

BAB V

KESIMPULAN DAN SARAN

A. Kesimpulan

Berdasarkan penelitian yang telah dilakukan ini dapat diperoleh kesimpulan bahwa.

Pertama, nilai afinitas yang dapat diprediksi dengan metode molekuler *docking*, diperoleh senyawa nicotiflorin pada target makromolekul α -G dan DPP4 dengan *score* berurutan -8,80 kkal/mol dan -9,20 kkal/mol serta senyawa luteolin-7-glucoside pada target makromolekul PTP-1B dan GK dengan *score* berurutan -9,50 kkal/mol dan -9,40 kkal/mol.

Kedua, quercetin-3-O-rhamnoside, nicotiflorin, rhaponticin, luteolin-7-glucoside, chrysoeriol, rhapontigenin, isorhamnetin-3-O-galactoside, orientin, dan isorhamnetin diprediksi memiliki model interaksi lebih baik dari ligan asli terhadap keempat target makromolekul antidiabetes.

Ketiga, profil farmakokinetik dari kedua tanaman diperoleh 16 senyawa dengan nilai afinitas dan model interaksi yang baik, menunjukkan bahwa senyawa chrysoeriol memenuhi aturan *Lipinski rules of five* yang menyatakan dapat digunakan secara oral, memiliki nilai absorpsi yang tinggi, dan tidak menembus sawar darah otak serta dapat dimetabolisme dengan baik sehingga senyawa chrysoeriol dapat diprediksi memiliki profil farmakokinetik terbaik.

B. Saran

Pertama, perlu dilakukan penelitian lebih lanjut mengenai analisis gugus fungsi yang terlibat dalam setiap interaksi guna mengetahui sisi aktif senyawa yang diteliti dan dapat digunakan sebagai acuan untuk modifikasi struktur menjadi senyawa yang lebih poten.

Kedua, dapat dilakukan penelitian lanjutan pada senyawa chrysoeriol dengan cara mengisolasi untuk memperoleh hasil yang murni dan mengetahui berapa besar perannya dalam tanaman tersebut sebagai antidiabetes.

Ketiga, perlu dilakukan studi lebih lanjut terkait farmakofor senyawa yang dilanjutkan dengan desain senyawa analog untuk meningkatkan aktivitasnya.

DAFTAR PUSTAKA

- [RSCB] Research Collaboratory for Structural Bioinformatics Protein Data Bank. <https://www.rcsb.org/pdb/home/sitemap.do> [23 Juni 2019].
- [USDA] United State Department of Agriculture. Plants Profile for *Leucaena leucocephala* (Lam.) (white leadtree). <https://plants.usda.gov/core/profile?symbol=LELE10> [21 Apr 2019].
- [USDA] United State Department of Agriculture. Plants Profile for *Trigonella foenum-graecum* L. (sicklefruit fenugreek). <https://plants.usda.gov/core/profile?symbol=TRFO80> [21 Apr 2019].
- Abdelmoaty MA, Ibrahim MA, Ahmed NS, Abdelaziz MA. 2010. Confirmatory studies on the antioxidant and antidiabetic effect of quercetin in rats. *Indian J Clin Biochem* 5(2): 188-192.
- Abdullah W, *et al.* 2016. The flavonoids and biological activity of *Cleome africana* growing in Egypt. *RJPBCS* 7:1092-1105.
- Abhay T, Ranit D, Abhinav A, Sanchit M, Meenu M, Saurabh S, Neha S, Gopal LK, Navneet K. 2018. Identification of molecular targets of potential antidiabetic drugs using prediction of activity spectra for substances and molecular docking. *IJGP*. 1-10.
- Accelrys Enterprise Platform. 2005. *Induction To The Discovery Studio Visualizer*. San Diego, California, USA : Accelrys Software Inc.
- Aertgeerts K, ye S, Tennant MG, Kraus ML, Rogers J, Sang BC, Skene RJ, Webb DR, Prasad GS. 2003. Crystal structure of human dipeptidyl peptidase IV in complex with decapeptide reveals details on substrate specificity and tetrahedral intermediate formation. *Protein Sci*. 13:412-421.
- Aguirre L, Arias N, Macarulla MT, Gracia A, Portillo MP. 2011. Beneficial effects of quercetin on obesity and diabetes. *The Open Nutra J* 4: 189-198.
- Al-Zubairi A.S. dan Eid E.E.M. 2010. Molecular targets in development of antidiabetic drugs. *International Journal of Pharmacology*. 6(6):784-795.
- Allredge BK, Corelli RL, Ernst ME, Guglielmo BJ, Jacobson PA, Kradjan WA, Williams BR. 2013. *Koda-Kimble & Young's Applied Therapeutics The Clinical Use of Drugs*. 10th ed. United States of America: Lippincott Williams & Wilkins, Pennsylvania.
- Anitha K, Gopi G, Girish, Kumar PS. 2015. Molecular docking study on dipeptidyl peptidase-4 inhibitor. *IJRDP*. 2(5):602-610.

- Aprijani, D.A., dan Elfaizi, M.A. 2004. *BIOINFORMATIKA: Perkembangan, Disiplin Ilmu dan Penerapannya di Indonesia*.
- Arwansyah, L., Ambarsar, T., Sumaryada. 2014. Simulasi docking senyawa kurkumin dan analognya sebagai inhibitor reseptor androgen pada kanker prostat. *Current Biochemistry* 1(1):14-24.
- Bahmani, M., Zargaran, A., Rafieian-Kopaei, M., Saki, K. 2014. Ethnobotanical study of medicinal plants used in the management of diabetes mellitus in the Urmia, Northwest Iran. *Asian Pac J Top Med*. 7(1):S348-S354.
- Bano D, Tabassum H, Ahmad A, Mabood A, Ahmad IZ. 2016. The medical significance of the bioactive compounds of *Trigonella foenum-graecum*. *Int. J. Res. Ayurveda Pharm* 7(4).
- Chakraborty, P and Ra,akrishnan, M. 2016. Role of P-glycoprotein in chemotherapeutic drug resistance and mechanisms of pump deactivation to overcome MDR in cancer cells. *A Critical Review*. 1(2):31-38.
- Corwin. J. 2009. *Buku Saku Patofisiologi* (3 ed.). (E. K. Yudha, Ed., & N.B. Subekti, Trans). Jakarta : EGC.
- Daina A, Michielin O, & Zoete V. 2017. SwissADME: a free web tool to evaluate pharmacokinetics, drug-likeness and medicinal chemistry friendliness of small molecules. *Scientific Repots* 1:13.
- DeLano Wl, Bromberg S. 2004. *PyMOL User's Guide*. California: DeLano Scientific LLC.
- Dipiro JT, Wells BG, Dipiro CV, Schwinghammer TL. 2015. *Pharmacotherapy Handbook*. Ninth Edition. USA: Mc Graw-Hill Education.
- Dominijanni S, Cipriani S, Malaguti M, Triolo L, Ansali F, Floccari F. 2017. Antidiabetic medication in patients with chronic kidney disease: what's new?. *Nephrol @ Point Care* 3:e17-e22.
- Ekayanti M., Sauriasari R., and Elya B.. 2018. Dipeptidyl peptidase IV inhibitory activity of traction from white tea ethanolic extract (*Camelia sinensis* (L.) Kuntze) ex vivo. *Pharmacogn. J* 10(1):190-193.
- Fatimah R. N. 2015. *Diabetes Melitus Tipe 2* [Abstrak]. Lampung : Universitas Lampung.
- Fong, E and Nemeth, E. 2013. Manipulation of the hepcidin pathway for therapeutic purpose. 98(11).
- Ganiswarna SG, Setiabudy R, Suyatna FD, Purwastyastuti, Nafrialdi. 2001. *Farmakologi Dan Terapi*. Jakarta: Bagian Farmakologi Fakultas Kedokteran – Universitas Indonesia.

- Ghosh S *et al.* 2014. Diosgenin from *Dioscorea bulbifera*: novel hit for treatment of type II diabetes mellitus with inhibitory activity against α -amylase and α -glucosidase. *Plos One* 9:1-9.
- Hasan, Mehedee dan Mustafizur Rahman. 2016. Effect of Fenugreek on Type 2 diabetic patients. *International Journal of Scientific and Research Publications* 1(6).
- Hassan RA, Tawfik WA, Abou-Setta M. 2014. The flavonoid constituents of *Leucaena leucocephala* growing in Egypt, and their biological activity. *Afr J Tradit Complement Altrern Med* 11:67-72.
- He Yangfeng, Lv Huanhuan, Wang Xiaoyan, Suo Yourui, Wang Honglun. 2014. Isolation and purification of six bioactive compounds from the seeds of *Trigonella foenum-graecum* L. using high-speed counter-current chromatography. *Separation Science and Technology* 49:580-587.
- Henzen Christoph. 2012. Monogenic diabetes mellitus due to defects in insulin secretion. *The European Journal of Medical Science*.
- Hevener KE, Zhao W, Ball DM, Babaoglu K, Qi J, White SW, *et al.* 2009. Validation of molecular *docking* programs for virtual screening against dihydropteroate synthase. *J Chem Inf Model.* (2): 444-60.
- Ilham Zul, Hamidon H, Rosji NA, Ramli N, Osman N. 2015. Extraction and quantification of toxic compound mimosine from *Leucaena leucocephala* leaves. *Procedia Chemistry* 16:164-170.
- Inbara SD and Muniappan M. 2018. Effect of *Trigonella foenum graecum* on alpha-glucosidase and dipeptidyl peptidase-IV inhibitory activity – an in vitro study. *Asian Journal Of Pharmaceutical And Clinical Research* 11:513-516.
- Jetté L, Harvey L, Eugeni K, Levens N. 2009. 4-Hydroxyisoleucine: a plant-derived treatment for metabolic syndrome. *Curr Opin Investig Drugs* 10(4):353-358.
- Kouranov, A., *et al.* 2006. The RCSB PDB information portal for structural genomics. *Nucleic Acids Res* 34:D303-D305.
- Lee, S.-Y., Park, S.-L., Hwang, J.-T., Yi, S.-H., Young-DoNam, & Lim, S.-I. 2012. Antidiabetic Effect of *Morinda citrifolia* (Noni) Fermented by. *Hindawi Publishing Corporation Evidence-Based Complementary and Alternative Medicine*.
- Lipinski, CA *et al.* 2001. Experimental and computational approaches to estimate solubility and permeability in drug discovery and development settings. *Advanced Drug Delivery Reviews.* 46 (1-3):3-26.

