

## Preparation of Flurbiprofen Derivative for Enhanced Brain Penetration

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**Abstract :** Nonsteroidal anti-inflammatory drugs (NSAIDs) are effective for relieving pain and reducing inflammation. They are nonselective inhibitors of two isoforms of COX, cyclooxygenase-1 (COX-1) and cyclooxygenase-2 (COX-2), and thereby inhibiting the production of hormone-like lipid compounds such as, prostaglandins and thromboxanes which cause inflammation, pain, fever, platelet aggregation, etc. In addition, recently there are many research articles reporting the neuroprotective effect of NSAIDs in neurodegenerative diseases, such as Alzheimer's disease (AD) and Parkinson's disease (PD). However, the clinical use of NSAIDs in these diseases is limited by low brain distribution. Therefore, in order to assist the in-depth investigation on the pharmaceutical mechanism of flurbiprofen in neuroprotection and to make flurbiprofen a more potent drug to prevent or alleviate neurodegenerative diseases, delivery of flurbiprofen to brain should be effective and sufficient amount of flurbiprofen must penetrate the BBB thus gaining access into the patient's brain. We have recently developed several types of guanidine-rich molecular carriers with high molecular weights and good water solubility that readily cross the blood-brain barrier (BBB) and display efficient distributions in the mouse brain. The G8 (having eight guanidine groups) molecular carrier based on D-sorbitol was found to be very effective in delivering anticancer drugs to a mouse brain. In the present study, employing the same molecular carrier, we prepared the flurbiprofen conjugate and studied its BBB permeation by mouse tissue distribution study. Flurbiprofen was attached to a molecular carrier with a fluorescein probe and multiple terminal guanidiniums. The conjugate was found to internalize into live cells and readily cross the BBB to enter the mouse brain. Our novel synthetic flurbiprofen conjugate will hopefully delivery NSAIDs into brain, and is therefore applicable to the neurodegenerative diseases treatment or prevention.

**Keywords :** flurbiprofen, drug delivery, molecular carrier, organic synthesis

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