

EFFECT OF "βCATECHIN" ON THE LIFE SPAN OF SENESCENCE ACCELERATED MICE (SAM-P8 STRAIN)

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SUMMARY

"βCATECHIN", a preparation of natural vitamins and phytochemicals, has been designed as an 'universal antioxidant' drink. Having previously demonstrated the scavenging action of a variety of free radicals by "βCATECHIN", we now report the effect of its long term administration on the life span of senescence accelerated mice (SAM-P8), a murine model system that offers many characteristics of mammalian aging with a shortened life span. Both male and female SAM (age: 10 weeks) maintained on "βCATECHIN" containing drinking water (1ml/kg b.w) showed significant extension of the mean life span as compared to their respective controls that received normal drinking water. Results show that administration of "βCATECHIN" increased the 50% mean survival rate by 8 weeks in case of female, and 7.5 weeks for male SAM. In addition to offering fresh evidence to the "free radical theory of aging", the results emphasize on the importance of a daily supplement of natural antioxidants, especially as a combination, to achieve the goal of a long and disease-free life.

KEY WORDS

catechin, natural antioxidants, anti-aging, SAM-P8, free radical scavenging, life span enhancer.

INTRODUCTION

Recent reports have reviewed aging as an accumulation of deleterious changes initiated by free radicals, a process that increases with age and determines the life span of an organism (1-5). However, some factors like dietary restriction (6), injection of spin traps like N-tert-α-phenyl-butyl nitron, PBN (7-8), chelating agents like phytic acid (9) and administration of antioxidant nutrients (10-11), have been reported to

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modulate life span and the incidence of certain age-related diseases via inhibiting the free radical mediated injury. Recently, natural antioxidants and other preparations of plant origin are increasingly gaining importance as potential anti-aging agents.

" β CATECHIN" has been designed as a model "universal antioxidant" drink, containing a combination of natural vitamins and phytochemicals. Our earlier report (12) demonstrated that " β CATECHIN" could inhibit the formation of thiobarbituric acid substances (TBARS) and increase the superoxide dismutase (SOD) activity in the iron-injected epileptic foci of rat cortex. In the same report, using specific spin traps and electron spin resonance spectroscopy (ESR), we demonstrated strong scavenging activity of 1,1-diphenyl-2-picrylhydrazyl (DPPH) radicals, superoxide and hydroxyl radicals by " β CATECHIN". In another ESR study, we observed that " β CATECHIN" could completely scavenge all the reactive oxygen species generated simultaneously during the oxidative photosensitization of riboflavin (13). Having demonstrated its strong scavenging action on a variety of free radicals, we examined the effect of long term administration of " β CATECHIN" on the life span of senescence accelerated mice (SAM), the prone strains of which, offer excellent models to study age-related changes, owing to their shortened life span and early manifestation of various signs of senescence similar to humans.

MATERIALS AND METHODS

Animals

Senescence accelerated mice (SAM-P8 strain) developed by Takeda *et al* (14) were kindly provided by the Kyoto University and were maintained in our animal facility under conventional conditions (25°C; humidity : 55%; 12hr light /12hr dark cycle). After acclimatization, the animals (10 weeks old) were randomized into two groups (Group A: 8 male + 11 female and Group B: 9 male+ 10 female). While, Group A (Control) animals received normal drinking water, those of Group B, received " β CATECHIN" containing water (1ml/kg b.w/day; comparable to human consumption level). The animals had free access to water and a standard diet (Oriental Yeast Co., Ltd., Tokyo, Japan), were weighed periodically and were allowed to die naturally.

" β CATECHIN"

" β CATECHIN" drink (50ml/bottle) used in the study was obtained from Sky Food Co., Ltd., Osaka (Japan).

