INTRODUCTION

The pharmacotherapy of the inflammatory diseases really began in the late 19th century, as chemists elaborated salicylic acid into acetylsalicylic acid (aspirin). The discovery of the clinical activity of phenylbutazone initiated research into laboratory animals on inflammatory diseases, and such models allied to a large screening program led to the introduction of indomethancin in the early sixties. Since that time, a plethora of structurally related carboxylic acids have been introduced as non-steroidal antiinflammtory drugs (NSAIDS) (Flower *et al.*, 1985).

There has been substantial progress in elucidating the action mechanism of non-steroial antiinflammatory drugs, and it is now possible to understand why such heterogeneous agents have the same basic therapeutic activities and often the same side effects. Indeed their therapeutic activity appears to depend to a large extent upon the inhibition of a defined biochemical pathways responsible for the biosynthesis of the prostaglandins and related autacoids (Brune, 1981).

Inflammation in patients with rheumatoid arthritis probably involves the combination of an antigen (gama globulin) with an antibody (rheumatoid factor) and complement, causing the local release of chemotactic factors that attract leukocytes. The leukocytes phagocytose, the complexes of antigen, antibody and complement which release many enzymes contained in their lysosomes. These lysosomal enzymes then cause injury to cartilage and other tissues, and this furthers the degree of inflammation. Cell-mediated immune reactions may also be involved. Prostaglandins are also released during this process. Non-steroidal antiinflammatory drugs inhibit these effects (Insel, 1991).

In addition to sharing many therapeutic activities non-steroidal antiinflammatory drugs share several undesirable effects. The most common is a propensity to induce gastric or intestinal ulceration that can sometimes be accompanied by a secondary anemia from the resultant blood loss.

There are other side effects of these drugs that probably depend upon their capacity to block endogenous prostaglandin biosynthesis: these include disturbances in platelet function and the prolongation of gestation or

spontaneous labor. Platelet function appears to be disturbed because NSAIDS prevent the formation by the platelets of thromboxane A_2 (TXA_2), a potent aggregation agent. These accounts for the tendency of these drugs to increase the bleeding time.

Non steroidal antiinflammatory drugs have little effect on renal function in normal humans however, they decrease renal blood flow and the rate of glomerular filtration in patients with congestive heart failure or, cirrhosis with ascites, (Flower *et al.*, 1985).

Biochemical analysis may be utilized as markers or probes to demonstrate undesirable effects of drugs on internal organs and body systems. Also, it is an application of biochemical technology in the illucidation of toxicological aspects of medication.

The aim of this research is to elucidate the toxicological side effects of two commonly used non steroidal antiinflammatory drugs i.e., piroxicam and pirprofen. Besides, an attempt was carried out to minimize their harmful side effect by using methyl androstenolone acetate as anabolic steroid compound.