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In Silico Study on Testing Antidiabetic Compounds Candidate from Azaphilone *Monascus* sp.

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Monascus sp. can be used as an ingredient in rice fermentation to produce red rice, called Angkak. In Asia, Angkak is used as traditional medicine and food containing bioactive compounds, one of which is monakolin that has the potential to be a nutraceutical. *Monascus* sp. produces five main pigments: red (monascorubramin, rubropunktamin), orange (monascorubrin, rubropunktatin), and yellow (monaskin, ankaflavin) which have biological activity. In subsequent developments, many new pigments were found which derivatives of the main pigments *Monascus* sp. are, but information regarding their biological effects is still very limited. The purpose of this study was to determine the pigment derivative compounds of *Monascus* sp. as a candidate compound for antidiabetic drugs. This study used 57 pigment derivative compounds *Monascus* sp. which is done *In silico*. 2GPA protein (Glycogen Phosphorylase) is used as an antidiabetic receptor. The software used in this research includes ChemDraw, Marvin Sketch, Molegro Molecular Viewer, Biovia Discovery Studio, and Autodock. The ADME study was conducted using PreADMET web-based software. The results of the drug scan test on the MPs4 isolate compound have a value that meets the requirements in all parameters such as molecular weight, proton donor, proton acceptor, Log p and molar refractory. The ADME test results on the MPs4 Isolate compound have a value that meets the requirements in all parameters of Caco2, HIA (Human Intestinal Absorption), and in PPB (Protein Plasma Binding). The results of the docking, the Isolate MPs4 compound are the best compounds and meet the requirements because they have smaller binding affinity than natural ligands and comparison ligands (Glibenclamide). The results of this study, MPs4 isolate can be used as a candidate for new antidiabetic drugs, but still requires further research, including *In vitro* and *In vivo* tests.

Key words: antidiabetic, azaphilone, docking, *in silico, Monascus* sp.

Monascus sp. dapat digunakan sebagai bahan fermentasi beras sehingga menghasilkan beras berwarna merah yang disebut Angkak. Di Asia, Angkak digunakan sebagai pengobatan tradisional dan juga makanan yang mengandung senyawa bioaktif, salah satunya adalah monakolin yang berpotensi sebagai *nutraceutical*. *Monascus* sp.menghasilkan pigmen utama yaitu merah (monaskorubramin, rubropunktamin,), orange (monaskorubrin, rubropunktatin), dan kuning (monaskin, ankaflavin) yang memiliki aktivitas biologis. Pada perkembangan berikutnya, ditemukan banyak pigmen baru yang merupakan turunan dari pigmen utama *Monascus* sp., tetapi informasi mengenai efek biologisnya masih sangat terbatas. Tujuan penelitian ini adalah untuk mengetahui senyawa turunan pigmen *Monascus* sp. sebagai senyawa kandidat antidiabetes. Penelitian ini menggunakan 57 Senyawa Turunan pigmen *Monascus* sp. secara *In silico*. Sebagai reseptor antidiabetes digunakan protein 2GPA(Glikogen Fosforilase). Perangkat lunak yang digunakan dalam penelitian ini meliputi ChemDraw, Marvin Sketch, Molegro Molecular Viewer, Biovia Discovery Studio, danAutodock. Studi ADME dilakukan dengan software berbasis web PreADMET. Hasil uji *drug scan*menunjukkan senyawa Isolate MPs4 memiliki nilai yang memenuhi syarat dalam semua parameter seperti berat molekul, donor proton, akseptor proton, Log p dan *refractory molar*. Hasil uji ADME pada senyawa Isolate MPs4 memiliki nilai yang memenuhi syarat dalam semua parameter Caco2, HIA (Human Intestinal Absorption), maupun pada PPB (Protein Plasma Binding). Hasil uji *docking* menunjukkan senyawa Isolate MPs4 menjadi senyawa yang terbaik dan memenuhi syarat karena memiliki *binding affinity* lebih kecil daripada ligan alami dan ligan pembanding (Glibenklamid). Hasil dari penelitian ini, Isolate MPs4 dapat dijadikan salah satu kandidat obat baru antidiabetes, namun masih memerlukan penelitian lebih lanjut diantaranya uji *In vitro* dan *In vivo*.

Kata kunci: bakteri pelarut fosfat, fosfor, kultur murni dan campuran, pertanian, tanah

Diabetes mellitus is a disease that characterized by disruption of carbohydrate metabolism and hyperglycemia, protein, and fat related to a lack of insulin secretion. Polyuria, polydipsia, weight loss, tingling, polyphagia are symptoms that are felt by people with Diabetes Mellitus (Fatimah 2015).

The mechanism of DM type 2 is a decrease in

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insulin sensitivity (insulin resistance) and failure of pancreatic beta cell function which results in decreased production of insulin that cause hyperglycemia (Perkeni 2015).

Monascus sp.can be used as rice fermentation material to make red rice, called Angkak. In Asia, Angkak is used as traditional medicine and food, contains bioactive compounds. One of them is a monacolin compound, which has potential as a nutraceutical (Nguyen *et al*. 2017).

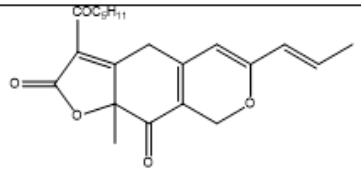
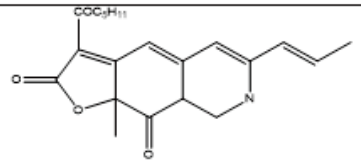
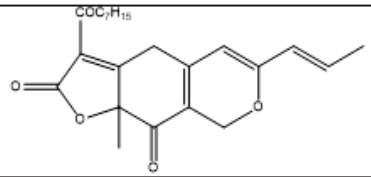
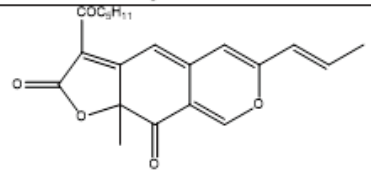
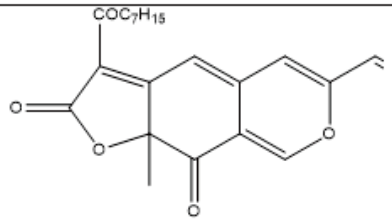
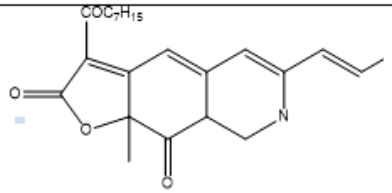
Research on *Monascus* sp. pigments is growing rapidly, including the discovery of new pigments, which are derived from the main pigments: yellow, orange and red. The research data obtained is still a separate data from any research journals, so that complete data are needed, particularly information regarding biological activity. From the six major pigments, 57 derivatives have been found until now. (Yuliana *et al*. 2017).

As seen from Table 1, some pigments derived from *Monascus* sp. include red (monascorubramin, rubropunktamin), orange (monascorubrin, rubropunctatus), and yellow (monaskin, ankaflavin) which have biological activity.

Monascus sp. pigments widely used as a food coloring and flavoring in the food industry, especially for fish such as fish paste, surimi and meat products such as sausages and ham. In addition, this pigment can be used not only in the food sector, but also in the cosmetic and pharmaceutical industries (Seyedin *et al.* 2015).

Pigments that have the potential to reduce blood

Table 1 The main pigments structure of *Monascus* sp.
(Yuliana *et al*. 2017)

No	Chemical Structure	Chemical Formula	Pigment
1		$C_{21}H_{26}O_3$	Monascin
2		$C_{21}H_{23}NO_4$	Rubropunctamine
3		$C_{23}H_{30}O_5$	Ankalfavin
4		$C_{21}H_{22}O_5$	Rubropunctatin
5		$C_{23}H_{26}O_5$	Monascorubin
6		$C_{23}H_{27}O_5$	Monascorubamine

glucose levels are rubropunctamine (red) and rubropunctatine (orange) pigments (Sulistyaning 2013).

