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Pharmacological and biochemical activities of Tenoxicam (Ro 12-0068), a new non-steroidal anti-inflammatory drug

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Abstracts

Tenoxicam, a new non-steroidal anti-inflammatory drug has been compared with piroxicam and indomethacin in a range of pharmacological and biochemical inflammation test systems. In a chronic (17-day) adjuvant arthritis in the rat, tenoxicam and piroxicam were equally effective in reducing several indices of inflammation and were less ulcerogenic and better tolerated than indomethacin. The oxicams reduced the oedematous and cellular components of a carrageenan pleurisy at 4 hours while at 24 hours they increased exudate volume and selectively inhibited the accumulation of mononuclear cells. These agents also reduced the inflammatory component of a delayed hypersensitivity response to methylated bovine serum albumin in the mouse. The oxicams were about 100-fold less active than indomethacin as inhibitors of prostaglandin synthetase but all three compounds reduced about equally the release of prostaglandin E_2 from phagocytosing rat PMN and interleukin 1-stimulated human rheumatoid synovial cells. The compounds had no effect on the release of superoxide anion, lysosomal enzymes or collagenase from cultured cells, neither did they inhibit isolated collagenase. Only indomethacin stabilized albumin against heat denaturation.

Introduction

Tenoxicam (Ro 12-0068) is a thienothiazine derivative (Fig. 1) belonging to the oxicam class of non-steroidal anti-inflammatory drugs [1]. In animal models tenoxicam has shown good anti-inflammatory and analgesic activity, with evidence of only weak prostaglandin synthesis inhibition as assessed by indirect methods [2–4]. In human studies the compound has been shown to be rapidly absorbed with a bioavailability of more than 99% and a half-life of about 70 hours, thus allowing once-daily administration (data on file, Hoffmann-La Roche & Co.). Various clinical studies have indicated that tenoxicam, at a daily dose of 20 mg or 40 mg is effective in rheumatoid arthritis [5–8], osteoarthritis [9, 10] and gout [6, 7]. In the present work further pharmacological and biochemical studies on tenoxicam are described which help to elucidate the possible mechanism(s) of action when compared with piroxicam and indomethacin, an aryl alkanoic acid type of anti-inflammatory drug.

Materials

Tenoxicam and piroxicam were supplied as micronized powders by Dr R. Pfister (Hoffmann-La Roche & Co., Basle). Indomethacin was purchased from Sigma (London) Chemical Co. Ltd.

Methods

Adjuvant arthritis – chronic (17-day) study

Adjuvant arthritis was induced in groups of 5 rats (AHH/R, female 115–170 g) by the method of NEWBOULD [11]. In summary, the right hind paw of each rat was injected into the sub-plantar surface with 0.1 ml adjuvant consisting of a homogenized suspension of heat killed *M. tuberculosis* (human strains C, DT and PN), 5 $mg \cdot ml^{-1}$ in liquid paraffin. One group of three normal rats, in which no adjuvant was injected was also set up to reflect normal weight gain.

Drugs were prepared as sonicated aqueous suspensions in 0.5% w/v sodium carboxymethylcellulose containing 0.05% v/v Tween 80. They were administered each morning (except for the first week-end) from the day of adjuvant injection.

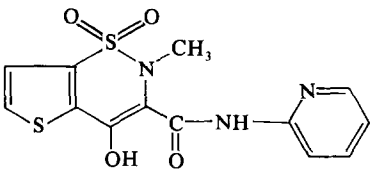

Figure 1
Structure of tenoxicam