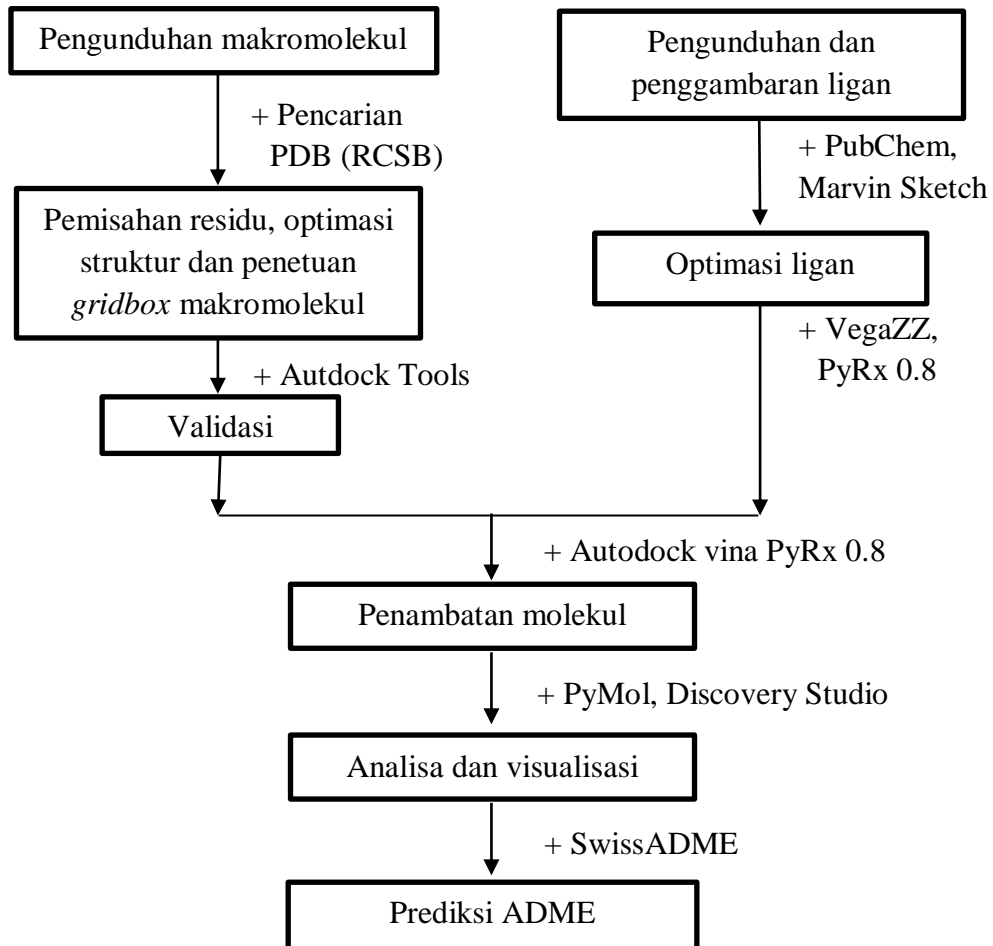
- Lipinski, CA. 2004. Drug discovery today. *Technologie*. 1 (4):337-341.
- Mahbub J, Mou RA, Sikta SA, Rahman A, and Dash PR. 2018. Biological and medicinal significance of *Trigonella foenum-graecum*. *IJLSR* 4:15-26.
- Manteno, J., Burgos, E., Perez, C., & Lopez, M. 2011. A review on the dietary flavonoid kaempferol. *Mini-review a in Medicinal Chemistry*. 11:298-344.
- Mealey, KL., Waiting, D., Rauning, DL., Schmidt, KR., Nelson, FR.. 2010. Oral bioavailability of P-glycoprotein substrate drugs do not differ between ABCB1-1 Δ and ABCB1 wild type dogs. *J. vet. Pharmacol Therap.* (33):453-460.
- Morris GM, Godsell DS, Halliday RS, Geuy R, Hart WE, Belew RK, Olson AJ. 1998. Automated docking using Lamarckian genetic algorithm and an empirical binding free energy function. *J Comp Chem*. 19(14): 1639-1662.
- Patil P., Mandal S., Tomar SK., Anand S. 2015. Food protein-derived bioactive peptides in management of type 2 diabetes. *European Journal of Nutrition*.
- Patil R, Das S, Stanley A, Yadav L, Sudhakar A, Varma AK. 2010. Optimized hydrophobic interaction and hydrogen bonding at the target-ligand interface leads the pathways of drug-designing. *PLOS One*. 5(8):1-10.
- Patrick Graham L. 2013. An Introduction to Medicinal Chemistry Fifth Edition. United Kingdom: Oxford University Press.
- Pedretti, A., Mazzolari, A., & Vistoli, G. 2004. VegaZZ: a versatile toolkit for drug design and protein modeling. *J Comput Chem* 25(13):1605-1612.
- Prasetyo Niko. 2011. *MarvinSketch to Chemoinformatics*. <https://neax502.wordpress.com/2011/11/26/marvinsketch-to-chemoinformatics/> [20 Juni 2019].
- Rachmatiah T, Nurvita H, dan D Rizna Triana. 2015. Potensi antidiabetes pada tumbuhan petai Cina (*Leucaena leucocephala* (Lam) De Wit). *Saintech* 25:115-118
- Raheleh A, Hasanloo T, Khosroshahli M. 2011. Evaluation of trigonelline production in *Trigonella foenum-graecum* hairy root cultures of two Iranian masses. *Plant Omics J* 4(7):408-411.
- Ramadhani DL. 2016. Penambatan Molekul (*Molecular Docking*): Pengenalan. <https://dhnlr.com/tekno/penambatan-molekul-molecular-Docking-pengenalan> [20 Juni 2019].
- Ramya T. Sri, V. Sathyanathan, Kumar D. P. 2011. Chowdhari M. Docking Studies on Synthesized Quinazoline Compounds Against Androgen Receptor. *Int. J. Pharm & Ind. Res* 1(4):266-269.

- Rathore SS, Saxena SN, Kakani RK, Singh B. 2013. Rapid and mass screening method for galactomannan content in fenugreek seeds. *Int J Seed Spices* 3(2): 9193.
- Rettie AE, Jones JP. 2005. Relevansi klinis dan toksikologis dari CYP2C9: interaksi obat-obat dan farmakogenetika. *Ulasan Tahunan Farmakologi dan Toksikologi*. 45:477-94.
- Salib JY, Michael HN, Eskande EF. 2013. Anti-diabetic properties of flavonoid compounds isolated from *Hyphaene thebaica* epicarp on alloxan induced diabetic rats. *Pharmacognosy Research* 5:22-29.
- Sandeep et al. 2011. AUDDock LE: A GUI for virtual screening with AUTODOCK Vina. *BMC research Notes* 4(445).
- Shandar, H.K., Kumar, B., Pasher, S., Tiwari, P., Salhan, M. & Sharma, P. 2011. A review of phytochemistry and pharmacology of flavonoids. *International Pharmaceutica Scientia*. 1(1):37.
- Saputri KE, Fakhmi N, Kusumaningtyas E, Priyatama D, dan Santoso B. 2016. Docking molekuler potensi anti diabetes melitus tipe 2 turunan zerumbon sebagai inhibitor aldose reduktase dengan autodock-vina. *Chimica et Natura Acta* 4:16-20.
- Saqib, U., dan Siddiqi, MI. 2008. Probing ligand binding interactions of human alpha glucosidase by homology modeling and molecular docking. *IJIB*. 2(2):116-121.
- Shargel, L., Yu, A., & Wu, S. 2005. *Biofarmasetika dan Farmakokinetika Terapan*, Edisi kedua. Surabaya: Airlangga University Press. 167-187.
- Sihabuddin M *et al.* 2011. Penetapan parameter farmakokinetik gendarusian A dalam urin subyek pria setelah pemberian sediaan ekstrak etanol daun *Justicia gendarussa* Burm. F. *Jurnal Medika Planta* 4:59-68.
- Silvita, D.S., Herry S. Sastramiharja, Dadang Rukanta. 2015. Pemberian Infusa Biji Petai China (*Leucaea Leucocephala*) dalam Menurunkan Kadar Gula Darah Uasa Pada Mencit Model Diabetes. Prosiding Penelitian Sivitas Akademika Unisba. Universitas Islam Bandung.
- Sougata G, Piyush M, Abhishek D, Ajay BP, Pramod M, Adersh A, Navanath K, Mahemud LS, Boppana R, Vaishali SS, Dilip DD, Balu AC. 2014. Diosgenin from *Dioscorea bulbifera*: novel hit of treatment of type II diabetes mellitus with inhibitory activity against α -amylase and α -glucosidase. *PLOS ONE*. 9(1-9).
- Sun H., Wang D., Song X., Zhang Y., Ding W., Peng X., Zhang X., Li Y., Ma Y., Wang R., Yu P. 2017. Natural prenylchalconaringenins and prenylnaringenins as antidiabetic agents: α -glucosidase and α -amylase

