ANTINFLAMMATORY ACTIVITY AND GASTROPROTECTIVE EFFECT OF THE ANTIOXIDANT COMPOUND IACVITA IN RATS

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IACVITA, bis (1-hydroxy-2,2,6,6,-tetramethyl-4-piperidinyl) decanoate (Medestea International), is a compound with antioxidant activity. Potential therapeutic indications for IACVITA were identified in the treatment of ROS (Reactive Oxygen Species) related diseases and ischaemic disturbances i.e. TIA (Transient Ischaemic Attack). The aim of the present study was to investigate the antinflammatory activity of this compound in rats, using the carrageenan-induced paw oedema and the cotton pellet granuloma assays in acute and chronic experimental conditions, respectively. Sprague-Dawley rats were treated intraperitoneally (i.p.) or orally with IACVITA, solubilized in water, at doses of 10, 25 and 50 mg/kg. Indomethacin, dosed orally at 2.5 mg/kg, was used as reference antiflogistic drug. All treatments were performed 30 min before tests. For statistical analysis of the data, one way analysis of variance (ANOVA) and Dunnett's or Newman-Keuls post tests were used. As expected, indomethacin inhibited the development of hind-paw oedema, produced by intraplantar injection of carrageenan solution. IACVITA, at all used dosages, exerted a significant antinflammatory effect after i.p. injection. This effect was not exerted after oral IACVITA treatment, suggesting a critical bioavailability of the compound when administered by this way. In the cotton pellet granuloma assay, the i.p. treatment with IACVITA, at doses of 25 and 50 mg/kg, for 7 consecutive days, significantly (P<0.01) reduced the weight of cotton pellet, in comparison with the vehicle group (11.6±1.4 and 11.4±1.5 for IACVITA 25 and 50 mg/kg, respectively vs. 23.0±2.1) as well as indomethacin treated rats (11.9±0.9). Then, we investigated the potential gastric toxicity of IACVITA alone, using an arbitrary scale (score from 0=normal mucosa to 5=perforating ulcers). IACVITA at both dosages (25 and 50 mg/kg), administered orally or i.p. didn't affect the integrity of gastric mucosae. Following these results we tested the ability of IACVITA to affect the severity of indomethacin-induced gastric ulcers. When this compound was administered orally, at the dose of 50 mg/kg, 15 min after indomethacin, it was only partially able to counteract indomethacin-induced gastric ulcers (2.5±0.2 vs. 3.8±0.1; P<0.01), whereas it was clearly able to prevent gastric ulcers (0.7±0.1 vs. 3.8±0.1; P<0.001) when administer 15 min in advance, interestingly suggesting that IACVITA could be used as a gastric protective agent. From these data it might be suggested that IACVITA exert an antiflogistic activity with a mechanism of action apparently different from the classical FANS. This concept seems to be corroborated by the demonstration that IACVITA did not induce gastric lesions when injected alone and did not affect prostaglandine PGE2 levels.