

## Effects of ginseng powder in aging rats

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## Abstract

The survival ratio in aging male rats given 0.1% or 1.0% ginseng and aging female rats given 0.1% ginseng was clearly higher than in untreated control rats, and similar changes were noted in the survival function. No remarkable changes in body weight were recognized. However, extremely aggressive behavior was observed in all rats given ginseng, and the animals showed significantly greater hair loss and changes in their setae.

**Key words** aging, ginseng, survival ratio, survival function, rat

## Introduction

In recent years, research on aging has rapidly advanced in a wide range of fields from the molecular level to studies on organs, blood vessels, nerves and the whole body, and further investigations are now actively in progress. On the other hand, although crude herbal drugs have been empirically classified into three groups, *i.e.*, upper, middle and lower medicines, upper medicines being ascribed tonic properties promoting perpetual youth and longevity, this has not been scientifically demonstrated. Ginseng, a representative upper medicine, was prescribed in the first ancient Chinese textbook of medicines, "Shen-Nong-Ben-Cao-Jing (神農本草經)" (considered to have been compiled in the Late Han Dynasty), and described as having antidotal, life-supporting, body-lightening, activating, perpetual youth-inducing and life-prolonging actions.<sup>1)</sup> In the present study, as a basic investigation of a crude drug in relation to aging, changes in body weight and the possibility of life-prolonging effects were investigated in rats given ginseng.

## Materials and Methods

Male and female (quadripara) Wistar rats were raised on pellet chow containing 0.1% or 1.0% ginseng powder (produced by mixing ginseng with CE-7, manufactured by CLEA Japan Inc., Tokyo, Japan) from 52 weeks after birth. Each group was composed of 30 rats. Food and water were given *ad libitum*. The animals were raised in a temperature- and humidity-controlled room ( $22 \pm 1^\circ\text{C}$ ,  $65 \pm 5\%$ ) with light cycles of 12 hr on (6 : 00 a.m. to 6 : 00 p.m.) and 12 hr off (6 : 00 p.m. to 6 : 00 a.m.). Ginseng powder (produced by the Monopoly Agency of the Republic of Korea) was supplied by Nikkan Korai Ninjin Co., Ltd., Kobe, Japan. The body weight of each rat was recorded every month, and the survival function was calculated according to Colton's formula.<sup>2)</sup>

## Results

*Changes in body weight and behavior*

Observation of changes in body weight from 52 weeks after birth revealed that male control rats maintained their initial weight, about 460 g,

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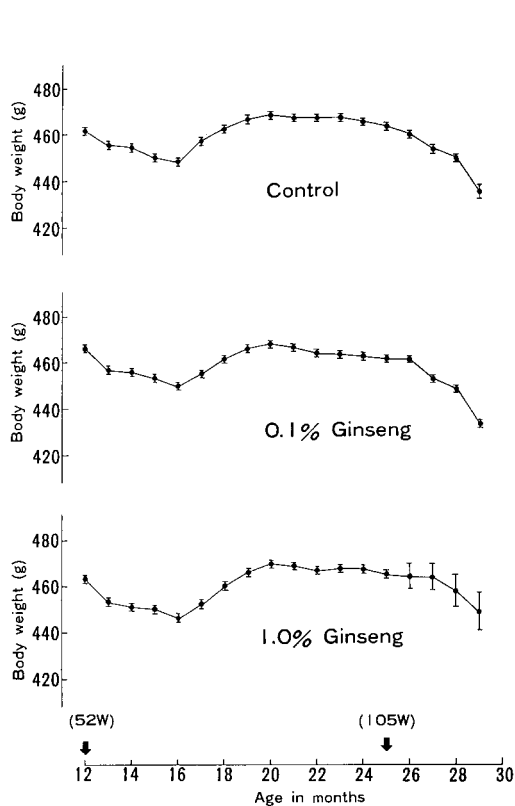


Fig. 1 Body weight in male rats.