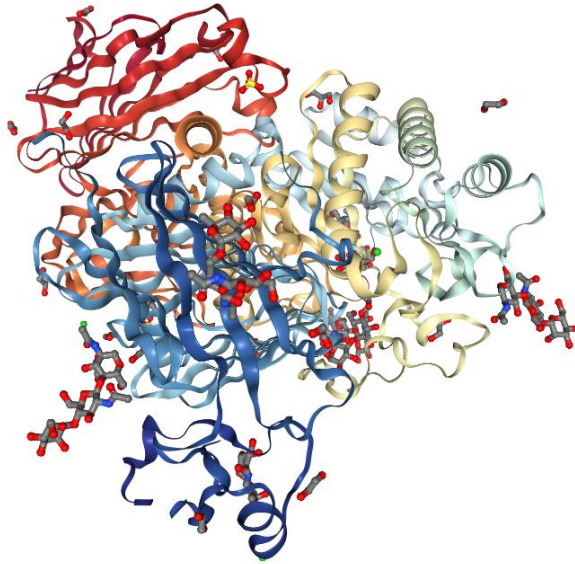
- inhibition and in vitro antihyperglycemic and antihyperlipidemic effects. *J. Agric. Food Chem* 65:1574-1581.
- Sun J, Qu C, Wang Y, Huang H, Zhang M, Li H, Zhang Y, Wang Y, Zou W. 2016. PTP1B, A Potential Target of Type 2 Diabetes Mellitus. *Molecular Biology* 5:1-6.
- Syahputra, G., Ambarsari, T., Sumardaya. Docking simulation of curcumin and its analogs as inhibitors on 12-lipoxygenase enzymes. *Jurnal Biofisika*. 10(1):48-58.
- Tamrakar, Akhliesh Kumar, Chandab K Maurya, dan Amit K Rai. 2014. *PTP1B inhibitors for type 2 diabetes treatment: a patient*. *Informa Healthcare* 24(10):1-15.
- Trisnawati SK, Setyorogo S. 2013. Faktor risiko kejadian diabetes mellitus tipe II di puskesmas Kecamatan Cengkareng Jakarta Barat. *Jurnal Ilmiah Kesehatan* 5:6-11
- Trott, O., and Olson, A. 2009. Software news and update autodock vina: improving the speed and accuracy of Docking with a new scoring function, efficient optimization, and multithreading. *Journal of Computational Chemistry* 0:1-7.
- Troot, O and Olson A.J. 2009. Software news and update autodock vina: improving the speed and accuracy of docking with a new scoring function, efficient optimization, and multithreading. *Journal of Computational Chemistry*. 31:455-461.
- Trott, O and Olson, A. 2010. NIH Public Access. *Journal of Computational Chemistry* 31:455-461.
- Trott O and Olson AJ. 2010. AutoDock Vina: Improving the speed and accuracy of Docking with a new scoring function, efficient optimization and multithreading. *Journal Of Computational Chemistry*. 31:455-461.
- Umaru IJ, Samling B, Umaru HA. 2018. Phytochemical screening of *Leucaena leucecophala* leaf essential oil and its antibacterial potentials. *MOJ Drug Design Developmen & Therapy* 2:224-228.
- Verma K. Sant dan Thareja, Suresh. 2016. Molecular docking assisted 3D-QSAR study of benzylidene-2, 4-thiazolidinedione derivatives as PTP-1B inhibitor for the management of Typr-2 diabetes mellitus. *Royal Society of Chemistry*. 1-11.
- Wagle A, Seong SH, Shrestha S, Jung HA, and Choi JS. 2019. Korean thistle (*Cirsium japonicum* var *maackii* (Maxim.) Matsum.): a potential dietary supplement against diabetes and alzheimer's disease. *MDPI* 24:1-19.

- Wang B, LP Yang, Zhang XZ, Huang SQ, Bartlam M, Zhou SF. 2009. Wawasan baru ke dalam karakteristik structural dan relevansi fungsional enzim sitokrom P450 2D6 manusia. *Ulasan Metabolisme Obat*. 41(4):573-643.
- Wani M, Sarvar FA, Agrawal J, Deshpande J, Mathew S, Khetmalas M. 2012. Qualitative phytochemical analysis and antimicrobial activity studies of *Gymnema sylvestre* R. *Br. Acta Biologica Indica* 1(1):121-124.
- Wen X, Wang JS, Neuvonen PJ, Backman JT. 2002. Isoniazid adalah inhibitor berbasis sitokrom P450 1A2, 2A6, 2C19, dan 3A4 isoform dalam mikrosom hati manusia. *Eur J Clin Pharmacol*. 57(11):799-804.
- Xie ZQ. 2010. Exploiting Pubchem For Virtual Screening NIH Public Access.
- Zanger UM, Schwab M. 2013. Cytochrome P450 enzyme in drug metabolism: regulation of gene expression, enzyme activities; and impact of genetic variation. *Pharmacology & Therapeutic*. 138:103-141.
- Zamboni VR, Ponzano BC, Iacono R, Ferrara, Germany S, Bourne Y, Parenti G, Moracci M, Sulzanbacher G. 2017. Structure of human lysosomal acid α -glucosidase-a guide for the treatment of pompe disease. *Nature Communications*. 1-10.
- Zayed MZ, Samling B. 2016. Phytochemical constituents of the leaves of *Leucaena leucocephala* from Malaysia. *Inernational Journal of Pharmacy and Pharmaceutical Sciences* 8:174-179.
- Zhou J. 2010. Multi-drug resistance in caner. *Business*. 596.

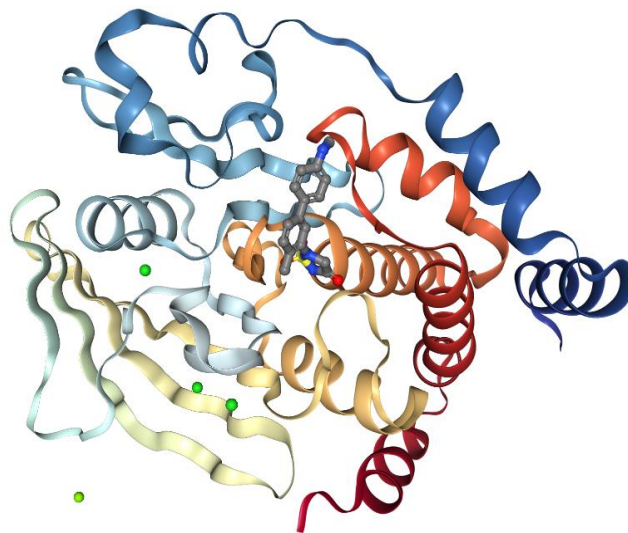
LAMPIRAN

Lampiran 1. Skema Jalannya Penelitian

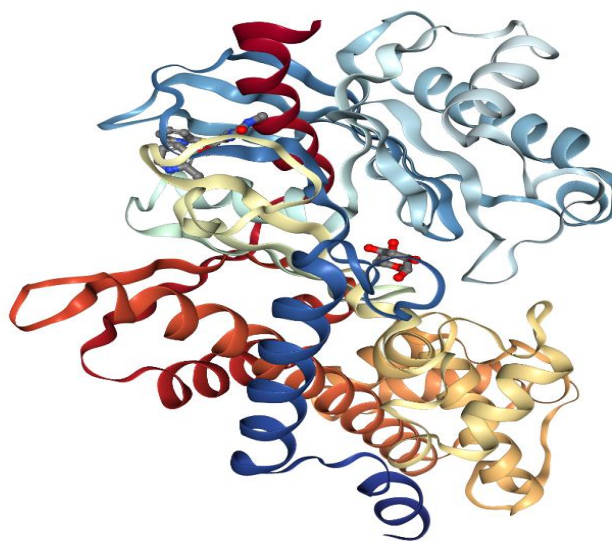
Lampiran 2. Struktur 3D Makromolekul



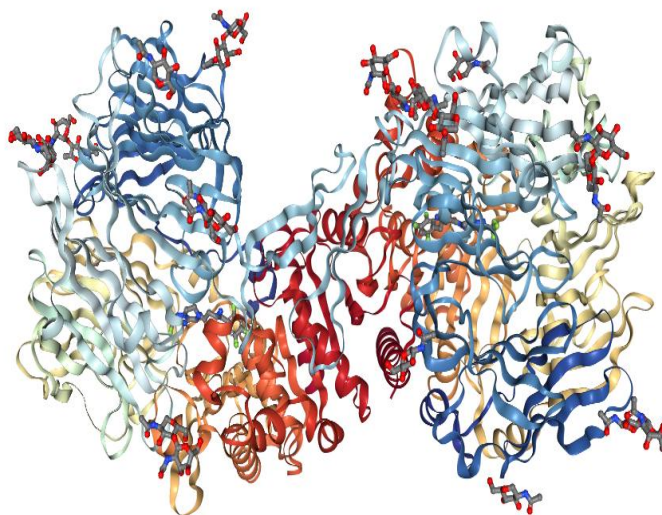
α -G (2QOE)



PTP-1B (5T19)


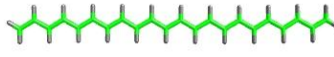
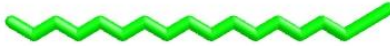
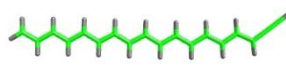

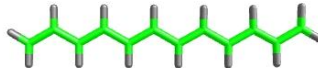
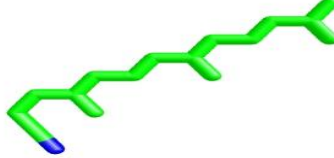
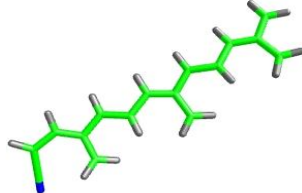
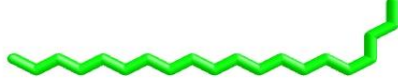
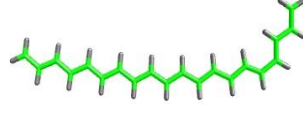
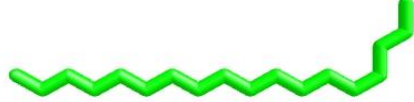
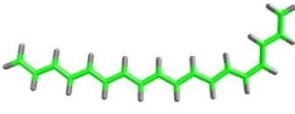
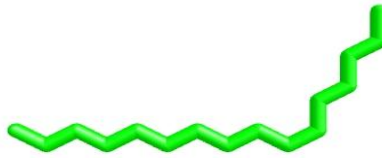
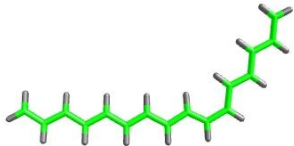