The purpose of this study was to determine the pigment derivative compounds of *Monascus* sp. as a candidate compound for antidiabetic drugswith *In Silico* test.

MATERIALS AND METHODS

The tools used in this study are personal computers with processor specifications: Intel CORE i7, 4.0 GB RAM; 64 bit Operating System, Operating System: Windows 10 Pro. The software used is Marvin Sketch version 5.2.5.1, Molegro Molecular Viewer (MMV) version 2.5,ChemdrawUltra, Biovia Discovery Studio 2017, Autodock, and web programs such as PreADMET, PRODRG2, Pharm Mapper and PDBsum. All software is open source. The materials in this study include the receptors that have been identified, downloaded from protein data bank (PDB) and 57 dyestuff compounds isolated from azaphilone derivatives from *Monascus* sp.

Ligand Preparation. Ligands were drawn using ChemDraw software and then optimized by protonation at 7.4 pH at Marvin Sketch (Ruswanto *et al.* 2014).

The procedure is performed on Azaphilone-derived ligands and then stored in the mol2 format. Optimization of the structure aims to see the conformation of molecules and see the low potential energy that has been adjusted based on pH conditions in the body.

Drug Scan. Drug observation was carried out on dyestuff compounds derived from *Monascus* sp.by considering Lipinski's rule of five as well as oral and ligand bioavailability. The parameters used were<500 g / mol molecular weight, <5hydrogen bond donors, <10 hydrogen bond acceptors, and 40-130 molar refractory.These parameters can be determined with the help of Marvin Sketch software (Ruswanto 2015).

Receptor Preparation. There are 5 enzyme structures (receptors) for antidiabetic: 1C8L (Glicogen Phosporilase A), 1H5U (Glicogen Phosporilase B), 2FW3 (Karnitin Palmitoyltranspherase 2), 2QMJ (Maltase Glucoamilase), and 2GPA (Glicogen Phosporilase).

Pdb format is created after the codes 1C8L, 1H5U, 2FW3, 2QMJ, 2GPA are downloaded from PDB (Protein Data Bank). Then it is prepared to separate from its natural ligand, adding hydrogen and removing solvent molecules (Ruswanto *et al.* 2018).

ADMET Study. ADMET compounds Profiling is done by applying the ADMET descriptor algorithm and the ADMESTAR database that freely available at (http://admetexp.org) (Qidwai 2017).

Docking Method Validation. Before the compound docking process is carried out with protein, the docking method is validated using Autodock 4.2.6. to see the Root Mean Square Deviation (RMSD)as docking validityparameters (Lelita *et al.* 2017).

Validation was done by using natural ligand re-docking on each receptor were used. Re-docking is the process of separating the natural ligand crystal structure docking receptor then carried back to the receptor. The docking parameter is valid if the RMSD value from the redocking results is ≤ 2.0 Å (Sherman *et al.* 2006).

The value of RMSD indicate acceptable accuracy, whereby if the value of RMSD <2 Å means indicates that the smaller the error of the docking results, so it can be said to be valid (Lelita *et al.* 2017).

Molecular Tethering. Test compounds and proteins downloaded from PDB were prepared with Autodock 4.2.6, before the tethering process, the parameters, dimensions, and the coordinates of the grid box were adjusted. The dimensions of the grid box are adjusted to the size of each ligand, while the coordinates of the grid box are adjusted based on the coordinates of the center of its natural ligand. Before that, the location of the gridboxwas determined using the Autodock program Tools. Grid Box is the location of the ligand mooring space which will be docking and have settingsincludes center_x, center_y, and center_z. To determine the size of a grid box is setby using spacing (armstrong). The placement of the Gridboxis based on the location of the test ligand and the active side of the protein.The grid box used is X = 31,864, Y = 21,182, and Z = 26,477.The parameter used is the calculation of 100 times runs GA (genetic algorithm). Compounds for testing and prepared proteins are put together in one folder for further gridding and docking (Yuliana *et al.* 2019).

RESULTS

Drug Scan. On the results of the drugscan test on Azaphilone derivatives in Table 2, shows that not all azaphilone derivatives fulfill the Lipinski's Rule of Five parameters requirements. Such as Glycyl Rubropuntatin, Isolate MPs3, Isolate MPs2, Isolate MPs1, N-glutaryl Monascurobamine,N-

Table 2 Drug scan test result

No	Name of Compound	Drug Scan				
		Molecular weight	Proton Donor	Proton Acceptor	Log P	Refractory Molar
		< 500 g/mol	< 5	< 10	< 5	40-130
1	GlycylRubropunctatin	413.470	1	11	3,33	114,09
2	Isolate MPs4	439.552	1	9	4,32	126,87
3	Isolate MPs3	439.508	1	11	4,08	123,54
4	Isolate MPs2	538.645	5	14	3,74	161,46
5	Isolate MPs1	510.591	5	14	2,85	152,26
6	N-glutarylMonascurobamine	511.571	2	15	4,30	138,82
7	N-glutarylRubropunctamine	483.517	2	15	3,41	129,62
8	PP-V	412.461	3	10	3,26	125,22
9	N-glycosylrubropunctamine	557.640	4	17	2,65	149,92
10	N-glycosylmonascurobamine	585.694	4	17	3,54	159,12
11	Compound R3	374.433	1	10	2,05	101,41
12	Red Derivat 1	453.535	1	11	4,65	128,03
13	Red Derivat 2	425.481	1	11	3,76	118,83
14	Red Derivat 3	497.544	2	15	4,01	134,07
15	Red Derivat 4	469.490	2	15	3,12	124,87
16	Red Derivat 5	453.535	1	11	4,65	128,03
17	Red Derivat 6	425.481	1	11	3,76	118,83
18	Red Derivat 7	497.544	2	15	4,01	134,07
19	Red Derivat 8	469.490	2	15	3,12	124,87
20	Un Named	375.465	3	9	1,16	103,91
21	Monascopyridine A	355.434	0	7	4,23	98,81
22	Monascopyridine B	383.488	0	7	5,12	108,01
23	Monascopyridine C	357.450	1	9	3,90	99,88
24	Monascopyridine D	343.467	1	7	4,61	100,56
25	New Red Pigmen	375.465	3	9	1,16	103,91
26	Monascuskaodione A	356.418	0	8	3,36	100,67
27	Monascuskaodione B	384.472	0	8	4,27	109,87
28	Red Shandong 1	303.402	4	7	0,54	91,77
29	Red Shandong 2	331.456	4	7	1,43	100,98
30	Monankarin AB	358.3851	2	8	2.38	98,10
31	Monankarin CD	372.4117	2	7	2.90	103.14
32	Monankarin E	358.3851	2	7	2.53	98.67
33	Monankarin F	356.4123	2	6	2.99	103.21
34	Monascusone A	254.2790	3	6	-0.99	67.08
35	Monascune B	302.3218	0	7	1.64	82.07
36	FK 17-P2B2	236.2637	2	5	0.35	66.34
37	Xantomonascin A	388.4111	2	8	4.00	102.20
38	Xantomonascin B	414.4914	2	8	3.76	126.81
39	Y3	448.571	6	8	0.34	115.88
40	Monapurones A	330.4180	1	6	2.98	97.87
41	Monapurones B	344.4446	0	5	3.93	101.83
42	Monapurones C	344.4446	0	5	3.93	101.83
43	Monaphilones A	374.5137	1	6	4.61	111.50
44	Monaphilones B	332.4339	1	6	3.27	97.70
45	Monaphilones C	336.4657	1	7	4.14	95.95
46	Monashexenone	320.4232	1	7	3.70	92.33
47	Rubropuctin	358.4712	1	6	4.02	107.15
48	Monarubrin (Y,BF)	330.4180	1	6	3.13	97.95
49	Yellow II	372.4547	1	7	4.31	116.32
50	Purpureus one	390.5131	0	8	5.43	107.95
51	Monascuspiloin	360.4440	1	6	3.11	101.32
52	Monaphilol A	384.4654	1	6	3.62	111.10
53	Monaphilol B	356.4123	1	6	2.73	101.89
54	Monaphilol C	440.5287	1	8	3.59	125.32
55	Monaphilol D	412.4755	1	8	2.70	116.12
56	Monasfluor A	354.4394	0	5	3.98	104.30
57	Monasfluor B	384.4654	0	7	4.27	109.87

