DESIGN AND SYNTHESIS OF TRPA1 RECEPTOR MODULATORS AS EMERGING OPPORTUNITIES TO TREAT PAIN AND INFLAMMATION-RELATED DISORDERS

Transient receptor potential (TRP) channels constitute a large family of diverse ion channel proteins with impact on sensory signalling pathways. TRPA1 is the only known member of the ankyrin subfamily that, behaving as a chemosensor of by-products of oxidative/nitrative stress resulting from tissue damage and/or inflammation, plays a fundamental role in pain signalling. Furthermore, TRPA1 activation promotes the release of inflammatory neuropeptides. This dual function as a detector and instigator of inflammatory agents makes TRPA1 a gatekeeper of chronic inflammatory disorders of the skin, airways, and gastrointestinal tract. The ongoing project is aimed to validate emerging opportunities in these therapeutic areas mainly offered by the blockade of TRPA1 receptor.

GOALS

• Design, synthesis and in vitro biological evaluation of new TRPA1 antagonists with high potency, selectivity, improved metabolic properties and water solubility

INSTRUMENTS AND METHODS

The compounds are synthesized with the standard equipment for traditional liquid phase synthesis. Flash chromatography and preparative HPLC, mass spectrometry, analytical HPLC, NMR, IR techniques will be used to isolate and characterize the synthesized compounds.

MAIN SUBJECTS Medicinal chemistry, organic chemistry, pharmacology, molecular biology

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