Abstract

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Antiulcer activity of Cyperus alternifolius in relation to its UPLC-MS metabolite fingerprint: a mechanistic study

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Background Gastric ulcer is one of the main prevalent gastrointestinal multi-etiological disorders with many associated complications and adverse effects. Our aim was to develop safer antiulcer therapies based on methanol ethyl acetate extracts of tubers and aerial parts from Cyperus alternifolius. Methods Gastric ulceration was experimentally generated by administration of single oral doses of indomethacin (30?mg/kg) to fasted rats. The animals received methanol ethyl acetate extracts of C. alternifolius tuber and methanol ethyl acetate extracts of aerial parts at two dose levels (50 100?mg/kg). Ranitidine (50?mg/kg) was used as standard anti-ulcer drug. After 4?h, the ulcer number and the total ulcer score were determined and TNF-? was assessed. Also, pathological and histochemical examination for gastric mucosa were performed. The metabolome heterogeneity of the different extracts was explored using (UPLC-MS) aided by supervised pattern recognition, i.e., orthogonal partial least squares discriminate analysis (OPLS-DA). A second OPLS-DA model was employed to link the UPLC-MS derived metabolome of the different extracts to their antiulcer activity to identify activity mediating metabolites. Results The extracts significantly reduced ulcer number, total ulcer score and TNF-? content in the stomach. Methanol ethyl acetate extracts of tubers were most effective even more than ranitidine. In parallel, the histopathological examination showed an improvement of damaged mucosa. A high PAS reaction was observed in the treated groups indicating a relieve of the mucosal layer. A mechanistic clue of the C. alternifolius antiulcer potential was provided by the identification of its bioactive compounds using OPLS-DA. Both methanol extracts of tubers and aerial parts were more enriched in phenolic acids. The ethyl acetate extract of the aerial part was more abundant in two aldehydes. A mechanism of action was postulated based on their reported actions viz. ?-carbonic anhydrase inhibition, anti-inflammatory and analgesic activity by its antioxidant activity and downregulation of several inflammatory mediators. Conclusion This is the first study to report on the antiulcer activity of C. alternifolius tubers with identification of the key bioactive compounds and the mode of action. Future phytochemical and biological evaluation of the identified bioactive compounds are needed to confirm the plant tubers as safer alternative adjunct therapy compared to conventional antiulcer drugs.