INNOVATIVE DELIVERY SYSTEMS AND TARGETING OF DRUGS TO THEIR ACTION SITES

The aim of the project is the formulation of innovative systems able to target neuroactive and anticancer drugs to their action sites. In general, neuro-active drugs are not able to reach the brain at therapeutic concentrations and several anticancer agents show the multidrug resistance phenomenon.
Similarly, antiretroviral drugs used in the treatment against AIDS have trouble in reaching body sites, such as macrofages and central nervous system (CNS) which represent protective "sanctuaries" toward HIV.
These effects are mainly due to the active efflux transport (AET) systems, that recognize and efflux in the bloodstream the drugs that have reached the brain, the cancer cells or the macrophages. The design of appropriate prodrugs, pharmaceutical co-crystals, or micro- and nanoparticulate systems can allow to obtain formulations that, upon non-invasive administrations, are able to target the drugs to their action site. In particular, we are designing innovative formulations constituted by prodrugs or pharmaceutical co-crystals able to elude the AET systems. It is foreseen to study the encapsulation of prodrugs into microparticles in order to obtain nasal formulations for improved CNS delivery. Moreover, new biocompatible nanoparticle systems able to modulate capture by macrophages will be developed. In this regard, it is expected that nanoparticles inducing high up-take-activity of macrophages could be used to eradicate macrophage infections, while nanoparticles able to limit the up-take-activity of macrophages can act as "stealth" nanoparticles, which, following their administration in the bloodstream, can target solid tumors *via* passive targeting phenomena, such as enhanced permeability and retention (EPR) effect.
Lastly, it is planned to study essential oil nanoemulsions with neuronal and antitumor activity in order to improve bioavailability and selectivity of their therapeutic activity.

GOALS

- Nasal formulations based on polymeric or lipidic microparticles for the drug targeting in the central nervous system.
- Essential oils showing therapeutic activity: formulative and bioavailability studies.
- Micro- and nanoemulsion formulative studies of essential oils showing therapeutic activity.
- Development of cellular models for the in vitro studies of drug permeation across physiologic barriers.
- Nanoparticulate formulations based on bile acids prodrugs for the targeting of anti-HIV drugs in macrophages.
- Development of cellular models for the in vitro studies of new strategies able to elude the multidrug resistance phenomenon of anticancer drugs.
- Pharmaceutical co-crystals: studies of dissolution, permeability and bioavailability.

INSTRUMENTS AND METHODS
HPLC techniques for the in vitro and in vivo quantitative analysis of the drugs and their related prodrugs. Emulsion or nanoprecipitation methods for the formulation of the particulate systems. Cell culture of monolayers for permeation studies of the prodrugs and their parent drugs by HPLC. Pharmacokinetic studies in physiologic fluids.

MAIN SUBJECTS
Pharmaceutical technology, medicinal chemistry, biology

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