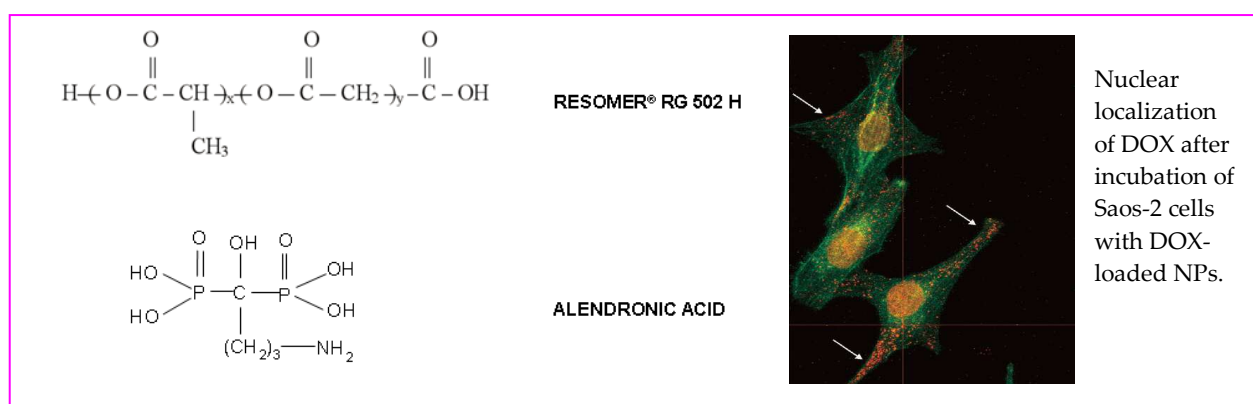


## A novel biomaterial for the production of osteotropic drug nanocarriers in bone cancer therapy

Prof. Rosario Pignatello – University of Catania – Consorzio TEFARCO Innova

The University of Catania, in collaboration with the Institute Rizzoli of Bologna, has produced a new biodegradable polymeric material, obtained by conjugating a poly(lactic-co-glycolic) acid (PLGA) derivative with alendronate. With this copolymer nanoparticles have been produced and loaded with doxorubicin as a model anticancer drug. This bone-seeking system showed both *in vitro* and *in vivo* that the encapsulation of the drug did not affect its anticancer activity.



### 1. Description of the product

Osteotropic drug delivery systems have been proposed as a mean to give drugs affinity to bone tissues. Drugs or proteins have been chemically linked to bone-seeking agents like bisphosphonates (BPs); alternatively, drug-loaded nanoparticles (NPs) have been used to target specific tissues, such as tumors. In this research the above approaches were merged by synthesizing a **novel bone-seeking polymer conjugate**, from which targetable nanoparticles can be produced. An amino-BP, alendronate (ALE) was covalently bonded to a biodegradable polymer, poly(lactic-co-glycolic acid) (50:50 PLGA) containing a free end carboxylic group. This copolymer showed full blood compatibility and absence of cytotoxicity *in vitro*.

By a specific solvent evaporation method, NPs with mean size in a 200-300 nm range were prepared from this conjugate. Their sterilization was achieved by gamma irradiation, confirming their potential as injectable drug nanocarriers. Due to the presence of the BP residue, PLGA-ALE nanoparticles were adsorbed onto hydroxyapatite to a higher extent than pure PLGA NPs.

The prepared conjugate thus represents a novel biomaterial able to give NPs, which can be loaded with drugs, such as anticancer agents, and addressed to osteolytic or other bone diseases. In this respect, preliminary *in vitro* and *in vivo* studies were made using doxorubicin (DOX) as a model anticancer drug. DOX-loaded NPs showed a tumor cell growth inhibitory activity *in vitro* comparable to the free drug; *in vivo*, both DOX-loaded NP and free DOX reduced the incidence of metastases from bone tumors in mice.

### 2. Innovative aspect of the product

This study represents the first approach described in the literature in which the two 'classical' strategies of the osteotropic prodrugs and drug-loaded nanoparticles have been merged into a single solution.

The proposed nanocarriers associate the possibility of loading a variety of drugs, namely anticancer agents but also antimicrobial compounds, proteins or peptides, fluorescent probes for diagnostic, etc., while keeping their osteotropic (targeting) feature.

### 3. Main advantages of the offer

- The PLGA-ALE copolymer showed complete biocompatibility *in vitro* and was not cytotoxic to endothelial cells and trabecular osteoblasts.
- Small nanoparticles were easily produced from the PLGA-ALE conjugate. These nanoparticles showed affinity *in vitro* towards hydroxyapatite.
- High drug loading values were achieved with doxorubicin.
- Theranostic approaches seem also to be exploitable with this nanocarrier.
- The main advantage remains the use of PLGA (Resomer®) polymers, classified as GRAS by US FDA and widely used in many medicines for human applications.

### 4. Technology key words

Anticancer drug delivery; Drug targeting; Bone-seeking systems; Nanoparticles; Osteotropic drug carriers (ODDS); Alendronate; PLGA; Doxorubicin.

### 5. Current Stage of Development

Available for demonstration – field tested.

### 6. Intellectual Property Rights

No IPR issue applied

#### Technical and scientific publications

A novel biomaterial for osteotropic drug nanocarriers. Synthesis and biocompatibility evaluation of a PLGA-alendronate conjugate.

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In vitro antitumor effects of bone-targeted nanoparticles loaded with doxorubicin

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## CONTACT

info@biopharmanet.eu

Tel.: +39 0521 905073 Fax: +39 0521 905006