Novel of (–)-menthone and (+)-camphor hydrazones as promising agents with dual effects

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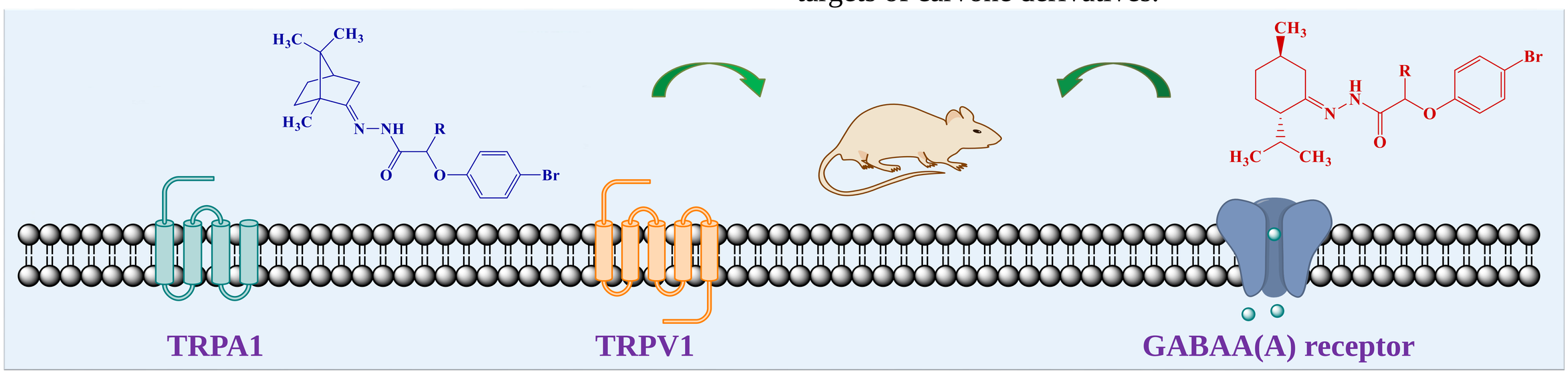
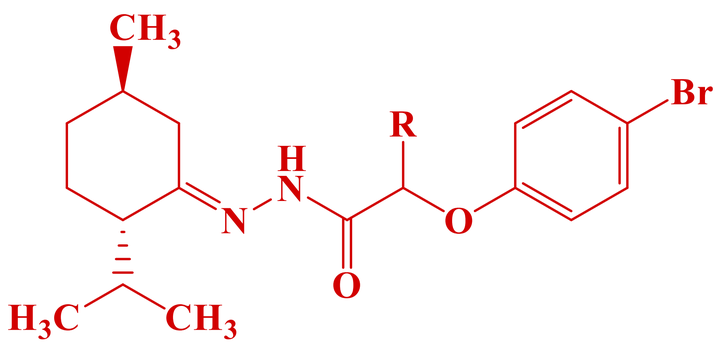
Aim: The present study aims to the development and synthesis of novel potential analgesic and anticonvulsant agents based on bioactive compounds from natural sources. For this purpose, a series of hydrazones has been obtained via (–)-menthone or (+)-camphor condensation with hydrazides of *para*-bromophenoxyacetic acids.

Methods: The structure of (–)-menthone and (+)-camphor hydrazones was characterized by ^{13}C-NMR, ^{1}H-NMR, FT-IR, ESI- and FAB-mass spectrometry. All compounds have been synthesized and purified up to 99% purity confirmed by high-performance liquid chromatography (HPLC); thermal behavior of menthone and camphor derivatives was performed by differential scanning calorimetry (DSC).

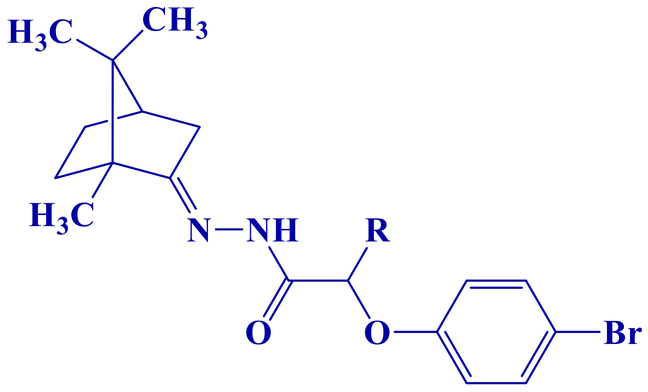
Results: The influence of obtained compounds on the central and peripheral nervous system was reliably confirmed by evaluating their anticonvulsant and analgesic activity. The present findings indicate that all above-mentioned compounds possess antiseizure action throughout 24 h after oral administration on PTZ-induced and maximal electroshock seizure (MES) convulsion models. Analgesic effect of (–)-menthone and (+)-camphor hydrazones was elucidated after transdermal delivery via chemical-induced pain models. In this study, pain in experimental animals was caused by selective agonists of TRP channel – capsaicin and allyl isothiocyanate (AITC) via their subplantar injection. All the tested compounds were found to suppress painful sensation produced by noxious stimuli indicating TRP channels (specifically, TRPV1 and TRPA1) as molecular targets of carvone derivatives.