glutarylrubropunctamine, N-glycosylrubropunctamine, N-glycosylmonascurobamine, Red Derivat 1, Red Derivat 2, Red Derivat 3, Red Derivat 4, Red Derivat 5, Red Derivat 6, Red Derivat 7, Red Derivat 8, Monascopyridine B, Y3, Purpureus one, while the Azaphilone derivative compounds that fulfill Lipinski's rules are Isolate MPs4, PP-V, Compound R3, Un Named, Monascopyridine A, Monascopyridine C, Monascopyridine D, New Red Pigment, Monascuskaodione A, Monascuskaodione B, Red Shandong 1, Red Shandong 2, Monankarin C-D, Monankarin A-B, Monankarin E, Monankarin F, FK 17-P2B2, Monascusone A, Monascusone B, Monasfluor A, Monasfluor B, Xantomonascin A, Xantomonascin B, Monapurones A, Monapurones B, Monapurones C, Monaphilol D, Monaphilol A, Monaphilol B, Monaphilol C, Monaphilones B, Monaphilones A, Monaphilones C, Monashexenone, Rubropuctin, Monarubrin (Y,BF), Yellow II, Monascuspiloin, so that it can be used as a candidate for drug compounds for further testing.

Receptor Preparation. There are 5 enzyme structures (receptors) for antidiabetic, which is 1C8L, 1H5U, 2FW3, 2QMJ, 2GPA. To separate them from the original ligand, the addition of hydrogen and the removal of solvent moleculesare needed. Then the enzymes / receptors that have been downloaded and stored in the form of PDB were analyzed using PDBSum.

Figure 1 showed that the 2GPA receptor shows a stable structure because the percentage of residue in the most favored region is 89.7% and in the disallowed region is 0.1%. The quality of the protein structure is considered good if the residue in the disallow region is less than 15% and the amino acid residue in the most favored region is greater than 50%. The greater percentage of amino acid residues in the most favored and the lower percentage of residues in the disallowed region, the better the quality of the structure. So it can be said that the protein structure of 2GPA receptor has good quality and can be used for further analysis.

ADMET Study. Based on ADME test results using web-based PreADMET software in Table 2, Azaphilone derivative compounds have medium permeability values, which are in the range of 4-70%. The process of absorption in the human intestine is in a good range that is in the range of 70-100%.

Then for the binding of proteins in the blood compound ; MPs4 Isolate, MPs3 Isolate, Red Derivate 1, Red Derivate 5, Monascopyridine B, Monascopyridine D, Monascuskaodione B, Xantomonascin A, Xantomonascin B, Monaphilones A, Rubropuctin, Monascopyridine B, Monascopyridine D, Monascuskaodione B, Xantomonascin A, Xantomonascin B, Monaphilones A, Rubropuctin, Monarubrin (Y, BF) Yellow, Monaphilol A, Monaphilol B, Monasfluor A, Monasfluor B have a high value of> 90% showing a strong bond with plasma proteins in the body.

Docking Method Validation. Validation is done by Autodock 4.2.6. Based on the data from Table 4, the result shows that the 2GPA PDB is valid where the RMSD value has fulfil the ≤2 requirements, which is have value of 0.77. Meanwhile the 1H5U, 2FW3, 1C8L PDB are not valid because the RMSD result shows that the valuesexceed the specified ≤ 2 range. The RMSD results of those three GDP codes are 2.85, 2.03, and 3.41. In the other hand, the 2QMJ PDB still fulfills the requirements, it have value of 1.28, but when the RMSD value of the 2GPA PDB compared with the 2QMJ PDB, it can be confirmed that the RMSD of the 2GPA PDB is smaller, because if the RMSD value is getting smaller, it shows that the position of the ligand is better because it getting near to the original conformation.

Molecular Tethering. As can be seen from Figure 2, the receptor used with the docking ligand obtained an RMSD value of <2.0 Å, it shows that it has fulfilled the validity requirements.

DISCUSSION

A protein structure is declared good if the most favored regions are ≥ 90% and disallowed regions less ≤ 1%. Another parameter used in the selection of receptors is that the RMSD value must be ≤ 2, because if the RMSD value is getting closer to zero then the original ligand with a copy of the ligand is increasingly similar. From these parameters, the enzyme / receptor with the code 2GPA (Glycogen Phosphorylase) fulfills the requirements because it has an RMSD value of 0.77.

Caco2 cells are the distribution of drugs through intestinal epithelium that derived from human colon adenocarcinomas that have multiple transport routes. HIA is the result of absorption and bioavailability processes that are evaluated from the amount of expenditure through bile, urine, and feces. PPB (Protein plasma binding) is a part of the drug that is available in a free form for circulation to all tissues in the body (Nursamsiar *et al.* 2016).

Validation of docking is done with water and without water, it is intended to determine the effect of

Table 3 Test Results of ADME Azaphilone derivatives

No	Name of Compund	Caco2 (nm/sec)	HIA (*Human Intestinal Absorption*) %	PPB (*Protein Plasma Binding*)%
1	Glycyl Rubropuntatin	20.9325 Medium	96.702970 Good	87.663371 Weakly Bonded
2	Isolate MPs4	25.6923 Medium	99.303546 Good	92.314035 Strongly Bonded
3	Isolate MPs3	21.5677 Medium	98.309963 Good	90.416630 Strongly Bonded
4	Isolate MPs2	8.92909 Medium	78.193552 Good	78.061242 Weakly Bonded
5	Isolate MPs1	9.25845 Medium	74.407933 Good	64.976138 Weakly Bonded
6	N-glutaryl Monascurobamine	19.8389 Medium	92.538271 Good	90.486415 Strongly Bonded
7	N-glutaryl Rubropuctamine	19.7598 Medium	90.311224 Good	88.136616 Weakly Bonded
8	PP-V	4.01366 Medium	92.923736 Good	86.114618 Weakly Bonded
9	N-glucosyl rubropuctamine	12.4451 Medium	85.412276 Good	65.185992 Weakly Bonded
10	N-glucosyl monascurobamine	12.5306 Medium	87.690078 Good	79.078783 Weakly Bonded
11	Compound R3	17.4163 Medium	95.677133 Good	73.231309 Weakly Bonded
12	Red Derivat 1	22.1952 Medium	98.668455 Good	90.932647 Strongly Bonded
13	Red Derivat 2	21.2765 Medium	97.891289 Good	88.641765 Weakly Bonded
14	Red Derivat 3	20.5128 Medium	91.491229 Good	89.736964 Weakly Bonded
15	Red Derivat 4	20.4423 Medium	88.981951 Good	86.838945 Weakly Bonded
16	Red Derivat 5	22.1952 Medium	98.668455 Good	90.932647 Strongly Bonded
17	Red Derivat 6	21.2765 Medium	97.891289 Good	88.641765 Weakly Bonded
18	Red Derivat 7	20.5128 Medium	91.491229 Good	89.736964 Weakly Bonded
19	Red Derivat 8	20.4423 Medium	88.981951 Good	86.838945 Weakly Bonded
20	Un Named	17.9896 Medium	89.666473 Good	66.572743 Weakly Bonded
21	Monascopyridine A	26.367 Medium	98.750840 Good	91.953695 Strongly Bonded
22	Monascopyridine B	32.7272 Medium	98.912525 Good	93.500167 Strongly Bonded
23	Monascopyridine C	22.7729 Medium	96.648798 Good	89.685299 Weakly Bonded
24	Monascopyridine D	22.9611 Medium	96.270412 Good	97.268350 Strongly Bonded
25	New Red Pigmen	17.9896 Medium	89.666473 Good	66.572743 Weakly Bonded
26	Monascuskaodione A	28.3725 Medium	98.770329 Good	88.897997 Weakly Bonded
27	Monascuskaodione B	36.0846 Medium	98.771155 Good	92.381422 Strongly Bonded
28	Red Shandong 1	13.6843 Medium	85.719545 Good	71.398196 Weakly Bonded
29	Red Shandong 2	14.2523 Medium	87.122330 Good	87.278357 Weakly Bonded
30	Monankarin AB	21.4435 Medium	93.56731 Good	85.58307 Weakly Bonded
31	Monankarin CD	21.9971 Medium	93.909198 Good	87.093425 Weakly Bonded
32	Monankarin E	21.4031 Medium	93.567883 Good	84.456494 Weakly Bonded
33	Monankarin F	35.5122 Medium	93.789307 Good	88.543275 Weakly Bonded
34	Monascusone A	19.3778 Medium	78.683369 Good	34.939799 Weakly Bonded
35	Monascune B	22.9891 Medium	97.536574 Good	61.438550 Weakly Bonded

