

## Capsaicin Derivatives Enhanced Activity of $\alpha 1\beta 2\gamma 2$ S-Aminobutyric Acid Type a Receptor Expressed in *Xenopus laevis* Oocytes

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**Abstract :** Epilepsy is one of the most common neurological diseases affecting more than 50 million of people worldwide. Epilepsy is a state of recurrent, spontaneous seizures with multiple syndromes and symptoms of different causes of brain dysfunction, prognosis, and treatments; characterized by transient, occasional and stereotyped interruptions of behavior whereby the excitatory-inhibitory activities within the central nervous system (CNS) are thrown out of balance due to various kinds of interferences. The goal of antiepileptic treatment is to enable patients to be free from seizures or to achieve control of seizures through surgical treatment and/or pharmacotherapy. Pharmacotherapy through AED plays an important role especially in countries with epilepsy treatment gap due to costs and availability of health facilities, skills and resources, yet there are about one-third of the people with epilepsy have drug-resistant seizures. Hence, this poses considerable challenges to the healthcare system and the effort in providing cost-effective treatment as well as the search for alternatives to treatment and management of epilepsy. Enhancement of  $\gamma$ -aminobutyric acid (GABA)-mediated inhibitory neurotransmission is one of the key mechanisms of actions of antiepileptic drugs. GABA type  $\alpha$  receptors (GABAAR) are ligand-gated ion channels that mediate rapid inhibitory neurotransmission upon the binding of GABA with a heteropentameric structure forming a central pore that is permeable to the influx of chloride ions in its activated state. The major isoform of GABA receptors consists of two  $\alpha 1$ , two  $\beta 2$ , and one  $\gamma 2$  subunit. It is the most abundantly expressed combinations in the brain and the most commonly researched through *Xenopus laevis* oocytes. With the advancing studies on ethnomedicine and traditional treatments using medicinal plants, increasing evidence reveal that spice and herb plants with medicinal properties play an important role in the treatment of ailments within communities across different cultures. Capsaicin is the primary natural capsaicinoid in hot peppers of plant genus *Capsicum*, consist of an aromatic ring, an amide linkage and a hydrophobic side chain. The study showed that capsaicins conferred neuroprotection in status epilepticus mouse models through anti-ictogenic, hypothermic, antioxidative, anti-inflammatory, and anti-apoptotic actions in a dose-dependent manner. In this study, five capsaicin derivatives were tested for their ability to increase the GABA-induced chloride current on  $\alpha 1\beta 2\gamma 2$ S of GABAAR expressed on *Xenopus laevis* oocytes using the method of two-microelectrode voltage clamp. Two of the capsaicin derivatives, IS5 (N-(4-hydroxy-3-methoxybenzyl)-3-methylbutyramide) and IS10 (N-(4-hydroxy-3-methoxybenzyl)-decanamide) at a concentration of 30  $\mu$ M were able to significantly increase the GABA-induced chloride current with  $p=0.002$  and  $p=0.026$  respectively. This study were able to show the enhancement effect of two capsaicin derivatives with moderate length of hydrocarbon chain on this receptor subtype, revealing the promising inhibitory activity of capsaicin derivatives through enhancement of GABA-induced chloride current and further investigations should be carried out to verify its antiepileptic effects in animal models.

**Keywords :**  $\alpha 1\beta 2\gamma 2$  GABA receptors,  $\alpha 1\beta 2\gamma 2$ S, antiepileptic, capsaicin derivatives, two-microelectrode voltage clamp, *Xenopus laevis* oocytes

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