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THE POTENTIAL OF NOCALLISA (NANOCAPSULES BASED ON*ALLIUM ASCALONICUM* SKIN) AS AN ALTERNATIVE FOR *SYSTEMIC LUPUS ERYTHEMATOSUS* THERAPY

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ABSTRACT

Lupus is an autoimmune inflammatory disease, one of lupus's types is systemic lupus erythematosus (SLE). SLE is often relatedto multisystemic inflammation due to abnormal immune function.Besides that, Allium ascalonicum is the main agricultural commodity of the Indonesian people which is only used for its tubers, while the skin only become organic waste for the environment. Compounds that dominate the skin of Allium ascalonicum are quercetin (flavonoids).Quercetin has anti-inflammatory activities that have potential in the treatment of SLE. So, the researchers made an innovation by utilizing quercetin in Allium ascalonicum skinforSLE's therapy in the form of nanocapsules so it can be consumed orally. This research used an experimental method with in-silico approach. This research proven that quercetin has potential as an anti-inflammatory agentthrough the results of PASS analysis with a Pa of 0.689. Quercetin with a single dose of the drug 1190 mg/kg known to be feasible as a drug substance with proven feasibility in various pharmaceutical aspects and 4th toxicity shows a low level of toxic impat to the body if this nanocapsules are consumed orally.

Keywords:*Systemic Lupus Erythematosus, Allium ascalonicum, nanocapsules, therapy.*

1. Introduction

Backgrounds

Lupus is a chronic autoimmune disease that can affect many organ systems. There are four main types of lupus, neonatal lupus, discoid lupus, drug-induced lupus, dan systemic lupus erythematosus (SLE). SLE is one of lupus's type that is often suffered by patients. Patients will sustain periodic flares with various levels of severity or incident without signs or symptoms which can be observed. SLE is linked to multisystemic inflammation caused by abnormal immune function. SLE can cause congenital and adaptive immune system activation that leads to autoreactive B cells activation by T cells(Ameer, et.al., 2022).

The usual therapeutic approach to lupus signs and symptoms depends on the type and severity of the disease. Patients with mild to moderste levels of lupus are generally given drugs such as NSAIDs, anti-malarial agents and corticosteroids to treat the symptoms. As the disease progresses, high doses of corticosteroids and immunosuppressive agents are given to control the disease(Maidhof& Hilas, 2012).

Quercetin is one of the flavonoid compounds of the flavonol group(Serafini, et.al., 2010). Quercetin, a flavonoid found in fruits and vegetables, has biological properties that can improve mental or physical performance and reduce the risk of infection. Quercetin has the anti-carcinogenic ability,anti-inflammatoryactivity, anti-virus, antioxidants, and psychostimulants(Li, et.al., 2016). The highest concentration of quercetin are found in onions, shallots, broccoli, apples, tea, andwine (Anand David, et.al., 2016).

Allium ascalonicum is one of the major agricultural commodities that society

urgently needs(Kementerian Pertanian Republik Indonesia, 2013). *Allium ascalonicum*are classified as kind of spice and used extensively as seasoning to enhance the flavor of dishes. The local shallot species commonly consumed by the people around Semarang Regency is *Allium ascalonicum*. Current conditions show that people only use the tubers as a cooking ingredient, while the shallot skins are only thrown away as waste. Shallot skin has various potentials to be developed into more useful products. The colored shallot skin indicates that the shallot skin contains polyphenolic substances. Shallot skin contains many active chemical compounds such as alkaloids, flavonoids, saponins, tannins, glycosides and steroids or triterpenoids(Manullang, 2010). Compounds that dominate the shallot skin are quercetin and steroids.

The utilization of natural ingredients as an alternative in the treatment of systemic lupus erythematosus has a great opportunity to be developed. Quercetin contained in shallot skin which has anti-inflammatory and antioxidant abilities is expected to be a new alternative in the treatment of lupus. The form of innovation that can be done is to pack shallot skin in capsule form so that it can be consumed orally. In addition, shallot skin extract will be processed to form nanoparticles which will make it more easily absorbed by the body.

This research was conducted to find out a potential compound of flavonoid especially quercetin and also theeffectiveness of *Allium ascalonicum*skin nanocapsulesas an alternative to treatment for Systemic Lupus Erythematosus.

