An Examination of Hepatic Effects during Diclofenac or Celecoxib Administration in the Presence or Absence of Rebamipide

East Tennessee State University

Purpose
Two isoforms of cyclooxygenase (COX-1 and COX-2) are inhibited by nonsteroidal anti-inflammatory drugs (NSAIDs). Nonselective NSAIDs (diclofenac) and COX-2-selective inhibitors (celecoxib) produce adverse effects through reduced prostaglandin production. Rebamipide, a prostaglandin synthesis inducer, has been utilized to prevent NSAID-induced gastric injury. This study examined the hepatic effects, oxidative stress and histopathology, of diclofenac or celecoxib in the presence or absence of rebamipide.

Methods
On days 1 and 2, following randomization into six groups (n≥5), rats received two daily administrations of either placebo or rebamipide (30 mg/kg). On day 3 in addition to a single placebo or rebamipide treatment, one placebo and one rebamipide group received celecoxib (40 mg/kg); while two other groups (placebo and rebamipide) were administered diclofenac (10 mg/kg). The remaining groups continued initial treatment. Upon sacrifice (day 4), excised livers were stored at -80 °C. A certified pathologist, blinded to the study, examined the hematoxylin and eosin stained liver sections. Colorimetric assays detected malondialdehyde (MDA) and total glutathione, oxidative stress biomarkers. Biomarker data underwent ANOVA and was presented as mean±SEM.

Results
All slides presented within normal histological limits having no inflammation, injury, or necrosis. Control MDA levels ranged from 7.65 to 10.33 µmol/g. Compared to control (8.85±0.46 µmol/g), no treatment group, celecoxib (7.91±0.80 µmol/g), diclofenac (7.68±0.42 µmol/g), rebamipide (9.92±0.41 µmol/g), celecoxib+rebamipide (8.86±0.54 µmol/g), or diclofenac+rebamipide (8.44±0.36 µmol/g), presented significance (p>0.130). Total glutathione levels ranging from 8.30 to 10.38 µmol/g were detected in controls. No significant difference (p>0.307) was observed between the treatment groups, celecoxib (11.08±1.08 µmol/g), diclofenac (10.46±0.82 µmol/g), rebamipide (11.22±0.89 µmol/g), celecoxib+rebamipide (9.95±0.86 µmol/g), or diclofenac+rebamipide (8.96±1.01 µmol/g), compared to control (9.81±0.39 µmol/g).

Conclusion
The absence of significant oxidative stress or histopathology indicates that at the dose examined neither celecoxib, diclofenac, rebamipide, celecoxib+rebamipide, nor diclofenac+rebamipide produced hepatic injury.