Hirszfeld Institute of Immunology and Experimental Therapy
Polish Academy of Sciences

Boron nitride nanoparticles as compounds dedicated to boron neutron capture therapy

Bożena Szermer-Olearnik[1], Anna Wróblewska[1], Agnieszka Szczygieł[1], Stanisław Cudziło[2],

Jagoda Mierzejewska[1], Katarzyna Węgierek-Ciura[1], Elżbieta Pajtasz-Piasecka[1]

[1]Hirszfeld Institute of Immunology and Experimental Therapy, Polish Academy of Sciences, Wrocław, Poland
[2]Military University of Technology, Faculty of Advanced Technologies and Chemistry, Warsaw, Poland

Background:

Boron neutron capture therapy (BNCT) is classified as a targeted anti-cancer radiotherapy based on boron delivery to tumor cells and irradiation of the affected area with a neutron beam. One of the leading challenges for the development of BNCT is the search for new boron-rich compounds that will allow to achieve the required concentration of ^{10}B isotope in cancer cells. Boron nitride nanoparticles, due to their high boron content, are becoming an object of interest for application in BNCT. The problem that needs to be solved is the way of their delivery to the cancer cells. We propose an original approach to use macrophages/monocytes for boron delivery to the tumor microenvironment. These professional phagocytic cells are widely distributed in the body tissues and are strongly associated with cancer tissues.

Experimental design:

The newly synthesized boron nitride nanoparticles (MUT, Warsaw, Poland) have been characterized in terms of shape and size of the particles using transmission electron microscopy and dynamic light scattering measurement. In order to evaluate the toxicity of tested nanoparticles, the MTT cell viability assay and Annexin V/propidium iodide apoptosis assay (BD Biosciences) were conducted on RAW 264.7 monocyte/macrophage-like cells (ATCC, TIB-71). Additionally, to determine cytokines production by these cells, an ELISA assay (enzyme-linked immunosorbent assay; eBioscience, BD Biosciences) was performed. The BPA (4-Borono-L-phenylalanine; Sigma-Aldrich) was used as reference compound.

Results:

The results showed a low polydispersity (PdI) of obtained nanoparticles – 0,243 and 0,233 for BN-1 and BN-6 adequately. The average particle size in the preparations was 190 nm (Fig.1 and Fig. 2). RAW 264.7 cells tolerated boron nitride in a concentration below 100 µg/ml (Fig 3). No cytotoxic effect of examined compounds on RAW 264.7 cells was demonstrated at a concentration of 10 µg/ml (Fig. 4). Besides, the higher concentration of both boron nitride compounds induced considerable production of tumor necrosis factor alpha (TNF-α) and this effect was accompanied with decreased production of IL-10, especially in the highest concentration of BNs (Fig. 5).

Low polydispersity of boron nitride (BN-1, BN-6) nanoparticles

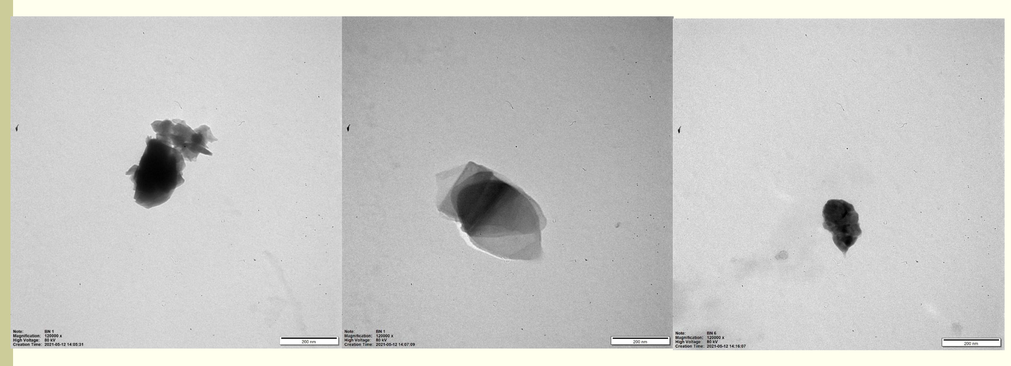
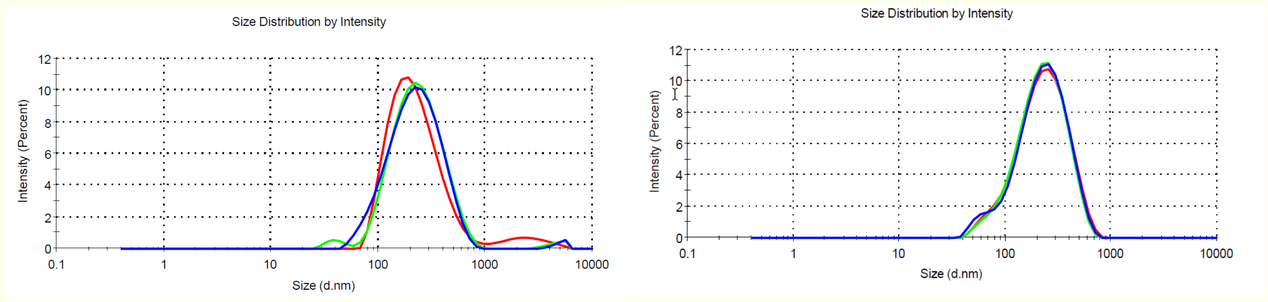