2. Method and Experimental Details

Types, Time, and Location of Research

This research used experimental method by using in-silico approach or computational calculations that result in quantitative data. This research was conducted from 17th May 2023 until 28th June 2023 in several places.The experiments were conducted in Chemistry Laboratory of SMA Negeri 3 Semarang, Chemistry Laboratory of Universitas Negeri Semarang, and Pharmacy Laboratory of SMK Islam Sudirman Ungaran. Meanwhile, the in-silico analysis was conducted in each team member's house.

Several variables were analyzed in this research. The independent variable in this research is nanocapsules based on shallot (*Allium ascalonicum*) skin extract. The dependent variable in this research is the potential and effectiveness of shallot (*Allium ascalonicum*) skin extract in the form of nanocapsules for systemic lupus erythematosus therapy. The control variable in this research is shallot (Allium ascalonicum) skin.

Research Ingredients and Tools

The required ingredients to conduct this research are 125 grams of shallot (Allium ascalonicum) skin simplicia, 1.25 liters of food-grade ethanol 70%, 20 grams of starch, 10 grams of talcum powder, and 5 grams of magnesium stearate. Moreover, there are numerous tools that are required to conduct this research. The tools for making shallot (Allium ascalonicum) skin extract are blender, beaker glass, measuring cup, reagent bottle, stirring rod, maceration vessel, scale, funnel, filter paper, rotary evaporator, black plastic, and rubber band. Then, the extract processing device into nanoparticles is an ultrasonicator. Afterward, the tools for making the nanocapsules are parchment paper, scale, porcelain mortar and pestle, porcelain spoon, ceramic bowl, beaker glass, pipette, 20 mesh sieve, 10 mesh sieve, and 02 size capsule.

Experiment

The experiment was started by preparing the nanocapsules. First, the shallot skins were processed by maceration method in order to collect the extract. Second, the extracts were tested for phytochemicals to determine the content of

active chemical substance. Third, the process of synthesizing nanoparticles in shallot skin extract was carried out using the ultrasonification method, then a PSA (Particle Size Analyzer) test was carried out to determine the particle size. Fourth, the nanoparticles skin extract, starch, talc, and magnesium stearate were mixed using a certain formula, then packed into the capsule.

Data Processing Methods

The data obtained from the test results are quantitative data through a series of in-silico computational processes.First, the researchers determined the structure of compounds used in *Systemic Lupus Erythematosus* therapy using PubChem software. Second, the active potential of the compounds contained in *Allium ascalonicum*) with ideal conditions (Potential active (Pa) > 0.1) were predicted through Way2Drug software. The third processes istarget protein analysis by several software (PharmMapper, SuperPred, and Swiss Target Prediction) with the largest percentage role in *SystemicLupus Erythematosus* therapy.Fourth, after selected a protein that plays the biggest role, the target protein will be modeled in 3 dimensionsthrough Swiss-Model software. Furthermore, researchers validated the structure of the compound usingERRAT graphic processing by Saves Webserver 6.0. Fifth, stereochemical properties of target protein was evaluated through the Ramachandran plot by Saves Webserver 6.0. Sixth, carried out molecular docking between ligand and macromolecule using PyRx and visualized with PyMol. Seventh, the docking results are converted in a two-dimensional form to determine the interactions between the amino acids and their residues through ProteinPlus webserver. Eigth, Swiss-ADME webserver is used to analyze drugsimilarity, pharmacochemical, and physicochemical. Last step is Toxicity test of drug candidates for *SystemicLupus Erythematosus*therapy using ProTox software.

3. Result and Discussion

Simplisia

The simplicia sample of shallot skin (*Allium ascalonicum L.*)used in this study was 125 grams. The shallot skins were obtained from the field in Weleri, Kendal Regency. This ingredient are washed with clean water and dried in the sun before being processed into simplicia powder using a blender.

Maceration

The extraction process used in this research is the maceration method. Where this process is carried out by immersing simplicia in 70% ethanol(food grade) with a ratio of 1:10 (simplicia (grams) : 70% ethanol (milliliter)). Soaking was carried out for five days and then processed in a rotary evaporator 50°C with a rotation of 60 rpm. The maceration process produces 22.21 grams of shallot skin extract.

Phytochemical Test

From the phytochemical tests that we have carried out, we obtained data indicating that shallot skin extract contained polyphenolic substances with a positive overall value (+), including flavonoids.

