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Certificate of Mini-Oral Presentation

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This is to certify that

Dykall Naf'an Dzikri

Puskesmas Tasikmadu

Exploring Indonesian phytochemicals as novel PPAR-γ activators for type II diabetes mellitus therapy : an In Silico Study

has been nominated as a presenter on
outstanding abstract submission to
ICoLA 2024
which was held at CONRAD Seoul, Republic of Korea
on September 26(Thu)~28(Sat), 2024.

Ick-Mo Chung
President

Jaetaek Kim
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MOP1-F-1

Virtual screening of Indonesian phytochemicals reveals hinokinin, dihydroguaiaretic acid, and deoxylapachol as novel GPR40 activators for type 2 diabetes mellitus

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Objectives: GPR40 is a class A G-protein coupled receptor (GPCR) found in the pancreas, intestine, brain, and other tissues. GPR40 agonists can enhance insulin levels directly by stimulating the pancreatic beta cells and indirectly by the synergistic effect of elevated plasma levels of the incretin GLP-1. Some evidence has shown that natural compounds have therapeutic effects for some human diseases. Therefore, this study aimed to identify Indonesian phytochemicals virtually as GPR40 for type II diabetes mellitus (DM) therapy.
Methods: A computational investigation was conducted employing molecular docking techniques to analyze the interactions among GPR40 (PDB: 4PHU), TAK-875, and phytochemicals sourced from Indonesia. The phytochemicals were obtained from HerbalDB and met the criteria for Lipinski's rule for drug availability. Macromolecule preparation was done using AutoDock, while the molecular docking process used PyRx. Protein-ligand interaction was visualized using Pymol. The indicators for data analysis were binding energy score must lower than TAK-875 (-10,1 kcal/mol), Root-Mean-Square Deviation (RMSD) score ≤ 2 Å, and bound with GPR40 residues where TAK-875 bind, such as Tyr 91, Arg183, Ala83, Phe87, Gly139, Leu158, Phe142 and Arg2258.
Results: The docking results showed that Hinokinin, Dihydroguaiaretic acid and Deoxylapachol had better potential activity to activate GPR40 than TAK-875. Hinokinin, Dihydroguaiaretic acid, and Deoxylapachol had lower binding scores (-10.2±0.1 kcal/mol) than the standard ligand. In addition, they bound to GPR40 at Tyr 91, Arg183, Ala83, Phe87, Gly139, Leu158, Phe142 and Arg2258 residues. Hinokinin, derived from plants like Chamaecyparis and Zanthoxylum, exhibits antioxidant, anticancer, antiviral, and antitrypanosomal properties. Dihydroguaiaretic acid, sourced from the creosote bush, is a phenolic lignan with antioxidant, anti-inflammatory, and potential anticancer properties. Deoxylapachol is a cytotoxic component with antifungal and anticancer activities.
Conclusions: New GPR40 activators from Indonesian phytochemicals named Hinokinin, Dihydroguaiaretic acid, and Deoxylapachol have been discovered as novel potential therapies for type II DM.
Keywords: GPR40

MOP1-F-2

In silico study: exploring Indonesian phytochemicals as DPP-IV inhibitors for Type II diabetes mellitus therapy

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Objectives: Dipeptidyl peptidase IV (DPP-IV) is enzyme that degrades incretins to reduced abnormal visceral adipose tissue metabolism and insulin secretion. DPP-IV inhibitors increase the levels of GLP-1 and GIP leading beta-cell insulin secretion in the pancreas, reducing postprandial and fasting hyperglycemia, and improving blood glucose control without inducing hypoglycemia. Some evidence has shown natural compounds have therapeutic effects for human diseases. This study aimed to determine Indonesian phytochemicals virtually as DPP-IV inhibitors for type II diabetes mellitus (DM) therapy.
Methods: In silico study using molecular docking between DPP-IV (PDB : 5J3J), Sitagliptin, and Indonesian phytochemicals. The phytochemicals were obtained from HerbalDB and met the criteria for Lipinski's rule for drug availability. Macromolecule preparation was done using AutoDock, while the molecular docking process used PyRx. Protein-ligand interaction was visualized using Pymol. The indicators for data analysis were binding energy score must lower than Sitagliptin (-8.6 kcal/mol), root-mean-square deviation (RMSD) score ≤2 Å, and bound with DPP-1V residues where Sitagliptin bind, such as Glu`205, Glu206, Tyr662, and Arg358.
Results: The docking results showed that 1.10-Phenanthroline Monohydrate, Roxburghine B, and Lanuginosine had better potential activity to inhibit DPP-IV than Sitagliptin. 1.10-Phenanthroline Monohydrate, Roxburghine B, and Lanuginosine had lower binding scores (-8.7±0.1, -8.7±0.1, and -8.7±0.1 kcal/mol, respectively) than the standard ligand. In addition, they bound to DPP-IV at Glu`205, Glu206, Tyr662, and Arg358 residues. 1.10-Phenanthroline Monohydrate, Roxburghine B, and Lanuginosine are originally isolated from the seed of the plant Zea mays, the leaves and stems of the plant Uncaria gambir, and the leaves of the plant Annona mucirata, respectively.
Conclusions: New DPP-IV Inhibitor from Indonesian phytochemicals named 1.10-Phenanthroline Monohydrate, Roxburghine B, and Lanuginosine have been discovered as novel potential therapy for type II diabetes mellitus.
Keywords: DPP-IV inhibitors, Indonesian phytochemicals