Table 3 Test Results of ADME Azaphilone derivatives -Continued-

No	Name of Compund	Caco2 (nm/sec)	HIA (*Human Intestinal Absorption*) %	PPB (*Protein Plasma Binding*)%
36	FK 17-P2B2	0.993 Rendah	90.43201 Good	56.07652 Weakly Bonded
37	Xantomonascin A	19.6124 Medium	88.865206 Good	96.842726 Strongly Bonded
38	Xantomonascin B	26.5245 Medium	94.538788 Good	94.764093 Strongly Bonded
39	Y3	19.3732 Medium	50.125685 Medium	67.649190 Weakly Bonded
40	Monapurones A	26.9554 Medium	95.760530 Good	86.135746 Weakly Bonded
41	Monapurones B	44.272 Medium	97.697949 Good	88.300451 Weakly Bonded
42	Monapurones C	44.272 Medium	97.697949 Good	88.300451 Weakly Bonded
43	Monaphilones A	48.8546 Medium	96.052979 Good	94.089855 Strongly Bonded
44	Monaphilones B	40.8229 Medium	96.054536 Good	90.112573 Strongly Bonded
45	Monaphilones C	26.9554 Medium	95.760530 Good	86.135746 Weakly Bonded
46	Monashexenone	22.609 Medium	95.857284 Good	88.158433 Weakly Bonded
47	Rubropuctin	46.2928 Medium	96.050080 Good	95.896405 Strongly Bonded
48	Monarubrin (Y,BF)	40.5147 Medium	96.071613 Good	92.263384 Strongly Bonded
49	Yellow II	34.2219 Medium	96.423561 Medium	91.738989 Strongly Bonded
50	Purpureus one	31.1835 Medium	98.247814 Good	90.721848 Strongly Bonded
51	Monascuspiloin	30.4892 Medium	96.468903 Good	90.306522 Strongly Bonded
52	Monaphilol A	36.7103 Medium	96.501044 Good	95.427557 Strongly Bonded
53	Monaphilol B	29.408 Medium	96.568439 Good	91.926288 Strongly Bonded
54	Monaphilol C	34.038 Medium	97.366571 Good	89.549401 Weakly Bonded
55	Monaphilol D	27.7997 Medium	97.311031 Good	83.639250 Weakly Bonded
56	Monasfluor A	49.808 Medium	97.649968 Good	92.794086 Strongly Bonded
57	Monasfluor B	36.0846 Medium	98.771155 Good	92.381422 Strongly Bonded

Information: Caco-2 : Low <4 ; Medium 4-70 ; High > 70
HIA : Bad 0-20 % ; Medium 20-70 % ; Good 70-100 %
PPB : Strongly Bonded > 90 % ; Weakly Bonded < 90 %

Table 4 Docking validation results

RECEPTORS	GRID BOX			RMSD
	X	Y	Z	
2GPA	**31.864**	**21.182**	**26.477**	**0.77**
1H5U	28.47	21.132	31.662	2.85
2QMJ	-29.911	7.647	-17.894	1.28
2FW3	23.57	4.509	34.021	2.03
1C8L	27.833	20.552	31.813	3.66

water on the docking process. In validation the presence of water shows physiological conditions in the body, because water will affect the ligand bond to the receptor and also the formation of hydrogen bonds with the receptor, besides this validation can also show the comparison of the position of the original ligand with the comparative ligand against the receptor when they are docked. The RMSD value is a parameter that can be used, because if the RMSD value obtained from the validation results is ≤2, that is mean the result is good.

Molecular tethering of pigments from *Monascus* sp. was carried out on 57 pigment compounds of *Monascus* sp. with 2 GPA receptor. For the results of interaction and molecular tethering showed in Table 5.

There are only 2 pigments that have smaller binding energy valueswhen compared with antidiabetic drugs

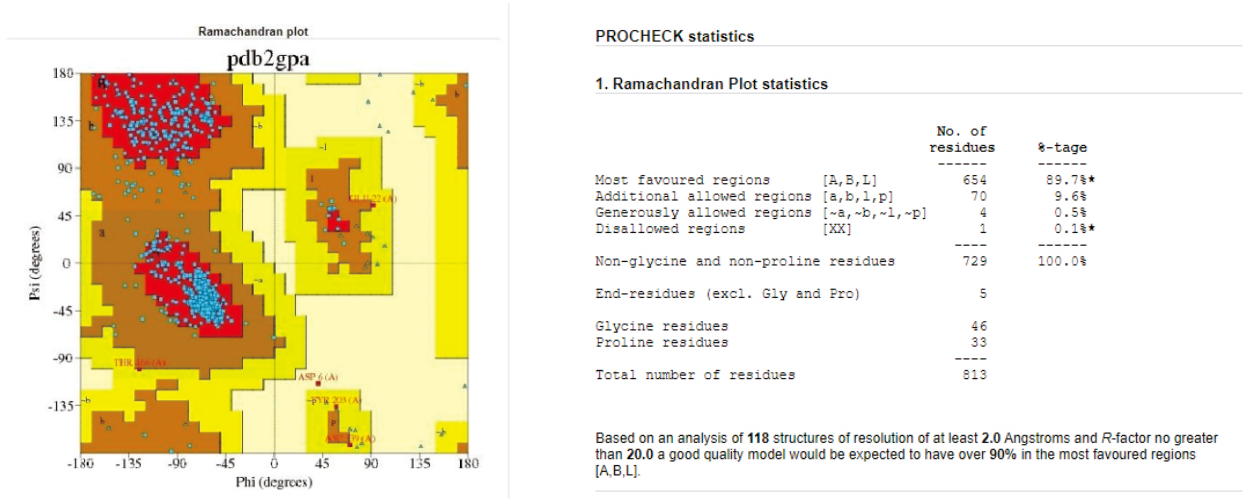


Fig 1 Visualization results of Ramachandran plot and procheck statistics.

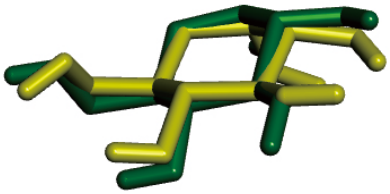


Fig 2 Visualization of docking result. Docking ligand (yellow) Natural ligand (green).