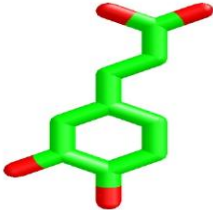
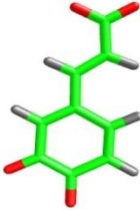
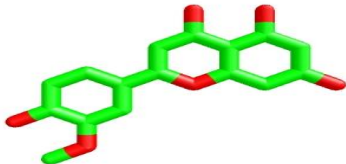


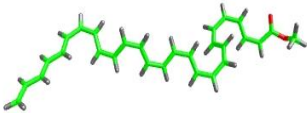



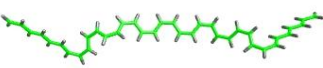
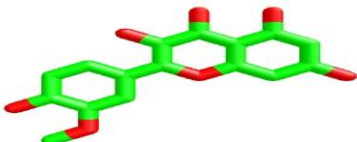
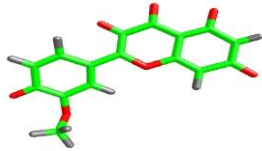
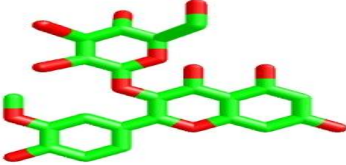

GK (4RCH)

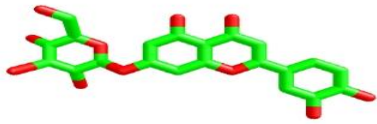

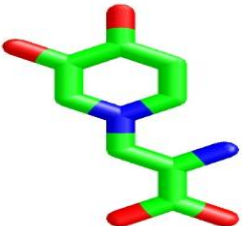


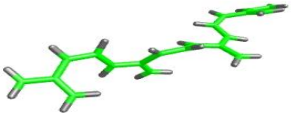
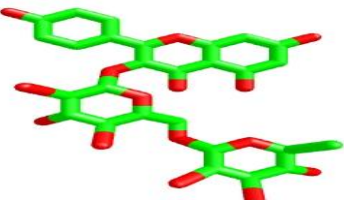
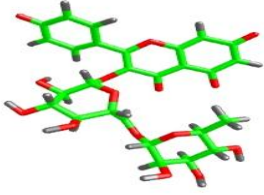
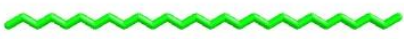
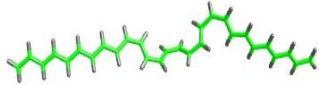

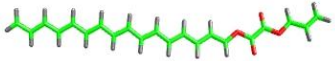

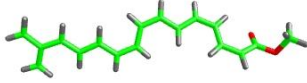

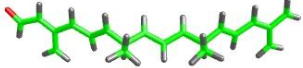


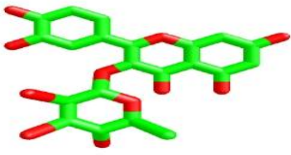


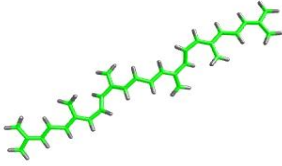

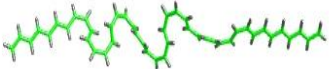
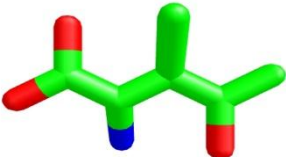
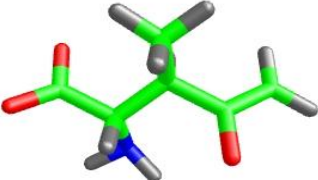
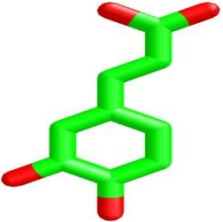
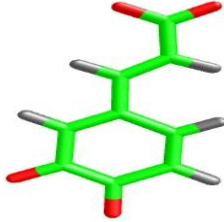
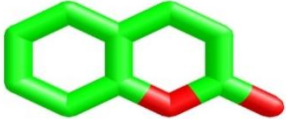

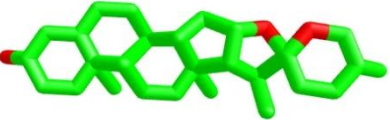

DPP4 (2QOE)



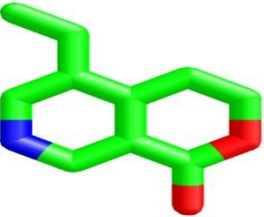



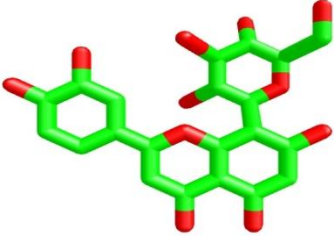

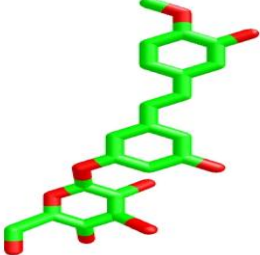

Lampiran 3. Hasil Sebelum dan Sesudah Optimasi Ligan Uji



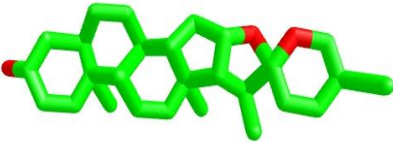
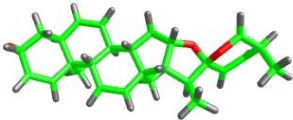
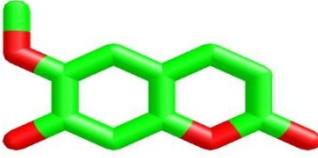

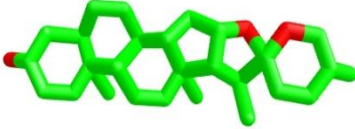
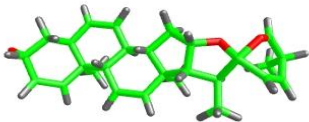
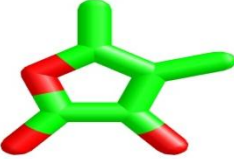
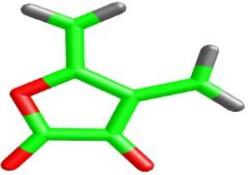
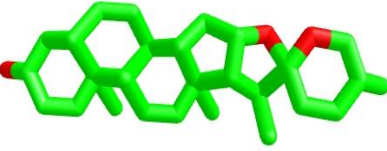
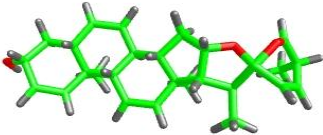
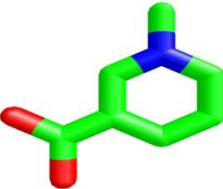
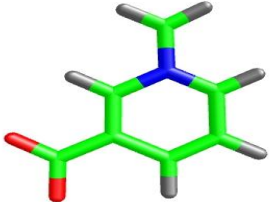
Ligan	Sebelum Optimasi	Sesudah Optimasi
<i>L. leucocephala</i>		
1-Docosene		
1-Octadecyne		
2-Dodecene		
Farnesyl Cyanide		
5-Eicosene		
5-Octadecene		
7-Hexadecene		



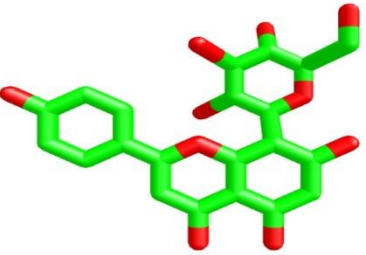

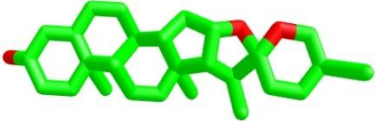
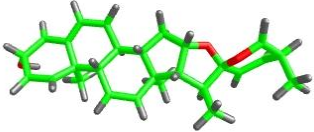

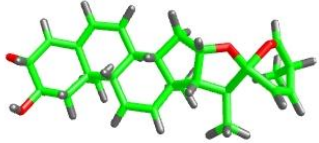
Asam cafeat		
Chrysoeriol		
Methyl Heptacosanoate		
Hexacosane		
Hexatriacontane		
Isorhamnetin		
Isorhamnetin 3-O-galactoside		

Luteolin-7-glucoside		
Mimosine		
Neophytadiene		
Nicotiflorin		
Octacosane		
Oxalic acid allyl hexadecyl ester		
Methyl 14-Methylpentadecanoate		
Phytol		

Quercetin-3-O-rhamnoside		
Squalene		
Tetratetracontane		
<i>T. foenum-graecum</i>		
4-hydroxy isoleucine		
Caffeic acid		
Coumarin		
Diosgenin		

Galactomannan	 A ball-and-stick model of Galactomannan, showing a branched chain of green carbon atoms with red oxygen atoms and white hydrogen atoms. The structure consists of a main chain of mannose units with galactose units branching off.	 A ball-and-stick model of Galactomannan, showing a branched chain of green carbon atoms with red oxygen atoms and white hydrogen atoms. The structure consists of a main chain of mannose units with galactose units branching off.
Gentianine	 A ball-and-stick model of Gentianine, showing a complex polycyclic structure with green carbon atoms, red oxygen atoms, and white hydrogen atoms. It features a central ring system with a blue nitrogen atom and a red sulfur atom.	 A ball-and-stick model of Gentianine, showing a complex polycyclic structure with green carbon atoms, red oxygen atoms, and white hydrogen atoms. It features a central ring system with a blue nitrogen atom and a red sulfur atom.
Isovitexin	 A ball-and-stick model of Isovitexin, showing a complex polycyclic structure with green carbon atoms, red oxygen atoms, and white hydrogen atoms. It features a central ring system with a blue nitrogen atom and a red sulfur atom.	 A ball-and-stick model of Isovitexin, showing a complex polycyclic structure with green carbon atoms, red oxygen atoms, and white hydrogen atoms. It features a central ring system with a blue nitrogen atom and a red sulfur atom.
Orientin	 A ball-and-stick model of Orientin, showing a complex polycyclic structure with green carbon atoms, red oxygen atoms, and white hydrogen atoms. It features a central ring system with a blue nitrogen atom and a red sulfur atom.	 A ball-and-stick model of Orientin, showing a complex polycyclic structure with green carbon atoms, red oxygen atoms, and white hydrogen atoms. It features a central ring system with a blue nitrogen atom and a red sulfur atom.
Rhaponticin	 A ball-and-stick model of Rhaponticin, showing a complex polycyclic structure with green carbon atoms, red oxygen atoms, and white hydrogen atoms. It features a central ring system with a blue nitrogen atom and a red sulfur atom.	 A ball-and-stick model of Rhaponticin, showing a complex polycyclic structure with green carbon atoms, red oxygen atoms, and white hydrogen atoms. It features a central ring system with a blue nitrogen atom and a red sulfur atom.

