ANTICANCER ACTIVITY OF ARTEMISININ-LOADED HYPERBRANCHED DENDRITIC NANOCARRIERS

E. Halevas[1], B. Mavroidi[1], C. Kokotidou[2,3], A. Mitraki[2,3], M. Pelecanou[1], M. Sagnou[1]*

[1]Institute of Biosciences & Applications, National Centre for Scientific Research "Demokritos", 15310 Athens, Greece

[2]Department of Materials Science and Technology, University of Crete, Heraklion, Greece

[3]Institute of Electronic Structure and Laser (IESL) FORTH, Greece

*(*sagnou@bio.demokritos.gr)*

ABSTRACT

Worldwide, breast cancer constitutes the most common and lethal type of cancer diagnosed in women with an expected death rate of 25.3 per 100,000 of patients in 2018 [1].

Advancements in nanotechnology have led to the development of novel anticancer nanomaterials with both diagnostic and therapeutic potential and the design of specific antitumor drug delivery nano-formulations with high drug entrapment efficiency, improved tissue and/or organ selectivity, enhanced therapeutic index, reduced cytotoxicity against healthy tissues, and controllable release rates of their therapeutic load [2].

2,2-Bis(hydroxyl-methyl)propionic acid (bis-MPA) hyperbranched dendritic scaffold is a novel class of biodegradable non-toxic nanomaterials with potential drug delivery applications. Their wide variety of modifiable structural and surface characteristics along with their intrinsic physico-chemical properties such as biocompatibility, bioavailability, self-assembly, reactivity, chemical recognition, adhesion to various surfaces, as well as luminescence and electrochemical properties have established bis-MPAs as effective drug nanocarriers [3].

Artemisinin (ART) belongs to the class of sesquiterpene lactones and it is present in the *Artemisia annua* sweet wormwood. Along with its semi-synthetic derivatives they constitute a group of well-known, well tolerated and Nobel prize winner (2015) antimalarial drugs [4]. ART has also been shown to possess antiangiogenic, anti-epileptic, anti-inflammatory, anti-sedative, anti-cataleptic, antibacterial, anti-viral and skin protective properties [5]. Recent *in vitro* and *in vivo* studies and human clinical trials have demonstrated the promising anticancer potential of ART against colorectal, lung, cervical, and breast cancers [6]. However, its low aqueous solubility and bioavailability, inadequate selectivity towards tumor cells, short half-life, non-selective toxicity profile, acquired drug resistance and high production cost limit its use as an effective anticancer drug candidate.

In an effort to develop novel, multifunctional pharmaceutical nanomaterials with enhanced bioavailability and targeted antitumor activity against breast cancer we have: a) synthesized Artemisinin-loaded G4-PEG6k-OH bis-MPA nano-matrices, b) investigated structural and textural properties of the newly synthesized materials by different and complementary characterization techniques, c) evaluated loading and release profile and d) assessed cytotoxicity effects of free and encapsulated Artemisinin in MCF-7 and MDA-MB-231 breast cancer cells and normal NIH-3T3 mouse embryonic fibroblast. Our results demonstrated the superiority in cytotoxic activity of the encapsulated ART against cancer cells, compared to the free drug, and even more important, the lack of toxicity against normal cells.

References

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