Synthesis, kinetics and pharmacological evaluation of prodrugs of NSAIDs with drugs of herbal origin

The non-steroidal anti-inflammatory drugs (NSAIDs) are among the most widely prescribed drugs worldwide. NSAIDs are widely used for indications extending from inflammation and pain to cardiovascular and genitourinary diseases. Despite the intensive research that has been aimed at the development of NSAIDs, their clinical usefulness is still restricted by their gastrointestinal side effects like gastric irritation, ulceration, bleeding, and perforation and in some cases may develop into life threatening conditions. There are different mechanisms suggested for the GI injury. i) Suggest a Local irritation produced by acidic group of the NSAIDs. ii) Inhibition of prostaglandins in GI tract. There is another, it is thought, according to which the generation of reactive oxygen species is a significant cause of the formation of gastric mucosal lesions. These observations indicate that antioxidants may be used to prevent NSAIDs induced gastric ulcers. During the past few decades, a large number of naturally occurring compounds have been identified as antioxidants, which are viewed as promising therapeutic agents for treating free radical mediated diseases including NSAID induced peptic ulcers. Large number of herbs and spices are recognized as source of natural antioxidants and studies have confirmed their efficacy for the treatment of gastrointestinal ulcers. Based on these observations, it has been suggested that coadminstration of antioxidants and NSAIDs in formulated dosage form may possibly decrease the risk of NSAIDs induced gastrointestinal side effects. However, there are potential advantages in giving such co-administered drugs having complementary pharmacological activities in the form of a single chemical entity. Such agents are named as mutual prodrugs which are designed with improved physicochemical properties and release the parent drug at the site of action. The project is aimed to synthesis and evaluation of NSAIDs-antioxidants mutual prodrugs as safer NSAIDs.