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بالرسالة صفحات لم ترد بالأصل

A PILOT STUDY ON SIDE EFFECTS OF SOME NONSTEROIDAL ANTI-INFLAMMATORY DRUGS

THESIS

SUBMITTED FOR PARTIAL FULFILMENT FOR THE DEGREE OF M.SC. IN RHEUMATOLOGY AND REHABILITATION

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IN THE NAME OF ALLAH,
THE MOST BENEFICIENT,
THE MOST MERCIFUL

TO

MY PARENTS AND MY SISTERS

ACKNOWLEDGEMENT

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CONTENTS

CONTENTS

INTRODUCTION

Nonsteroidal anti-inflammatory drugs (NSAIDs) are used commonly for a variety of rheumatic disorders. Over 35 million NSAID prescriptions and billions of over-the-counter aspirin, ibuprofen, and naproxen preparations are sold annually allover the world *(**Paulus, 1985**)*, and more than 1% of the American population uses these drugs on a daily basis *(**McCarthy, 1989**)*. For the majority of individuals, they are well tolerated; nevertheless, in a significant minority, gastrointestinal (GI) side effects may result in serious complications necessitating their discontinuation *(**McCarthy, 1989**)*. Physicians are responsible for appropriately prescribing these medications must balance their anti-inflammatory and analgesic benefit against their potential for inducing serious toxicity. Adverse effects from these medications as a group is reported to the food and drug administration more frequently than from any other medication class *(**Lanza, 1984**)*.

Although adverse events affect only a small proportion of those taking NSAIDs, their widespread use translates into a substantial number of affected persons. Furthermore, complications associated with these side effects contribute considerably to increased morbidity and mortality, and treatment of these common but debilitating diseases entails significant costs *(**Lichtenstein et al, 1995**)*.

Worldwide, there are over 100 NSAIDs either marketed or at an advanced stage of development *(**Rainsford, 1987**)*. This group of drugs has acquired a certain notoriety in recent years because seventeen individual agents have been withdrawn or had clinical studies terminated following toxicity *(**Rainsford, 1987**)*. In many instances the unwanted effects are, to a degree, common to the whole class *(**Henry, 1988**)*.

The review will concentrate on the serious toxicity of the drugs which are in current widespread use and, where it is relevant, will highlight individual drugs which seem to be associated with exceptional risks.

Historical overview of NSAIDs

Rev. Edmond Stone, 1763 said: 'There is a bark of an English tree, which I have found by experience to be a powerful astringent, and very efficacious in curing aguish and intermitting disorders.' *(Wright, 1995)*

Sixty-five years after the Rev. Edmond Stone made his observation; salicin crystals were isolated from willow bark. Within 10 years the term 'salicylic acid' was coined. By 1860, salicylic acid was being synthesized, and in 1874, large-scale production was under way *(Weissman, 1991)*. Within 3 years, acute rheumatic fever, gout and chronic polyarthritis were being managed with salicylates. In 1898, aspirin (acetylsalicylic acid) was discovered. Since that time, a plethora of NSAIDs have been developed and marketed. According to an informal poll of a symposium audience *(Decisions in Non Steroidal Anti-inflammatory Prescribing, International League Against Rheumatism, 5 July 1993, Barcelona, Spain)*, these agents' popularity can be attributed to the following characteristic, ranked in order of importance: anti-inflammatory action, pain relief, tolerability, patient compliance and speed of action *(Wright, 1995)*.

Classifications of NSAIDs

The NSAIDs can be classified on the basis of their chemical structures (Fig. 1), as follows:

(I)Acidic Agents:

(A) Arylcarboxylic Acids:

(1) Salicylic acids:

Aspirin in its various forms, salsalate, Cholinesalicylate and sodium salicylate.

(2) Anthranilic acids (fenamates)

Flufenamic acid, mefenamic acid, meclofenamic acid, niflumic acid.

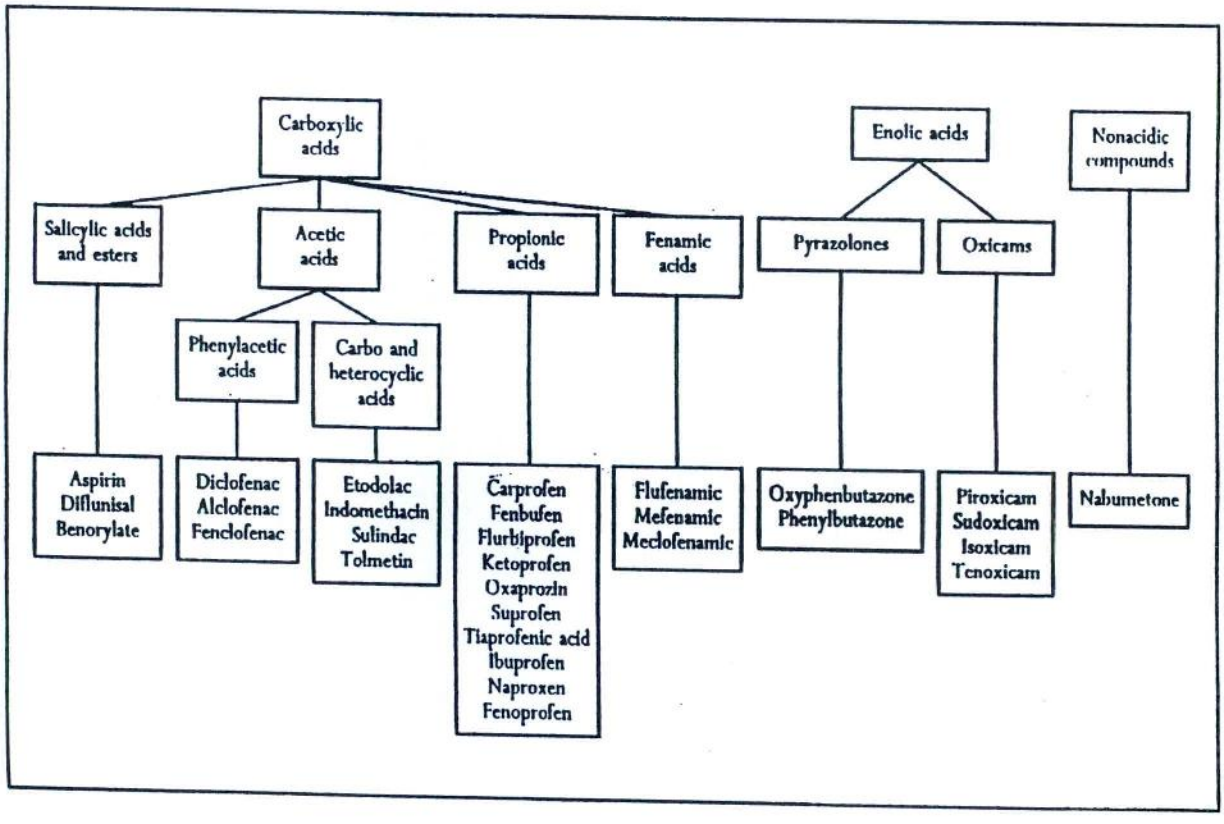

Fig. 1: Classification of NSAIDs by chemical class (from Thompson & Dunne, 1995).