Rhapontigenin		
Sarsasapogenin		
Scopoletin		
Smilagenin		
Sotolone		
Tigogenin		
Trigonellin		

Vicenin-2	 <chem>O=C(O)C1=CC=C(C=C1)C2=CC(=C(C=C2)OC3=CC(=O)C(OC4=CC=CC=C4)C5=CC=CC=C5C6=CC=CC=C6C7=CC=CC=C7)C8=CC=CC=C8</chem>	
Vitexin	 <chem>O=C(O)C1=CC=C(C=C1)C2=CC(=C(C=C2)OC3=CC(=O)C(OC4=CC=CC=C4)C5=CC=CC=C5)C6=CC=CC=C6</chem>	
Yamogenin	 <chem>O=C(O)C1=CC=C(C=C1)C2=CC(=C(C=C2)OC3=CC(=O)C(OC4=CC=CC=C4)C5=CC=CC=C5)C6=CC=CC=C6C7=CC=CC=C7</chem>	
Yuccagenin	 <chem>O=C(O)C1=CC=C(C=C1)C2=CC(=C(C=C2)OC3=CC(=O)C(OC4=CC=CC=C4)C5=CC=CC=C5)C6=CC=CC=C6C7=CC=CC=C7C8=CC=CC=C8</chem>	

Lampiran 4. Data Hasil Docking

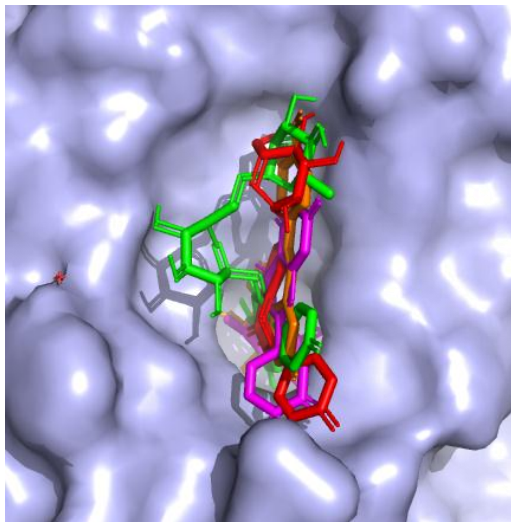
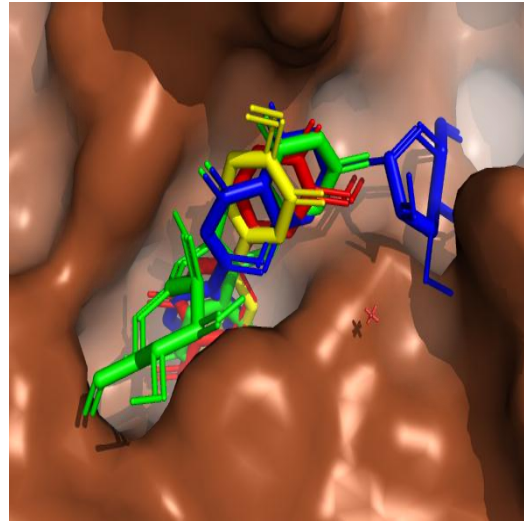
A. Data Hasil Docking *L. leucocephala*

<i>L. Leucocephala</i> Compound	$\Delta G_{\text{binding}} \pm \text{SD}$			
	α -Glucosyl 5NN8	PTP1B 5T19	GK 4RCH	DPP4 2QOE
Ligan asli	-8.43 \pm 0.05	-9.60 \pm 1.00	-9.60 \pm 1.00	-8.28 \pm 0.29
Kontrol Positif	-8,40 \pm 0,00	-8,60 \pm 0,05	-8,10 \pm 0,00	-8,90 \pm 0,38
1-Docosene	-5.03 \pm 0.15	-5.13 \pm 0.17	-5.13 \pm 0.17	-4.73 \pm 0.17
1-Octadecyne	-4.88 \pm 0.21	-5.10 \pm 0.22	-5.10 \pm 0.22	-4.80 \pm 0.37
2-Dodecene	-5.08 \pm 0.10	-5.38 \pm 0.10	-5.38 \pm 0.10	-5.03 \pm 0.29
Farnesyl Cyanide	-6.03 \pm 0.19	-6.80 \pm 0.34	-6.80 \pm 0.34	-6.10 \pm 0.34
5-Eicosene	-5.13 \pm 0.25	-5.23 \pm 0.17	-5.23 \pm 0.17	-4.95 \pm 0.21
5-Octadecene	-5.05 \pm 0.03	-5.35 \pm 0.30	-5.35 \pm 0.30	-5.18 \pm 0.15
7-Hexadecene	-5.25 \pm 0.13	-5.18 \pm 0.21	-5.18 \pm 0.21	-5.05 \pm 0.31
Asam cafeat	-5.90 \pm 0.00	-7.50 \pm 0.00	-7.50 \pm 0.00	-6.30 \pm 0.00
Chrysoeriol	-6.90 \pm 0.00	-8.90 \pm 0.00	-8.90 \pm 0.00	-8.13 \pm 0.59
Methyl Heptacosanoate	-5.08 \pm 0.24	-5.10 \pm 0.16	-5.10 \pm 0.16	-5.25 \pm 0.47
Hexacosane	-4.95 \pm 0.24	-4.80 \pm 0.14	-4.80 \pm 0.14	-4.63 \pm 0.10
Hexatriacontane	-5.00 \pm 0.14	-4.65 \pm 0.17	-4.65 \pm 0.17	-5.43 \pm 0.29
Isorhamnetin	-7.20 \pm 0.00	-8.50 \pm 0.00	-8.50 \pm 0.00	-8.33 \pm 0.10
Isorhamnetin 3-O-galactoside	-8.00 \pm 0.24	-8.20 \pm 0.00	-8.20 \pm 0.00	-8.25 \pm 0.31
Luteolin-7-glucoside	-8.30 \pm 0.00	-9.50 \pm 0.00	-9.50 \pm 0.00	-8.40 \pm 0.00
Mimosine	-5.63 \pm 0.10	-6.48 \pm 0.13	-6.48 \pm 0.13	-6.15 \pm 0.10
Neophytadiene	-5.65 \pm 0.10	-6.00 \pm 0.12	-6.00 \pm 0.12	-5.73 \pm 0.33
Nicotiflorin	-8.80 \pm 0.00	-8.10 \pm 0.00	-8.10 \pm 0.00	-9.20 \pm 0.00
Octacosane	-4.83 \pm 0.10	-4.83 \pm 0.30	-4.83 \pm 0.30	-4.40 \pm 0.18
Oxalic acid allyl hexadecyl ester	-4.98 \pm 0.22	-5.80 \pm 0.29	-5.80 \pm 0.29	-5.80 \pm 0.55
Methyl 14-Methylpentadecanoate	-4.83 \pm 0.19	-5.68 \pm 0.15	-5.68 \pm 0.15	-5.35 \pm 0.17
Phytol	-5.58 \pm 0.29	-6.13 \pm 0.30	-6.13 \pm 0.30	-5.93 \pm 0.15
Quercetin-3-O-rhamnoside	-8.33 \pm 0.05	-8.20 \pm 0.00	-8.20 \pm 0.00	-9.20 \pm 0.00
Squalene	-6.70 \pm 0.14	-6.83 \pm 0.42	-6.83 \pm 0.42	-7.15 \pm 0.58
Tetratetracontane	-4.78 \pm 0.13	-4.45 \pm 0.17	-4.45 \pm 0.17	-5.37 \pm 0.15

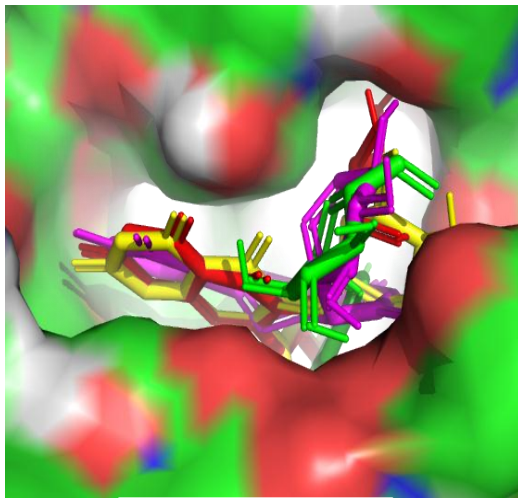
B. Data Hasil Docking *T. foenum-graecum*