Fig.1 TEM visualization of boron nitride nanoparticles.



A B

Fig. 2 Size distribution curves of boron nitride nanoparticles BN-1 – A, BN-6 - B.

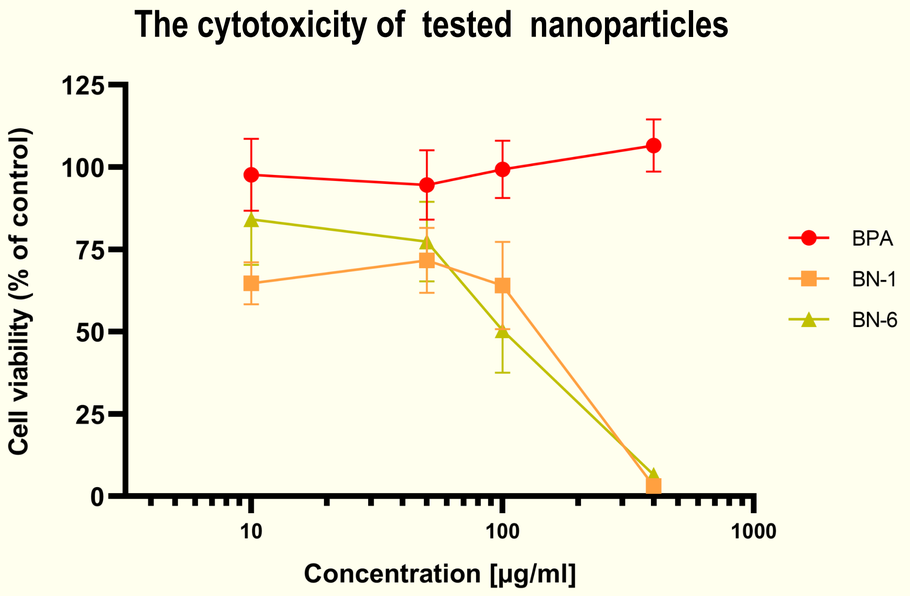


Fig. 3 MTT cell viability assay conducted on RAW 264.7 monocyte/macrophage-like cells.

