

Design, synthesis, physicochemical characterization, and biological evaluations of new drugs for inflammatory-based disease treatment.

Acute or chronic inflammation is a natural response of the body against pathogens and harmful stimuli. Acute inflammation is a part of innate immunity, initiated by immune cells, that persists only for a short period. Chronic inflammation, on the other hand, is long-term inflammation that occurs only when the pro-inflammatory condition persists. This pathological state can trigger several types of chronic diseases, including cancer, cardiovascular disease, and neurological disease, through dysregulation of various signalling pathways. Targeting these pathways has high potential in the prevention and treatment of chronic diseases.

Currently, available drugs often lack affinity for a specific pathway and spread randomly within cells. As a result, they are often ineffective and have a wide spectrum of side effects. Moreover, because many inflammatory-based diseases involve disruption of numerous cellular signalling pathways, polypharmacotherapy is the current approach used to treat them. It consists of the chronic intake of several drugs that are not all essential for adequate treatment. In addition, the administration of drug cocktails has many pharmacokinetic and pharmacodynamic limitations.

The objective of the present project is the design, synthesis and physicochemical characterization of novel molecular hybrids representing multi-target drugs. In particular, the conjugation of several pharmacologically active substructures is a useful approach to generate a variety of hybrid structures capable of acting against multiple targets. At the same time, chemical modifications of well-known drugs will be evaluated to improve their pharmacodynamics and toxicological profiles. In particular, by means of the prodrug strategy, conjugation of parent drugs with carriers will be carried out.

Optimization of the synthetic strategy will be carried out according to the principles of green chemistry and through the application of energy-efficient techniques (microwaves and ultrasound).

Hybrids and prodrugs with a promising physicochemical profile will be tested in in-vitro and in-vivo models and molecular modelling studies will be carried out as well.

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