

Antinociceptive Activity of Structural Analogues of Rotundifolone: Structure-Activity Relationship

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Rotundifolone, a monoterpene isolated from the essential oil of the leaves of *Mentha × villosa*, is a constituent of several essential oils and known to have antinociceptive activity. Our recent study demonstrated that the analogues of rotundifolone showed also a significant antinociceptive effect. In the present report, to investigate the correlation between the structure and antinociceptive activity, rotundifolone and its analogues were evaluated in the acetic acid-induced writhing test in mice. All compounds showed to be more antinociceptive than rotundifolone against the pain response induced by acetic acid. Comparing the antinociceptive effect of rotundifolone with limonene oxide and (+)-pulegone, the results demonstrated that the epoxide group contributes as much as the ketone group to the antinociceptive activity of rotundifolone. Similarly, pulgone oxide and carvone epoxide were more antinociceptive than rotundifolone, thereby suggesting that the position of the functional group on the ring also influences the antinociceptive activity. (–)-Carvone produced maximal inhibition of the writhing response and was slightly more active than (+)-carvone. The study showed that by appropriate structural modification it may be possible to develop novel antinociceptive agents.

Key words: Rotundifolone, Monoterpenes, Analgesic Activity, *p*-Menthanes