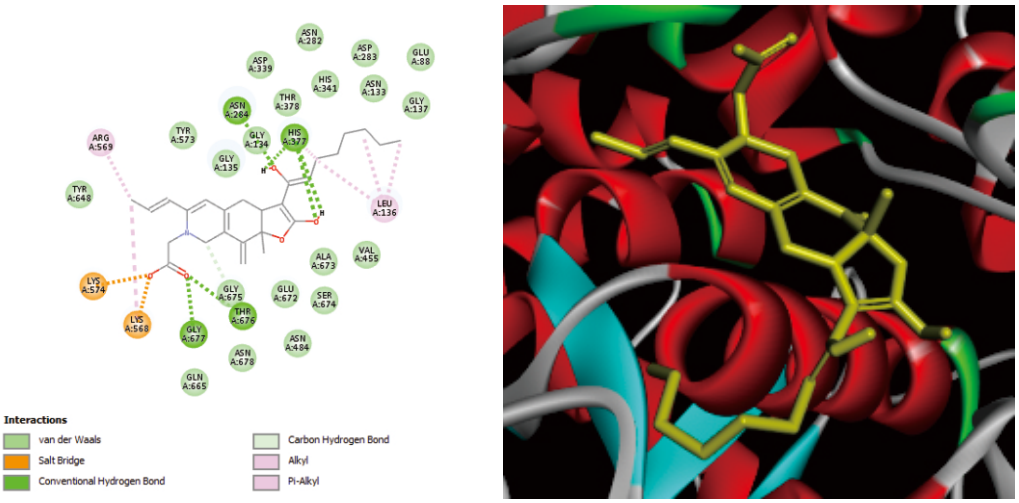


Fig 3 Visualization of 2D and 3D docking results for Isolate MPs4 compounds with 2 GPA receptor.

on the market (Glibenclamide), The value of free energy bonds on Isolate MPs4 refers to the smallest value, because the value is -11.58 kcal / mole which indicates it has the most stable position.

Ligands from Glibenclamide produce Asn284, Gly675 hydrogen bonds. This interaction is also found in Isolate MPs4 that shows the affinity of Isolate MPs4 is better than the comparative ligand (Glibenclamide). The visualization of 2D and 3D docking results for Isolate MPs4 compounds with 2 GPA receptor can be seen from Figure 3.

The next lowest free energy bond value is the Red Derivate 6. Red Derivate 6 compound has a smaller binding energy when compared to original ligands and comparative ligands (Glibenclamide) so that they have a stable conformation. The bonds that occur in Red Derivatives 6 are hydrogen bonds, namely Asn284 and Gly675 which are also found in original hydrogen ligand and comparative ligand (Glibenclamide) bonds. Therefore, Red Derivate 6 has the potential to become

Table 5 The results of docking pigment tests from *Monascus* sp. with 2 GPA (Glycogen Phosphorylase) receptor

No	Compounds	Run	Binding Affinity kkal/mol	HydrogenBond	Amino Acid (Residue Contact)
1	Glibenclamide (comparison)	55	-10.48	ASN284 GLY675	ASN282, ALA383, PHE286, PHE285, HIS341, ASP339, THR378, ALA673, HIS377, ASN484, SER674, LEU139, GLY675, THR676, GLU672,GLY135, GLY677, VAL567, ARG569, TYR648, GLY134, LYS574, ASN133, LEU136, LYS568, ASP284, GLU88, ASN284
2	Original Ligand	32	-6.08	LEU136 ASN284 GLU672 SER674 GLY675 ASN484	LEU136, ASN284,GLU672, SER674, GLY675, ASN484, LYS574, TYR573, HIS377, ALA673, THR676, VAL455, LEU139, GLY135
3	Glycyl-rubropunctatine	28	-10.11	THR676 ASN484 HIS377	THR676, ASN484, HIS377, ARG569, TYR648, LYS568, LYS574, ASN678, GLY677, GLU672, GLN665 GLY675, ALA673, SER674, VAL455, LEU139, GLU88, ASN133, GLY137, ASP283, ASN284, LEU136, GLY135, GLY134
4	Isolate MPs4	21	-11.58	GLY677 THR676 HIS377 ASN284	GLY677, THR676, HIS377 ASN284, ARG569, TYR648, LYS574, LYS568, GLN665, GLY675, ASN678, GLU672, ASN484, ALA673, SER674, VAL455, LEU136, GLY137, GLU88, ASN133, ASP283, HIS341, ASN282, ASP339, THR378, GLY134, GLY135, TYR573
5	Isolate MPs3	40	-9.78	TYR537 GLU672 ALA673 HIS377 THR676 GLY677	TYR537, GLU672, ALA673 HIS377, THR676, GLY677, ASP339, ASN284, GLY135, LEU136, THR378, GLU88, ASN133, ASP283, GLY134, ARG569, TYR648, LYS568, LYS574, ASN678, GLY675, ASN484, SER674, VAL455
6	Isolate MPs2	47	-7.45	HIS377 GLU672 GLY675 LYS680	HIS377, GLU672, GLY675, LYS680, THR378, ASP339, ALA383, PHE285, ASP283, ASN282, ASN284, LEU136, ARG569, HIS341, ASN133, VAL567, GLY677, GLY134, TYR648, ARG138, THR676, GLY135, ASN678, GLN665, SER674, TYR573, ALA673, VAL455
7	Isolate MPs1	83	-9.53	GLN665 SER674 GLY677 THR676 GLY675 HIS377	GLN665, SER674, GLY677, THR676, GLY675, HIS377, LYS568, GLU672, TYR573, ALA673, VAL455, HIS341, THR378, ASP339, LEU136, ASN284, ASP283, LEU139, GLY135, GLY134, ARG569, LYS574, TYR648, ASN678, GLY694, ALA695, SER667, ASN696, VAL567
8	N-glutaryl Monascurobamine	52	-9.30	LEU136 ASP283	LEU136, ASP283, LYS574, LYS568, VAL567, GLY677, THR676, LYS680, GLY135, GLU672, ARG138, GLY675, SER674, ALA673, TYR573, HIS377, GLY137, ASN133, ASP339, ASN284, GLY134, PHE285, HIS341, ALA383, ASN282, ARG569, TYR648
9	N-glutaryl Rubropuctamine	18	-9.66	ASP283 LEU136 THR676	ASP283, LEU136, THR676, GLY137, ASN133, ASN282, GLU88, PHE285, ALA383, ASN284, GLY134, ARG569, HIS341, LYS574, TYR648, LYS568, VAL567, GLY677, LYS680, ARG138, GLY675, GLU672, SER674, GLY135, ALA673, TYR573,HIS377
10	PP-V	89	-9.99	LEU136 ASP283 THR676	LEU136, ASP283, THR676, PHE285, PHE286, ASN133, GLY137, HIS341, GLY134, GLY135, LYS574, LYS568, GLN665, GLY675, GLY677, GLU672, SER674, ALA673, VAL455, TYR573, HIS377, ASN284, THR378, GLU88, ASP339, ASN282, ALA383
11	N-glycosyl rubropuctamine	15	+7.08	ASN284 HIS377 ASN484 GLY135	ASN284, HIS377, ASN484, GLY135, HIS341, PHE285, ALA383, LEU384, ASP339, THR378, ALA673, GLU672, VAL455, SER674, GLY675, LYS568, LYS574, VAL567, GLY677, THR676, ARG138, LEU139, ASP283, ASN133, GLU88, ASN282, LEU136

Table 5 The results of docking pigment tests from *Monascus* sp. with 2 GPA (Glycogen Phosphorylase) receptor -Continued-

