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Pharmacokinetic, Biodistribution, and Toxicity Study of Boronophenylalanine in Hepatocellular Carcinoma Cells and Tumor-bearing Mouse Model

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Objectives

To systematically evaluate the cellular uptake, safety profile, and pharmacokinetics of boronophenylalanine (BPA) in hepatocellular carcinoma (HCC), and validate its clinical potential for boron neutron capture therapy (BNCT) in liver cancer.

Methods

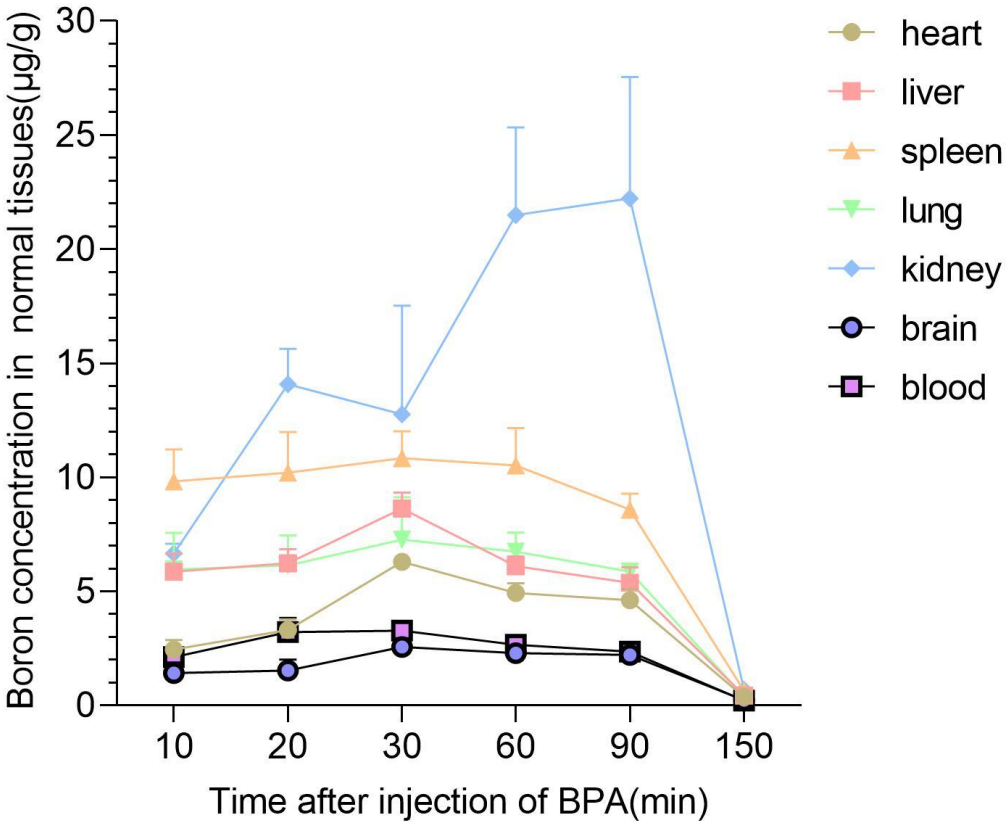
Boron uptake analysis: Quantified intracellular boron accumulation in HCC cell lines (Hepa1-6, HepG2) using inductively coupled plasma atomic emission spectroscopy (ICP-AES) under varying concentrations and time points.
Cytotoxicity assessment: Evaluated BPA-induced toxicity in HCC cells via CCK-8 assays at 24 h.
Safety evaluation: Conducted hemolysis assays on erythrocytes exposed to BPA (0.1–1 mg/mL).
Pharmacokinetic profiling: Measured boron distribution and clearance in Sprague-Dawley rats using blood sampling and ICP-AES.
In vivo targeting efficacy: Assessed tumor-specific boron accumulation and clearance in cell-derived xenograft models using tumor-to-normal tissue (T/N) and tumor-to-blood (T/B) ratios.

