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Título	Sex-specific effects of Eugenia punicifolia extract on gastric ulcer healing in rats
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Resumo	<p>AIM: To evaluate the sex-specific effects of a hydroalcoholic extract from Eugenia punicifolia (HEEP) leaves on gastric ulcer healing.</p> <p>METHODS: In this rat study involving males, intact (cycling) females, and ovariectomized females, gastric ulcers were induced using acetic acid. A vehicle, lansoprazole, or HEEP was administered for 14 d after ulcer induction. Body weight was monitored throughout the treatment period. At the end of treatment, the rats were euthanized and the following in vivo and in vitro investigations were performed: macroscopic examination of the lesion area and organ weights, biochemical analysis, zymography, and evaluation of protein expression levels. Additionally, the concentration-dependent effect of HEEP was evaluated in terms of subacute toxicity and cytotoxicity.</p> <p>RESULTS: Compared to the vehicle, HEEP demonstrated a great healing capacity by substantially reducing the ulcerative lesion area in males (52.44%), intact females (85.22%), and ovariectomized females (65.47%), confirming that HEEP accelerates the healing of acetic acid-induced gastric lesions and suggesting that this effect is modulated by female sex hormones. The antiulcer effect of HEEP was mediated by prostaglandin E2 only in male rats. Overall, the beneficial effect of HEEP was the highest in intact females. Notably, HEEP promoted the expression of vascular endothelial growth factor (intact vs ovariectomized females) and decreased the expression of Caspase-8 and Bcl-2 (intact female vs male or ovariectomized female). Additionally, HEEP enhanced fibroblast</p>



	<p>proliferation and migration into a wounded area in vitro, confirming its healing effect. Finally, no sign of subacute toxicity or cytotoxicity of HEEP was observed. CONCLUSION: In gastric ulcers, HEEP-induced healing (modulated by female sex hormones; in males, mediated by prostaglandin) involves extracellular matrix remodeling, with gastric mucosa cell proliferation and migration.</p>
Fomento	