RESULTS AND DISCUSSION

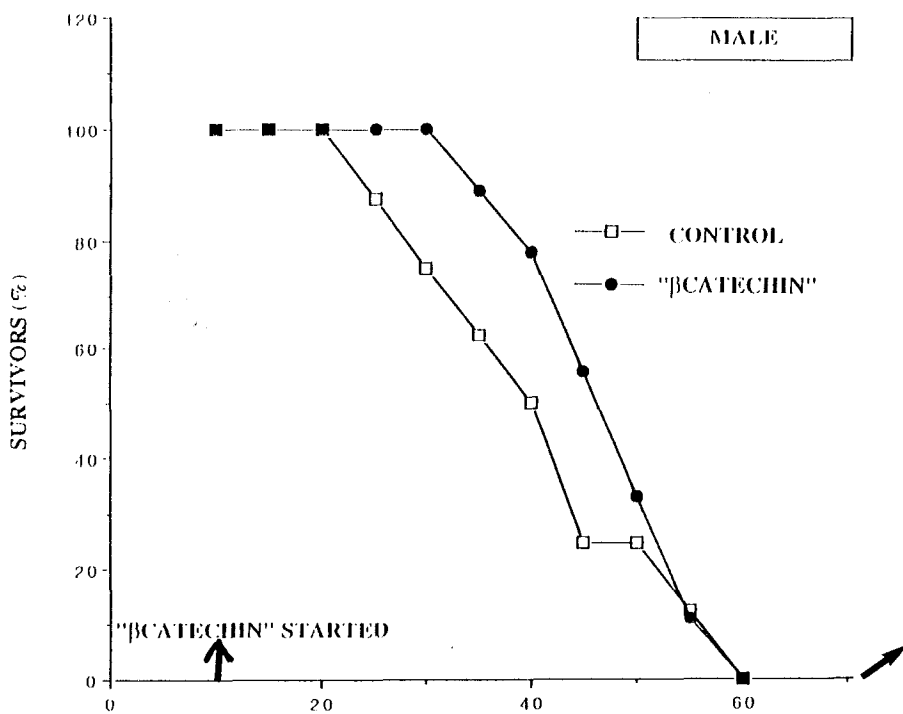
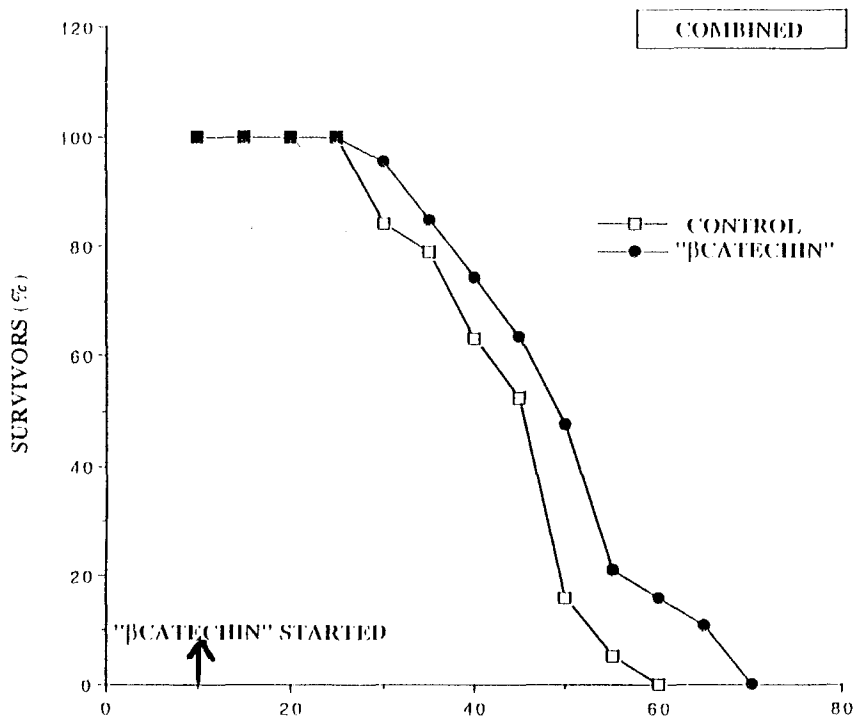
Figure 1 depicts the effect of " β CATECHIN" administration on the life span of male and female SAM. The calculated mean of 50% survival rate, in case of male SAM was 40 weeks for the control group, while that of the " β CATECHIN"

administered animals was 47.5 weeks. The female SAM receiving "βCATECHIN" treatment showed 59 weeks as mean of 50% survival rate, while that of their respective control SAM was 51 weeks. Our data depicts that the 50% mean survival rate of female SAM was over 11 weeks longer than the male SAM. This difference between the sexes was found to persist even in the "βCATECHIN" treated animals. Although inbred mice are genetically homogenous, there are often considerable variations in their biological life spans and hence data from the two sexes was analyzed individually as well.

A wide variety of antioxidants, via inhibiting the free radical reactions, are shown to enhance the life span in various model systems (10-11). Intraperitoneal administration of spin trap PBN has been shown to prolong the life span of SAM (7) and to reverse the age-related changes in gerbil brain (8) only at chronic levels. Other synthetic antioxidants like butylated hydroxy toluene (BHT), that could inhibit free radical reactions become toxic beyond certain levels (15). Hence, natural antioxidants and dietary supplements are being focused on as potential life span enhancers. Many herbal medicines and preparations of natural plant extracts, Toki-shakuyaku-san: TJ-23 (17); Sho-saiko-to-go-keishi-ka-shkuyakuto: TJ-960 (16) and ginseng root extract (18), that could inhibit lipid peroxidation and free radical reactions, are shown to inhibit age-related changes as well.

