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Rational Basis for the Use of Bergamot Essential Oil in Complementary Medicine to Treat Chronic Pain

L Rombolà¹, D Amantea, R Russo, A Adornetto, L Berliocchi, L Tridico, M T Corasaniti, S Sakurada, T Sakurada, G Bagetta, L A Morrone

Affiliations

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Abstract

In complementary medicine, aromatherapy uses essential oils to improve agitation and aggression observed in dementia, mood, depression, anxiety and chronic pain. Preclinical research studies have reported that the essential oil obtained from bergamot (BEO) fruit (*Citrus bergamia*, Risso) modifies normal and pathological synaptic plasticity implicated, for instance, in nociceptive and neuropathic pain. Interestingly, recent results indicated that BEO modulates sensitive perception of pain in different models of nociceptive, inflammatory and neuropathic pain modulating endogenous systems. Thus, local administration of BEO inhibited the nociceptive behavioral effect induced by intraplantar injection of capsaicin or formalin in mice. Similar effects were observed with linalool and linalyl acetate, major volatile components of the phytocomplex. Pharmacological studies showed that the latter effects are reversed by local or systemic pretreatment with the opioid antagonist naloxone hydrochloride alike with naloxone methiodide, high affinity peripheral μ -opioid receptor antagonist. These results and the synergistic effect observed following systemic or intrathecal injection of an inactive dose of morphine with BEO or linalool indicated an activation of peripheral opioid system. Recently, in neuropathic pain models systemic or local administration of BEO or linalool induced antiallodynic effects. In particular, in partial sciatic nerve ligation (PSNL) model, intraplantar injection of the phytocomplex or linalool in the ipsilateral hindpaw, but not in the contralateral, reduced PSNL-induced extracellular signal-regulated kinase (ERK) activation and mechanical allodynia. In neuropathic pain high doses of morphine are needed to reduce pain. Interestingly, combination of inactive doses of BEO or linalool with a low dose of morphine induced antiallodynic effects in mice. Peripheral cannabinoid and opioid systems appear to be involved in the antinociception produced by intraplantar injection of β -caryophyllene, present in different essential oils including BEO. The data gathered so far indicate that the essential oil of bergamot is endowed with antinociceptive and antiallodynic effects and contribute to form the rational basis for rigorous testing of its efficacy in complementary medicine.

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