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ABSTRACT

Cordyceps sinensis has traditionally been used in China as a strategy to combat aging. We have reported the effects of *Cordyceps sinensis* Cs-4 (Cs-4) a mycelia fermentation product of *C. sinensis*, in glucose-lipid-energy metabolisms, anti-fatigue, and endurance enhancement. In this study, we examined the effect of Cs-4 on lifespan extension and antioxidant status in mice. For the lifespan-extension study, 250 mice 12 months of age (both sexes) received either vehicle or Cs-4 (0.5, 1.0 or 1.5g/kg diet). Caloric intake was adjusted to match the levels for controls twice per week. Compared to controls, the Cs-4 dosage group's 75% survival time was extended 94-108 days, 50% survival time extended 10-66 days, 25% survival time extended 29-44 days, and 12.5% survival time extended 7-50 days (86 weeks so far; treatment continues). The Kaplan-Meier Survivor analysis revealed the extended lifespan and the reduced risks of death by Cs-4. The antioxidant activity was tested in mice (6 months old) that received 60 days of vehicle or Cs-4 (0.5, 1.0 or 1.5 g/kg diet) and a single dose of 11Gy ⁶⁰Co gamma-radiation on day 60. Compared to controls, Cs-4 prevented the depletion of plasma total thiol-groups, GSH and GSH-peroxidase, liver CAT, SOD, and GSH-reductase (p<0.05) caused by radiation exposure. Cs-4 also prevented the radiation-induced increases in liver protein carbonyls and 8-OHdG (p<0.05) observed in the control group. In conclusion, Cs-4 supplementation significantly improves the body's antioxidant capacity and extends the lifespan in mice, supporting the traditional anti-aging uses of Cs-4 in humans.

INTRODUCTION

- Cordyceps sinensis* is traditionally believed to have anti-aging activities and to promote longevity.
- C. sinensis* and its mycelia fermentation product *C. sinensis* Cs-4 have a broad spectrum of health benefits, including the therapeutic activities of improving cardiovascular, liver, lung, and kidney functions. (Zhu et al. J Altern Compl Med. 4:289-303, 429-457,1998)
- We reported the endurance enhancement and anti-fatigue properties of Cs-4 and the improvement of energy, glucose, and lipid metabolisms by Cs-4 in animals and humans. (Dai et al. J Altern Compl Med. 7:231, 2001; Zhao et al. J Altern Compl Med. 8:309, 2002; Xiao et al. Chin J Integrat Med. 10:187, 2004; Li et al. Chin J Clin Pharmacy 16:274, 2007; Li et al. Shanghai J Prevent Med. 20:367, 2008; Wang et al. 2008 Symposium Chin Assoc Med Mycol. pp157-164)
- The aim of this study was to test the lifespan-extension effect and antioxidant activity of Cs-4 in mice.



***Cordyceps sinensis* (Berk.) Sacc. 冬虫夏草**
(Collected from Qinghai-Tibetan plateau of China)

Isolation & Purification
Cs-4 (A fungal strain of *Paecilomyces hepiali* Chen et Dai)

Industrial Fermentation

***Cordyceps sinensis* Cs-4**

冬虫夏草
Cordyceps sinensis

LIFESPAN EXTENSION (STUDY 1)