Table 1 Phytochemical test result

Numb.	Parameters	Result
1.	Alkaloid	(+)
2.	Steroid	(+)
3.	Terpenoid	(+)
4.	Flavonoid	(+)
5.	Phenolic	(+)
6.	Saponin	(+)

One of the derivatives of flavonoid compounds is quercetin which is found in shallot skin extract (*Allium ascalonicum*). This compound has functions as anti-carcinogenic, anti-inflammatory, antioxidants, anti-virus, and psychostimulants, this is in line with a journal published by Li, et.al, 2016.

PSA Test Result

From the PSA test that we have carried out, we obtained an average size of 170.3 nanometers where these particles correspond to the ideal size of nanoparticles in drug delivery according to previous literature studies which stated thatthe size of the nanoparticle needed in a drug delivery system is 50-300 nm (Sabdoningrum, 2021).

Below is the average calculation and analysis table of the particle sizes we have tested.

Calculation Results

Peak No.	S.P.Area Ratio	Mean	S. D.	Mode
1	1.00	199.1 nm	63.2 nm	181.7 nm
2	---	--- nm	--- nm	--- nm
3	---	--- nm	--- nm	--- nm
Total	1.00	199.1 nm	63.2 nm	181.7 nm

Cumulant Operations

Z-Average : 170.3 nm
PI : 0.485

Figure 1 PSA's calculation result

The initial particle size of shallot skin is 0.34 nanometers. After one run with 84 transformations, a particle size of 8510.56 nanometers was obtained. If each change in size is averaged, a result of 170.3 nanometers will be obtained. In addition, the graph above proves that the percentage of particle size reduction from extracts of shallot skin reaches above 90% or it can be said that the extract particles can transform into particles that are able to penetrate into the spaces between cells almost perfectly.

Structural Formula

Structure of the active compounds in *Allium ascalonicum* skin was obtained through the 'PubChem' website. The resulting output structure is a conversion of the molecular formula of the compound which is adjusted again using the Canonical SMILES (Simplified Molecular Input Line Entry System).

Quercetin has a molecular formula$C_{15}H_{10}O_7$. With the results of CanonicalSMILESC1=CC(=C(C=C1C2=C(C(=O)C3=C(C=C(C=C3O2)O)O)O)O).Therefore, the output structure of the compound obtained is.

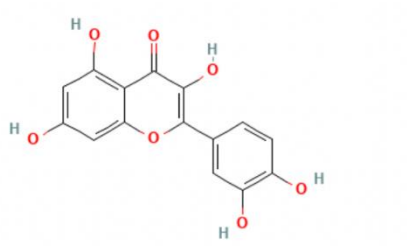

Figure 2 Quercetin's molecular formula

Potency of Active Compounds

This analysis used the website 'Way2drug'. This website is a spectrum analyzer of the biological activity of a chemical compound that uses the PASS (Prediction of Activity Spectra for Substances) software base for predictions of various types of biological activity based on the structure of organic compounds. The output that will show in this analysis is a table listing activities that can be produced by chemical compounds, with details of Pa (activation potential) and Pi (inactivation potential). The main indicator of the activity of a compound is when Pa>Pi.

Biological activity in quercetin compounds that have an important role in therapy*Systemic Lupus Erythematosus* including antioxidants, anti-inflammatory,immunosuppressant, non-steroidal anti-inflammatory agent, membrane permeability inhibitor, histamine releaseinhibitors, Tcell inhibitors, and membrane integrity antagonist.

The following table isPa and Pi results from each biological activity of quercetin compounds based on PASS analysis.

Table 2 PASS analysis result

Activity	Pa	Pi
Membrane permeability inhibitor	0,938	0,003
Antioxidant	0,872	0,003
Histamine releaseinhibitors	0,720	0,004
Anti-inflammatory	0,689	0,017

Membrane integrity antagonist	0,454	0,056
Non-steroidal anti-inflammatory agent	0,439	0,018
Immunosuspersant	0,344	0,088
T cell inhibitors	0,124	0,02

Determining Target Protein

The determination of the target protein required three stages of intensive analysis through several softwares. The results of the three analyzes will then be compared simultaneously to create a 'Protein Mapping', in which the mapping results are the elimination of several target proteins that do play a role in therapy.Systemic lupus erythematosus.

First, we used PhamMapper software, it is a server designed to identify candidate protein targets through newly discovered molecules contained in drugs, natural products, or other compounds with unidentified binding targets, with a pharmacophore mapping approach.

Second, we used Swiss-Target software, it is a server that analyzes the prediction of the most likely macromolecular target of a small molecule, which is assumed to be bioactive.In this analysis, the researcher narrows the species object down to *Homo sapiens*only.

