INTRODUCTION

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Nonsteroidal anti-inflammatory drugs are among the most commonly used drugs throughout the world. The drugs have been proven to be effective in the treatment of acute and chronic painful and inflammatory musculoskeletal conditions **(Simon, 2000).**

Nonsteroidal anti-inflammatory drugs are associated with considerable mortality and morbidity, and an excess risk of serious upper gastrointestinal (GI) events continues for up to 1 year after discontinuation **(Martin et al., 2000).** The chronic use of traditional NSAIDs for pain and inflammation is limited by their gastrointestinal and renal toxicity **(Tegeder et al., 2000).**

Nonsteroidal anti-inflammatory drugs can be classified broadly into two types based on their chemical structure. Most NSAIDs are carboxylic acids; but a few, most noticeably phenylbutazones, are enolic acids. Carboxylic acid containing drugs include salicylate derivatives (e.g., aspirin), carbocyclic and heterocyclic acid derivatives (e.g., indomethacin), fenamic acid derivatives (e.g., mefenamic acid), propionic acid derivatives (e.g., ibuprofen) and phenyl acetic acid derivatives (e.g., diclofenac). Enolic acid containing drugs include oxicam derivatives (e.g., meloxicam) and pyrazoles (e.g., phenylbutazone). Non-acidic group compounds include nabumenton **(Derle et al., 2006).**

Nonsteroidal anti-inflammatory drugs within a group will tend to have similar characteristics and tolerability. There is a little difference in clinical efficacy between the NSAIDs when used at equivalent doses. Rather, differences among compounds tended to be with regards to compound's elimination half-life), route of dosing regimens (related to the administration, and tolerability profile **(Wikipedia, 2008).**

Based on the selectivity of COX inhibition function, NSAIDs can be grouped into two pharmacologic classes: nonspecific COX inhibitors and selective COX-2 inhibitors, the coxibs **(Bronstein, 2004).**

The discovery of COX-2 in 1991 raised the hope of developing an effective NSAID without the gastric problems characteristic of these agents. It was thought that selective inhibition of COX-2 would result in anti-inflammatory action without disrupting gastroprotective prostaglandins **(Wikipedia, 2008).**

Based on recent studies using the carrageenan pleurisy mode in rats, the existence of a COX-3 enzyme has been theorized **(Bronstein, 2004).**

The relatively selective COX-2 inhibiting oxicam, meloxicam, was the first step towards developing a true COX-2 selective inhibitor. Coxibs, the newest class of NSAIDs, can be considered as true COX-2 selective inhibitors, and include celecoxib, rofecoxib, valdecoxib, parecoxib and etoricoxib **(Wikipedia, 2008).**

There is no evidence of a clinically meaningful efficacy difference between COX-2 inhibitors and traditional NSAIDs. Efficacy differences between COX-2 inhibitors may exist and further research is required to characterize these drugs **(Loewen, 2002).**

Meloxicam, nimesulide, and etodolac were identified in the 1980s as potent anti-inflammatory drugs with low ulcerogenic activity in the rat stomach. In some instances this was also shown to parallel low activity against prostaglandin synthesis in the rat stomach. After the discovery of COX-2 these three drugs were each found to be selective COX-2 inhibitors **(Vane, 2000).** Meloxicam is one of 26 new molecular entities

approved by Food & Drug Administration in 2000. Meloxicam is a new addition to the nonsteroidal anti-inflammatory drug family in the United States, but it has a track record of prior use in millions of patients across more than 100 countries **(Davies and Vinson, 2001).**

Etodolac, an acetic acid derivative, has been under clinical investigations since 1979 and has showed a favorable safety profile in over 11,000 patients of varying age **(Mabee et al., 1995).**

Inhibitors of cyclooxygenases (COXs) are the most widely used drugs. Selective cyclooxygenase (COX)-2 inhibitors that are in widespread clinical use were developed to avoid side effects of conventional NSAIDs, including gastrointestinal and renal toxicity.

Nonsteroidal anti-inflammatory drugs gastropathy is associated with substantial morbidity and mortality, which result in high costs to both the patient and society **(Roth, 1996).**

Two of the most widely prescribed selective COX-2 inhibitors; meloxicam and etodolac, were studied to estimate the extent of their hepatorenal and genotoxic effects in order to encourage or discourage their clinical use.