METHODS

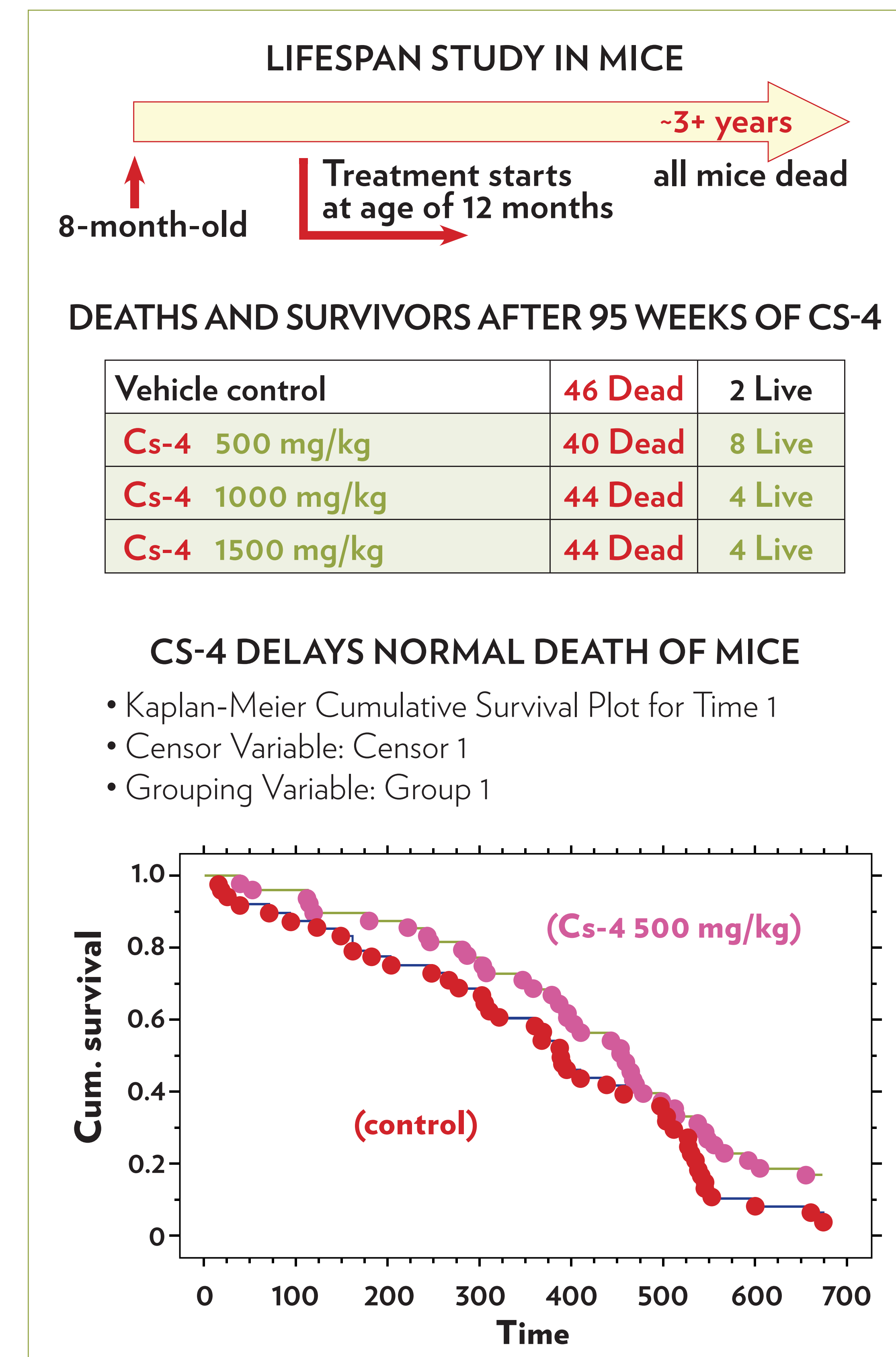
8-month-old mice fed normal chow until 12 months of age. At 12 months, mice were randomized into one of four groups matched for gender and weight.

GROUPS:

- Control: Normal mouse chow
- Treatment 1: Chow containing Cs-4: 500 mg/kg BW
- Treatment 2: Chow containing Cs-4: 1000 mg/kg BW
- Treatment 3: Chow containing Cs-4: 1500 mg/kg BW

DIET AND ENDPOINTS:

- Caloric intake of treatment groups was adjusted bi-weekly to match the intake of the control group
- Deaths recorded daily
- Lifespan study is ongoing



ANTIOXIDANT & BIOCHEMICAL STUDIES (STUDY 2)

METHODS

Mice were randomized into five groups and treated for 64 consecutive days by gavage. Mice received 11Gy ⁶⁰Co gamma-radiation on day 60 to induce oxidative stress and damage (except non-radiation control group). The study was completed on the fourth day and the liver and blood samples of all mice were collected and analyzed for antioxidant enzymes and biochemical markers of oxidative stress.

