Prenyloxycoumarins with antioxidant and lipoxygenase inhibitory activity: Synthesis, bioactivity evaluation and encapsulation in biodegradable poly(lactic acid) nanoparticles

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Oxyprenylated natural products (isopentenyloxy-, geranyloxy- and the less spread farnesyloxy- compounds and their biosynthetic derivatives) represent a family of secondary metabolites that have been considered for years just as biosynthetic intermediates of C-prenylated derivatives. Only in the last decade these natural products have been recognized as interesting and valuable biologically active phytochemicals.

Prenyloxycoumarins are secondary metabolites commonly present in plants belonging to the families of Rutaceae and Umbelliferae. Several of these coumarins were shown to possess valuable pharmacological properties. Among them, auraptene (7-geranyloxycoumarin) which is isolated from the peel of citrus fruit (Citrus natsudaidai Hayata) has been reported to have chemopreventive effects on chemically induced carcinogenesis and possess antioxidant activity.

In this work, the synthesis of the natural product auraptene as well as its analogue, 4-methyl-7-geranyloxycoumarin will be presented. The compounds were evaluated in vitro for their antioxidant activity as well as for their ability to inhibit soybean lipoxygenase, as an indication of their potential anti-inflammatory activity.

Nanoencapsulation of bioactive compounds can provide protection against unwanted degradation and also improve their bioavailability and delivery properties. In order to investigate the possibility of enhancing the stability of the synthesized prenyloxycoumarins against photo- and air-oxidation as well as modifying their aqueous solibility, the compounds were encapsulated in biodegradable poly(lactic acid) (PLA) nanoparticles. Encapsulation in PLA 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.