ABSTRAK

Alzheimer merupakan penyakit otak yang bersifat progresif, berjalan lambat dan mengakibatkan demensia. Pengobatan terhadap alzheimer yang sudah ada dengan mekanisme penghambat asetilkolinesterase seperti: Fisostigmine, Tacrine, Donepezil, dan Rivastigmin mampu menghambat pemburukan penderita alzheimer. Namun, obat-obatan tersebut memiliki efek samping seperti mual, muntah, diare, dan nyeri otot, sehingga diperlukan pengembangan obat alzheimer baru dengan efek samping yang lebih rendah. Pada penelitian ini telah dilakukan uji *in silico* pada 10 senyawa turunan fenoksi halida fenil sebagai inhibitor enzim asetilkolinesterase, kemudian dilakukan sintesis dari senyawa yang memiliki energi bebas ikatan terendah (ΔG_{bind}). Hasil uji *in silico* menunjukkan senyawa *N*-(4'-klorofenil)-2-fenoksiasetamida memiliki nilai ΔG_{bind} -7,80 Kkal/mol. Senyawa tersebut disintesis dengan mereaksikan 2-fenoksiasetil klorida dan 4-kloroanilin dengan katalis piridin. Senyawa hasil sintesis berupa serbuk kuning kecoklatan dengan rendemen sebesar 82,5% dan jarak lebur 116,7-118,8 ^{o}C. Hasil analisis dengan kromatografi lapis tipis (KLT) menunjukkan bercak tunggal dengan R_f sebesar 0,925. Hasil elusidasi struktur dengan spektrofotometri inframerah, spektrometri massa, dan spektroskopi ^{1}H dan ^{13}C-resonansi magnetik inti menunjukkan senyawa hasil sintesis adalah *N*-(4'-klorofenil)-2-fenoksiasetamida.

Kata kunci: *N*-(4'-klorofenil)-2-fenoksiasetamida, alzheimer, uji *in silico*, substitusi nukleofilik asil, inhibitor asetilkolinesterase

ABSTRACT

Alzheimer's is a brain disease that is progressive, progresses slowly and results in dementia. Treatment of existing Alzheimer's with acetylcholinesterase inhibitor mechanisms such as: Fisostigmine, Tacrine, Donepezil, and Rivastigmin can inhibit the deterioration of Alzheimer's sufferers. However, these drugs have side effects such as nausea, vomiting, diarrhea and muscle pain, so it is necessary to develop new Alzheimer's drugs with lower side effects. In this research, an in silico test was carried out on 10 phenoxy phenyl halide derivatives as inhibitors of the acetylcholinesterase enzyme, then the compounds with the lowest bond free energy (ΔG_{bind}) were synthesized. The results of the in silico test showed that the compound N-(4'-chlorophenyl)-2-phenoxyacetamide had the lowest ΔG_{bind} -7.80 Kcal/mol. The compound was synthesized by reacting 2-phenoxyacetyl chloride and 4-chloroaniline with pyridine catalyst. The synthesized compound is a brownish yellow powder with a yield of 82.5% and a melting range of 116.7 to 118.8 ^{o}C. The results of analysis using thin layer chromatography (TLC) showed a single spot with an Rf of 0.925. The results of structural elucidation by infrared spectrophotometry, mass spectrometry, and 1H and 13C-nuclear magnetic resonance spectroscopy showed that the synthesized compound was N-(4'-chlorophenyl)-2-phenoxyacetamide.

Keywords: *N-(4'-chlorophenyl)-2-phenoxyacetamide, Alzheimer's, in silico test, acyl nucleophilic substitution, acetylcholinesterase inhibitors*