Morphological alteration in mitochondria following diclofenac and ibuprofen administration.

ABSTRACT

This study was conducted to identify and to compare the mitochondrial morphological alterations in livers of rats treated with various doses of diclofenac and ibuprofen. Hundred and forty-four male Sprague Dawley rats were dosed with 3, 5 and 10 mg kg⁻¹ diclofenac and ibuprofen in saline via intraperitoneal injection for 15 days. The control group was administered with saline in a similar manner. Four rats were euthanised every 3 days until day 15. While 200 mg kg⁻¹ diclofenac and ibuprofen-treated rats (n = 4) were euthanized 10 h post-treatment. The livers were removed, cleaned and a section across the right lobe was taken and fixed in 4% (v/v) glutaraldehyde for electron microscopy analysis and the remaining samples were kept at -80°C for Western blot analysis. Five milligram per kilogram and 10 mg kg⁻¹ diclofenac-administered rats for 15 days revealed the presence of enlarged mitochondria, irregular and ruptured mitochondrial membranes. While rats administered with 10 mg kg⁻¹ ibuprofen also showed the presence of mitochondria with irregular membrane structure and ruptured membranes. Western blotting analysis of mitochondrial fractions revealed the expression of cytochrome c in all samples and complete absence of cytochrome c expression in the cytosolic fraction of all samples after day 15. Analysis in 200 mg kg⁻¹ diclofenac and ibuprofen-treated groups, revealed expression of cytochrome c in both mitochondrial and cytosolic fractions. This observation indicates that both diclofenac and ibuprofen may alter the morphology of mitochondria, leading to cytochrome c release into the cytosol. Further studies needs to be conducted to investigate on the activity of the mitochondria following both treatments.

Keyword: Cytochrome c; Hepatotoxicity; Mitochondria; Non-steroidal anti-inflammatory drugs.