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ANALGESIC ACTIVITY AND MECHANISM OF ACTION OF THE MONOTERPENE p-CYMENE IN THE RAT MODEL OF INFLAMMATORY PAIN

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p-Cymene is a monoterpene phenol, an active ingredient of essential oils extracted from various plants (Cumin, Thyme...). In addition to its anti-inflammatory and anti-oxidant activities, the analgesic activity of p-Cymene has recently been considered..

The aim of this study was to examine the analgesic effect of p-Cymene, and to compare it with the same effect of standard analgoantipyretic diclophen, and especially to examine the possibility of the interaction of p-Cymene and non-selective and selective NO-synthase inhibitors L-NAME and aminoguanidine (AG) on carrageenan-induced hypernociception in female rats.

Inflammatory pain (hypernociception) was induced by intraplantar (i.pl.) administration of carrageenan (500µg) into the rat hind paw. Electronic von Frey apparatus (ELUNIT, Belgrade) was used to determine paw withdrawal threshold induced pressure as the painful stimulus, and the effect was measured in grams (q).

p-Cymene (5-50 mg/kg,p.o.), given 50 min before i.pl. injection of carrageenan, produced significant (p<0.01,p<0.001) dose-dependent antinociception. p-Cymene (25 mg/kg,p.o.) and diclophen (10 mg/kg,p.o.) exhibited a similar antinociceptive activity in intensity and duration. p-Cymene (5 mg/kg,p.o.) coadministered with L-NAME or AG (5 mg/kg and 0.3 mg/kg,i.p.) caused a significantly higher (p<0.01, p<0.001) antinociceptive effect compared to the effect of p-Cymene alone. Also, in the presence of NO donor L-arginine (10 mg/kg,i.p.) the antinociceptive effect of the combination of p-Cymene + L-NAME and p-Cymene + AG, showed significant attenuation (p<0.05,p<0.01,p<0.001) throughout the whole measurement (1-6 hours).

p-Cymene leads to a dose-dependent antinociceptive effect in carrageenan-induced hypernociception, with intensity and duration similar to the antinociceptive effect of diclophen. p-Cymene, non-selective and selective NOS inhibitors (L-NAME and AG) administered together have a synergistic effect in carrageenan-induced hypernociception which is significantly reduced in the presence of L-arginine. On the basis of these results, we conclude that p-Cymene has analgesic activity based on the modulation of the L-arginine-NO system.