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Effect of D-galactose on Weight Gain in Animal Model of Aging

Dwi Sunu Datrianto[1], Yonathan Alvin Maruli Asi Sihotang[2], Topas Wicaksono Priyo Jr[3], Surya Agus Prihatno[3], Teguh Budipitojo[4], and Yosua Kristian Adi[3*]

[1]Graduate from Sains Veteriner Magister, Faculty of Veterinary Medicine, Universitas Gadjah Mada, 55281 Yogyakarta, Indonesia
[2]Student from Sains Veteriner Magister, Faculty of Veterinary Medicine, Universitas Gadjah Mada, 55281 Yogyakarta, Indonesia
[3]Department of Reproduction and Obstetrics, Faculty of Veterinary Medicine, Universitas Gadjah Mada, 55281 Yogyakarta, Indonesia
[4]Department of Anatomy, Faculty of Veterinary Medicine, Universitas Gadjah Mada, 55281 Yogyakarta, Indonesia

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***Corresponding author:** Yosua Kristian Adi

Abstract **Original Research Article**

D-galactose is widely used as an inducing reagent for animal models of aging. The aging model by D-galactose induction has similarities with natural old. In this study, we described the effect of D-galactose administration in rats against their body weight. Thirty healthy male rats aged 2 months were divided into 2 groups. Control group was treated with aqua sterile as placebo, while D-galactose group was treated with 3 mg/kg BW of D-Galactose orally every day for 6 weeks. The rats in both groups were measured using digital weigher every week. The data were analyzed descriptively for the average of body weight (g) each week and statistically for the average of weight gain (%) after 6 weeks using t-test. The average of body weight in control group from week-0 until week-6 were 119± 16.24; 144± 20.24; 160± 27.37; 170± 29.08; 179± 32.79; 197± 32.37; and 208± 32.07, while in D-galactose group were 129± 13.92; 151± 15.94; 164± 24.63; 173± 25.37; 182± 27.15; 192± 25.55; and 197± 25.55. Statistical analysis using t-test showed that there was a significant difference of average weight gain in both groups ($p<0.05$). The average of weight gain in control group and D-galactose group was 75.59%±21.19% and 53.76%±21.79%, respectively. D-galactose could decrease the weight gain in rat model of aging.

Keywords: Aging, Animal Model, D-Galactose, Rats, Weight Gain.

INTRODUCTION

Weight loss occurs due to reduced feed intake. Increased weight loss followed by an increase in the duration of fasting. This weight loss will be optimal when the feeding time is constant [1]. Age can affect weight loss after reducing feed intake [2] and the younger rats lost a higher percentage of body weight than the older mice [3]. Aging is accompanied by a host of metabolic changes, including modulation of mitochondrial function, a decline in insulin sensitivity and alterations in substrate utilization [4]. Aging encompass decrease body functions and increase death risk with increasing adult age [5]. This decline is characterized by progressive changes in biochemistry, energy metabolism, and physiological or even fat storage capacity. [6]. Aged mice from several strains have a lower food consumption, lower energy expenditure, decreased olfactory and auditory senses, and pathological changes such as increased cancer risk [7]. Body fat mass shows different dynamics: while fat stores increase until 1-2 years of individual age, mice lose fat with older age [6].

Rate of metabolism has been associated with aging and body mass has been associated with lifespan. Smaller animals have a higher metabolic rate and exhausting a finite number of metabolic events leads to death [8, 9]. Aging and death are a consequence of the toxins produced by metabolism. This suggests that increased metabolism per unit body weight in smaller animals results in higher free radical production, increased macromolecular oxidative damage, and cellular senescence [10]. Changes in the rate of metaboism are dynamic, weight loss and energy restriction affect the component of energy expenditure. Total daily energy expenditure has been shown to consistently decrease with weight loss. Weight loss occurs at a loss of metabolically active tissue, so that the basal metabolic rate decreases [11, 12].