Third, we used SuperPred software, it is a prediction server for ATC codes and compound targets. The Anatomical Therapeutic Chemical (ATC) classification system is used for the classification of drugs published by WHO. This classification is based on the therapeutic and chemical characteristics of a drug.

The following is a table of results from some of the target protein predictions.

Table 3 List of target protein in quercetin

Target	Common name	Uniprot ID	ChEMBL ID	Target Class
Lymphocyte differenttiation antigen CD38	CD38	P28907	CHEMBL4660	Enzyme
Aldo-keto reductase family 1 member B10	AKR1B10	O60218	CHEMBL5983	Enzyme
Tankyrase-2	TKNS2	Q9H2K2	CHEMBL 6154	Enzyme
Tankyrase-1	TNKS	O95271	CHEMBL 6164	Enzyme
DNA topoisomerase el (by homology)	TOP1	P11387	CHEMBL 1781	Isomerase
Telomerase reverse transcriptase	TERT	O14746	CHEMBL 2916	Enzyme

The above results show the range of target proteins from smallest to largest possible. The target protein belonging to the enzyme classification and which can help the process of SLE therapy is *lymphocyte differentiation antigen cd38* which has the common name CD38 with the code UniProt P28907, so this compound is a target protein obtained from the conversion of quercetin.

Validation Structure of Compounds

Validation structure of target proteinwas carried out usingERRAT graphic. ERRAT is awebserver to verify the protein structure determined by crystallography. Error values are plotted as a function of positionsliding 9-residue window. Functionerror based on the interaction statistics of the non-bonded atoms in the protein structure listed.

At this step, it requires the help of 'Saves Webserver version 6.0' so that the ERRAT graphical output can be calculated properly. 3D modeling of target protein*lymphosite differentiation antigen cd38* which has been stored with the .pdb file type (specifically for protein) is processed using a C++ program, so the following results are obtained.

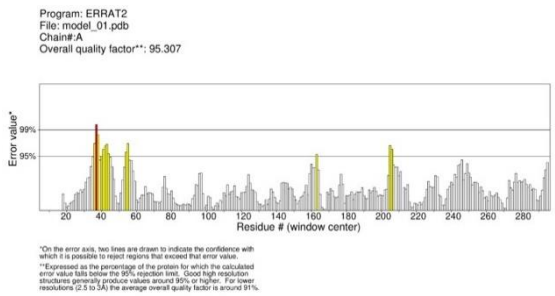

Figure 3 ERRAT graphiclymphocyte-cd38

The figure above is an ERRAT graph which shows the overall quality factor of the cd38 protein is 95.307% it can be seen too from the red graph at the residues range, this indicates a very high protein potential in terms of the possible error value of less than 5%.

Evaluation of Stereochemical Properties

Stereochemical properties evaluation of the model was carried out usingwebserver namely 'Saves Webserver version 6.0' but with special software in the form of Procheck through analysis of the Ramachandran plot.The Ramachandran plot is a two-dimensional plot that depicts amino acid residues. Inside there is a corner*phi* as the X axis and*psi* as the Y axis. The combined output of the two angle references is used as a basis for assessing the stereochemical quality of a protein or enzyme model. The assessment is adjusted to the percentage of amino acid residues that are in the highly favored region (most favoured regions) and prohibited areas (disallowed regions) of the Ramachandran plot.

Here is the result of the Ramachandran plot of proteinlymphocyte differentiation antigen cd38.