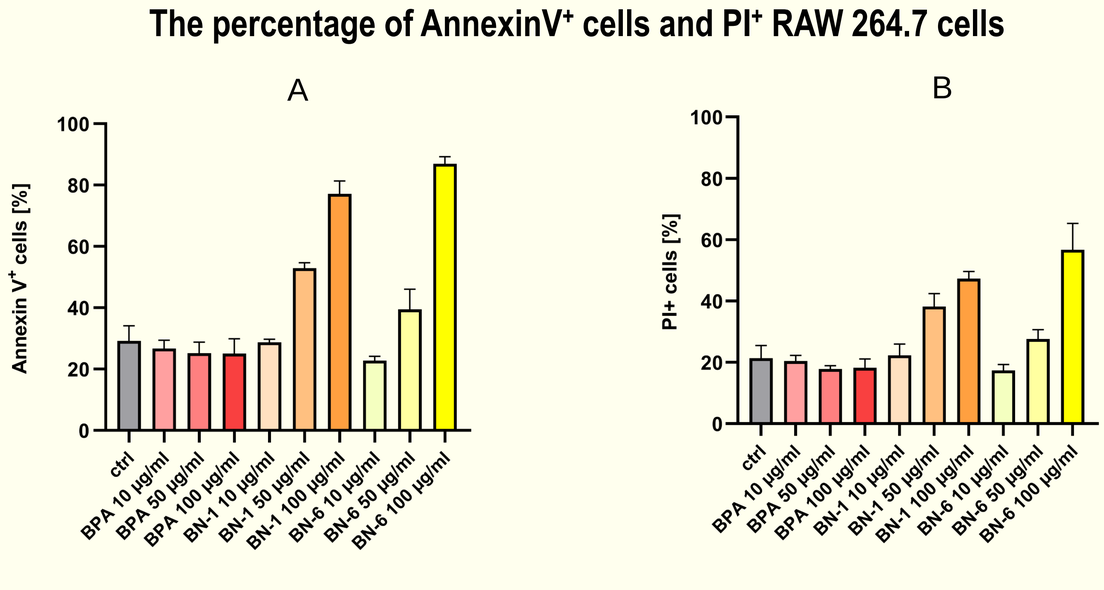


Fig. 4 Annexin V/propidium iodide apoptosis assay (A, B, respectively) Conducted on monocyte/macrophage-like cells after 72h exposure

Conclusions:

Both boron nitride nanoparticles due to their small size and low polydispersity can become potential candidates for BNCT. However, the influence on RAW264.7 cells was dose- and time-dependent. On the other hand, long exposition of cells on BN in concentration higher than 50 µg/ml leads to increase cell sensitivity followed by increase apoptosis and TNF-a production. Taken together, the observed influence of BN nanoparticles on macrophage cells could be used to modulate the tumor microenvironment in the future BNCT experimental therapy.

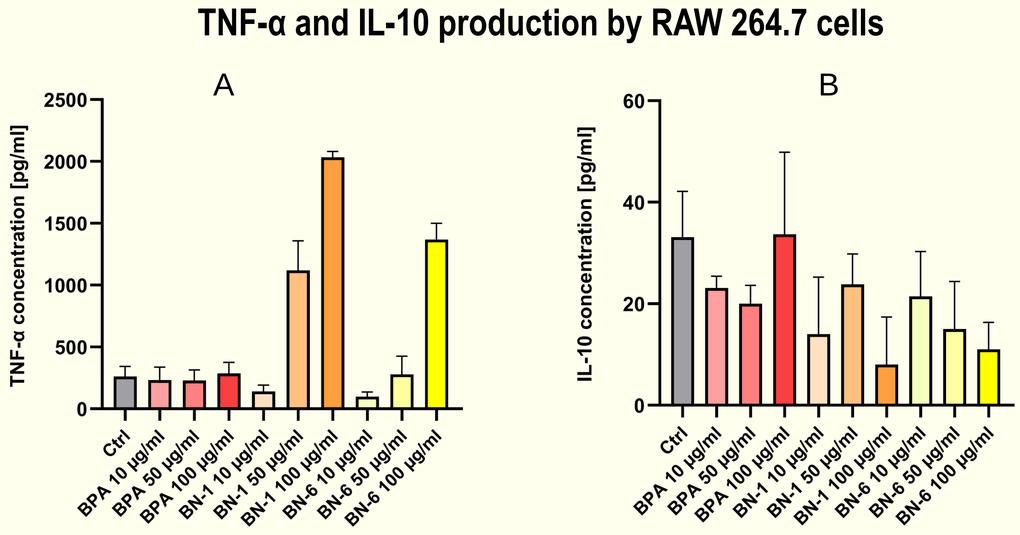


Fig. 5 TNF-α (A) and IL-10 (B) production after stimulation of RAW 264.7 monocyte/macrophage-like cells with boron nitride at various concentrations.