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ORIGINAL PAPER

Determination of ^{10}B in lymphoma human cells after boron carrier treatment: comparison of ^{10}BPA and immuno-nanoparticles

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Current cancer treatments lead to insufficient distribution of therapeutic agents in tumor cells due to their lack of selectivity often causing adverse effects in the normal cell uptake of the drug. The challenge is to design therapeutic drugs able to maximize the treatment of malignant cancers while minimizing their adverse effects. In this study, ^{10}B incorporation in the B chronic lymphocytic leukemia cell line MEC-1 was investigated. The cells were treated with L-*p*-^{10}borophenylalanine (^{10}BPA) and ^{10}boron immuno-nanoparticles (BNPs) loaded with ^{10}BPA with or without the anti-CD20 monoclonal antibody for different contact times. The uptake of ^{10}B by the cells was determined by the inductively coupled plasma mass spectrometry (ICP-MS) after acid mineralization. To obtain accurate and consistent data, the analytical procedure was optimized using factorial experimental design. It was observed that BNP loaded with ^{10}BPA and anti-CD20 represents the best carrier system for ^{10}B in B cells for long time (> 10 h) whereas ^{10}BPA seems to be the top drug for short time (< 4 h) procedures.

Keywords: boron-10 carrier, immuno-nanoparticles, in vitro experiments, human tumour cells

Introduction

It is well known that boron neutron capture therapy (BNCT) is based on a nuclear reaction that occurs when non-radioactive ^{10}B is irradiated with low-energy thermal neutrons to produce high linear energy transfer α particles and ^{7}Li nuclei. BNCT is effective when a sufficient amount of ^{10}B is selectively delivered to the tumor (around 20 μg g^{-1}), and enough thermal neutrons are absorbed by the cancer cells to sustain a lethal ^{10}B(n,α) ^{7}Li capture reaction (Barth et al., 2005). Because the high linear energy transfer (LET) particles have confined path lengths in tissue (5–9 μm), the lethality is limited to boron containing cells.

During the last 20 years, many different classes of boron delivery agents have been tested: initially boric acid and some of its derivatives were considered but with limited success due to the low selectivity and poor tumor retention (Goodwin et al., 1955).

Actually, the only two drugs declared to be applicable in clinical therapy are the sodium mercaptoundecahydrododecaborate ($Na_2B_{12}H_{11}SH$, BSH) and a dihydroxyboryl derivative of phenylalanine called L-*p*-^{10}borophenylalanine (^{10}BPA). In particular, ^{10}BPA (complexed with fructose to improve its water solubility) and ^{10}BSH have been used clinically in Japan, the United States, Europe, and Argentina (Barth et al., 2005).

The major challenge in the development of boron delivery agents is to design therapeutic agents able to maximize the treatment of malignant cancers in patients while minimizing adverse effects of the drugs. Most current anticancer agents do not substantially differentiate between cancerous and normal cells, which leads to systemic toxicity and adverse effects. This lack of differentiation significantly limits the maximum allowed drug dose, but the over expression of receptors or antigens in human cancers enables their efficient uptake by receptor mediated endocytosis.

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