Chapter I

Non-steroidal anti-inflammatory drugs (NSAIDs)

I.1 Introduction

Non-steroidal anti-inflammatory drugs (NSAIDs) are widely used for treatment of pain, fever and inflammation[1]. The worldwide NSAID market for both occasional and chronic users has been conservatively estimated over 60 million people, and certain NSAIDs (aspirin, naproxen, ibuprofen) are among the most popular over-the-counter medications[2,3]. Chronic NSAIDs therapy effectively reduces the symptoms of many painful arthritic syndromes, but invites adverse gastrointestinal (GI) complications ranging from stomach irritation to life-threatening GI ulceration, bleeding and perforation to more serious small-bowel ulceration[4-6]. At the tissue level, the most common clinical manifestation of NSAID-related GI damage is a combination of gastroduodenal erosions and ulcerations often called NSAID-induced gastropathy[5,6], affecting at least 25% of chronic NSAID patients. NSAID-induced gastropathy may limit long-term NSAID therapy and cause a significant financial burden to the healthcare system[5-9].

I.2 Mechanism of action

NSAIDs (including aspirin) act primarily by inhibiting the synthesis of prostaglandins from arachidonic acid. This anti-prostaglandin effect is to be the major mechanism of action of NSAIDs, it may produce analgesia by blocking prostaglandin-related pain impulse generation, or through inhibition of other pain mediators, such as bradykinin or histamine. Higher doses of NSAIDs also produce anti-inflammatory effects. Although the precise mechanism of the anti-inflammatory effects of NSAIDs are uncertain, it is thought to be related, in part, to prostaglandin inhibition. Prostaglandins are released from injured cells and cause erythema, vasodilatation and hyperalgesia. Other anti-inflammatory effects of NSAIDs are inhibition of leukocyte migration, inhibition of lysozymal enzymes, or interference with other cell processes, such as cell binding or transmemberane ion fluxes. An NSAID dose higher than that required to inhibit prostaglandin synthesis may be required for an optimal anti-inflammatory effect, suggesting that the inflammatory effect of NSAIDs are wholly due to their anti-prostaglandin effect[10,11].

I.3 Therapeutic uses of NSAIDs

Several medicinal uses of NSAIDs are reviewed such as pain, fever and platelet aggregation reduction. They are also used in the treatment of osteoarthritis, rheumatoid arthritis and enclosing spondylitis. Recent therapeutic uses are prevention of renal tissue damage[12] and early retinopathy[13].

I.4 Classification of NSAIDs

Non-steroidal anti-inflammatory drugs are classified according to their chemical structure into the following classes[14] (see **Table I.1**).

1-Salicylates
2-Anthranilates
3-Arylacetic acid derivatives
4-Arylpropionic acid derivatives
5-Pyrazolinone derivatives
6-Acidic enolic compounds
7-Arylsulfonamides
8-Salicylates