<i>T. foenum-graecum</i> Compound	$\Delta G_{\text{binding}} \pm \text{SD}$			
	α -Glucosyl 5NN8	PTP1B 5T19	GK 4RCH	DPP4 2QOE
Ligan asli	-8.43 \pm 0.05	-9.60 \pm 1.00	-8.30 \pm 0.08	-8.28 \pm 0.29
Kontrol positif	-8,40 \pm 0,00	-8,60 \pm 0,05	-8,10 \pm 0,00	-8,90 \pm 0,38
4-hydroxy_ isoleucine	-5.00 \pm 0.00	-5.40 \pm 0.00	-4.50 \pm 0.00	-5.20 \pm 0.00
Caffeic_acid	-5.90 \pm 0.00	-7.50 \pm 0.00	-6.47 \pm 0.06	-6.30 \pm 0.00
Coumarin	-5.90 \pm 0.00	-7.05 \pm 0.06	-0.61 \pm 0.00	-6.08 \pm 0.78
Diosgenin	-8.30 \pm 0.00	-7.63 \pm 0.10	-8.90 \pm 0.00	-9.00 \pm 0.00
Galactomannan	-6.93 \pm 0.50	-6.13 \pm 0.13	-7.53 \pm 0.06	-7.35 \pm 0.17

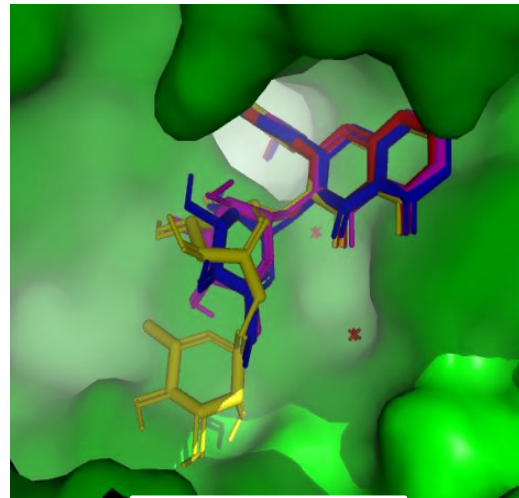
Gentianine	-5.43 ± 0.05	-6.90 ± 0.00	-6.20 ± 0.00	-5.80 ± 0.00
Isovitexin	-7.78 ± 0.05	-7.60 ± 0.00	-8.60 ± 0.00	-8.05 ± 0.06
Orientin	-6.93 ± 0.05	-7.90 ± 0.00	-9.10 ± 0.00	-7.40 ± 0.00
Rhaponticin	-8.28 ± 0.05	-8.20 ± 0.00	-9.07 ± 0.12	-8.40 ± 0.00
Rhapontigenin	-7.40 ± 0.00	-8.40 ± 0.00	-8.40 ± 0.00	-7.90 ± 0.00
Sarsasapogenin	-7.90 ± 0.12	-7.63 ± 0.05	-8.03 ± 0.46	-8.50 ± 0.00
Scopoletin	-5.60 ± 0.00	-7.50 ± 0.00	-6.70 ± 0.00	-5.98 ± 0.05
Smilagenin	-8.30 ± 0.00	-7.90 ± 0.00	-8.40 ± 0.00	-8.50 ± 0.00
Sotolone	-5.00 ± 0.00	-5.60 ± 0.00	-4.80 ± 0.00	-5.40 ± 0.00
Tigogenin	-8.40 ± 0.00	-7.78 ± 0.25	-7.90 ± 0.00	-8.80 ± 0.00
Trigonellin	-4.88 ± 0.05	-6.28 ± 0.25	-4.90 ± 0.00	-4.90 ± 0.08
Vicenin-2	-7.10 ± 0.00	-7.90 ± 0.00	-7.10 ± 0.00	-7.50 ± 0.00
Vitexin	-6.48 ± 0.05	-7.78 ± 0.05	-8.90 ± 0.00	-7.60 ± 0.00
Yamogenin	-8.08 ± 0.05	-8.50 ± 0.00	-9.10 ± 0.00	-8.60 ± 0.00
Yuccagenin	-8.30 ± 0.00	-7.73 ± 0.15	-8.20 ± 0.00	-8.80 ± 0.00

Lampiran 5. Binding site Target Makromolekul α - G (5NN8)

PTP-1B (5T19)

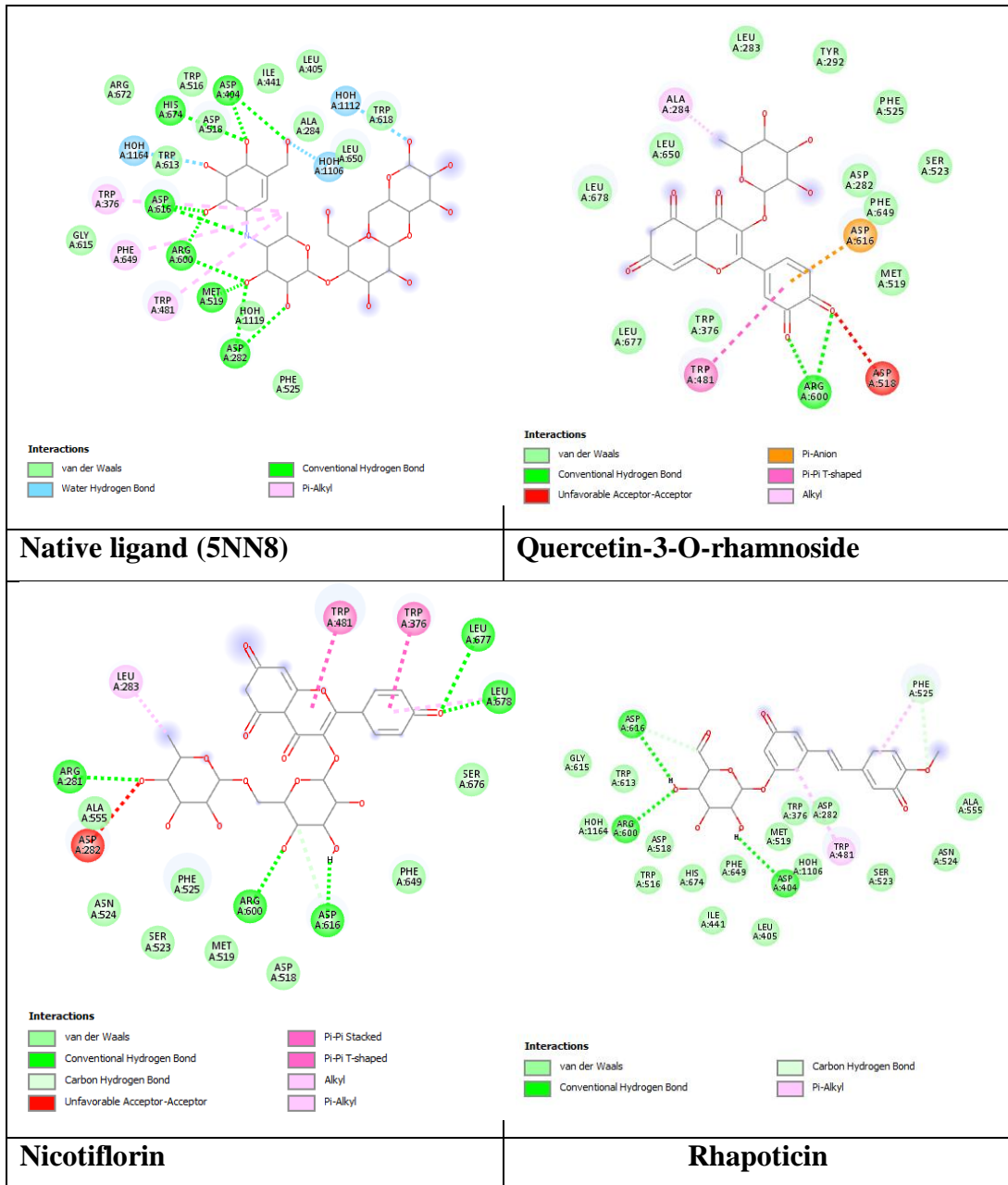


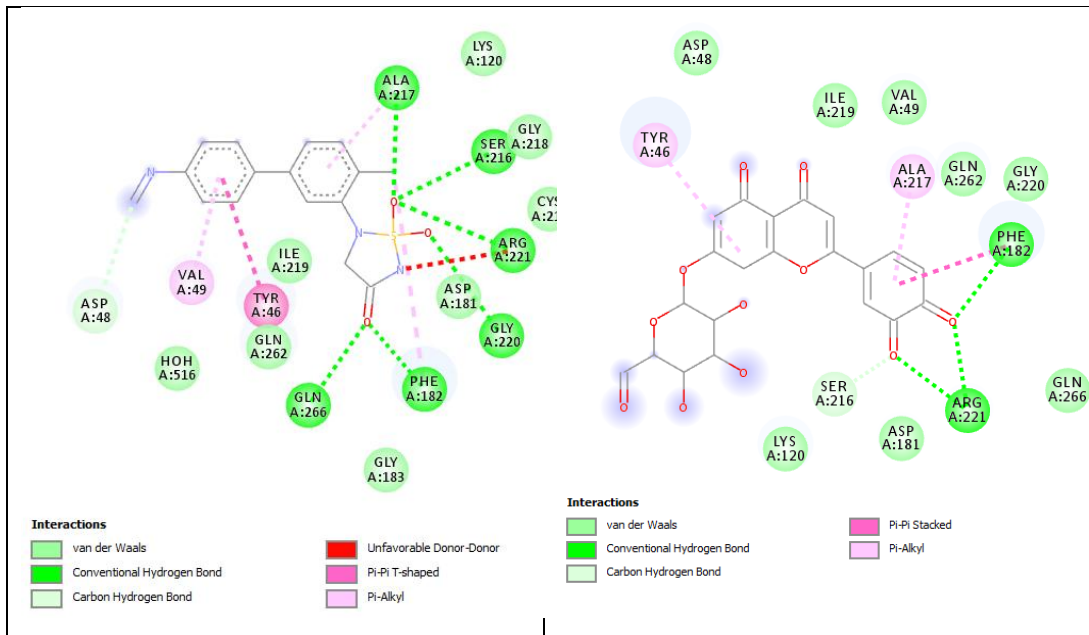
GK (4RCH)



DPP4 (5T19)

