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## 14-O-methylmorphine-6-O-sulfate, a novel opioid agonist displays peripheral antinociception following local or systemic administration

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**Background & Aim:** Convincing data supports the contribution of peripheral opioid receptors to total antinociception produced by systemic opioids. To achieve that, the physicochemical property of test drug should be accounted. Herein, we examined the antinociceptive effect of 14-O-methylmorphine-6-O-sulfate (14-O-MeM6SU), in the rat formalin test after systemic or local administration.

**Method:** Pain events were induced by intraplantar 2.5% formalin solution. Then, pain events were counted for 60 min, subdivided into 5 min periods. The 0-10 and 11-60 min time periods were named as phase I and phase II, respectively. Drugs were injected subcutaneously (s.c.) or intraplantarly (i.pl.), 15 or 5 min prior to i.pl. formalin injection, respectively. The impact of test compounds on both phases was studied. Additionally, righting reflex method was used to exclude the central effect of test compounds as its impact on sleeping time induced by inhaled isoflurane. Vehicle injections were used as control. One way ANOVA followed by Dunnett's post hoc test and unpaired t-test was used for the determination of significances in case of formalin test and righting reflex method, respectively.

**Results:** S.c. injections of 14-O-MeM6SU or morphine inhibited the pain events evoked by formalin in both phases. Co-administered naloxone methiodide (NAL-M), a peripherally acting opioid antagonist reversed the antinociceptive effect of certain s.c. 14-O-MeM6SU doses but not of morphine (Fig. 1.). Morphine injected into ipsilateral or contralateral paws showed antinociception in both pain phases. Interestingly, 14-O-MeM6SU in certain doses produced antinociception only after ipsilateral injections. Finally, 14-O-MeM6SU contrary to morphine in s.c. antinociceptive doses significantly prolonged the sleeping time of inhaled isoflurane. These results indicate that the novel morphine analogue reported to have high efficacy earlier by us, have limited access to CNS and may have peripheral antinociception that is of potential clinical value.

The antinociceptive effect of 14-O-MeM6SU with or without NAL-M in formalin test after s.c. administration

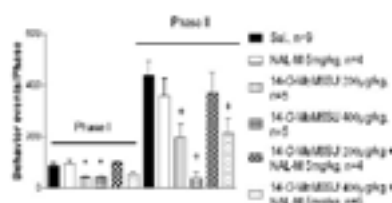


Fig. 1. The antagonistic effect of the systemically coadministered NAL-M on the antinociceptive effect of s.c. 14-O-MeM6SU. Each column represents the cumulative data of the given phase. \* vs. Sal Phase I; + vs. Sal; Phase II; p<0.05

### Biography

Mihaly Balogh is a PhD student and Assistant Research Associate at Semmelweis University (Budapest, Hungary) since 2015. He has experience in investigating different *in vivo* models of neuropathic (e.g. diabetic neuropathy) and inflammatory pain (e.g. CFA induced inflammation). He studies the role of the peripheral opioid system in analgesia and also acquired practice in several *in vitro* (e.g., western blot) and isolated organ assays. Beside his scientific work, he is involved in teaching pharmacology and pharmacotherapy at Semmelweis University for English and Hungarian students.

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