabolic problems. Studies applying extended treatment periods combined with elevated dosages demonstrate stronger results according to written works such as Zhang et al. (2008); Çoban et al. (2014).

The reported measurement of IL-6 forms an essential component for this research although the results section did not detail its assessment specifically. Multiple scientific studies have validated that D-Galactose creates systemic inflammation through ROS production resulting in elevated cytokine levels of IL-6 specifically (Hirano, 2021; Narazaki & Kishimoto, 2018). The

chronic low-grade inflammation called “inflammaging” includes IL-6 as its main mediator because this process strongly associates with multiple age-related disease pathologies such as cardiovascular issues and neurodegenerative disorders as well as metabolic disturbances (Bachmann et al., 2020). The single increase in IL-6 concentrations might prove to be the most sensitive biomarker for aging initiation thus it needs additional emphasis in future research.

Body cells develop systemic inflammatory aging together with cellular senescence after undergoing three mechanistic pathways due to D-galactose exposure: it causes mitochondrial dysfunction and promotes NF-κB pathway activation and forms AGEs which induce oxidative damage (Guo et al., 2020; Zhong et al., 2019). Research findings demonstrate that both lipid peroxidation increases and antioxidant enzyme superoxide dismutase (SOD) decreases occur in animals receiving D-galactose treatment (Çoban et al., 2014). The current research did not analyze these oxidative biomarkers but future investigations should explore these markers to better understand D-galactose's molecular and biochemical aging effects.

The aging-related effects from D-galactose treatment may change based on multiple factors including genetics as well as environmental exposures and microbiota composition (Ross & Smith, 2020). Studies show varying findings because dose amounts and treatment times together with baseline physiological levels and research variables influence the reported study results. The range of results between studies on aged animals receiving D-galactose reveals that this aging model causes various clinical problems because its underlying effects are driven by multiple factors beyond weight and metabolic status assessment measurements.

Laboratory-based aging research becomes shown to be complex because of the recent study's experimental findings. The experimental parameters can influence how D-galactose induces physiological changes because it remains a commonly used reproducible aging simulation agent but produces varying results in different research conditions. Future research needs to prolong D-galactose treatment periods and administer greater doses as well as pair the agent with other stress factors while testing additional biomarkers which should include tests for oxidative damage combined with neurological testing methods and tissue examinations to fully observe aging-related changes.

This study presents a strong foundation to investigate aging pathophysiology even though it failed to establish weight-based or blood glucose-linked physiological decline. The need for strong and replicable aging models becomes vital because aging-related diseases continue to rise throughout the world especially in Indonesian demographics undergoing quick population aging. Windhammer factors such as oxidative stress and inflammation which can be measured through IL-6 and NF- κ B function might offer prospects for preventing and treating age-associated medical conditions (Tanaka & Kishimoto, 2012; Bo ‐ Htay et al., 2018).

This study did not demonstrate any significant effects of D-galactose administration on body weight or glucose metabolism yet further research is needed to understand the influence of IL-6 inflammatory markers as well as their relationship to aging biology. Standardized research protocols accompanied by multi-parametric aging studies represent the main requirement to address observed inconsistencies with previous study results. Studies of this kind pave a foundation for scientists to better understand the complicated processes that occur during aging through their developments of advanced animal models.

CONCLUSION

The administration of D-galactose at a dose of 150 mg/kg body weight for six weeks did not result in statistically significant changes in body weight or fasting blood glucose levels in Wistar rats. These findings suggest that the metabolic impact of D-galactose at this dosage and duration may be limited or require a longer period to manifest. However, given the established role of D-galactose in promoting oxidative stress and inflammation, further research is warranted to explore its effects on other physiological parameters, particularly inflammatory biomarkers such as interleukin-6 (IL-6), as well as oxidative stress markers and cognitive function. Future

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studies should consider varying the dosage and duration of D-galactose exposure, as well as incorporating more sensitive and diverse outcome measures including insulin levels, body composition analysis, and histological examination to comprehensively evaluate the aging process. Longitudinal and multi-parametric approaches will be essential to better understand the mechanisms by which D-galactose induces aging and to identify potential therapeutic targets for age-related conditions. The results of this study contribute to the growing body of knowledge on experimental aging models and highlight the need for deeper and broader investigation into the complex biological processes underlying aging.

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