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Advanced Biotechnology: Modulation of doxorubicin cytotoxicity by smart gold nanoparticles multi-functionalized with natural compounds in targeting human cervical and breast cancer cells

Background: The conventional drug delivery approach comprises systemic administration of a specific drug that could be low on anticancer efficacy, nonspecific in targeting cancer cells, with severe side-effects. To address these challenges, the smart nano-inspired drug delivery systems with enhanced stability are designed and developed in the Research Center of Excellence in Physical Chemistry, Babeş -Bolyai University, to target specific cancer cells and improve doxorubicin, D, efficiency and specificity at its low concentration with minimal side-effects.

Objectives: Our research study was designed to assess the role of natural molecules, such as trans-resveratrol (R), piperine (P), and icariin (Ic), on targeting cervical and breast cancer cells and on sensitization of cancer cells to D action and thus, to minimize the D effective dose and its side effects.

Methods: Resveratrol was also used for the synthesis of GNP_R1 nanoparticles. The smart multi-functional GNP_s loaded with D, R, P, and Ic (e.g., GNP_R1@DRPIc) were successfully prepared and fully characterized by SPR, TEM, HR-TEM, XRD, AFM, DLS, and zeta potential in various biological media. The D cytotoxicity was tested on cancer

cell lines, using the MTT assay at 24 h and 48 h incubation time. The smart drug delivery is a cutting-edge innovative approach in current nanomedicines to ensure effective and safe administration of therapeutics to target sites.

Results: Our results demonstrate that the smart multi-functional GNP_s (such as GNP_R1@DR and GNP_R1@DRPIc) can effectively target the cervical and breast cancer cells and improve the bioavailability of therapeutic agents and enhance the doxorubicin cytotoxicity against cancer cells. **Conclusions:** This study provides compelling evidence that the smart GNP_R1@DRPIc innovative nanocarriers can enhance the therapeutic efficacy of doxorubicin against human cervical and breast cancer and offer a more advantageous alternative compared to doxorubicin monotherapy. Moreover, this research study provides a proof of innovative concept for possible medical application.

Keywords: smart drug delivery nanoparticles; smart multi-functionalized gold nanoparticles; green synthesis of gold nanoparticles; doxorubicin; resveratrol; piperine; icariin; cervical and breast cancer cell lines

SMART MATERIALS & STRUCTURES

March 30–31, 2026 Berlin

SRH University of Applied Sciences, Germany



BIOGRAPHY

Professor Maria Tomoaia-Cotisel completed PhD at Babes-Bolyai University (BBU, 1979) of Cluj-Napoca, Romania (RO), and postdoctoral studies from London University, King's College (1981, 1986, 1989), UK. She was the visiting scientist, at Philipps University of Marburg, (1989/1990), Germany, State University of New York at Buffalo (1990/1991), USA, National Institutes of Health, (1991-1993) and Molecular/Structural Biotech., Inc., (1994-1997), Bethesda, MD, USA. She is the founder and director of Research Center in Physical Chemistry (2006-) at BBU. She published over 300 original research papers, 5 patents in US, and 4 patents in RO, and 12 books in physical chemistry, including thermodynamics, chemical structure, biophysics, bionanomaterials, colloids and interfaces. She got awards, e.g., Gheorghe Spacu Award (1983, from the Romanian Academy), Alexander von Humboldt Award (1986, Germany), Japan Society for Promotion of Science and Technology Award (1986, Japan), and Fogarty Award (1991, USA) for science and technology. She received the Chemical Thermodynamics book award (2021) from Academy of Romanian Scientists. Research Interests and achievements include: various aspects of nanobiomaterials, advanced nanotechnology for biomedical applications, nanostructured advanced smart materials for drug delivery targeted to various tissues and cells, colloidal systems, cell membrane models as monolayers, Langmuir-Blodgett layers, liposomes, micelles and vesicles, multi-substituted hydroxyapatite based bioceramics for osteoporotic bone remodeling and regeneration, nanomaterials for tissue engineering, nano- and micro-biocomposites, biomimetic self-assembled scaffolds, porous bioresorbable scaffolds, regenerative medicine, cancer cellular therapy, nanoparticles of gold and silver for cancer therapy, biomolecular immobilization and surface modification strategies. Over 100 invited keynote conferences and plenary lectures at International Conferences, Symposia, Congresses and Workshops.

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