D-galactose is widely used as an inducing reagent for animal models of aging and aging was associated with physiopathological processes in the body [13, 14]. D-galactose not only has an aging effect, but also an effect on heart damage that causes

dysfunction [15], skin aging [16], male reproductive system, decrease in sperm count and increase the ratio of immotile and abnormal morphological sperm [17], bone mass loss [18], liver damage [19], increase lipid peroxidase and decrease Superoxide dismutase (SOD) activity. So, the aim of the study was to determine the effect of dgalactose in reducing weight gain significantly.

MATERIALS AND METHOD

Ethical Approval

1. This study has been approved by the Ethical Committee with the reference number 0023/EC-FKH/Int./2020 of the Universitas Gadjah Mada.

Experimental Animal

2. Thirty healthy male Wistar rats 200-250 grams were used in this study. For one week of Feed and environmental adaptation, rats were fed with basal feeding and ad libitum drinking water. Rats were divided into 2 groups, control groups (n = 15) and D-galactose treated groups (n = 15). Control group was treated with aqua sterile as placebo, while D-galactose group was treated with 3 mg/kg BW of D-Galactose orally every day for 6 weeks. The rats in both groups were measured using digital weigher every week. The data were analyzed descriptively for the average of body weight (g) each week and statistically for the average of weight gain (%) after 6 weeks using t-test.

RESULT AND DISCUSSION

The results show in Table 1 below was the body weight for six weeks in the treatment group and the control group.

Table-1: Weighing the body weight of the rats (g) every week in the control group and the treatment group

	W	R1	R2	R3	R4	R5	R6	R7	R8	R9	R10	R11	R12	R13	R14	R15
C	0	136	135	126	94	98	109	114	124	95	120	122	150	135	111	115
	1	165	168	143	118	112	139	139	169	112	159	143	170	155	127	142
	2	191	192	160	115	120	165	165	190	130	179	160	195	134	133	166
	3	213	178	157	120	129	182	178	201	145	202	167	212	151	146	163
	4	234	161	163	135	136	170	198	208	167	227	170	228	146	160	181
	5	250	177	191	142	155	204	207	240	168	238	191	235	193	177	182
	6	262	196	202	151	172	224	220	256	178	248	198	232	205	184	191
T	0	139	144	150	135	119	132	116	140	106	106	144	130	127	114	130
	1	166	165	163	161	142	163	138	157	132	124	176	160	145	126	154
	2	184	165	195	163	160	176	159	173	148	140	196	177	168	95	156
	3	183	159	212	142	185	161	176	180	160	160	203	193	178	110	189
	4	190	178	226	146	195	200	193	192	168	160	188	195	194	110	191
	5	187	196	228	157	208	202	214	201	180	192	206	195	208	121	189
	6	180	199	248	175	208	216	221	213	181	195	206	200	198	127	187

C= Control; T= Treated; R= Rat

The results showed that in the control group and treated group, the body weight had increased continuously until the end of the week. The average body weight of the rats increased every week in the control group and the treated group.

The average body weight each week could be seen in Table 2 below.

Table-2: Average body weight (g)

	Control	Treated
Week 0	119 ± 16.24	129 ± 13.92
Week 1	144 ± 20.24	151 ± 15.94
Week 2	160 ± 27.37	164 ± 24.63
Week 3	170 ± 29.08	173 ± 25.37
Week 4	179 ± 32.79	182 ± 27.15
Week 5	197 ± 32.37	192 ± 25.55
Week 6	208 ± 32.07	197 ± 26.78

From the calculation of the average body weight of rats each week, it could be seen that the control group and the treatment group had increased. However, the weight gain in the control group was higher than the treatment group.

The flow change of average body weight could be seen in Figure 1 below.

