NSAIDs AND THE DIGESTIVE MUCOSA: MOLECULAR MECHANISMS OF DAMAGE AND REPAIR

De Ponti Fabrizio

Department of Pharmacology, University of Bologna, Bologna, Italy

Non-steroidal anti-inflammatory drugs (NSAIDs) are widely used for their analgesic, anti-inflammatory and, for some of them, antiplatelet actions (1, 2). The serious side-effects affecting the digestive mucosa are a matter of concern and pose a significant obstacle to their use. I will review the molecular mechanisms by which NSAIDs iduce gastrointestinal toxicity, taking into account both COX-dependent and COX-independent effects. Concerning the former mechanism, it is important to recognize that both COX isoforms are expressed in the gut and not only in the upper gut mucosa (3). COX-independent effect may derive from the acidic nature of some compounds as well as from additional pharmacological properties of some agents.

Apart from the well known damage caused in the upper gut, enteropathy is also a recogized side-effect of NSAIDs and will be reviewed providing an outline of the use of functional measurement of NSAID-induced changes in the gastrointestinal tract. Specifically, the open questions regarding the use of NSAIDs in patients with inflammatory bowel disease (4) will be addressed.

The progress in our understanding of the pathogenesis of the gastrointestinal effects of NSAIDs have resulted in the development of a number of novel compounds. Those strategies that also provide new insights into the molecular aspects of NSAID action (e.g. NO- and hydrogen sulfide-releasing compounds) will be briefly mentioned. Finally, the use of intestinal permeability measurements for assessment of some of these strategies will be discussed.