Statistics: All results are expressed as mean ± SEM. Statistical significance was determined by Student's *t*-test at $P < 0.05$ that was considered as significant compared to control group.



R = CH_3 (**1**)
R = C_2H_5 (**2**)
R = *n*-C_3H_7 (**3**)



R = CH_3 (**4**)
R = C_2H_5 (**5**)
R = *n*-C_3H_7 (**6**)

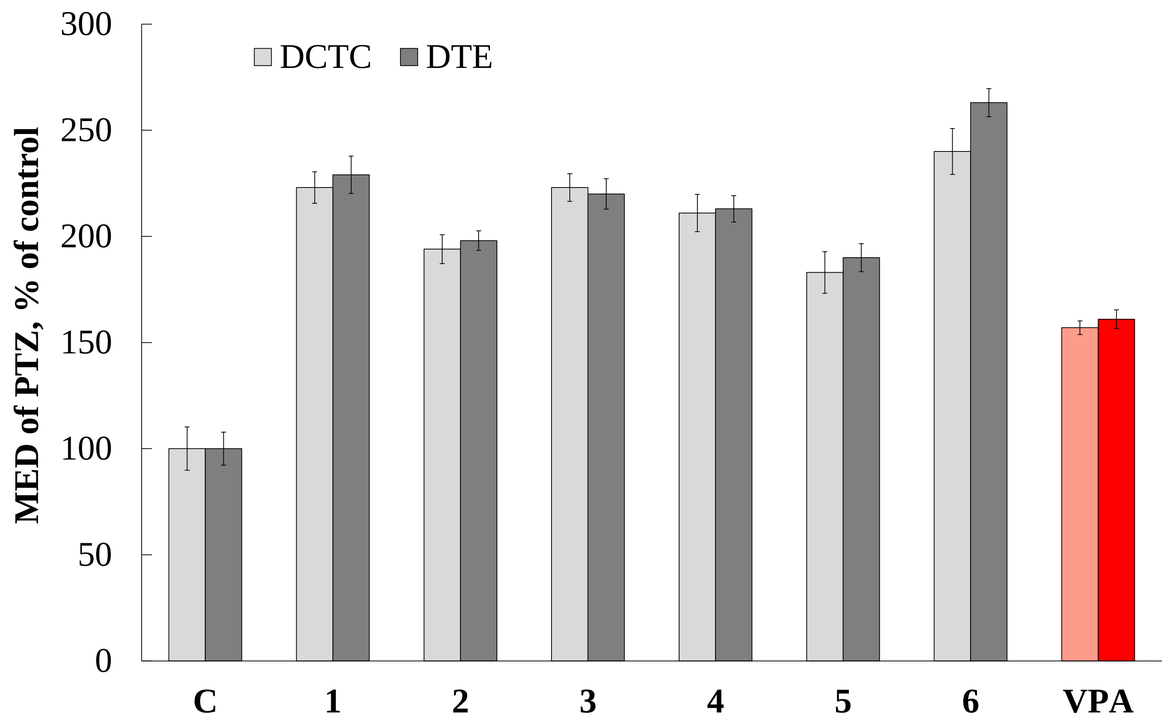


Figure. Anticonvulsant activity of hydrazones **1**-**6** in PTZ-test at 3 h after single oral administration; VPA – Valproic acid.

Conclusion: Thus, the current study reveals a strategy for drug development possessing simultaneously pain relief and antiseizure action. This idea is implemented by targeted synthesis of (–)-menthone and (+)-camphor derivatives – hydrazones as promising agents with dual effects.

The 7th International Electronic Conference on Medicinal Chemistry
01–30 NOVEMBER 2021 | ONLINE