Piroxicam-β-Cyclodextrin
A Review of its Pharmacodynamic and Pharmacokinetic
Properties, and Therapeutic Potential in Rheumatic Diseases
and Pain States

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Summary

Piroxicam-β-cyclodextrin is a complex of the established nonsteroidal anti-inflammatory drug (NSAID) piroxicam and an inert cyclic macromolecule, β-cyclodextrin. In clinical trials in patients with rheumatic diseases or pain arising from other conditions, it was as effective an analgesic as standard piroxicam, and showed a faster onset of action on the first day of treatment.

In short term pharmacodynamic studies in healthy volunteers, piroxicam-β-cyclodextrin was equivalent to or tended to show less gastrointestinal mucosal toxicity than standard piroxicam, as assessed by endoscopy and faecal blood loss. However, no data are available on its comparative gastrointestinal mucosal effects from long term clinical trials using similar measures. Preliminary findings from a clinical study suggest piroxicam-β-cyclodextrin caused fewer gastroduodenal lesions than tenoxicam. As with other NSAIDs, the majority of adverse events associated with piroxicam-β-cyclodextrin in clinical trials were gastrointestinal in origin, with epigastric pain, heartburn and nausea the most common.

Thus, piroxicam-β-cyclodextrin is an effective agent in patients with rheumatic diseases or other pain states. When rapid analgesia is required in the initial treatment of acute pain, the faster onset of action of piroxicam-β-cyclodextrin may be an advantage over the parent compound; however, this is unlikely to be important during long term therapy. The results of further long term trials are awaited before firm conclusions can be reached regarding the gastrointestinal tolerability of piroxicam-β-cyclodextrin compared with that of standard piroxicam and other NSAIDs.

Pharmacodynamic Properties

Piroxicam-β-cyclodextrin is a NSAID with anti-inflammatory, analgesic and antipyretic properties. Limited data available on the analgesic and anti-inflammatory effects of piroxicam-β-cyclodextrin suggest that it is equivalent to piroxicam in animal and human models of pain. The effects of piroxicam-β-cyclodextrin on the gastrointestinal mucosa have been more extensively studied.

Findings from endoscopy and faecal blood loss studies suggest that piroxicam-β-cyclodextrin is equivalent to, or shows a trend to be less toxic than, the parent molecule in healthy volunteers aged 20 to 50 years. However, none of these trends reached statistical significance.

In these studies, total endoscopy scores were similar for both drugs. In 2 studies of 1 month’s duration, piroxicam-β-cyclodextrin 20 mg/day tended to cause less cumulative faecal blood loss than piroxicam 20 mg/day after 2 to 4 weeks’ treatment. In all studies piroxicam-β-cyclodextrin showed a trend towards greater gastric mucosal damage, or significantly more damage, than placebo.

Pharmacokinetic Properties

Administration of piroxicam-β-cyclodextrin as a single dose in fasting volunteers resulted in mean plasma piroxicam concentrations 0.25 and 0.5 hours after administration that were, respectively, 3 to 10 and 1.3 to 3 times higher than after standard piroxicam administration in 2 comparative studies.

Although food slowed the absorption from both products, plasma concentrations of piroxicam were still 2 to 4 and 1.3 to 1.4 times higher 0.5 and 2 hours after administration of piroxicam-β-cyclodextrin than after standard piroxicam. However, after multiple-dose administration the only difference was at 0.25 hours after administration, when the plasma concentration of piroxicam was 1.3 times higher after piroxicam-β-cyclodextrin than piroxicam. The area under the plasma