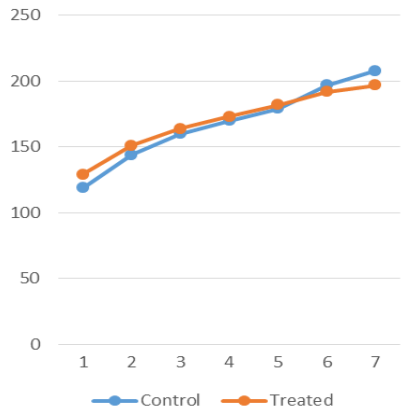

Fig-1: Illustration of average body weight

In the flow changes of body weight, there were a difference body weight gain between the control group and the treatment group. This difference could be seen from the two lines in the image. In the picture showed that the blue line at the end of the week was higher than the orange line.

The weight gain of rats could be seen in Table 3 below.

Table-3: Body Weight Increased (%)

	Control	Treated
Rat 1	45.18	11.4
Rat 2	51.85	29.49
Rat 3	54.66	29.62
Rat 4	60.31	38.19
Rat 5	60.63	43.05
Rat 6	62.29	43.84
Rat 7	65.76	52.14
Rat 8	66.08	53.84
Rat 9	75.51	55.9
Rat 10	87.36	63.63
Rat 11	92.64	65.33
Rat 12	92.98	70.75
Rat 13	105.5	74.78
Rat 14	106.45	83.96
Rat 15	106.66	90.51
Averge	75.59±21.19	53.762±21.79

From the calculation of the average weight gain, it can be seen that the treatment group has a lower average body weight gain than the control group. Statistical analysis using t-test showed that there was a significant difference in the mean weight gain in the two groups P= 0.026534911 (<0.05).

In this study, D-Galactose was shown to reduce body weight. This could be seen from the average weight gain that decreases over time. Excess D-galactose in the body will be reduced by galatose reductase and produce galacticol which causes osmotic stress. Eexcess D-galactose would also cause an oxidation process initiated by galacto oxidase and produces hydrogen peroxide. High hydrogen peroxide caused a decrease in Superoxide dismutase (SOD) [20].

Superoxide dismutases (SODs) were metalloenzymes that were found in all kingdoms of life. SODs form the first line of defense against reactive oxygen species (ROS)-mediated injury [21]. SOD was a very important antioxidant defense against oxidative stress in the body [22]. Several studies revealed the therapeutic potential and physiological importance of SOD [23]. SOD was the main antioxidant in cells responsible for eliminating oxygen. Many studies had revealed the important role of oxidative stress in carcinogenesis [24, 25]. There was some clear evidence showing that ROS acted as an endogenous carcinogen by inducing mutations in cells [26-28].

In addition, Galactose initiates non-enzymatic glycation reactions. After weeks to months, resulting in advanced glycation end products (AGEs). AGEs will react with its receptors (RAGE) and produce ROS. ROS was a collective term that includes radical (hydroxyl radical, OH, or superoxide O_2) and non-radical (hydrogen peroxide, H_2O_2) derivatives of oxygen[29]. ROS is produced through activation of NADPH oxidase [20]. Activation of glucose mitochondrial oxidative metabolism will cause an increase in oxidative stress so that ROS will be formed [30]. Many studies have found that ROS is involved in weight control by exerting different effects on hypothalamic neurons. This results in satiety and controlled hunger behavior [31].

ROS also have implications for the long-term consequences of hunger and satiety. For example, the fact that satiety is associated with the highest level of ROS production in the hypothalamus indicates that proopiomelanocortin (POMC) cells are more exposed to ROS-induced damage than neuropeptide Y/Agouti-related protein (NPY/AgRP). NPY/AgRP neurons, which do not produce elevated ROS levels even if highly active. Thus, it is not unreasonable to anticipate that over time, POMC neurons might become impaired, a process that is in line with the declining ability of animals and humans to lose weight as they become older [32]. An elevated ROS production also has an autoregulatory effect on POMC neurons, further increasing their activity. These cellular events act to suppress feeding behavior and decreasing further food intak [33].

CONCLUSION

Giving D-Galactose to aging animal models could reduce weight gain.

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