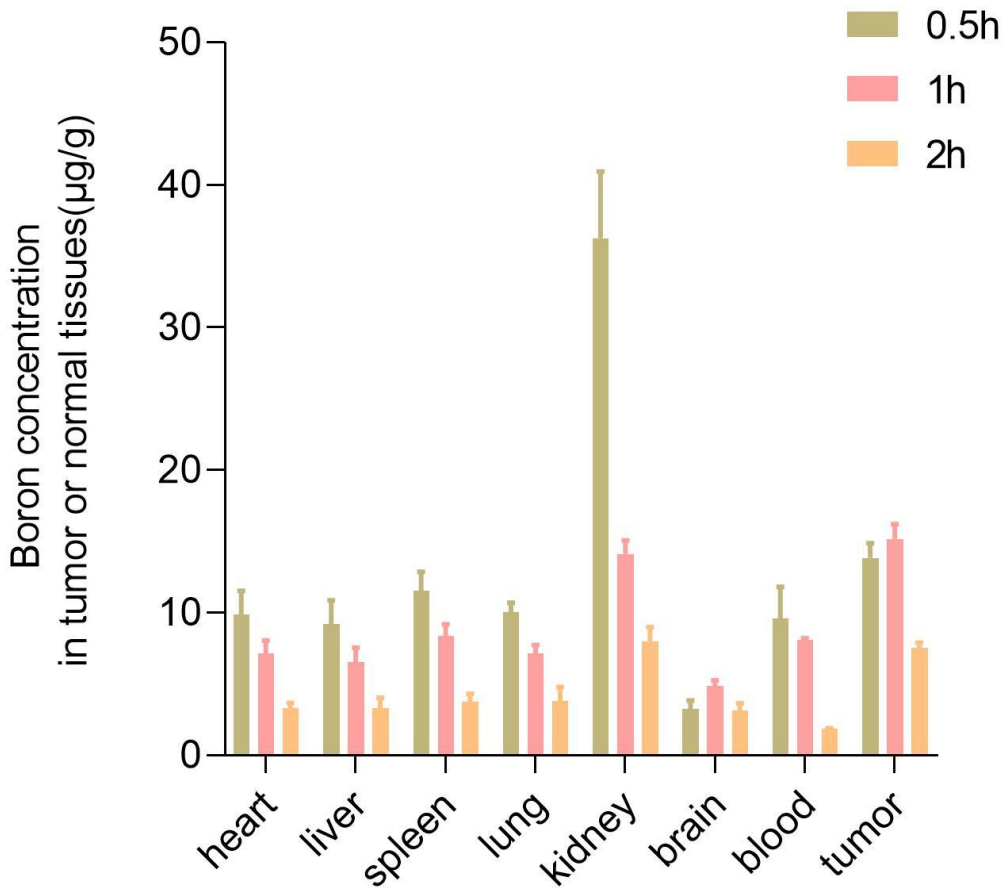
Results

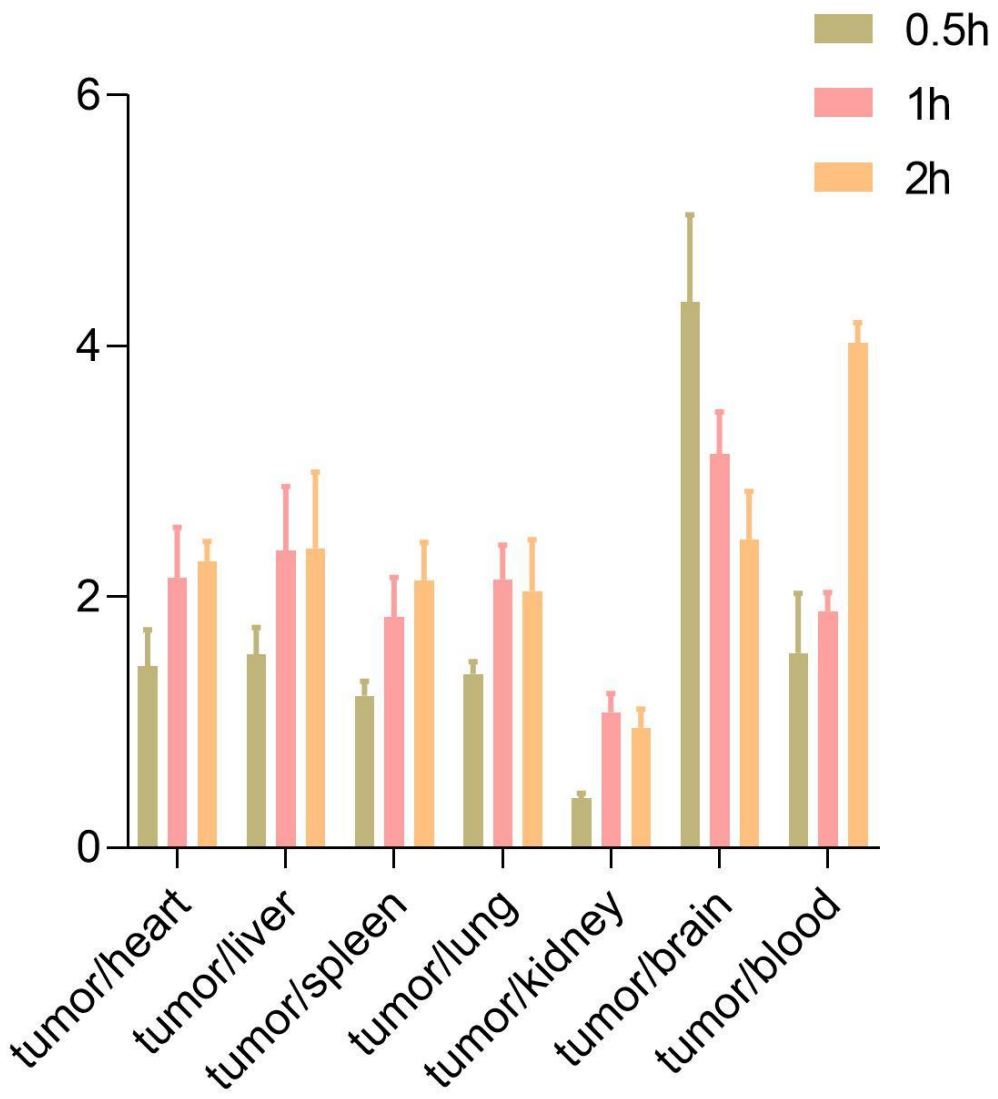
Boron uptake: Concentration- and time-dependent accumulation in HCC cells, plateauing at 6 h.
Cytotoxicity: Significant cell viability reduction observed at 24 h ($p < 0.05$).
Safety: No hemolysis detected at clinically relevant BPA doses (0.1–1 mg/mL).
Pharmacokinetics: Rapid systemic boron distribution (peak plasma concentration at 25 ± 5.8 min) with a blood half-life of 74.71 ± 52.22 min.
Tumor targeting: In xenograft models, T/N > 2 and T/B > 4 at 2 h post-injection, followed by rapid systemic clearance.

Conclusions

BPA demonstrates selective enrichment in HCC tumors, favorable pharmacokinetic properties (rapid uptake and clearance), and low systemic toxicity, fulfilling key criteria for BNCT agents. This study provides foundational evidence supporting BPA's clinical utility in BNCT for HCC, addressing a critical gap in basic research and advancing dual-targeted radiotherapy strategies at the cellular level.


Boron concentration in normal tissues(μg/g)
30
25
20
15
10
5
0
10
20
30
60
90
150
Time after injection of BPA(min)
heart
liver
spleen
lung
kidney
brain
blood


Boron concentration
in tumor or normal tissues(μg/g)
50
40
30
20
10
0
0.5h
1h
2h
heart
liver
spleen
lung
kidney
brain
blood
tumor


0.5h
1h
2h
6
4
2
0
tumor/heart
tumor/liver
tumor/spleen
tumor/lung
tumor/kidney
tumor/brain
tumor/blood