ABSTRACT

SYNTHESIS AND IN SILICO EVALUATION OF ANALGESIC ACTIVITY OF N-(4-TERTIARY-BUTYLBENZOYL)-*p*-AMINOPHENOL

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Pain is one of the most common health problems in the world even though many types of analgesic drugs have been developed. The most popular and widely used analgesic in Indonesia is a *p*-aminophenol derivative, paracetamol. In high doses, it can cause methemoglobinemia and liver failure. To reduce this toxicity, structure modification can be done to its amine group. This research aims to synthesize and evaluate the analgesic activity of new modified *p*-aminophenol derivative, *N*-(4-tertiary-butylbenzoyl)-*p*-aminophenol, with in silico approach as a new prospective analgesic drug. *N*-(4-tertiary-butylbenzoyl)-*p*-aminophenol was synthesized by reacting *p*-aminophenol with 4-tertiary-butylbenzoyl chloride through Schotten-Baumann nucleophilic acylation reaction. Aceton and triethylamine were used as solvent and catalyst respectively, then the synthesized compound was recrystallized using hot water. The percentage yield of this synthesis was 39%. Its purity was analyzed by melting range test and thin-layer chromatography. The structure of the compound was confirmed with a UV-Vis spectrophotometer, infrared spectrophotometer, and nuclear magnetic resonance spectrometer. The analgesic activity prediction was evaluated by *in silico* method using Molegro Virtual Docker program. Analgesic activity of *N*-(4-tertiary-butylbenzoyl)-*p*-aminophenol was compared to paracetamol using the COX-2 receptor (ID PDB: 5IKR). It was found that *N*-(4-tertiary-butylbenzoyl)-*p*-aminophenol gives a lower rerank score than paracetamol, -88,1054 and -61,3547 respectively. The amino acid residue interactions suggest that this new *p*-aminophenol derivative is predicted to be able to inhibit COX-2. With these findings, it can be concluded that *N*-(4-tertiary-butylbenzoyl)-*p*-aminophenol has higher analgesic activity than paracetamol using in silico evaluation method.

Keywords: Synthesis, in silico study, *N*-(4-tertiary-butylbenzoyl)-*p*-aminophenol, paracetamol, analgesic activity.