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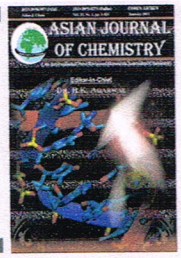

Analyzing the Interaction of Shellegueain A, a Bioactive Compound of Pakis Tangkur (*Selliguea feei* or *Polypodium feei*) to Cyclooxygenase Enzyme by Molecular Docking

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Shellegueain A is an active compound contained in pakis tangkur (*Selliguea feei* or *Polypodium feei*). This compound has been proven to show analgesic activity by decreasing writhing response in acetic acid-induced rats. It also showed antiinflammatory activity by significantly reducing oedema in carrageenan-induced rat's paw. The purpose of this study was to examine the binding modes of shellegueain A against COX-1 and COX-2 in terms of hydrogen bonds and docking energy, to understand its analgesic and antiinflammatory properties. The simulation indicated that shellegueain A did not interact with either COX-1 or COX-2 enzymes, while afzelechin (a monomeric metabolite of shellegueain A) did by making hydrogen bonds with Met522.

Key Words: Cyclooxygenase, Shellegueain A, Afzelechin, Selliguea feei, Molecular docking.

INTRODUCTION

Pakis tangkur, (*Selliguea feei*), which can be found wildly grown at Tangkuban Perahu Mountain in West Java,, has been empirically used as a pain reducer. Shellegueain A, a novel sweet trimeric proanthocyanidin with a double-linked A units, is a bioactive compound of this plant. The structure of this substance was established as epiafzelechin-(4β → 8, 2β → O → 7)-epiafzelechin-(4β → 8)-afzelechin[1]. Afzelechin is the monomer subunit of shellegueain A (Fig. 1).

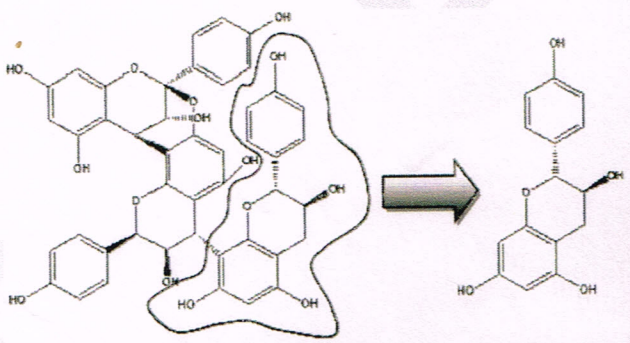

Fig. 1. 2D structures of shellegueain A (left) and afzelechin (right)

Cyclooxygenase (COX) plays an important role in inflammatory response. This enzyme has been analyzed by x-ray crystallography at a resolution of 3.0 Å and visualized as a homodimer with 587 amino acid residues per chain thus yielding a molecular weight of 67230 daltons[2]. Two isoforms of the cyclooxygenase enzyme, which are COX-1 and COX-2, exist. These two isoforms share a sequence identity of 60 % denoting that the overall structures of the enzyme isoforms are highly conserved. The overall structures of COX-1 and COX-2 are highly conserved although COX-2 was shown to have a much larger non-steroidal anti-inflammatory drug binding site due to the substitution of a valine for isoleucine (Fig. 2) at position 523 in the active site[3]. The cyclooxygenase active

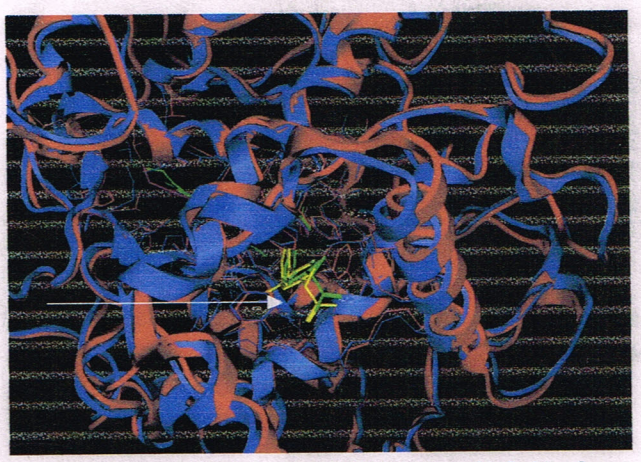

Fig. 2. Alignment of COX-1 (red) and COX-2 (blue) with flurbiprofen co-crystalized in both enzymes. White arrow shows two molecules of flurbiprofen (coloured in green and yellow) which are located at the same site in the binding pocket of both enzymes