Penambatan molekuler beberapa senyawa analog kurkumin turunan dibenzilidenasikloheksanon pada siklooksigenase-2

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Abstrak

Siklooksigenase (Cyclooxygenase - COX) merupakan enzim yang mengkonversi asam arakidonat menjadi prostaglandin. Prostaglandin berperan penting dalam menimbulkan respons inflamasi dan berbagai respons fisiologis lainnya. Dikenal dua jenis isozim siklooksigenase, COX-1 dan COX-2. Aktivasi siklooksigenase-2 umumnya terinduksi oleh rangsangan dan tidak terus-menerus sehingga menjadi target inhibisi dari obat-obat selektif inhibitor siklogenase terbaru. Kurkumin, senyawa aktif dari Curcuma longa, dan analog alamiahnya memiliki aktivitas inhibisi sikloksigenase-2 yang teramati secara in vitro dan in vivo pada penelitian sebelumnya. Pada penelitian ini, dilakukan pengujian secara in silico melalui penambatan molekuler untuk mengamati aktivitas inhibisi siklooksigenase-2 beberapa analog kurkumin turunan dibenzilidenasikloheksanon. Dari hasil penambatan molekuler kemudian analog diperingkatkan konstanta inhibisinya, Ki. Analog yang paling poten sebagai inhibitor COX-2 dari hasil penelitian ini adalah analog III. Daerah pengikatan substrat penting untuk COX-2 yang teramati pada penelitan ini meliputi residu-residu Tyr 355, Phe 381, Tyr 385, Leu 384, dan Trp 387.
<hr>Cyclooxygenase (COX) is an enzyme that converting arachidonic acid (AA) to prostaglandin. Prostaglandin has an important role of inducing inflammation and other physiological responses. There are two types of cyclooxygenase isozyme, COX-1 and COX-2. Cyclooxygenase-2 activation in general was induced by stimulation and was not constitutive therefore it became inhibition target of the newer selective cyclooxygenase inhibitor drugs. Curcumin, active compound from Curcuma longa, and its natural analogues were shown to have cyclooxygenase-2 inhibition activity. This activity has been observed by in vitro and in silico method in the previous researches. In this research, in silico test was done using molecular docking method to observe cyclooxygenase inhibition activity of some dibenzilydenecyclohexanone derived curcumin analogues. From the result of molecular docking, the analogues were ranked based on its G binding energy and inhibition constant, Ki. In this research, the most potential analogue as COX-2 inhibitor was analogue III. Important binding area of the COX-2 substrate was comprised of Tyr 355, Phe 381, Tyr 385, Leu 384, and Trp 387 residues.