MOP2-C-1

Exploring Indonesian phytochemicals as novel PPAR-γ activators for type II diabetes mellitus therapy: an In Silico Study

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Objectives: Peroxisome proliferator-activated receptor γ (PPAR-γ) is highly expressed in adipose tissue, regulating adipogenesis, lipid metabolism, and insulin sensitivity. Activation of PPAR-γ improves insulin sensitivity and enhances glucose metabolism. It acts as a master regulator of adipogenesis, stimulating the production of small insulin-sensitive adipocytes. Therefore, this study aimed to identify Indonesian phytochemicals virtually as PPAR-γ for type II diabetes mellitus (DM) therapy.
Methods: In silico study using molecular docking between PPAR-γ (PDB: 2PRG), Rosiglitazone, and Indonesian phytochemicals. The phytochemicals were obtained from HerbalDB and met the criteria for Lipinski's rule for drug availability. Macromolecule preparation was done using AutoDock, while the molecular docking process used PyRx. Protein-ligand interaction was visualized using Pymol. The indicators for data analysis were binding energy score must lower than Rosiglitazone (-7,8 kcal/mol), root-mean-square deviation (RMSD) score ≤2 Å, and bound with PPAR-γ residues where Rosiglitazone bind, such as Ser289, His323, Tyr473, and Gln286.
Results: The docking results showed that Lumichrome, Cubebin, and 3-O-Methylcalopocarpin had better potential activity to activate PPAR-γ than Rosiglitazone. Lumichrome, Cubebin, and 3-O-Methylcalopocarpin had lower binding scores (-8.8±0.1, -8.6±0.1, and -8.1±0.1 kcal/mol, respectively) than the standard ligand. In addition, they bound to PPAR-γ at Ser289, His323, Tyr473, and Gln286 residues. Lumichrome is a derivative of riboflavin (vitamin B2) and can be found in a variety of plants. Cubebin is a compound found in the Piper cubeba plant, also known as Cubeb or Java pepper. This plant is native to Java and Sumatra in Indonesia. 3-O-Methylcalopocarpin is found in the Calophyllum species of plants. Calophyllum inophyllum, also known as Tamanu, Foraha, or Alexandrian laurel, is a tree found in the mangrove ecosystems of Indonesia.
Conclusions: New PPAR-γ Activators from Indonesian phytochemicals named Lumichrome, Cubebin, and 3-O-Methylcalopocarpin have been discovered as novel potential therapy for type II DM.
Keywords: PPAR-γ

MOP2-C-2

Genetic analysis of HMGCR variants reveals potential association with New Onset Statin-induced Diabetes Mellitus (NODM)

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Objectives: Statins widely prescribed for hypercholesterolemia therapy, but statin use increase risk of new-onset diabetes mellitus (NODM). The HMGCR gene encodes 3-hydroxy-3-methylglutaryl-CoA reductase, the rate-limiting enzyme that playing important role in cholesterol biosynthesis. This study investigates the potential association between HMGCR variants and NODM risk using in silico methods.
Methods: We identify deleterious mutations and classify functional single nucleotide polymorphisms (SNPs) in the HMGCR gene by using SIFT, PolyPhen, CADD, REVEL, Meta LR and Mutation asessor. We also use Prosite- ExPasy to determine mutation location in protein domain.
Results: We analyzed 10.125 variant alelles and identifying 739 alleles are exonic variant. Forteen alleles were predicted to be potentially deleterious and probably damaging. Analysis using Prosite- ExPasy detected mutations within the Proline-rich domain (Procar), sterol-sensing domain (SSD) and hydroxymethylglutaryl-coenzyme A reductase (HMG-Co-A) domain. One allele, rs1430662318, located in the Procar domain, could potentially affect the structural stability of the protein, which might influence the overall response to statins. Three alleles, rs538995429, rs757219169, and rs1760364727, were found within the SSD domain. The SSD domain is crucial for the regulatory function of HMG-CoA reductase. Variants in this domain may disrupt the enzyme's ability to respond to cellular cholesterol levels, leading to altered lipid metabolism. The remaining ten alleles were located within the HMG-CoA reductase domain, which is directly involved in the enzyme's catalytic activity. Variants in this domain are likely to have the most significant impact on the enzyme's function. This variability could influence the therapeutic efficacy and side effect profile of statins, including the risk of developing diabetes.
Conclusions: The presence of specific variants in the HMGCR gene, especially those located in critical functional domains such as the Procar, SSD, and especially HMG-CoA reductase domains, can increase the risk of new-onset diabetes induced by statin.
Keywords: Genetic variant, Statin, Diabetes