

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

Ozgur Yesilyurt¹, Mutlu Cayirli², Yusuf Serdar Sakin¹, Melik Seyrek¹, Ahmet Akar¹ and Ahmet Dogrul¹

¹Gulhane Academy of Medicine, Turkey

²Mevki Military Hospital, Turkey

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 with PF-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.

oyesilyurt@gata.edu.tr

Notes: