UAEU

جامعة الإمارات العربية المتحدة
United Arab Emirates University

The College of Graduate Studies and the College of Medicine and Health Sciences Cordially Invite You to a

Master Thesis Defense

Entitled

THE EFFECTS OF CAPSACICN ON THE FUNCTION OF HUMAN α7 NICOTINIC ACETYLCHOLINE RECEPTORS EXPRESSED IN XENOPUS OOCYTES

by

Asma Hassan Ali Muftah Alzaabi

Faculty Advisor

Prof. Murat Oz, Department of Pharmacology and Therapeutics
College of Medicine and Health Sciences

Date & Venue

01:30 PM
Thursday, 22 March 2018
Sheikha Fatima lecture Theater, College of Medicine and Health Sciences

Abstract

Capsaicin is a naturally occurring alkaloid derived from chili pepper fruits. Capsaicin is a unique compound due to its ability to trigger a desensitization after the initial neuronal excitation in the nerve terminal expressing TRPV1 as well as generation of long-lasting nerve defunctionalization at sufficient dosing. Capsaicin has a beneficial role in the treatment of pain, cancer, obesity, diabetes, gastrointestinal, cardiovascular, dermatological conditions, and several other pathologies. In this study, we investigated the effect of capsaicin on the function of a cloned α7 subunit of human nicotinic acetylcholine receptor (α7-nAChR) expressed in *Xenopus laevis* oocytes using the two-electrode voltage clamp method. Capsaicin showed maximum potency of inhibition of ACh-induced currents with an IC_{50} value of 8.6 µM (with 50% inhibition). The mechanisms of capsaicin's action on the α7-nAChR were further investigated and found to be independent of membrane potential. Furthermore, capsaicin (10 µM) did not affect the activity of Ca^{2+} dependent Cl^- channels since the extent of inhibition by capsaicin was unaltered by the intracellularly injected Ca^{2+} chelator BAPTA and perfusion with Ca^{2+}-free bathing solution containing 2 mM Ba^{2+}. The effect of capsaicin was associated with decreased ACh efficacy, and the inhibition was not reversed by increasing ACh concentrations, suggesting a non-competitive inhibition of nicotinic receptors. Capsaicin not only had an inhibitory effect on α7-nAChRs but also on the other members of cys-loop family of ligand-gated ion channels including: $\alpha_3\beta_2$, $\alpha_4\beta_4$, $\alpha_4\beta_2$, α1β1, and α3β4 nACh receptors, $5HT_3$ receptor, and glycine α_1 and α_3-receptor, while, it caused potentiation of glycine α_2-receptor function. In conclusion, our results indicate that capsaicin inhibits the function of the α7-nACh receptor, and emphasizes the importance of α7-nACh receptor for future pharmacological/ toxicological profiling.

Keywords: Capsaicin, Xenopus laevis oocytes, nicotinic acetylcholine receptors.