No	Compounds	Run	Binding Affinity kkal/mol	HydrogenBond	Amino Acid (Residue Contact)
12	N-glycosyl monascurobamine	90	+7.83	ASN484 SER674 HIS377 ASN284	ASN484, SER674, HIS377, ASN284, GLY677, LYS568, LYS574, GLY123, LEU139, GLY134, THR676, ARG569, ASP283, LEU136, ASN133, GLU88, ASN282, HIS341, PHE285, LEU384, THR378, ALA383, ASP339, ALA673, VAL455, GLU6782, GLY675
13	Compound R3	72	-9.90	ASP283 LEU136 HIS377 ASN484 GLY675 GLY677 THR676	ASP283, LEU136, HIS377, ASN484, GLY675, GLY677, THR676, GLU672, GLN665, ASN678, LYS574, GLY135, ASN284, ASN282, ASN133, GLU88, GLY137, GLY134, LEU139, VAL455, ALA673, SER674, LYS568
14	Red Derivat 1	19	-8.80	GLY675 GLU672 HIS377	GLY675, GLU672, HIS377, SER674, TYR573,ALA673,VAL455, LEU139, LEU136, THR378, ASN284, HIS341, ASP339, ALA383, PHE285, GLY135, ARG569, TYR648, GLY134, GLY677, THR676, VAL567, LYS568, LYS574
15	Red Derivat 2	18	-8.86	ASN484 LEU136 GLY137 ASP283 GLY135 THR676	ASN484, LEU136, GLY137, ASP283, GLY135, THR676, GLY675, ALA673, SER674, VAL455, TYR573, GLU672, ASN284, HIS377, ASP339, HIS341, ALA383, THR378, ASN282, GLU88, ASN133, GLY134, ARG569, LYS574, GLY677, LEU139
16	Red Derivat 3	78	-8.09	THR676 GLY677 GLU672 HIS377	THR676, GLY677, GLU672, HIS377, LYS568, GLY675, LYS574, TYR573, SER674, ALA673, VAL455, LEU139, THR378, HIS341, PHE285, ALA383, ASP339, LEU136,ASN284, GLY135, ASP283, GLY134, TYR648, ARG569, ASN133
17	Red Derivat 4	86	-8.51	GLY677 THR676 GLU672 HIS377	GLY677, THR676, GLU672, HIS377, GLY675, SER674,TYR573, ALA673, VAL455, THR378, LEU136, LEU139, ASN284,ASP283, GLY134, ASN133, ARG569, TYR648, LYS568, LYS574, ASN678, GLY135, GLN665
18	Red Derivat 5	57	-10.30	GLY677 THR676 HIS377	GLY677, THR676, HIS377, VAL455, LEU136, THR378, GLY137, ASN133, GLU88, ASN282, ASP283, ASN284, GLY134, GLY135, TYR573, TYR648, ARG569, LYS680, ASN678, LYS568, LYS574, GLY675, GLU672, ASN484, SER674, ALA673
19	Red Derivat 6	100	-10.63	GLY677 THR676 ASN484 HIS377	GLY677, THR676, ASN484, HIS377, LYS680, ASN678, GLY675, LYS568, LYS574, SER674, GLU672, VAL455, ALA673, LEU139, LEU136, ASP283, GLY137, ASN284, GLY135, GLU88, ASN133, GLY134, TYR648, ARG569
20	Red Derivat 7	2	-9.86	GLY677 ASN484 HIS377 ASN284	GLY677, ASN484, HIS377, ASN284, LYS568, TYR648, LYS574, LYS680, THR676, GLY675, GLU672, SER674, ALA573, VAL455, THR378, LEU136, PHE285, GLU88, ASN282, ASN133, HIS341, ASP283, GLY135, TYR573, ARG569, GLY134, ASN678, GLN665
21	Red Derivat 8	21	-9.50	GLY677 THR676 HIS377	GLY677, THR676, HIS377, ARG569, ASN678, LYS568, LYS574, TYR648, LYS680, GLY675, ARG138, ASN484, SER674, GLU672, ALA673, VAL455, LEU136, THR378, ASP339, ALA383, HIS341, PHE285, ASN284, GLY135, GLY134
22	Un Named	32	-9.11	GLY135 ASP283 GLY675 ASN484 HIS377 GLU672	GLY135, ASP283, GLY675,ASN484, HIS377, GLU672, GLY134, LEU136, THR676, LEU139, VAL455, SER674, ALA673, THR671, THR378, VAL379, ASN284, LEU380, TYR573, LYS574, LYS568, TYR648, ARG569

Table 5 The results of docking pigment tests from *Monascus* sp. with 2 GPA (Glycogen Phosphorylase) receptor -Continued-

No	Compounds	Run	Binding Affinity kkal/mol	HydrogenBond	Amino Acid (Residue Contact)
23	Monascopyridine A	49	-9.81	LEU136 ASP283 GLY135 GLU672	LEU136, ASP283, GLY135, GLU672, PHE286, ALA383, PHE285,SN284, ASN133, GLY137, GLY134, LYS574, THR676, GLY675, SER674, HIS377, ALA673, THR378, THR671, TYR573, VAL379, LEU380, ASP339, HIS341
24	Monascopyridine B	35	-9.21	HIS377 ALA673 LEU136 ASP283	HIS377, ALA673, LEU136, ASP283, LEU139, TYR573, GLY135, GLY137, GLY134, ASN133, ASN284, ASP339, PHE285, PHE286, ALA383, VAL567, HIS341, GLN665, LYS568, GLY677, ASN678, THR676, GLY675, THR378, GLU672, LYS574, SER674
25	Monascopyridine C	23	-8.59	SER674 GLY675 GLU672 GLY135 LEU136 ASP283 ASN284	SER674, GLY675, GLU672, GLY135, LEU136, ASP283, ASN284, THR378, HIS341, ALA383, PHE285, ASP339, LEU384, LEU139, VAL455, ASN484, ALA673, THR676, HIS377, TYR573, LYS574, GLY134
26	Monascopyridine D	59	-9.03	LEU136 ASP283 ASN284 GLU672	LEU136, ASP283, ASN284, GLU672, HIS341, ASP339, ALA383, PHE285, THR378, SER674, GLY675, ASN484, THR676, LEU139, VAL455, LYS574, ALA673, TYR573, GLY135, HIS377, GLY134
27	New Red Pigment	52	-9.59	ASP283 LEU136 HIS377 ASN484 GLY675 THR676 GLY677	ASP283, LEU136, HIS377, ASN484, GLY675, THR676, GLY677, VAL567, TYR648, LYS574, LYS568, GLY135, ASN284, ASN133, GLU88, GLY137, GLY134, VAL455, LEU139, SER674, ALA673, GLU672
28	Monascuskaodione A	76	-9.48	HIS377 ASN484 GLY675 THR676	HIS377, ASN484, GLY675, THR676, GLY677, LYS574, ASN678, LYS568, GLN665, GLU672, ASN284, ASP238, GLU88, ASN282, ASN133, LEU136, VAL455, LEU139, ALA673, SER674, GLY135
29	Monascuskaodione B	86	-9.46	HIS377 ASN484 GLY675 THR676	HIS377, ASN484, GLY675, THR676, VAL455, LEU139, ALA673, SER674, GLU672, GLY135, GLY677, LYS574, GLY134, LYS568, ARG569, TYR648, ASP283, LEU136, ASN284, ASN133, GLU88, GLY137
30	Red Shandong 1	60	-8.36	HIS377 ASN284 GLU672	HIS377, ASN284, GLU672, ALA673, VAL455, TYR573, LYS574, LEU139, ASN484, GLY675, GLY135, SER674, YHR676, LEU136, ASP283, GLY134, GLY137, GLU88, ASN133, HIS341, ASP339
31	Red Shandong 2	37	-8.15	GLY135 ASP283 LYS574 TYR573	GLY135, ASP283, LYS574, TYR573, HIS377, ASN133, ASN284, THR378, HIS341, ASP339, PHE285, ALA383, LEU136, GLY675, GLU672, THR676, GLY677, ASN678, GLN665, LYS568, VAL567, ARG569, GLY134, HIS571
32	FK 17-P2B2	55	-7.74	HIS377, ASN484, GLY675, GLU672, ASN284	LEU136, HIS377, ASN484, GLY675, GLU672, ASN284, ASN133, GLU88, ASP283, TYR573, GLY135, LYS574, SER674, THR676, ALA673, VAL455, LEU139.
33	Monankarin A-B	42	-8.39	GLU162, GLU273	ARG277, ILE275, VAL278, GLN295, ARG277, ASN274, ILE275, ALA246, SER245, ILE159, ARG160, GLU162, GLU273
34	Monankarin C-D	38	-8.17	VAL567, LYS568, GLU672, GLY675, HIS377, ARG569	LYS574, LEU136, GLN665, GLY677, ASN678, THR676, TYR573, SER674, ALA673, VAL455, ASN284, GLY135, ASP283, GLY134, TYR648, VAL567, LYS568, GLU672,GLY675, HIS377, ARG569