"βCATECHIN" has been designed as an antioxidant drink, containing ascorbate, green tea extract, dunaliella carotene, vitamin E and sunflower seed extract. The combination has been aimed at counteracting both water soluble and the lipid soluble free radicals. Our previous experiments (12-13) confirmed the universal scavenging activity of this preparation.

Significant elevations in the biochemical parameters, such as the malondialdehyde content, SOD activity along with a decrease in the endogenous glutathione content, have been reported in the tissues of SAM-P8 strain (19) and in other aging murine models (20). These changes are considered as consequences of the endogenous accumulation of free radicals with age. In fact, a positive relationship between antioxidant concentration in mammalian tissues and their life span has long been established by Cutler (11). Our previous work demonstrated an increase in the SOD activity and inhibition in the TBARS formation in the iron-induced epileptic foci of rat cerebral cortex by "βCATECHIN" (10). Also, a four week administration of "βCATECHIN" to Wistar rats decreased the TBARS formation in hippocampus and cerebral cortex and the hepatic levels of phosphatidylcholine hydroperoxide (PCOOH), MDA and 4-hydroxynonenal (M.V. R. Kumari, unpublished data). These effects could



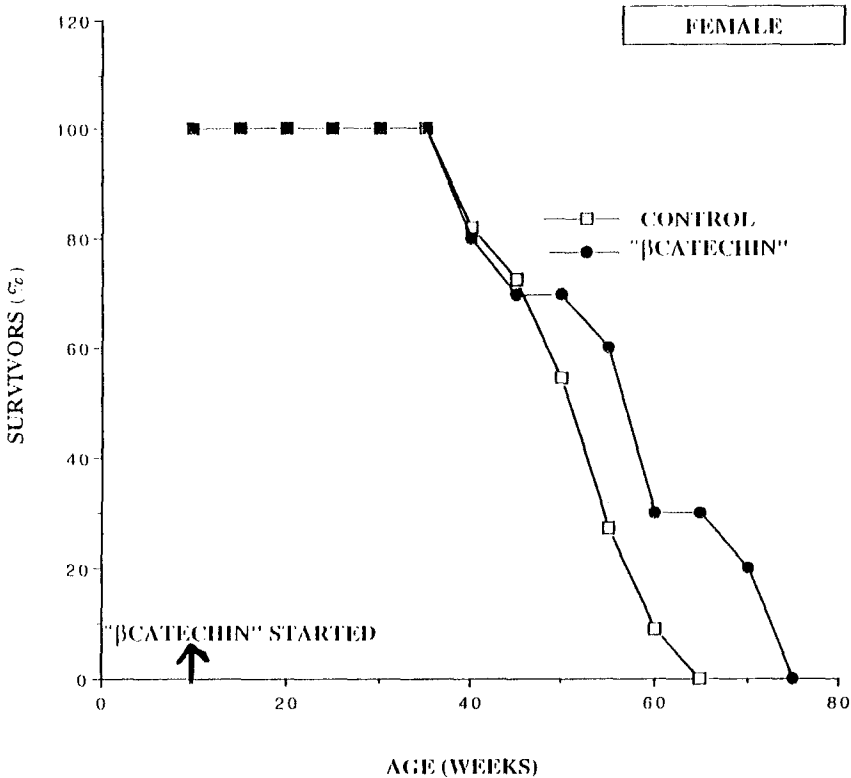


Figure 1. Effect of "βCATECHIN" administration on the life span of senescence accelerated mice (SAM-P8 strain)

probably be consequential to the direct free radical scavenging action of "βCATECHIN" (12-13).

The prolonged life span of SAM-P8 receiving "βCATECHIN" reported here, taken together with the data generated earlier, we suggest that the endogenous antioxidant defense pools of SAM receiving "βCATECHIN" treatment were relatively enriched (a) due to direct scavenging action of various components of "βCATECHIN" on the free radicals that could have otherwise attacked the intracellular targets, triggering aging and other free radical mediated diseases and (b) by protecting the intracellular antioxidants like glutathione and other thiols from depletion. These processes could have supposedly played a key role in the enhancement of life span of SAM maintained on "βCATECHIN". It would, therefore, be interesting to study the effect of "βCATECHIN" administration on other aging related processes and free radical mediated diseases.

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