

Studi in silico dan in vitro obat antidiabetes dengan sirt-1 = Study of antidiabetic drugs with sirt-1 through in silico and in vitro

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Abstrak

ABSTRACT

Dalam perkembangan penelitian, diketahui enzim SIRT-1 berperan penting dalam metabolisme gula darah dalam tubuh manusia dan dapat dijadikan target terapi untuk T2DM. Antidiabetes diyakini merupakan aktivator dari enzim tersebut. Dengan diaktifkannya SIRT-1 pada daerah aktivator, SIRT-1 dapat menurunkan resistensi insulin dan kadar gula darah. Namun belum pernah dilakukan penelitian efek antidiabetes terhadap daerah katalitik SIRT-1. Penelitian ini bertujuan untuk melihat aktivitas dari senyawa antidiabetes golongan sulfonilurea, meglitinid, biguanid, thiazolidindion, dan alfa-glukosidase inhibitor terhadap enzim SIRT-1 kode PDB: 4I5I secara in silico dan in vitro. Penelitian secara in silico dilakukan menggunakan AutoDock, dan dilanjutkan secara in vitro menggunakan alat Glomax Discover, kit SIRT-GloTM Assay and Screening System, dan sampel senyawa antidiabetes metformin dan gliklazid. Hasil penambatan pada senyawa antidiabetes terhadap daerah katalitik enzim SIRT-1 memberikan energi ikatan yang baik; glimepiride dengan hasil tertinggi yaitu -9,05 kkal/mol dan acarbose sebesar -2,01 kkal/mol. Hasil pengujian secara in vitro menunjukkan bahwa senyawa antidiabetes memiliki potensi aktivator dengan intensitas luminesens yang tinggi. Pada data di menit ke-30 dan ke-45, metformin memberikan EC50 sebesar 11,59 mM dan 25 mM; gliclazide, di sisi lain, memberikan EC50 yang lebih baik sebesar 6,609 mM dan 0,1008 mM. Data penelitian menunjukkan bahwa senyawa antidiabetes memiliki ikatan yang baik pada daerah katalitik, namun memiliki mekanisme yang lebih kuat sebagai aktivator enzim SIRT-1 terutama gliclazide.

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ABSTRACT

Researches throughout the years found that SIRT 1, a metabolism regulating enzyme, played a role in glucose metabolism and can be used as a targeted therapy for T2DM. Antidiabetic drugs are believed to be the activator of this enzyme. Activation of SIRT 1 can lower blood glucose and also improve insulin resistance. But research on the effect of antidiabetic drugs on the catalytic domain of SIRT 1 has never been done. This study aims to observe the activity of sulfonylurea, meglitinid, biguanid, thiazolidindion, and alpha glucosidase inhibitor antidiabetic drug classes against the SIRT 1 enzyme PDB code 4I5I through in silico and in vitro. In silico study was conducted using AutoDock, and confirmed through in vitro using Glomax Discover tool, SIRT GloTM Assay and Screening System kit, and metformin and gliclazide as samples of antidiabetic drugs. The result shows that the antidiabetic drugs has good binding energy towards the catalytic domain glimepiride has the smallest binding energy that is 9.05 kkal mol and acarbose with the biggest binding energy that is 2.01 kkal mol. In vitro results show that the antidiabetic drugs have the activator potency with high luminescence intensity. Data shown in minute 30 and 45, the EC50 of metformin are 11.59 mM and 25mM gliclazide, on the other hand, has better EC50 which are 6.609 mM and 0.1008 mM. This results show that antidiabetic drugs have a promising binding energy in the catalytic

domain, but have stronger mechanism as an activator towards SIRT 1 especially gliclazide.