

Área: ORG

TRPA1 Biomimetic Micellar Systems Utilizing Polyethyleneimine and Cysteine for Antinociceptive Drug Screening.

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Highlights

Biomimetic micellar systems as screening assays for antinociceptive drugs; Micellar systems based on cysteine-substituted polyethyleneimine (PEI); Biomimetic systems to accelerate the development of new drugs

Resumo/Abstract

TRPA1 is an ion channel involved in the nociceptive system, a sensory system that enables animals to detect and avoid stimuli potentially harmful to the body. TRPA1 is permeable to calcium and magnesium ions, and its pharmacology remains relatively limited. The development of new drugs relies heavily on animal testing as a key step. This project aims to mimic the TRPA1 channel using micellar systems based on polyethyleneimine (PEI), which can be applied as screening assays to accelerate the development of new drugs. For this purpose, PEI and its hydrophobic derivative, PEI-C12, were modified with cysteine — a key amino acid present in TRPA1. Different synthetic methods were tested, and the most effective involved solubilizing PEI or PEI-C12 in water, followed by the addition of EDC, NHS, and cysteine, with the reaction maintained at room temperature under stirring for 24 hours. After dialysis and drying, the reaction product was confirmed by ¹H NMR (15-17% of cysteine introduced). The modified polymers (PEI-CYS or PEI-C12-CYS) were used to prepare micellar dispersions encapsulating Eriochrome T (ErioT), achieving an encapsulation efficiency of 99%. With the dispersions prepared, assays were assembled using Tris-HCl buffer at pH 7, acetonitrile (required to facilitate ErioT release), MgCl₂ (to react with Erio T when released and change color), the micellar dispersion, and two different TRPA1 agonists (channel activators): ZnCl₂ and cinnamaldehyde, in varying concentrations (total volume of 2 mL). The tests with agonists aimed to observe a color change in the system due to the release of ErioT, indicating activation of the nociceptive channel. Concentrations were selected based on release assays over time (5 minutes to 24 hours). The ZnCl₂ concentration chosen for further testing was 50 μL of a 10 mmol ZnCl₂ solution. For cinnamaldehyde, the selected amount was 10 μL of the pure compound. Parallel assays were performed to compare the release in the presence and absence of dipyron (a TRPA1 antagonist drug), and the results were analyzed using UV-Vis spectroscopy. The spectra showed that dipyron inhibited the effect of cinnamaldehyde but not that of ZnCl₂, which aligns with *in vivo* reports. Therefore, further studies with other agonist and antagonist agents will be conducted; however, the system appears promising, as it mimics the TRPA1 response so far.

References

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