

December 10-12, 2018  
Rome, ItalyDorina E Coricovac et al., Nano Res Appl 2018, Volume 4  
DOI: 10.21767/2471-9838-C7-028

# Functionalization of betulinic acid by nanotechnology improved its *in vitro* antiproliferative activity

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In recent years, nanotechnology has become a key player in multiple biomedical fields, drug delivery being one of the domains where nanotechnological innovations are highly applied. Nanocarrier systems proved to be very useful in improving the physicochemical and pharmacological properties of different compounds, thus augmenting their effectiveness as therapeutic agents. Betulinic acid (BA) is a pentacyclic lupane-type triterpene of natural origin that exerts a plethora of biological effects, including antitumor, antiviral, anti-inflammatory, immunomodulatory, anti-angiogenic, hepatoprotective, etc. The main handicap of BA consists in very low water solubility what limits its use *in vivo*. To adjust this flaw and to improve its bioavailability, we prepared a nanoformulation of BA using silver and silver PEGylated (PEG) nanoparticles and verified its cytotoxic effects *in vitro* against a panel of tumor cell lines, as: human (A375) and murine melanoma (B164A5), lung (A549), breast (MCF-7 and MDA-MB-231) and hepatic carcinoma (HepG2) and on a healthy cell line – HaCaT – human immortalized keratinocytes. The obtained nanoformulation were characterized in terms of physicochemical properties by applying standard methods as transmission electron microscopy (TEM) and UV-VIS, that confirmed the development of stable solutions. The cytotoxicity was evaluated by the means of MTT (3-(4,5-Dimethylthiazol-2-yl)-2,5-Diphenyltetrazolium Bromide) and Alamar blue techniques, and the impact on cell migration and proliferation was measured using scratch assay. The nanoformulations of BA managed to inhibit the proliferation of all tumor cells at a higher extent as compared with the solution of BA in DMSO (dimethyl sulfoxide) used as the standard, whereas in the case of a healthy cell line, the toxic effect was minimum. The migration of tumor cells was also impaired by the nanoformulations. These preliminary results indicate that the antiproliferative effect of BA was improved.

Further studies are required to establish the mechanism of action of this nanoformulation and to prove its effectiveness *in vivo*.

## Recent Publications

1. Coricovac D, Dehelean C, Moaca EA, Pinzaru I, Bratu T, Navolan D and Boruga O (2018) Cutaneous melanoma-a long road from experimental models to clinical outcome: a review. *International Journal of Molecular Sciences* 19(6):E1566.
2. Pinzaru I, Coricovac D, Dehelean C, Moacă EA, Mioc M, Baderca F, Sizemore I, Brittle S, Marti D, Calina C D, Tsatsakis A M and Şoica C (2018) Stable PEG-coated silver nanoparticles - A comprehensive toxicological profile. *Food and Chemical Toxicology* 111:546-556.
3. Coricovac D E, Moacă E A, Pinzaru I, Cîtu C, Soica C, Mihali C V, Păcurariu C, Tutelyan V A, Tsatsakis A and Dehelean C A (2017) Biocompatible colloidal suspensions based on magnetic iron oxide nanoparticles: synthesis, characterization and toxicological profile. *Frontiers in Pharmacology* 8:154.
4. Gheorgheosu (Coricovac) D, Duicu O, Dehelean C, Soica C and Muntean D (2014) Betulinic acid as a potent and complex antitumor phytochemical: a minireview. *Anti-Cancer Agents in Medicinal Chemistry* 14(7):936-45.
5. Gheorgheosu (Coricovac) D, Jung M, Ören B, Schmid T, Dehelean C, Muntean D, Brüne B (2013) Betulinic acid suppresses NGAL-induced epithelial-to-mesenchymal transition in melanoma. *Journal of Biological Chemistry* 394(6):773-81.