until around 105 weeks after birth, thereafter showing a decreasing tendency. Similar findings were obtained for male rats given 0.1% or 1.0% ginseng (Fig. 1). As shown in Fig. 2, quadripara female rats weighed about 330 g at 52 weeks, being about 130 g lighter than male rats of the same age. This was probably the result of their previous four deliveries. There was a gradual increase in body weight until 85 weeks of age in both female control rats and those given ginseng; the weight reached about 370 g in controls, 390 g in rats given 0.1% ginseng, and 380 g in rats given 1.0% ginseng, showing a slightly greater increase among rats given ginseng. Thereafter, the weights in the three groups of female rats fluctuated at around the levels obtained at 85 weeks. Extremely aggressive behavior was observed in all rats given ginseng, and the appearance of their fur coat differed from that in control rats, showing significantly greater hair loss and

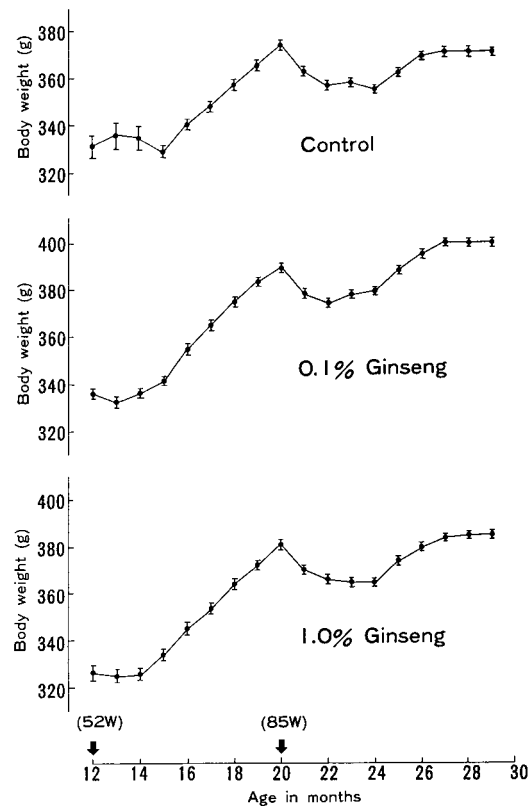


Fig. 2 Body weight in female rats.

changes in the setae.

#### Survival ratio

As shown in Fig. 3, male control rats began to die at 68 weeks, showing 50% survival at 104 weeks. Among rats given 0.1% ginseng, death occurred from 74 weeks after birth, showing survival ratios similar to those of the controls until 114 weeks, after which an obvious life-prolonging effect was observed among them. A similar life-prolonging effect was also found in rats given 1.0% ginseng. Effects on female rats are shown in Fig. 4. Death occurred among female control rats from 80 weeks, but they showed a survival ratio of 63% even at 120 weeks (the end of the experiment), exhibiting marked longevity as compared with male control rats. Although female rats given 0.1% ginseng also revealed a similar trend until about 110 weeks, 80% of them were alive at 120 weeks, showing a survival ratio higher than that for control rats. Among female rats

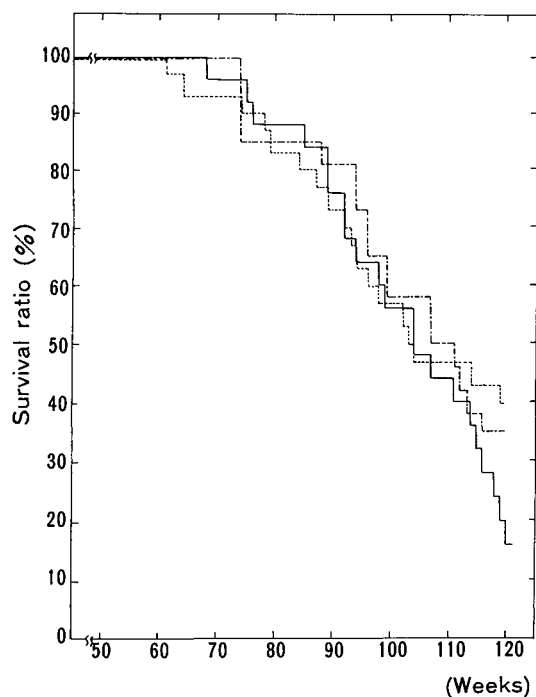


Fig. 3 Survival ratio in male rats.  
—, Control rats ; - - -, 0.1% ginseng-administered rats ; ·····, 1.0% ginseng-administered rats.

