Analisis In Silico Senyawa Flavonoid sebagai Angiotension Converting Enzyme Inhibitor (ACEI) = In Silico Analysis of Flavonoid as Angiotensin Converting Enzyme Inhibitor (ACEI)

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Abstrak

ABSTRAK
Hipertensi merupakan kondisi patologis ketika tekanan darah terlalu tinggi yang di atas normal. Diperkirakan 13 miliar orang menderita hipertensi dan penyakit ini menjadi salah satu penyebab utama kematian dini di seluruh dunia. Angiotensin Converting Enzyme (ACE) memiliki peran penting dalam pengaturan tekanan darah arteri. Angiotensin Converting Enzyme Inhibitor (ACEI) merupakan salah satu lini pertama untuk pengobatan hipertensi. Obat ini dapat menginhibisi ACE yang memecah angiotensin I untuk membentuk vasokonstriktor poten angiotensin II. Penelitian dilakukan dengan metode penapisan virtual menggunakan AutoDock Vina yang terdapat dalam PyRx untuk mencari kandidat ACEI yang berasal dari senyawa bahan alam flavonoid. Flavonoid telah diketahui bertindak sebagai komponen dalam diet yang efektif dalam menghambat ACE. Flavonoid, terutama glikosidanya, merupakan fitokimia yang paling vital dalam diet dan sangat menarik karena diketahui bioaktivitasnya yang beragam. Struktur kristalografi target makromolekul diperoleh dari pangkalan data PDB (PDB ID: 1O86). Optimasi dilakukan dengan ukuran grid box yang divariasikan serta ion Zn2+, Cl- & 6 molekul air yang dipertahankan terhadap makromolekul. Berdasarkan hasil penapisan virtual, didapatkan 10 senyawa bioaktif peringkat teratas diantaranya yaitu epigallocatechin 3-O-gallate-7-O-glucoside-4-O-glucuronide, theaflavin 3-O-gallate, theaflavin 3,3-O-digallate, eriocitrin atau eriodictyol 7-O-rutinoside, luteolin 7-O-diglucuronide, malvidin 3-O-(6-caffeoyl-glucoside), narirutin 4-O-glucoside, quercetin 3,4-O-diglucoside, peonidin 3-O-(6-p-coumaroyl-glucoside) dan delphinidin 3-O-glucosyl-glucoside. Senyawa tersebut menunjukkan afinitas pengikatan optimum terhadap target makromolekul ACE dengan energi ikatan berada direntang -10,3 kkal/mol hingga -10,9 kkal/mol yang dibandingkan dengan standar moeksipril (-9,1 kkal/mol). Hasil menunjukkan 10 senyawa tersebut dapat menjadi ligan potensial untuk mengobati hipertensi.
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<i>ABSTRACT
Hypertension is defined as condition of blood pressure that abnormally too high. An estimated of 1.13 billion people worldwide has hypertension and this disease is one of the most cause of premature death worldwide. Angiotensin Converting Enzyme (ACE) has an importent role in arterial blood pressure regulation. Angiotensin Converting Enzyme Inhibitor (ACEI) is one of the first line treatment for hypertension. This drug can inhibit ACE which cleaves angiotensin I to the form potent vasoconstrictor angiotensin II. This study was conducted by virtual screening method used AutoDock Vina in PyRx to search ACEI candidate from flavonoid natural compounds. Flavonoids have been known to act as components in the diet that are effective to inhibit ACE. Flavonoids, especially their glycosides, are the most vital phytochemicals in diet and are of great general interest due to their diverse bioactivity. The crystallographic structure of macromolecule target was obtained from PDB database (PDB :1O86). Optimization was performed by variying grid size and maintaning Zn2+, Cl- & 6 water molecules in the

macromolecule. Based on virtual screening results, the top ten ranking bioactive compounds was obtained. They are epigallocatechin 3-O-gallate-7-O-glucoside-4-O-glucuronide, theaflavin 3-O-gallate, theaflavin 3,3-O-digallate, eriocitrin atau eriodictyol 7-O-rutinoside, luteolin 7-O-diglucuronide, malvidin 3-O-(6-caffeoyl-glucoside), narirutin 4-O-glucoside, quercetin 3,4-O-diglucoside, peonidin 3-O-(6-p-coumaroyl-glucoside) and delphinidin 3-O-glucosyl-glucoside. Those compounds showed optimum binding affinity to ACE macromolecule target with binding energy range -10,3 kcal/mol to -10,9 kcal/mol as compared to the moexipril standard (-9,1 kcal/mol). The results indicated that 10 compounds could be the potential ligands to treat hypertension.<i/>