"Synthesis of bioactive coumarin analogues and their encapsulation in biodegradable poly(lactic-co-glycolic acid) (PLGA) nanoparticles. In vitro evaluation of their biological activity."

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Coumarins are benzopyrone analogues widely distributed in nature. The fused heterocyclic framework of coumarins has served as the prototype scaffold for the synthesis of a wide variety of analogues in order to investigate their biological activity. Coumarins possess a remarkable range of biological properties including antioxidant, anticancer, vasorelaxant, antiviral and anti-inflammatory.

In recent years, encapsulation of active ingredients in colloidal nanocarriers has tremendous potential for drug delivery in the pharmaceutical and cosmetics industry. It consists of the entrapment of a drug/compound inside a carrier material, in the aim of enhancing several physicochemical characteristics of the encapsulated substance while obtaining a more efficient and controlled drug delivery as well.

In this work we will present the synthesis, structure characterization and evaluation of biological activity of natural and synthetic coumarin analogues. Moreover, in order to tailor the physicochemical characteristics of the compounds (such as low water solubility, potential photosensitivity and air-oxidative decomposition), their encapsulation in PLGA nanoparticles was studied. PLGA was the polymer of choice as it is a biodegradable and biocompatible polymer which has been approved for use in therapeutic devices.

The structure characterization of the compounds was performed using NMR spectroscopy whereas their antioxidant activity was investigated using different in vitro assays. Encapsulation in PLGA nanoparticles was achieved via the emulsification-solvent evaporation technique. Size, polydispersity index and ζ-potential of the nanoparticles were measured by Dynamic Light Scattering method whereas the Encapsulation Efficiency (EE) was determined indirectly, using UV-Vis

spectroscopy. The potential antiproliferative effects of our coumarin analogues, either nano-encapsulated or not, have been tested in vitro against human neuroblastoma cell line SK-N-SH, through different cytotoxic assays.