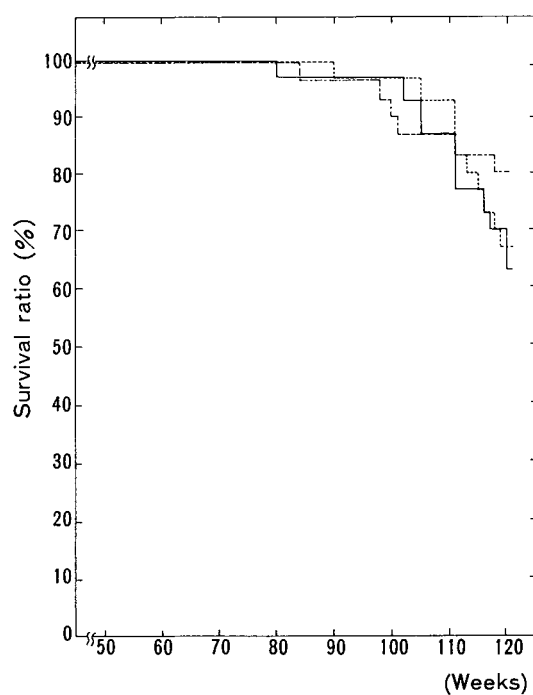


Fig. 4 Survival ratio in female rats.  
—, Control rats ; - - -, 0.1% ginseng-administered rats ; ·····, 1.0% ginseng-administered rats.

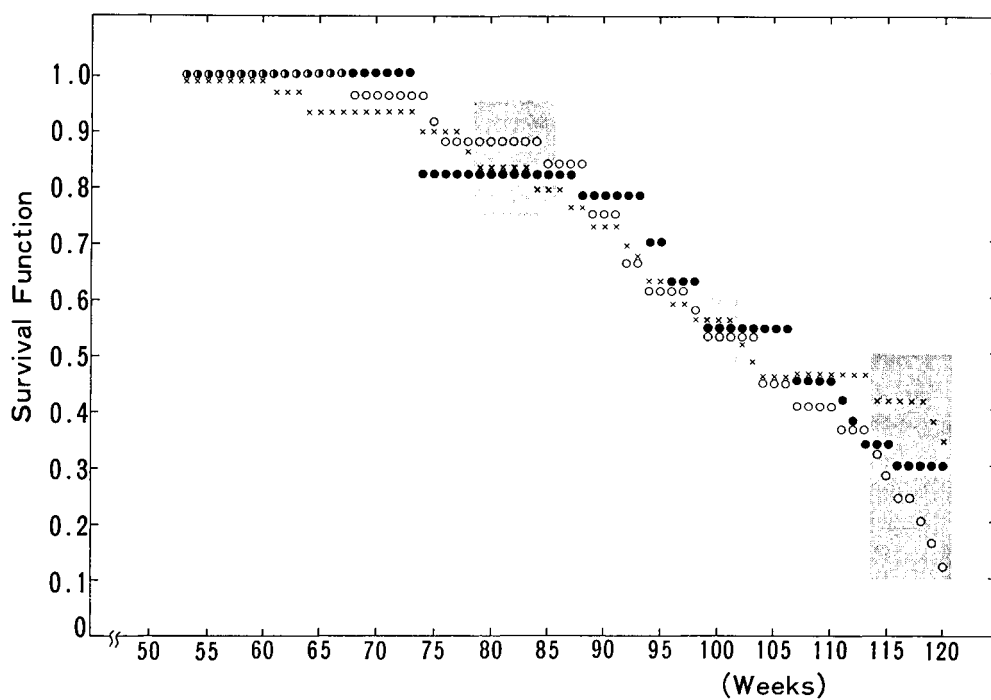


Fig. 5 Survival function in male rats.  
○, Control rats ; ●, 0.1% ginseng-administered rats ; ×, 1.0% ginseng-administered rats.