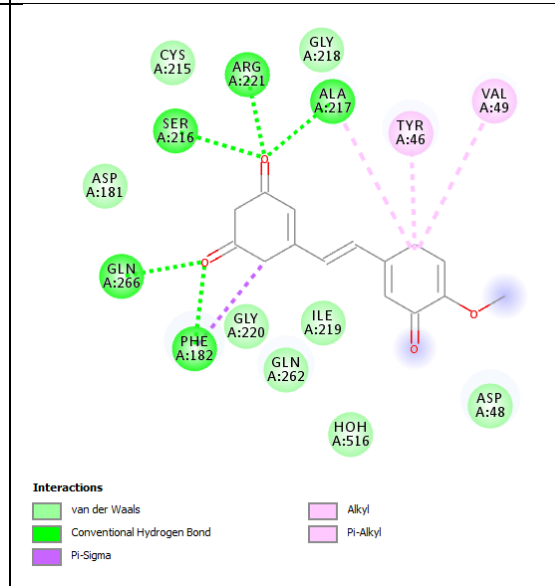
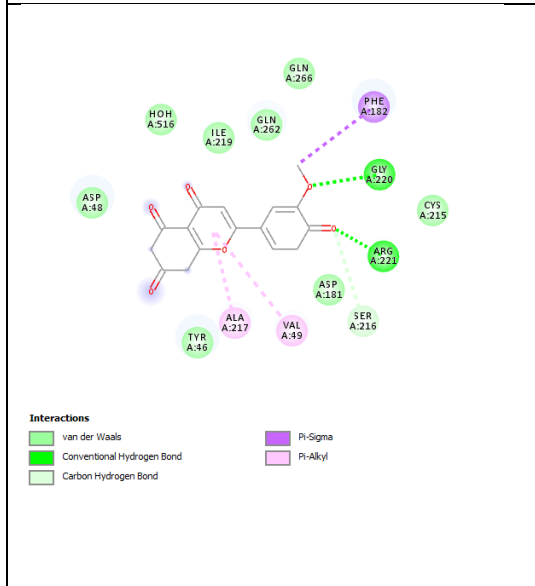
Lampiran 6. Interaksi Ligan Uji dengan masing-masing Makromolekul





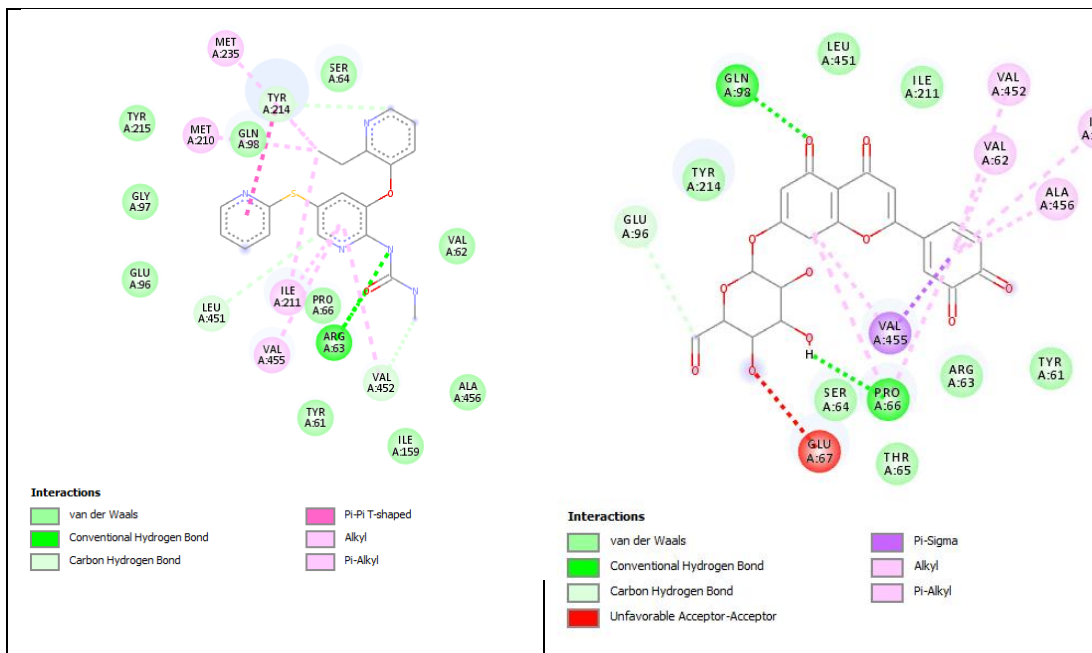
Native ligand (5T19)

Luteolin-7-glucoside



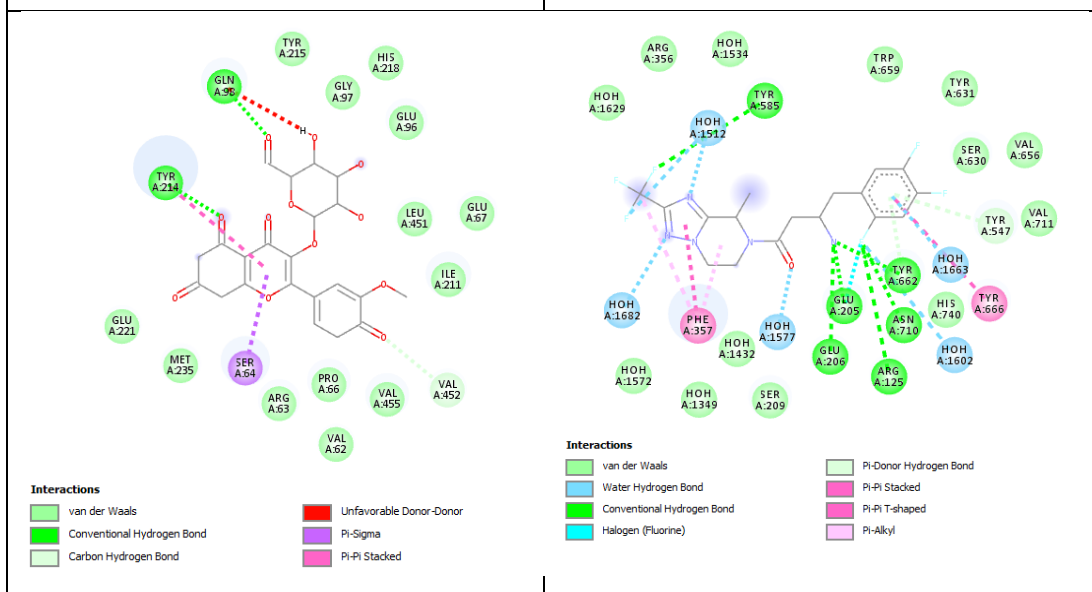
Chrysoeriol

Rhapontigenin



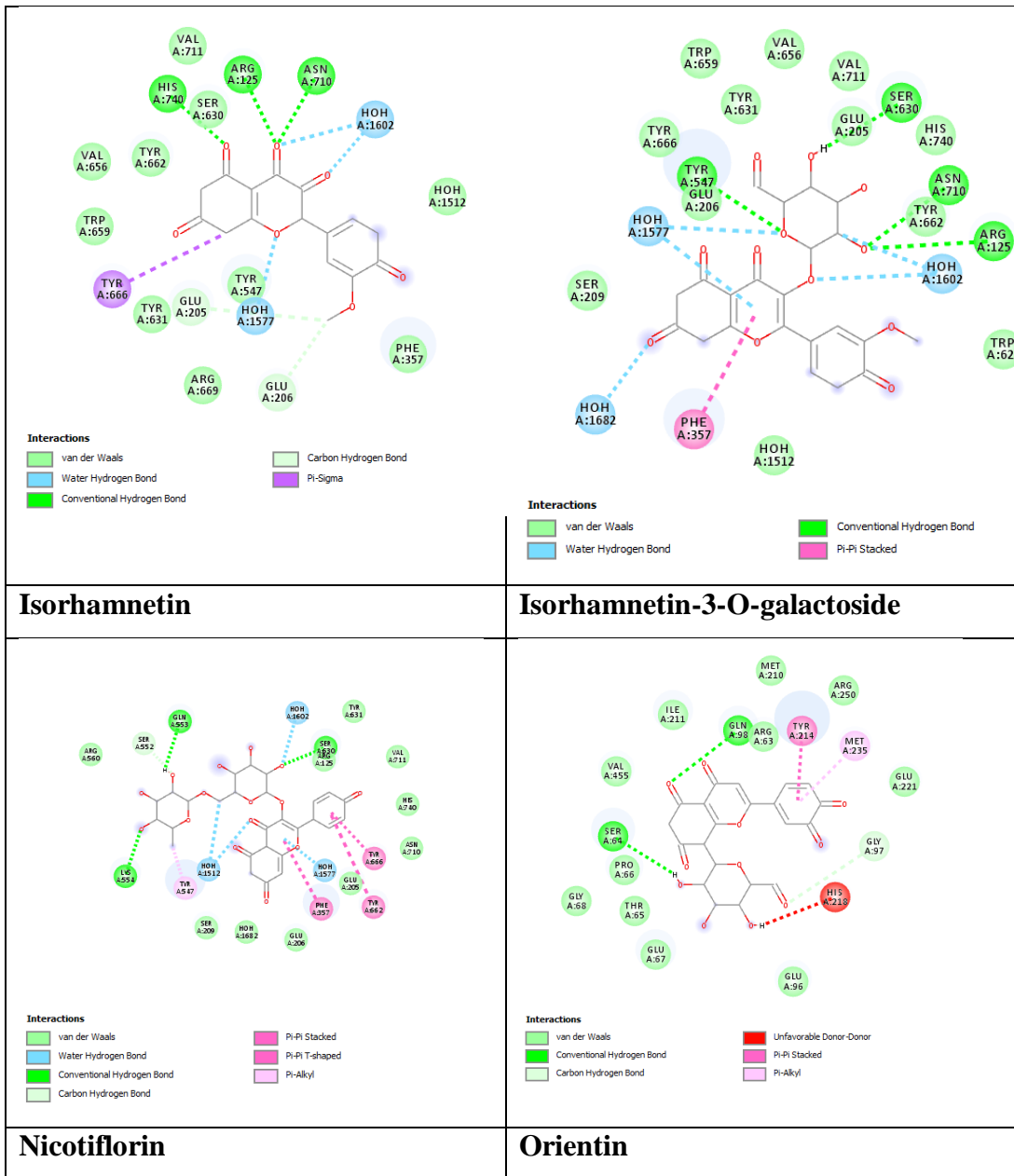
Native ligand (4RCH)

