

## **In vivo Evaluation of Novel Boron containing compound A-1 for BNCT**

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### **Abstract (447 words)**

**INTRODUCTION:** Boron neutron capture therapy (BNCT) is gaining attention as a state-of-the-art minimally invasive cancer treatment [1]. Up to now, clinical studies using boronophenylalanine (BPA) and sodium borocaptate (BSH) as <sup>10</sup>B delivery agents for neutron capture reaction have been conducted [2,3]. However, continuous administration of their high concentrations is needed to keep sufficient <sup>10</sup>B tumor concentration. Therefore, we have developed novel boron containing compound A-1, efficient in accumulation and retention in tumor.

**Materials and Methods:** After optimization of compound A-1, in vitro and in vivo study, 3x10<sup>6</sup> of mouse colon carcinoma (CT26) cells were injected in the right thigh of 5-week-old female Balb/c mice. Two weeks after injection tumor-bearing (avg. 360 mm<sup>3</sup>) mice were used in this study. Two dosage of boron containing compound A-1 (88.8 mg/kg with 24.1 mg[<sup>10</sup>B]/kg, n=5 and 250 mg/kg with 68.3 mg[<sup>10</sup>B]/kg, n=6) were administrated by tail vein injection 24 hours before irradiation. Fructose-BPA (500 mg/kg with 24.1 mg[<sup>10</sup>B]/kg, n=5) was administrated by tail vein injection 2 hours before irradiation as a positive control. Groups with irradiation only (n=4) and untreated mice (n=6) were used as controls.

The irradiation was performed with thermal neutrons with a flux of 1.8-4.0 x 10<sup>12</sup> neutrons/cm<sup>2</sup> over 1 hour at Kyoto University Research Reactor (KUR). The tumor size and body weight were measured in the period starting prior the treatment till 26 days after irradiation. And the tumor volume (mm<sup>3</sup>) was calculated as long diameter multiplied by the square of short diameter, and divided by 2.

**RESULTS:** The results of thermal neutron irradiation is shown in figure. The effect on body weight in all individuals was not found (a). The compound A-1 administrated group and BPA administrated group significantly suppressed the tumor growth as compared with other control groups (b). In particular, the compound A-1 (250 mg/kg) administrated group showed tumor growth inhibitory effect comparable to the BPA administrated group until 18th day.

**Conclusion:** We assume that compound A-1 is a candidate boron compound for further investigation that showed high accumulation in tumor even 24 hours after injection.

Fig. BNCT of tumor-bearing mice with  $^{10}\text{B}$ -enriched compounds A-1. (a) Mice body weight after thermal neutron irradiation. (b) Tumor growth ratio after 1 hour - thermal neutron irradiation ( $1.8\text{-}4.0 \times 10^{12}$  neutrons/cm<sup>2</sup>) with the injection of compound A-1 24 hours, and BPA 2 hours before irradiation, and irradiation only and untreated groups as controls. Comparison using the t-test was performed using mice 26 days after irradiation.

## REFERENCES

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