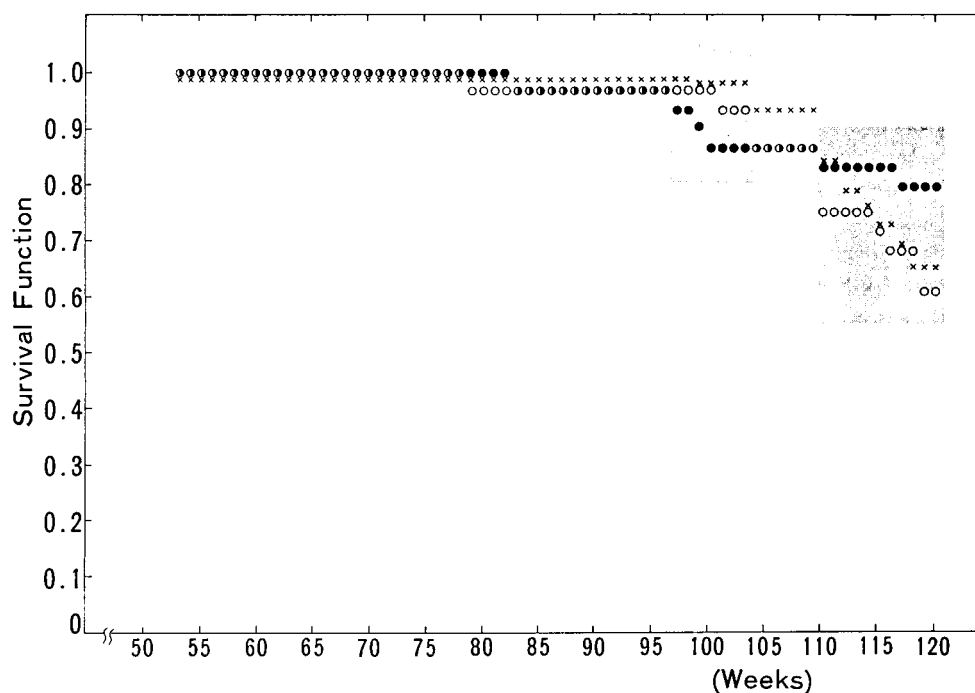


Fig. 6 Survival function in female rats.

○, Control rats ; ●, 0.1% ginseng-administered rats ; ×, 1.0% ginseng-administered rats.

given 1.0% ginseng, however, the results were almost the same as those obtained with controls, showing no such life-prolonging effect as that observed among female rats given 0.1% ginseng.

#### Survival function

As shown in Fig. 5, the survival function for male control rats decreased with lapse of time, showing a pattern similar to that of the survival ratio. On the other hand, male rats given 0.1% or 1.0% ginseng showed lower survival functions than those for controls in the first half of the administration period (at 79–85 weeks), but the values became higher than the control level after 114 weeks. At the 120th week, the survival function was determined to be 0.122 in control rats, while significantly higher values of 0.301 in the 0.1% ginseng group and 0.345 in the 1.0% ginseng group were obtained. The survival function was also lower in female rats given 0.1% ginseng than in controls at 97–103 weeks, but the value exceeded the control level after 110 weeks, as shown in Fig. 6. In contrast, there was no significant difference in the survival function

between female rats given 1.0% ginseng and female control rats.