Luteolin-7-glucoside



Isorhamnetin-3-O-galactoside

Native ligand (2QOE)



Lampiran 7. Data Lipinski Rules of Five dan Profil Farmakokinetik

A. Data Lipinski Rules of Five dan Profil Farmakokinetik *L. leucocephala*

<i>L. leucocephala</i> compound	Lipinski Rules				Druglikeness
	BM	HBA	HBD	Log P	
1-Docosene	308,58	0	0	8,67	Diterima
1-Octadecyne	250,46	0	0	6,84	Diterima
2-Dodecene	168,32	0	0	4,91	Diterima
Farnesyl Cyanide	231,38	1	0	4,60	Diterima
5-Eicosene	280,53	0	0	7,70	Diterima
5-Octadecene	252,48	0	0	6,97	Diterima
7-Hexadecene	224,43	0	0	6,24	Diterima
Asam cafeat	180,16	4	3	0,93	Diterima
Chrysoeriol	300,26	6	3	2,18	Diterima
Methyl Heptacosanoate	424,74	2	0	9,52	Diterima
Hexacosane	366,71	0	0	10,00	Diterima
Hexatriacontane	506,97	0	0	13,67	Ditolak
Isorhamnetin	316,26	7	4	1,65	Diterima
Isorhamnetin 3-O-galactoside	478,4	12	7	0,06	Ditolak
Luteolin-7-glucoside	448,38	11	7	0,15	Ditolak
Mimosine	198,18	5	3	1,96	Diterima
Neophytadiene	278,52	0	0	7,07	Diterima
Nicotiflorin	594,52	15	9	-1,13	Ditolak
Octacosane	394,76	0	0	10,81	Diterima
Oxalic acid allyl hexadecyl ester	354,52	4	0	6,15	Diterima
Methyl 14-Methylpentadecanoate	270,45	2	0	5,48	Diterima
Phytol	296,53	1	1	6,23	Diterima
Quercetin-3-O-rhamnoside	448,38	11	7	0,22	Ditolak
Squalene	410,72	0	0	9,38	Diterima
Tetratetracontane	619,19	0	0	16,54	Ditolak

<i>L. leucocephala</i> compound	Farmakokinetika							
	Absorpsi		Distri busi	Metabolisme				
	GI Abs	P-gp S	BBB P	CYP inhibitor				
				1A2	2C19	2C9	2D6	3A4
1-Docosene	Rendah	Ya	Tidak	Ya	Tidak	Tidak	Tidak	Tidak
1-Octadecyne	Rendah	Tidak	Tidak	Ya	Tidak	Tidak	Tidak	Tidak
2-Dodecene	Rendah	Tidak	Tidak	Ya	Tidak	Tidak	Tidak	Tidak
Farnesyl Cyanide	Tinggi	Tidak	Ya	Ya	Tidak	Ya	Tidak	Tidak
5-Eicosene	Rendah	Tidak	Tidak	Ya	Tidak	Tidak	Tidak	Tidak
5-Octadecene	Rendah	Tidak	Tidak	Ya	Tidak	Tidak	Tidak	Tidak
7-Hexadecene	Rendah	Tidak	Tidak	Ya	Tidak	Tidak	Tidak	Tidak
Asam_cafeat	Tinggi	Tidak	Tidak	Tidak	Tidak	Tidak	Tidak	Tidak
Chrysoeriol	Tinggi	Tidak	Tidak	Ya	Tidak	Ya	Ya	Ya
Methyl Heptacosanoate	Rendah	Ya	Tidak	Tidak	Tidak	Tidak	Tidak	Tidak
Hexacosane	Rendah	Ya	Tidak	Tidak	Tidak	Tidak	Tidak	Tidak
Hexatriacontane	Rendah	Ya	Tidak	Tidak	Tidak	Tidak	Tidak	Tidak
Isorhamnetin	Tinggi	Tidak	Tidak	Ya	Tidak	Tidak	Ya	Ya
Isorhamnetin 3-O-galactoside	Rendah	Ya	Tidak	Tidak	Tidak	Tidak	Tidak	Tidak
Luteolin-7-glucoside	Rendah	Ya	Tidak	Tidak	Tidak	Tidak	Tidak	Tidak
Mimosine	Tinggi	Tidak	Tidak	Tidak	Tidak	Tidak	Tidak	Tidak
Neophytadiene	Rendah	Ya	Tidak	Tidak	Tidak	Ya	Tidak	Tidak
Nicotiflorin	Rendah	Ya	Tidak	Tidak	Tidak	Tidak	Tidak	Tidak
Octacosane	Rendah	Ya	Tidak	Tidak	Tidak	Tidak	Tidak	Tidak
Oxalic acid allyl hexadecyl ester	Tinggi	Tidak	Tidak	Tidak	Tidak	Ya	Tidak	Tidak
Methyl 14-Methylpentadecanoate	Tinggi	Tidak	ya	Ya	Tidak	Tidak	Tidak	Tidak
Phytol	Rendah	Ya	Tidak	Tidak	Tidak	Ya	Tidak	Tidak
Quercetin-3-O-rhamnoside	Rendah	Tidak	Tidak	Tidak	Tidak	Tidak	Tidak	Tidak
Squalene	Rendah	Tidak	Tidak	Tidak	Tidak	Tidak	Tidak	Tidak
Tetratetracontane	Rendah	Ya	Tidak	Tidak	Tidak	Tidak	Tidak	Tidak

B. Data *Lipinski Rules of Five* dan Profil Farmakokinetik *T. foenum-graecum*

<i>T. foenum-graecum</i> compound	Lipinski Rules				Druglikeness
	BM	HBA	HBD	Log P	
4-hydroxy_ isoleucine	147,17	4	3	1,29	Diterima
Caffeic acid	180,16	4	3	0,93	Diterima
Coumarin	146,14	2	0	1,82	Diterima
Diosgenin	414,62	3	1	5,03	Diterima
Galactomannan	504,44	16	11	-5,28	Ditolak
Gentianine	175,18	3	0	0,05	Diterima
Isovitexin	432,38	10	7	1,97	Diterima
Orientin	448,38	11	8	-0,47	Ditolak
Rhaponticin	420,41	9	6	0,63	Diterima
Rhapontigenin	258,27	4	3	2,61	Diterima
Sarsasapogenin	416,64	3	1	5,24	Diterima
Scopoletin	192,17	4	1	1,52	Diterima
Smilagenin	416,64	3	1	5,42	Diterima
Sotolone	128,13	3	1	0,63	Diterima
Tigogenin	416,64	3	1	5,24	Diterima
Trigonellin	137,14	2	0	-0,61	Diterima
Vicenin-2	594,52	15	11	-1,98	Ditolak
Vitexin	432,28	10	7	-0,02	Diterima
Yamogenin	414,62	3	1	5,01	Diterima
Yuccagenin	430,62	4	2	4,17	Diterima

<i>T. foenum-graecum</i> compound	Farmakokinetika							
	Absorpsi		Distri busi	Metabolisme				
	GI Abs	P-gp S	BBB P	CYP inhibitor				
				1A2	2C19	2C9	2D6	3A4
4-hydroxy_ isoleucine	Tinggi	Tidak	Tidak	Tidak	Tidak	Tidak	Tidak	Tidak
Caffeic acid	Tinggi	Tidak	Tidak	Tidak	Tidak	Tidak	Tidak	Tidak
Coumarin	Tinggi	Tidak	Ya	Ya	Tidak	Tidak	Tidak	Tidak
Diosgenin	Tinggi	Tidak	Ya	Tidak	Tidak	Tidak	Tidak	Tidak
Galactomannan	Rendah	Ya	Tidak	Tidak	Tidak	Tidak	Tidak	Tidak
Gentianine	Tinggi	Tidak	Ya	Ya	Tidak	Tidak	Tidak	Tidak
Isovitexin	Rendah	Tidak	Tidak	Tidak	Tidak	Tidak	Tidak	Tidak
Orientin	Rendah	Tidak	Tidak	Tidak	Tidak	Tidak	Tidak	Tidak
Rhaponticin	Rendah	Ya	Tidak	Tidak	Tidak	Tidak	Tidak	Tidak
Rhapontigenin	Tinggi	Tidak	Ya	Ya	Tidak	Ya	Tidak	Ya
Sarsasapogenin	Tinggi	Tidak	Ya	Tidak	Tidak	Tidak	Tidak	Tidak
Scopoletin	Tinggi	Tidak	Ya	Ya	Tidak	Tidak	Tidak	Tidak
Smilagenin	Tinggi	Tidak	Ya	Tidak	Tidak	Tidak	Tidak	Tidak
Sotolone	Tinggi	Tidak	Ya	Tidak	Tidak	Tidak	Tidak	Tidak
Tigogenin	Tinggi	Tidak	Ya	Tidak	Tidak	Tidak	Tidak	Tidak
Trigonellin	Tinggi	Tidak	Tidak	Tidak	Tidak	Tidak	Tidak	Tidak
Vicenin-2	Rendah	Ya	Tidak	Tidak	Tidak	Tidak	Tidak	Tidak
Vitexin	Rendah	Tidak	Tidak	Tidak	Tidak	Tidak	Tidak	Tidak
Yamogenin	Tinggi	Tidak	Ya	Tidak	Tidak	Tidak	Tidak	Tidak
Yuccagenin	Tinggi	Ya	Ya	Tidak	Tidak	Tidak	Tidak	Tidak