ANTIOXIDANT ENZYMES:

- Superoxide dismutase (SOD)*
- Catalase (CAT)
- Glutathione peroxidase (GSH-Px)
- Glutathione reductase (GSH-Rd)*
- Glucose-6-phosphate dehydrogenase (G6PD)*

*Data not shown

MARKERS OF OXIDATIVE STRESS:

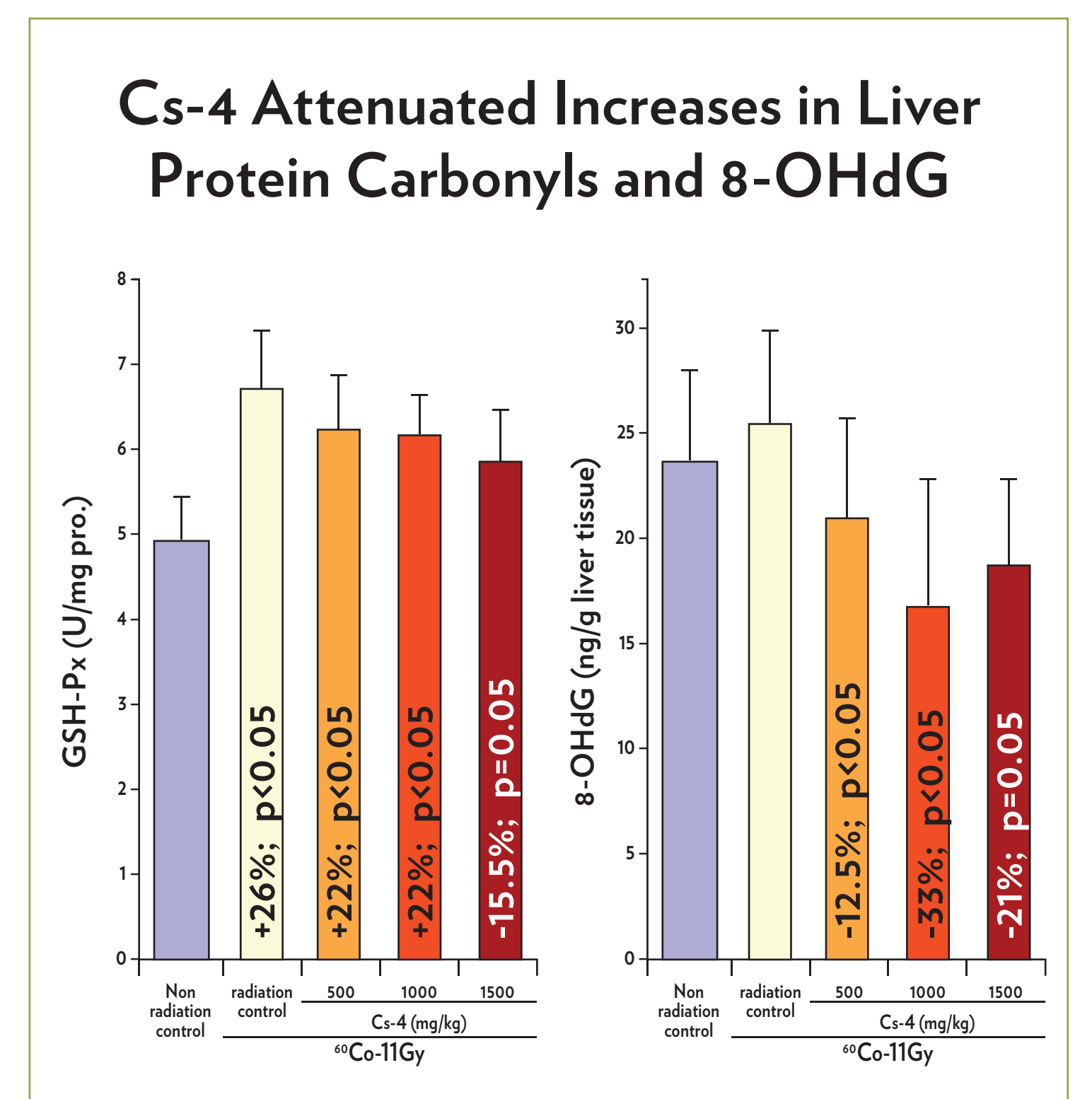
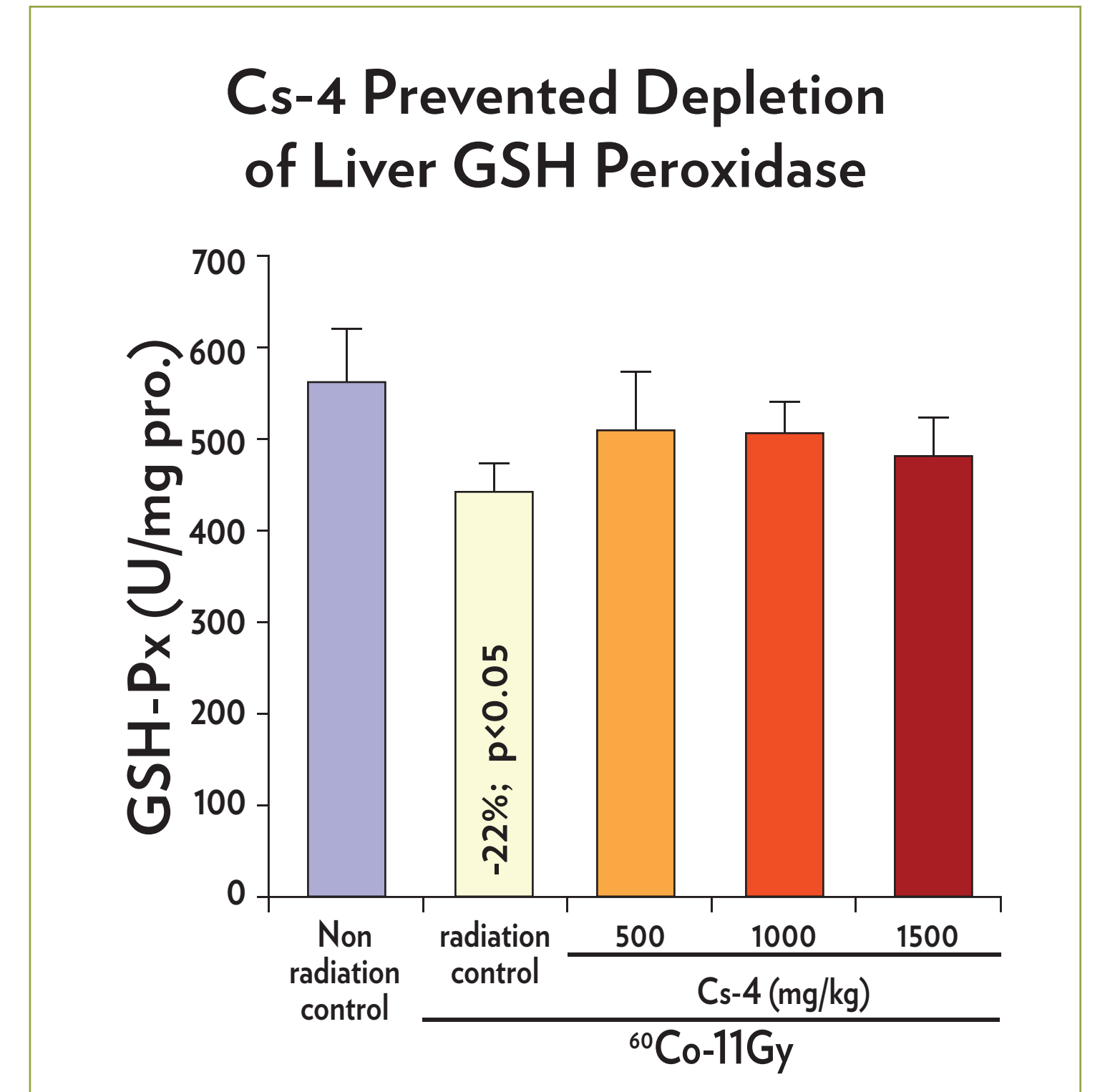
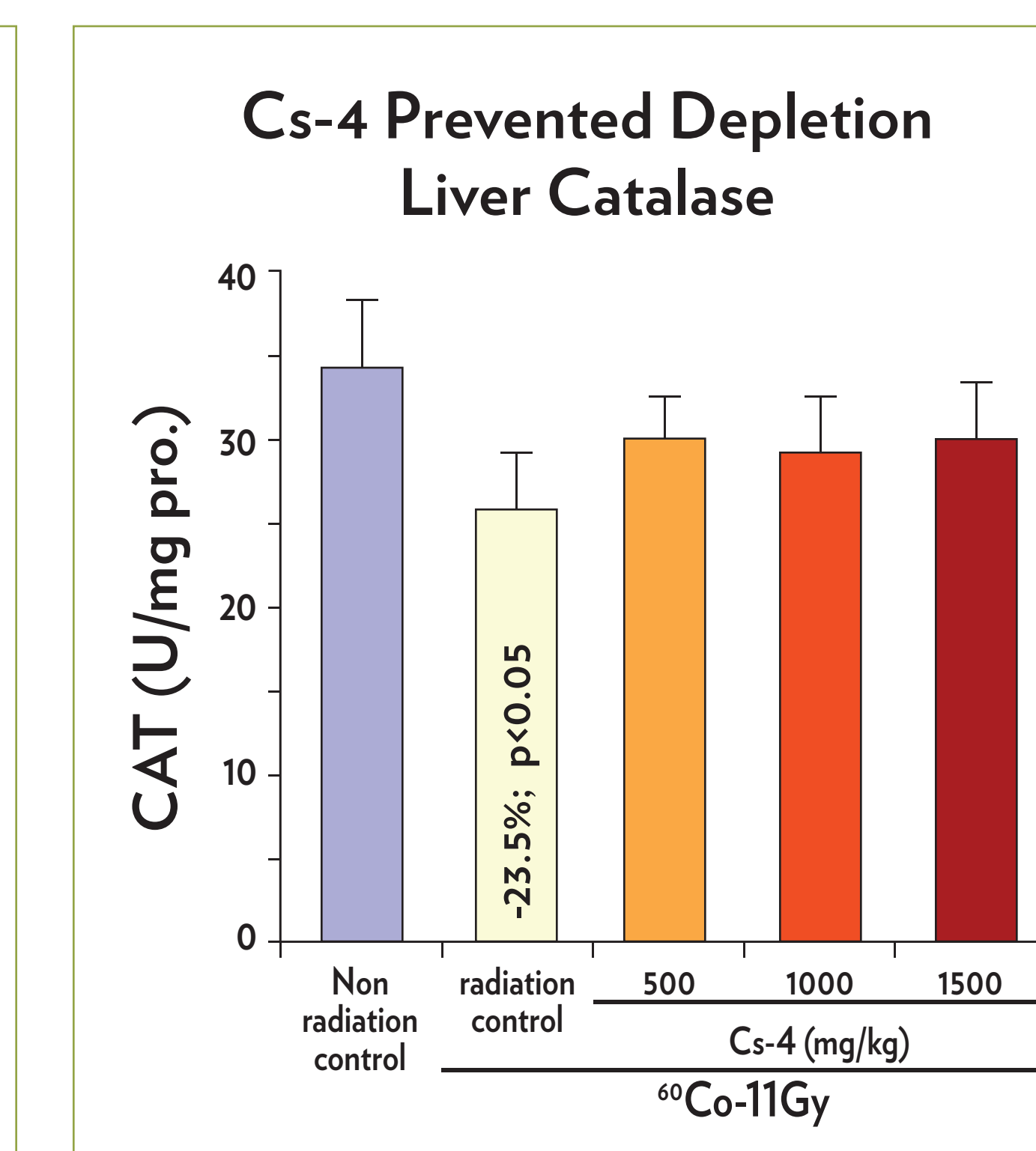
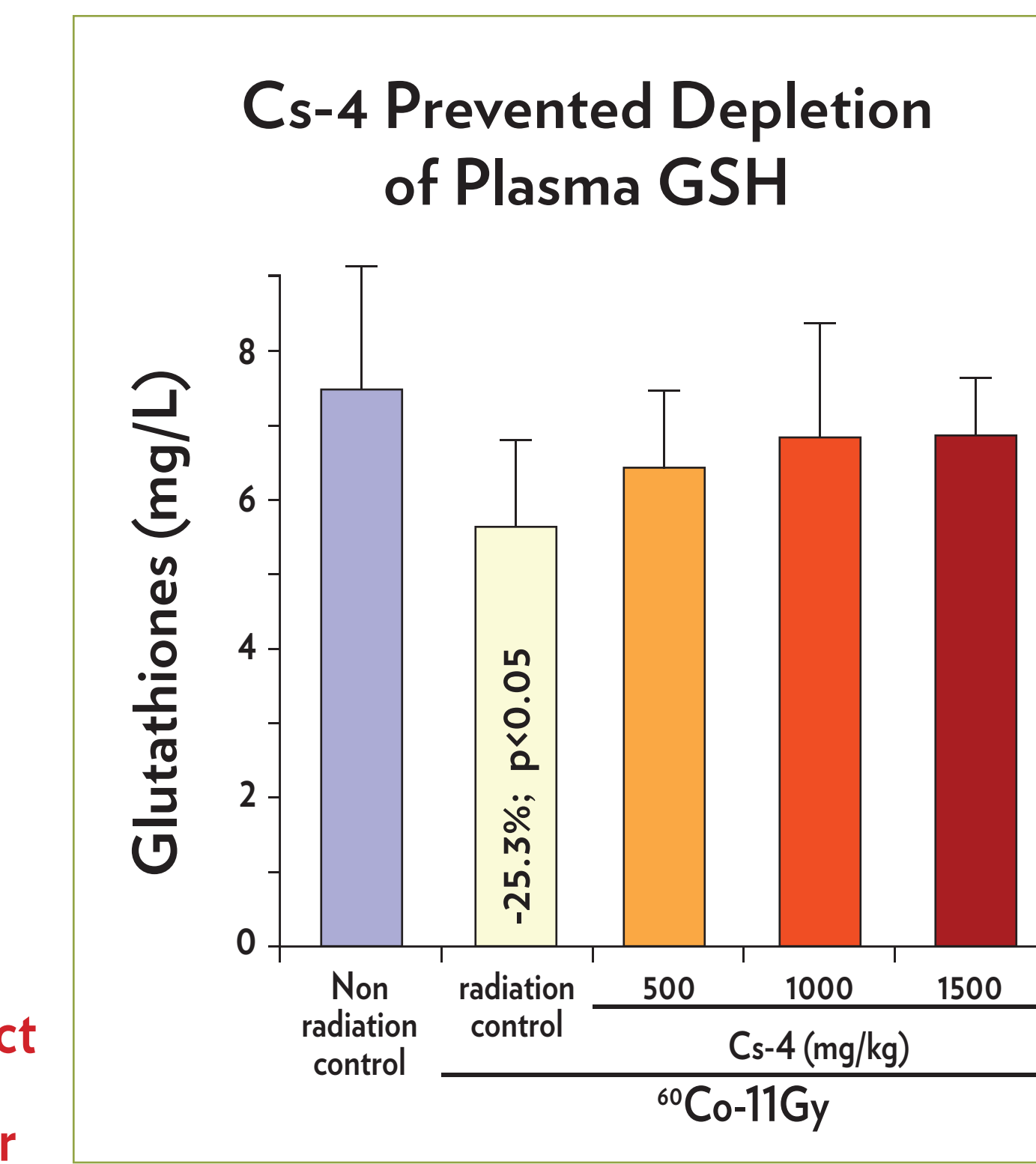
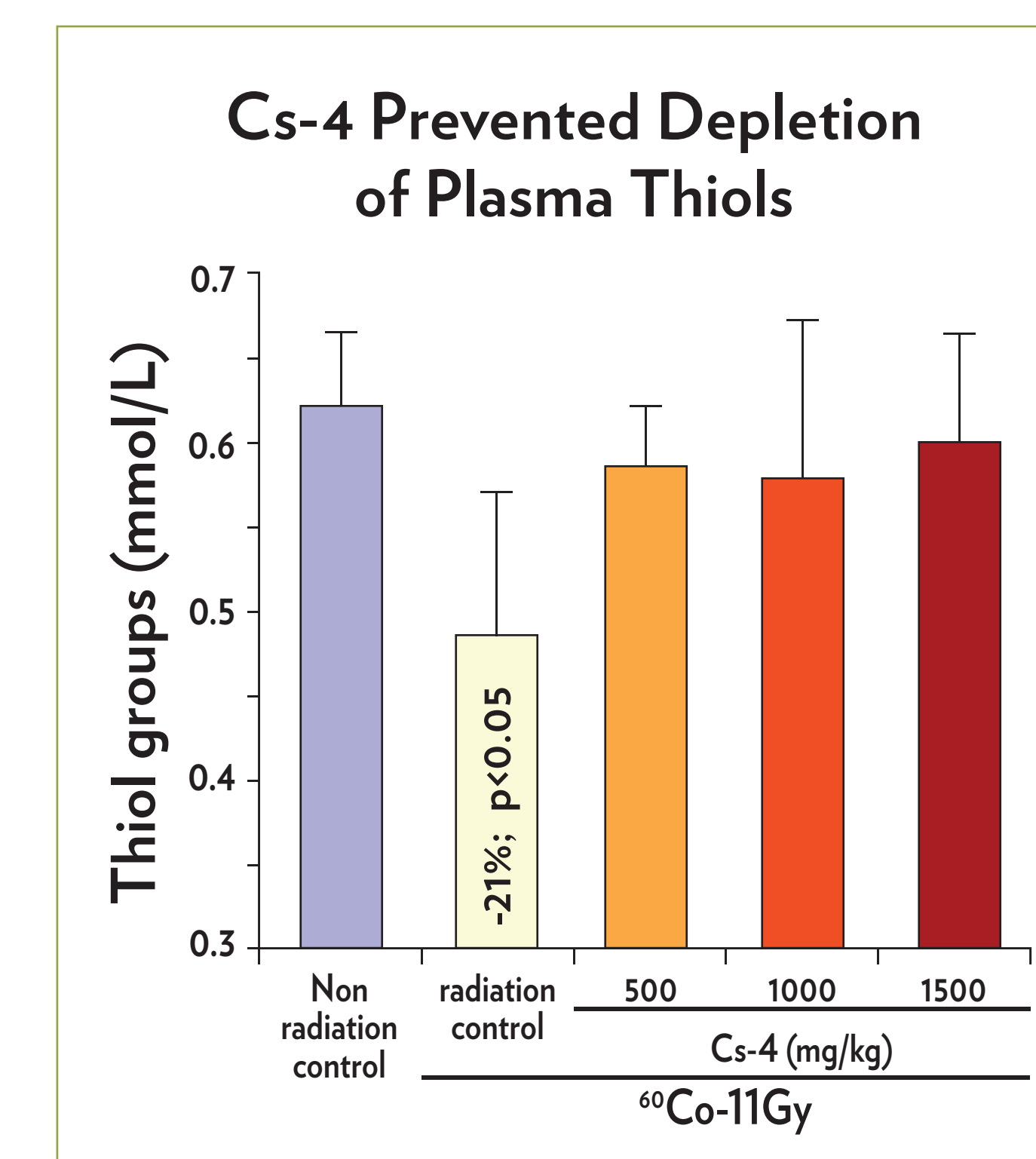
- Total thiol groups and glutathione
- Total protein carbonyl groups
- 8-OHdG in liver

Mice randomized into five groups:

Non-radiation control	(n=15)
Radiation control	(n=15)
Cs-4 500 mg/kg	(n=15)
Cs-4 1000 mg/kg	(n=15)
Cs-4 1500 mg/kg	(n=15)

0 (days) → 60 (days) → 63 (days)

⁶⁰Co (11Gy) → Collect blood & liver



SUMMARY & CONCLUSION

- Supplementation with *Cordyceps sinensis* Cs-4 prolongs lifespan in an aging mouse model.
- Cordyceps sinensis* Cs-4 supplementation increased antioxidant protection and reduced oxidative stress in mice exposed to radiation.
- Cordyceps sinensis* Cs-4 supplementation significantly improves the body's antioxidant capacity, protects against oxidative damage, and extends the lifespan in mice, supporting the traditional use of Cs-4 as an anti-aging strategy in humans.