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21. MOLECULAR INSIGHTS INTO NATURAL COMPOUNDS: ELECTROPHYSIOLOGICAL EFFECTS OF TRANS-CINNAMALDEHYDE AND EUGENOL ON NICOTINIC ACETYLCHOLINE RECEPTORS

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Natural extracts and essential oils, often containing a diverse array of bioactive compounds, are appealing sources for identifying new potential drug candidates in drug discovery. Bioactive compounds have been used in traditional medicine for centuries to treat a variety of diseases. In recent times, there has been a resurgence of interest in these bioactive compounds due to their medicinal properties. Research has shown that many of these compounds act on neurotransmitter receptors, particularly Cys-loop receptors such as the nicotinic acetylcholine receptor (nAChR). nAChRs are a family of acetylcholine-gated ion channels found in the central and peripheral nervous systems, playing key roles in processes like muscle contraction, memory, and attention.

The primary goal of this project was to investigate the molecular effects of two naturally occurring phenylpropanoids found in *Cinnamomum verum* oil, trans-cinnamaldehyde (TCA) and eugenol (EGN), on two types of mammalian nAChRs, both of which are involved in various pathological conditions. Since TCA and EGN are multitarget compounds, it is essential to understand the molecular mechanisms underlying their potential therapeutic and adverse effects.

Through single-channel recordings, we observed that TCA exerts a negative modulatory effect on both α7 and muscular nAChRs. In α7 receptors, TCA significantly reduces activity by decreasing the frequency of activation episodes without affecting the amplitude or open duration. In contrast, for muscular nAChRs, both TCA and EGN induce a concentration-dependent reduction in open channel duration within the micromolar range. This reduction is accompanied by a shift towards shorter durations in the main closed component.

The modulation of nAChRs by these compounds is pharmacologically significant and should be considered when evaluating the therapeutic potential of TCA and EGN. Our findings provide valuable insights into how natural compounds affect Cys-loop receptors, which are underexplored but critical targets for various therapeutic strategies.