



others

### Lithium-Neutron Capture Therapy

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One of the most promising methods of target tumor elimination is boron neutron capture therapy (BNCT) which is based on the uptake of isotope  $^{10}\text{B}$  by cancer cells and the subsequent irradiation with an epithermal neutron beam. Particles from the  $^{10}\text{B}(n,\alpha)^7\text{Li}$  nuclear reaction are characterized by short-range and high linear-energy transfer and are restricted mainly to the tumor cell which leads to local damage of the tumor. In 93.9% of cases, nucleus  $^7\text{Li}$  is emitted in an excited state and emits a 478 keV photon, which takes away 16% of energy of the reaction.

Isotope  $^6\text{Li}$  also has a large thermal neutron absorption cross section and may be used instead of boron for neutron capture therapy (NCT). In the  $^6\text{Li}(n,\alpha)^3\text{H}$  reaction, only particles with a high linear-energy transfer are emitted: a tritium nucleus and an  $\alpha$ -particle, thus 100% of the energy is released in tumor cells containing lithium. The data accumulated to date on the pharmacokinetics of lithium allow to effective monitoring of lithium concentrations to prevent the development of side effects. According to theoretical calculations, the concentration of  $^6\text{Li}$  in the tumor required for the successful lithium-neutron capture reaction should be  $\geq 20 \mu\text{g/g}$ .

*In vitro* experiments showed that cytotoxicity of lithium salts was observed in lithium concentrations of 160  $\mu\text{g/ml}$  and more, thus, lithium salts can be safely used in lithium concentrations minimally required for successful NCT. ICP AES study revealed that lithium accumulation in cancer cells was higher than boron accumulation after incubation with lithium and boron containing drugs in concentrations of 40  $\mu\text{g/ml}$ .

*In vivo* experiments revealed the maximal lithium accumulation in the tumor in mice with skin melanoma B16 30 minutes after lithium carbonate administration at a dose of 400 mg/kg which was 22.4  $\mu\text{g/g}$ . The tumor/skin lithium concentration ratio at this time point was 1.5; tumor/blood ratio – 2. Thus, lithium uptake by tumor tissue was quite effective, furthermore, the single administration of high doses of lithium carbonate did not cause the structural changes in the kidney. The expression of protein markers of acute kidney injury Kim1 and NGAL was increased 30 and 90 minutes after an administration of lithium carbonate and was gradually decreased to the control values after 7 days. Thus, lithium carbonate may be used in future experiments in lithium neutron capture therapy.

Acknowledgments:

This research was funded by the Russian Science Foundation (grant number 19-72-30005).