Design of Low-nanometer Scale Size Ag, Ni, and Co Nanocomposites *in situ* in a Polymer-Inorganic Carrier as a Promising Nanobiotechnology for Anti-Cancer Treatment

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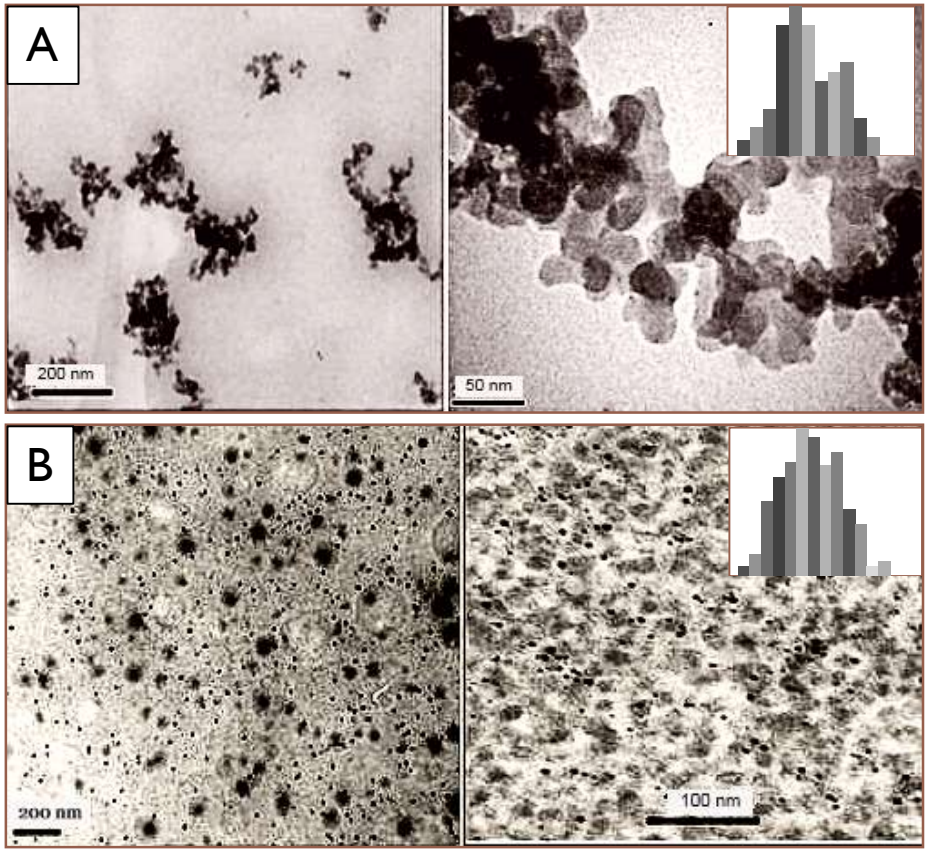


Fig. 1 A,B. TEM images of SiO2-g-PAAm matrix (A), AgNPs (B), NinPs (C), and CoNPs (D). Insets: particles size distribution; mean particles diameters: 21 nm (matrix), 6.1nm (AgNPs), 3 nm (CoNPs), and 1.5 nm (NiNPs).

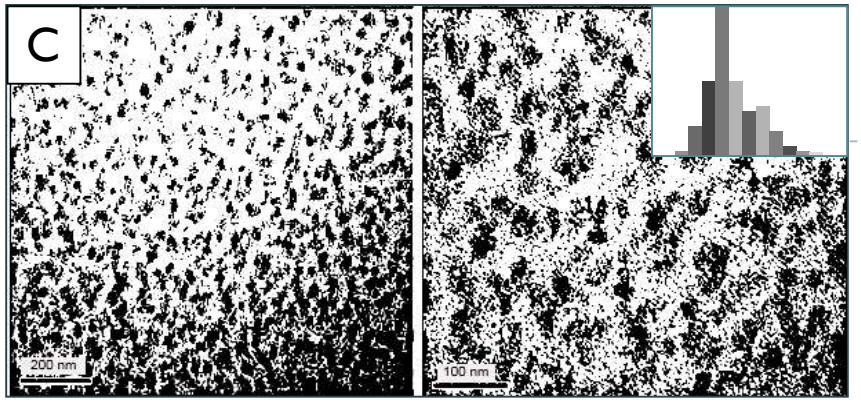
Background: Design of polymer-stabilized metal nanocomposites (MeNP) is a promising nanobiotechnology for nanomedicine and a fast developing field of research. Besides polymer-stabilized AgNPs with proved anti-cancer effects, which design is improved constantly, particular interest of researchers is directed to MeNPs with magnetic properties for targeted drug delivery in oncotherapy.