Table 5 The results of docking pigment tests from *Monascus* sp. with 2 GPA (Glycogen Phosphorylase) receptor -Continued-

No	Compounds	Run	Binding Affinity kkal/mol	HydrogenBond	Amino Acid (Residue Contact)
35	Monankarin E	70	-9.14	GLU672, LYS568, GLY135, ASP283, ASN284	LYS574, LEU136, HIS377, GLY134, ARG569, TYR648, VAL567, GLY677, GLN665, ASN678, THR676, GLY675, VAL455, SER674, ALA673, GLU672, LYS568, GLY135,ASP283, ASN284
36	Monankarin F	3	-8.71	GLY135, HIS377, ASN484, GLU672, LYS568, VAL567	LYS574, TYR573, ALA673, TYR648, ARG569, GLY134, LEU136, ASP283, ASN284, THR378, SER674, VAL455, LEU139, GLY675, GLN665, THR676, GLY677, ASN678, GLY135, HIS377, ASN484, GLU672, LYS568, VAL567
37	Monaphilones A	100	-8.46	THR676, GLU672, TYR573, HIS377	LYS568, ARG569, TYR648, LYS680, GLY134, GLY677, GLY135, ASN133, LYS574, ASN284, LEU136, ASP283, GLU88, ASN282, HIS341, VAL455, ALA673, SER674, GLY675, TYR90, THR676, GLU672, TYR573, HIS377
38	Monaphilones B	73	-8.35	LYS568, GLY677, THR676, GLU672, ASN284	TYR648, ARG569, VAL567, GLY134, ASN133, TYR90, ARG649, LYS608, SER674, VAL455, ASN484, GLY135, HIS377, LEU136, GLY675, TYR573, LYS574, LYS568, GLY677, THR676, GLU672, ASN284
39	Monaphilones C	69	-8.82	GLU672, GLY675, ASN484, HIS377	TYR573, LEU380, LYS568, ARG569, TYR648, GLY134, LYS574, THR378, THR671, VAL379, ASN284, ALA673, VAL455, SER674, LEU139, THR676, LEU136, GLY135, GLY677, GLU672, GLY675, ASN484, HIS377
40	Monapurones A	81	-9.55	TYR573, ASN284, THR676, GLY675, ASN484, HIS377,	GLU672, LYS568, ALA673, LEU380, VAL379, THR671, THR378, VAL455, LEU139, LEU136, SER674, GLY135, GLY677, ASN678, GLN655, VAL567, LYS574, TYR573, ASN284, THR676, GLY675, ASN484, HIS377
41	Monapurones B	27	-8.35	ASN484, HIS377	LYS568, LEU136, ALA383, VAL567, LYS574, GLY675, TYR573, ASN284, ASP339, THR378, PHE285, HIS341, GLU672, GLY677, THR676, GLY135, LEU139, ALA673, VAL455, SER674, ASP283, ASN484, HIS377
42	Monapurones C	94	-8.17	ASN484, LYS574	GLY675, LYS568, LEU136, SER674, LEU139, GLY135, THR676, GLY677, VAL567, GLN665, TYR573, ASN133, GLU672, ASN282,GLU88, HIS341, ASP283, ASN284, GLY137, THR378, HIS377, GLY134, VAL455, ALA673
43	Monarubrin (Y,BF)	15	-8.57	ASP283, ASN284, GLU672, HIS377	HIS341, GLN665, GLY675, LEU136, LYS568, ASN678, GLY677, THR676, GLY134, LYS574, ARG569, GLY135, TYR573, ALA673, THR378, ASP339, PHE285, ASP283, ASN284, GLU672, HIS377
44	Monascusone A	42	-8-08	ASP283, LEU136, SER674, GLU672	VAL455, ALA673, HIS377, THR378, ASN284, PHE285, HIS341, ASN282, ASN133, GLU88, GLY137, GLY134, GLY135. ASN484, GLY675, TYR573, ASP283, LEU136, SER674, GLU672
45	Monascusone B	23	-9.19	ASN484, HIS377	LEU136, LYS568, HIS341, ALA673, VAL455, LEU139, GLY135, SER674, THR676, VAL567, GLY677, GLU672, LYS574, GLY675, TYR573, ASN284, THR378, GLU88, ASN133, ASN484, HIS377
46	Monascuspiloin	74	-8.32	LYS574, THR676, GLY675, GLU672	TYR648, LYS568, ARG569, GLY134, ASN133, TYR90, LEU136, ALA383, ASP339, THR378, HIS377, ASN284, ALA673, SER674, TYR573, GLY135, GLY677, ASN678, LYS574, THR676, GLY675, GLU672
47	Monashexenoone	31	-9.50	GLU162, GLU273,	ARG277, ILE275, TYR161, VAL278, GLN295, ARG277, ASN274, ILE275, ALA246, SER245, ILE159, ARG160, GLU162, GLU273

Table 5 The results of docking pigment tests from *Monascus* sp. with 2 GPA (Glycogen Phosphorylase) receptor -Continued-