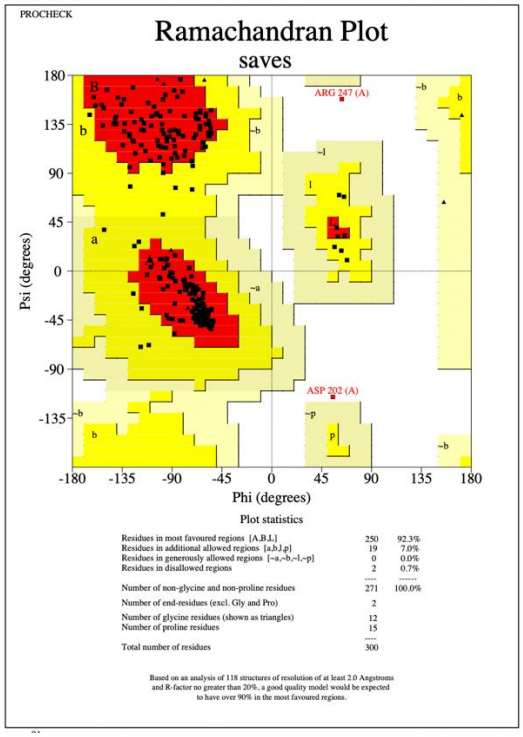

Figure 4 Ramachandran Plot of lymphocyte-cd38

The figure shows a map of the distribution of amino acid residues from the lymphocyte differentiation antigen cd38 protein. The distribution of the residue forms white to red areas. The white area is the disallowed region, while the red area is the most favored region. It is known that there is 92.3% residue in the most favored region and 0.7% residue in the disallowed region. This shows that the protein model used is of good quality.

Molecular Docking

Molecular docking iscomputational simulation using genetic-based methods that can be used to show the patterns of interaction between two molecules, natural compounds or ligand and receptor or protein by attaching a small molecule (ligand) to the active side of the receptor.

This analysis was done by 'PyMol' software to predict the interactions between *alfa-helix*with*beta-sheet*from the selected target protein. After getting the output from 'PyMol', the next step is docking using the 'PyRx' webserver. This webserver will minimize quercetin as a ligand, then the program will process the quercetin

comparison with*lymphocyte differentiation antigen cd38* using the Python module. Output from executioncompilerwill show a table of Binding affinity, RMSDlower bound, and RMSD upper bound.

Here are the resultsofmolecular docking among the active compounds of quercetin that have been decreaseswith target proteinslymphocyte differentiation antigen cd38.

Table 4 Resultsofmolecular docking

Ligand	Binding affinity	RMSD lower bound	RMSD upper bound
cd38_ quercetin	- 7.2	0.0	0.0
cd38_ quercetin	- 7.1	1.47	2.43
cd38_ quercetin	- 6.9	2.43	4.45

The lower of binding affinity value, indicates that the interaction between the ligand and the protein receptor are more stable. The RMSD value <2.0 indicates that the calculation is more accurate and the resulting error is less happens, so that the molecular docking in this research was successful, as proven by the smallest binding affinity value, which is -7.2 and both RMSD values are 0.0.

Visualization of Molecular Docking

Three- dimensional visualization that describes the interaction between the ligand and the target protein is obtained from 'PyMol' webserver. Meanwhile the two-dimensional one is from 'ProteinPlus' webserver, it containssub-software 'PoseView' to analyze the interaction lines between the results of molecular docking with amino acids and their residues.

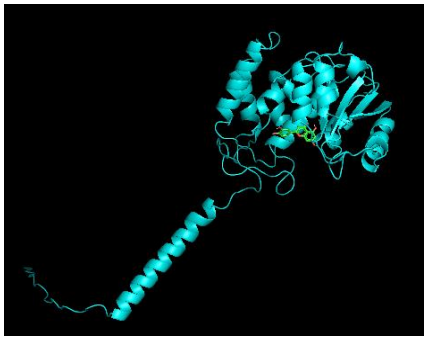

Figure 5 Visualization of macromolecule (lymphocyte-cd38)

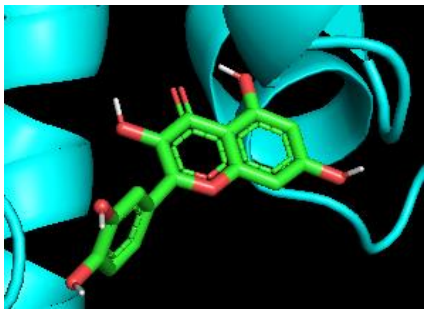

Figure 6 Visualization of ligand (quercetin)

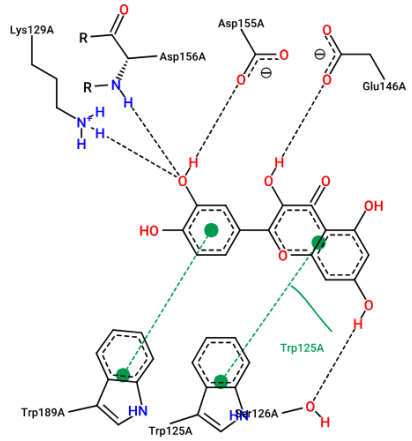

Figure 7 Visualization two-dimensional of molecular docking

From the interactions above, it can be seen that some of the amino acids formed include essential amino acids in the form of Lysine (Lys 129A) and Tryptophan (Trp 125A), conditionally non-essential amino acids in the form of Serine (Ser 126A), and non-essential amino acids in the form of Aspartic acid (Asp 155A and Asp 156A) and Glutamic acid (Glu 146A).