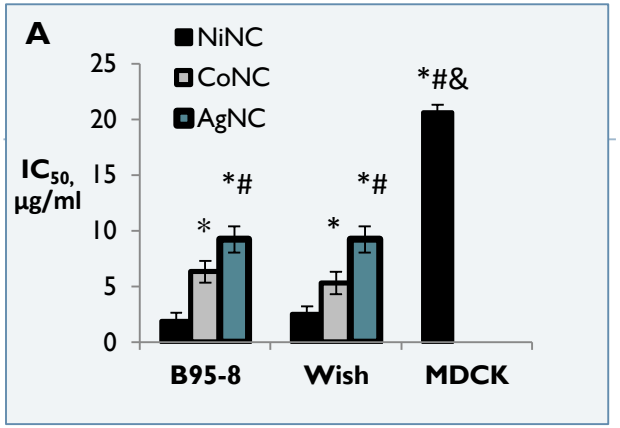
Aim: to evaluate *in vitro* anti-cancer properties of Ag, Ni, and Co nanocomposites obtained by borohydride reduction *in situ* in a polymer-inorganic hybrid matrix SiO_2-grafted polyacrilamide (SiO_2-*g*-PAAm) with SiO_2 core r_{av} 7 nm, M_{vPAA} ~ 800 kDa.

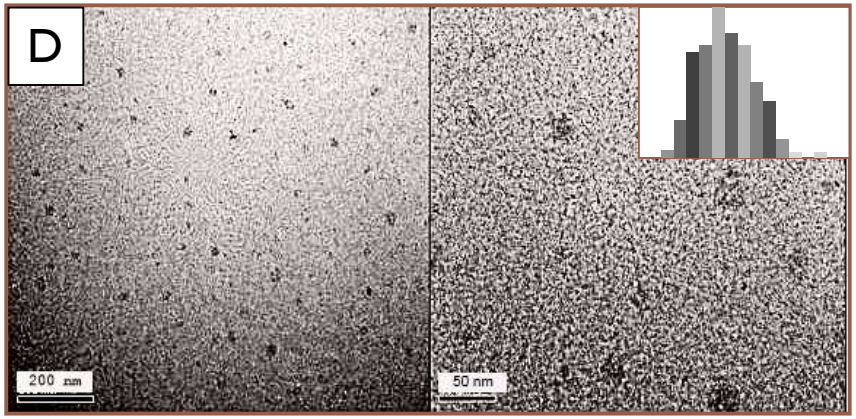
Methods: cell lines used were: marmosets' leucocytes transformed by Barr-Epstein virus (B95-8), Wish with marker chromosomes of HeLa cells, and MDCK (Madin-Darby canine kidney); MDCK served as control. Particle size was evaluated by transmission electron microscopy (TEM). Cell viability was estimated with MTT test.

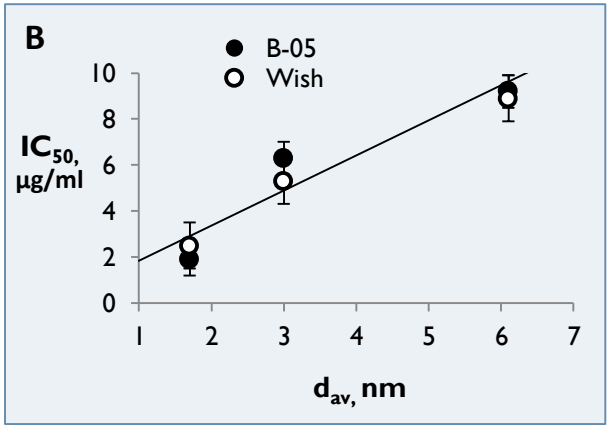
Results: Mean particle diameters (d_{av}) evaluated by transmission electron microscopy were 6.1 (Ag), 1.7 (Ni), and 3.0 (Co) nm. Matrix was estimated as ~21 nm (pure SiO_2-*g*-PAAm), 23 nm (CoNPs), and 31 nm (NiNPs). All MeNPs showed high anti-cancer activity (Fig. 2). NiNP exhibited highest toxicity to cancer cells: IC_{50} were 1.9 and 2.5 μg/ml for B95-8, and Wish, respectively. CoNP exhibited moderate toxicity: IC_{50} were 6.3 and 5.31 μg/ml for B95-8 and Wish cell lines, respectively. AgNP showed the least toxicity: IC_{50} 9.2 μg/ml for B95-8 and Wish cells similarly.

Of cell lines B95-8 cells were most sensitive to MeNPs.









The least toxicity was found for MDCK cells (Fig. 2A). Matrix contributed to cytotoxicity in B95-8 cells, but was not toxic to other cell types. Anti-cancer activity inversely correlated with d_{av}: AgNP < CoNP < NiNP (Fig. 2 B).

Fig. 2. The effect of Ag, Co, and NiNC on the viability of B-95, Wish, and MDCK cells. A: IC_{50}, µg/ml; B: the dependence of IC_{50} on mean particles diameter (d_{av}).

Conclusions: simple and cost-effective method of *in situ* synthesis of low-nanometer size MeNPs in a polymer-inorganic matrix allowed for obtaining Me nanoparticles with high anti-cancer activity, dependent on particle size, and much less toxic to control MDCK cells. Thus, Ag, Ni, and Co nanocomposites synthesized *in situ* in non-toxic SiO_2-*g*-PAAm matrix are promising nanobiotechnology for anti-cancer therapy, however the dependence of their effectiveness on Me and cancer cell types needs further studies.