#### Discussion

Among the effects of ginseng, tonic, robust, hemopoietic, stomachic, temperature-maintaining, fatigue-eliminating, ataractic and sedative actions have been cited.<sup>3)</sup> In modern Chinese medicine, ginseng is used for cases of insufficient vital force among cases of decreased general physiological condition.<sup>4)</sup> Because of its action of supplying vital force, promotion of general metabolic function is expected in cases of decreased energy or general function. Since the 1970s, when Oura *et al.* found that an extract of ginseng promoted biosynthesis of ribonucleic acid and protein,<sup>5-10)</sup> various studies have been carried out, ranging from the organ level including the liver, kidney, adipose tissue, adrenal gland and bone marrow, to the cellular level including hepatocytes, marrow cells, spermatids and fat cells and extending to cultured cells such as hepato-

ma cells, as reported by Igarashi, Okuda, Odashima, Kumagai, Saito and Yamamoto *et al.*<sup>11)</sup> The effects of ginseng on cellular metabolism and proliferation have been actively studied from various aspects. However, these experiments have focused on the effects produced during a period of several hours to weeks in young animals. In this regard, the present study used a different approach by investigating the effects of ginseng on the process of aging. Noticeable effects appeared at 110 or 115 weeks after birth, and the survival ratios of male rats given 0.1% or 1.0% ginseng were 35% and 37%, respectively, at 120 weeks, which were double the control level. Among female rats, a survival ratio of 80% was obtained for those given 0.1% ginseng, whereas the corresponding ratio for controls was 63%. Similar phenomena were observed with regard to the survival function. Also, female rats generally lived longer than male rats. Thus, an evident life-prolonging effect of ginseng was found in all rats excluding female rats given 1.0% ginseng. The mechanism of this effect remains to be elucidated. However, the authors previously demonstrated that ginseng saponins, especially ginsenoside-Rb<sub>2</sub>, promote or improve the *in vivo* metabolism of sugar, lipid and nitrogen.<sup>12-21)</sup> Shia *et al.*<sup>22)</sup> investigated the effects of ginseng saponins on fibroblasts from senile human and demonstrated a promoting effect on the glycolytic system, with evidence of an increase in phosphohexose isomerase and lactate dehydrogenase activities. These actions would seem to contribute to an increased life-prolonging effect. On the other hand, female rats given 1.0% ginseng showed a survival ratio or survival function similar to those of control rats, unlike the case in rats given 0.1% ginseng. Preliminary experiments have provided findings suggesting the presence of a lipid metabolism-improving action (decreased triglyceride, low-density lipoprotein-cholesterol and very-low-density lipoprotein, and increased high-density lipoprotein-cholesterol in serum) in rats given 1.0% ginseng for 150 weeks. From these results, it might be expected that alterations in the life-prolonging effect would be produced by several possible factors, including

the dose, time and period of ginseng administration. Although detailed investigations into the causes of death will be necessary to help clarify the pathology of longevity, previous experiments have suggested that in both controls and female rats given 1.0% ginseng, pneumonia, malignant tumor and pituitary adenoma were dominant causes of death, accounting for 80% of total deaths. The dominance of these conditions was more marked with increased age, closely resembling the pattern of death related to aging in humans. There were also some deaths due to general organ congestion. About 50% of control rats had tumors, which included pituitary adenoma and malignant tumors such as osteosarcoma, hepatoma, hemangiosarcoma, myosarcoma and malignant lymphoma; benign mastadenoma was frequent among female rats. In the groups of rats given 1.0% ginseng, about 35% had tumors, the incidence being slightly suppressed in comparison with controls.<sup>23)</sup>

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### 和文抄録

老化による和漢薬作用の基礎研究として、薬用人参投与ラットの生存率並びに生存関数について検討した。雄性ラットの0.1%と1.0%人参投与群、雌性ラットの0.1%投与群において対照群に比し明らかに延命作用が認められた。体重変化は対照群と人参群で著しい差異を認めなかったが、人参群では全例に極めて攻撃的な症状が観察され、毛並みも対照群と異なり、脱毛がやや多く、剛毛となる特徴が観察された。

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