No	Compounds	Run	Binding Affinity kkal/mol	HydrogenBond	Amino Acid (Residue Contact)
48	Purpureus one	10	-8.20	LEU136, ASP283, ASN484, GLY675, SER674, GLY677	ARG569, LYS574, GLY135, ASN284, GLY134, TYR90, ASN133, TYR573, HIS377, VAL455, THT676, THR378, LYS680, GLU672, VAL567, TYR648, LYS568, ALA673, LEU136, ASP283, ASN484, GLY675, SER674, GLY677
49	Robropuctin	4	-9.22	GLY672, ASN284, HIS377, GLY135, ASP283	TYR648, ARG569, LYS568, HIS341, TYR90, ASN133, TYR573, ALA673, THR378, ASP339, PHE285, LEU136, LYS574, ALA383, GLY675, GLY134, GLY672, ASN284, HIS377, GLY135, ASP283
50	Xantomonascin A	89	-9.12	HIS377, SER674, LYS574, LEU136, ASP283	HIS341, TYR573, ALA673, THR671, THR378, VAL455, ASN284, ASP339, PHE285, ASN282, GLU88, ASN133, GLY134, ARG569, GLY135, LYS568, THR676, GLU672, GLY675, HIS377, SER674, LYS574, LEU136, ASP283
51	Xantomonascin B	9	-10.13	ASP283, LEU136, THR676, HIS377, SER674	LYS574, ALA383, TYR573, HIS341, ASP339, ASN284, THR378, THR671, ALA673, GLU672, VAL455, GLY675, GLY677, GLY135, ARG569, LYS568, GLY134, ASN133, GLU88, ASN282, PHE285, ASP283, LEU136, THR676, HIS377, SER674
52	Y3	87	-9.29	ASP283, GLY677, THR676	LYS574, LYS568, GLN665, ASN678, GLY675, ALA673, SER674, VAL455, ASN484, LEU139, HIS377, THR378, LEU136, GLY135,ASN133, GLY137, ASN284, GLY134, ARG569, TYR573, GLU672, ASP283, GLY677, THR676
53	Yellow II	64	-8.80	HIS377, LEU136, ASP283	ALA383, HIS341, ASP339, THR378, ALA673, SER674, GLU672, GLY675, THR676, LYS568, GLY677, LYS574, GLY135, GLY134, GLY137, ASN133, ASN282, ASN284, GLU88, PHE285, PHE286, HIS377, LEU136, ASP283
54	Monaphilol A	63	-9.13	ASP283, GLU672, ASN284, HIS377	TYR648, ARG569, LYS568, LEU136, HIS341, PHE285, ASP339, THR378, GLY675, GLY135, TYR573, LYS574, GLY134, ASN133, HIS571, ASN282, ASP283, GLU672, ASN284, HIS377
55	Monaphilol B	15	-8.93	ASP283, ASN284, GLU672	TYR648, ARG569, LYS568, LEU136, HIS341, ASN282, PHE285, ASP339, HIS377, THR378, TYR573, GLY675, GLY135, LYS574, GLY134, ASP283, ASN284, GLU672
56	Monaphilol C	42	-9.96	ASP283, LEU136, THR676, GLU672, GLY675, ASN484, HIS377,	LYS574, LYS568, ALA383, HIS341, ALA673, VAL455, SER674, TYR573, THR378, ASN284, PHE285, ASP339, ASN133,GLU88, GLY134, GLY137, VAL576, GLN665, GLY677, ALA673, ASP283, LEU136, THR676, GLU672, GLY675, ASN484, HIS377
57	Monaphilol D	48	-9.94	HIS377, ASN484, THR676, LEU136, ASP283	HIS341, LYS568, GLU672, VAL455, SER674, LEU139, ALA673, TYR573, ASN284, THR378, PHE285, ALA383, ASP339, GLY134, GLY137, GLY135, LYS574, ASN678, GLN665, VAL567, GLY677, GLY675, HIS377, ASN484, THR676, LEU136, ASP283
58	Monasfluor A	87	-8.92	HIS377, ASN484, GLY675, THR676,	LEU136, VAL455, LEU139, SER674, ALA673, GLY677, LYS568, ASN678, GLN665, LYS574, GLU672, GLY135, TYR573, ASN284, ASP283, ASN282, GLU88, ASN133, HIS377, ASN484, GLY675, THR676
59	Monasfluor B	16	-9.47	HIS377, ASN484, THR676,	HIS377, ASN484, THR676, LEU136, ASN133, GLY134, GLY137, GLU88, ASP283, ASN284, SER667, GLN665, ASN696, LYS568,GLY677, GLY675, LYS574, ASN678, GLY135, ALA673, LEU139, SER674, VAL455.

an antidiabetic drug that works on the glycogen phosphorylase receptor.

As conclusion, from drug scan test results on the Isolate MPs4 compound have the values that fulfill all parameters' requirements such as molecular weight, proton donors, proton acceptors, log p and molar refractory. ADME test results on Isolate MPs4 compounds have the values that fulfill all parameters' requirements of Caco2, HIA (Human Intestinal Absorption), as well as on PPB (Plasma Protein Binding). The docking test results on the Isolate MPs4 compound were the best and qualified because it have smaller binding affinity than original ligands and comparative ligands (Glibenclamide). Therefore, MPs4 isolate can be used as a candidate for new antidiabetic drugs, but still requires further research, including *In vitro* and *In vivo* tests.

REFERENCES

Fatimah RN. 2015. Diabetes melitustipe 2 [Type 2diabetes mellitus]. Artikel Review Medical Faculty Lampung University. 4(5):94.

Lelita R, Gunawan R, Astuti W. 2017. Studi docking molekular senyawa kuersetin, kalkon dan turunannya sebagai inhibitor selkankerpayudara mc-7 (*Michigan cancer foundation*-7) [Study of molecular docking compounds of quercetin, chalcone and their derivatives as mc-7 (*Michigan cancer foundation*-7) breast cancer cell inhibitor. J Atomik. 2(2):190-196.

Nguyen T, Karl M, Santini A. 2017. *Red yeast rice*. Foods. 6(3):19. doi:/10.3390/foods6030019.

Nursamsiar N, Toding AT, Awaluddin A. 2016. Studi *in silico* senyawa turunan analog kalkon dan pirimidin sebagai antiinflamasi: prediksi absorpsi, distribusi, dantoksisitas [In-silico study chalcone and pyrimidine analog derivatives as anti-inflammmatory: prediction of absorption, distribution, and toxicity]. PHARMACY: Pharm J of Indones. 13(1):92-100.doi: 10.30595/pji.v13i1.891.

Omran Z, Rauch C. 2014. Acid-mediated Lipinski's second rule: application to drug design and targeting in cancer. EurBiophys J 43(1):199–206. doi: 10.1007/s00249-014-0953-1.

Qidwai T. 2017. QSAR modeling, docking and ADMET studies for exploration of potential anti-malarial compounds against *Plasmodium falciparum*. In silico pharm. 5(1):6.

Rudjianto A, Yuwono A, Shahab A, Manaf A, Pramono B, Lindarto D, Purnamasari D, Sanusi H, Zufry H, Novida H, Suastika K, Sucipto KW,Sasiarini L, Dwipayana MP, Saraswati MR, Soetedjo NN, Soewondo P, Soelistijo SA, Sugiarto, Langi YA. 2015. Konsensus pengelolaan dan pencegahan diabetes melitus tipe2 di Indonesia [Consensus of management and prevention of type 2 diabetes mellitus in Indonesia]. Pengurus Besar Perkumpulan Endokrinologi Indonesia (PB Perkeni), Jakarta.

Ruswanto R, Nofianti T, Mardianingrum R, and Lestari T. 2018. Desain dan studi in silico senyawa turunan kuwanon-H sebagai kandidat obat anti-HIV [Design and in silico study of kuwanon-H as anti-HIV drug candidate]. Valensi. 4(1):57-66.

Ruswanto R. 2015. Desain dan studi interaksi senyawa n'-(3, 5-dinitrobenzoyl)-isonicotinohydrazide pada *Mycobacterium tuberculosis* enoyl-acyl carrier protein reductase (INHA) [Design and interaction study of the compound n '- (3, 5-dinitrobenzoyl) - isonicotinohydrazide on *Mycobacterium tuberculosis*enoyl-acyl carrier protein reductase (INHA)]. Jurnal Kesehatan Bakti Tunas Husada. 12(1):192-201.

Ruswanto R. 2015. Molecular docking empat turunan isonicotinohydrazide pada *Mycobacterium tuberculosis* enoyl-acyl carrier protein reductase (INHA) [Molecular docking of four isonicotinohydrazide derivatives in *Mycobacterium tuberculosis* enoyl-acyl carrier protein reductase (INHA)]. Jurnal Kesehatan Bakti Tunas Husada, 13(1).

Seyedin A, Hatamian-ZarmiA, Rasekh B, Mirderikvand M. 2015. Natural pigment production by Monascuspurpureus: Bioreactor yield improvement through statistical analysis. Appl Food Biotechnol. 2(2):23-30.

Sherman W, Beard HS, Farid R. 2006. Use of an induced fit receptor structure in virtual screening. Chem Biol Drug. 67(1):83-84.

Singgih M, Permana B, Maulidya SAI, Yuliana, A. 2019. Studi in silico metabolit sekunder kapang*Monascus* sp. Sebagai kandidat obat antikolesterol dan antikanker [In silico study of *Monascus* sp. as candidates for anti-cholesterol and anticancer drugs]. ALCHEMY. 15(1):104-123.

Sulistyaning AR, Wirawanni Y. 2013. Pengaruh pemberian angkak (*red yeast rice*) terhadap kadar glukosa darah puasa pada wanita prediabetes [the effect of red yeast rice on fasting blood glucose levels in prediabetic women] (Doctoral dissertation, Diponegoro University).

Yuliana A, Singgih M,Julianti E, Blanc P. 2017. Derivates of azaphilone *Monascus* pigments. Biocatalysis and Agricultural Biotechnology. 9(1):183-194.