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Systemic and spinal administration of FAAH, MAGL inhibitors and dual FAAH/MAGL inhibitors produce anti-pruritic effect in mice

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The increase of endocannabinoid tonus by inhibiting fatty acid amide hydrolase (FAAH) or monoacylglycerol lipase/MAGL inhibitors have also been described to get enhanced endocannabinoid therapeutic effect. Recent studies reported that systemic administration of FAAH and MAGL inhibitors elicit anti-pruritic effect. The effects of dual FAAH/ MAGL inhibitors on pruritus in comparable FAAH and MAGL inhibitors are not investigated yet. Additionally, it is well known that spinal cord is an important site in the modulation of itch, but there is no study to investigate the potential contribution of spinal site of action of FAAH, MAGL and dual FAAH/MAGL inhibitors on pruritus. In this study, we examined and compared dose related anti-pruritic effects of selective FAAH inhibitor PF-3845, selective MAGL inhibitor JZL184, and dual inhibitor JZL195 on intradermal serotonin-induced scratching model following their intraperitoneal or intrathecal administration in mice. Serotonin (25 µg) was injected intradermally in a volume of 50 µl into the rostral part of skin on the back of male Balb-C mice (23-28 gr) and scratches were counted for a 30 min observation period. Both systemic or intrathecal treatments withPF-3845, JZL184 or JZL195 produced similar dose dependent anti-pruritic effects. Our results suggest that endocannabinoid degrading enzymes FAAH and MAGL involve in pruritic process at spinal level and FAAH, MAGL or dual FAAH/MAGL inhibitors have promising anti-pruritic effects when given systemically or intrathecally.

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Neonicotinoids as a potential threat to honey: Liquid chromatography analysis

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Neonicotinoids are a relatively new class of the insecticides chemically related to nicotine. In less than 20 years, neonicotinoids become the most widely used class of insecticides. Their presence now accounts for at least one quarter of the world insecticide market. Different studies in Europe and USA have demonstrated that sub lethal amounts of neonicotinoids cause disorientation, reduced communication, impaired learning and memory, reduced longevity and disruption of honeybee brood cycles. Moreover, residues of these insecticides may be found in the final products of bees such as honey, pollen, beeswax, propolis etc. The European Commission has banned the use of imidacloprid, thiamethoxam and clothianidin in crops attractive to pollinators in 2013 emphasizing the awareness of potential harmful impact of the neonicotinoids on honeybees and their products. Therefore, monitoring and determination of trace levels of the neonicotinoids in honey are necessary and demands highly efficient, selective and sensitive analytical techniques. The aim of this study was to develop and optimize analytical methods based on liquid chromatography with dispersive liquid-liquid microextraction (DLLME) and QuEChERS sample preparation procedures for the simultaneous analysis of seven neonicotinoids (dinotefuran, nitenpyram, thiametoxam, clothianidin, imidacloprid, acetamiprid and thiacloprid) in honey samples. The liquid chromatographic conditions were optimized by Response Surface methodology with Box-Behnken design and Derringer´s desirability. The optimized method was validated to fulfill the requirements of SANCO/12495/2011 standard for both sample pretreatment procedures. For the first time more than 100 honey samples from Republic of Serbia were analyzed.

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