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Effectiveness of GABA agonist for treatment in mice with complete freud's adjuvants induced chronic pain: molecular modeling approach

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ABSTRACT

The present study was designed to investigate the effectiveness of gaba agonist in behavioral changes of inflammatory mice with molecular docking approach. Forty mice were divided into 8 groups i.e. sham, gabapentin (10, 30 and 100 nmol), baclofen (1, 10 and 30 nmol) and negative control. Chronic pain was induced by inflammatory agent such as Complete Freud's Adjuvant (CFA). On day 8 after intraplantar injection of CFA, mice were treated by intrathecal with normal saline (sham and negative control groups), gabapentin and baclofen with three different doses, once a day for seven consecutive days. Latency time toward thermal stimulus was measured on days 1,2,8,9,11 and 15 after induction. The molecular docking was examined by Mollegro virtual docker program. The result showed that intrathecal injection of gabapentin and baclofen increased time latency toward thermal stimulus compared to negative control. There were differences between gabapentin and baclofen doses for chronic pain treatment. Molecular docking showed that the differences of effective dose were related to type of amino acid binding between gabapentin and baclofen.

***Key Words*:** Gabapentin, baclofen, dorsal horn, CFA, molecular docking.

INTRODUCTION

Generally, many diseases are represented with pain. Although pain is a simple condition, but without an appropriate therapy will lead to chronic pain condition. Chronic pain incidence impacts to many several problems in patient life such as economic, social and psychology (Breivik, 2005; Mallen, *et al*., 2005). International Association for the study of Pain (IASP) define that pain is an unpleasant sensory and emotional experience, usually associated with actual and potential tissue damage (IASP, 2011). Chronic pain incidence is the most symptom that was happened in 1 of 6 people on the population (Xie, 2011). The prevalence of chronic pain in Europe was estimated to 55.2% (Picavet and Schouten, 2003; Harstall and Ospina, 2003). There were no clearly estimation in Indonesia, but Kartini (2007) showed that 25-50% of geriatry patient have pain. Until now, chronic pain treatment is still a challenge because of its complex mechanism. Morphine as the first treatment have a lot of weakness and the effectiveness of this drug for chronic pain treatment is still debated (Baron *et al*., 2010; Hahm *et al*., 2011). So, we need an alternative new strategy, one of them is GABAergik agonist drugs such as gabapentin and baclofen (Wang *et al*., 2007).

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MATERIALS AND METHODS

Chemicals and Drugs

Gabapentin, Baclofen, Complete Freud's Adjuvant (CFA) and Neutral Buffer Formalin (NBF) 10% were pharmaceutical analysis and purchased from Sigma. Aether for anaesthetic was pharmaceutical analysis and purchased from E-Merck.

Experimental Animals

Forty 8-week-old mice (males) were used for the experiment. They were purchased and kept in the Animal House, College of Pharmacy, University of Airlangga, Surabaya, East Java, Indonesia. The temperature of the room was maintained at 26-28°C with a 12-hour light/12-hour dark cycle. Forty mice were divided into eight group i.e. sham, negative control, gabapentin treatment (10, 30 and 100nmol) and baclofen treatment (1, 10 and 30nmol). All