Analysis of Drug Similarity, Pharmacochemical, and Physicochemical

Evaluation of drug candidates is generally carried out through analysis of similarity properties with absorption

profiles and resemblance todrug (drug-likeness), distribution, metabolism, and excretion (ADME). This analysis was performed with the 'Swiss-ADME' webserver where the output panel will list all the values in the ADME parameters. Graphic output (Bioavailability Radar) includes all molecules submitted in BOILED-Egg plots and executed with enhanced CADD tasks to estimate gastrointestinal uptake and global brain penetration, they are two main aspects of ADME affecting pharmacokinetics.

Evaluation of drug-like properties is generally carried out according to the Lipinski rule (rule of five) whereas predictions of ADME can provide information regarding oral bioavailability, cell permease, metabolism, and elimination which are the pharmacokinetic and pharmacodynamic characteristics of a drug molecule. The following is a table of Lipinski's rules.

Table 5 Lipinski Rules (Rule of Five)

Aspect	Sub-aspect	Ideal Value
Physicochemical	Molecular weight	≤ 500
	Num. H-bond acceptors	≤ 10
	Num. H-bond donors	≤ 5
Lipophilicity	iLOGP	≤ 4,15

Results of Bioavailability Radar accompanied by a tablesections one-panel-per-molecule output (Physicochemical Properties, Lipophilicity, Pharmacokinetics, Drug Likeness and Medicinal Chemistry) of quercetin compounds:

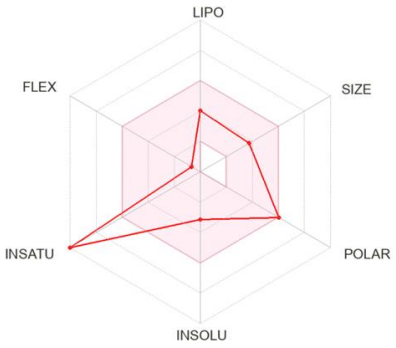

Figure 8 Results of Bioavailability RadarResults of Bioavailability Radar

Physicochemical Properties	
Formula	C15H10O7
Molecular weight	302.24 g/mol
Num. heavy atoms	22
Num. arom. heavy atoms	16
Fraction Csp3	0.00
Num. rotatable bonds	1
Num. H-bond acceptors	7
Num. H-bond donors	5
Molar Refractivity	78.03
TPSA	131.36 Å²
Lipophilicity	
Log $P_{o/w}$ (iLOGP)	1.63
Log $P_{o/w}$ (XLOGP3)	1.54
Log $P_{o/w}$ (WLOGP)	1.99
Log $P_{o/w}$ (MLOGP)	-0.56
Log $P_{o/w}$ (SILICOS-IT)	1.54
Consensus Log $P_{o/w}$	1.23
Water Solubility	
Log *S* (ESOL)	-3.16
Solubility	2.11e-01 mg/ml ; 6.98e-04 mol/l
Class	Soluble
Log *S* (Ali)	-3.91
Solubility	3.74e-02 mg/ml ; 1.24e-04 mol/l
Class	Soluble
Log *S* (SILICOS-IT)	-3.24
Solubility	1.73e-01 mg/ml ; 5.73e-04 mol/l
Class	Soluble
Pharmacokinetics	
GI absorption	High
BBB permeant	No
P-gp substrate	No
CYP1A2 inhibitor	Yes
CYP2C19 inhibitor	No
CYP2C9 inhibitor	No
CYP2D6 inhibitor	Yes
CYP3A4 inhibitor	Yes
Log K_p (skin permeation)	-7.05 cm/s
Druglikeness	
Lipinski	Yes; 0 violation
Ghose	Yes
Veber	Yes
Egan	Yes
Muegge	Yes
Bioavailability Score	0.55
Medicinal Chemistry	
PAINS	1 alert: catechol_A
Brenk	1 alert: catechol
Leadlikeness	Yes
Synthetic accessibility	3.23

Figure 9 Sections one-panel-per-molecule output

According to the Lipinski rule, the quercetin compound fulfills all the criteria. Molecular weight is 302.24 g/mol, Num. H-bond acceptors are worth 7, Num. H-bond donors are worth 5, and iLOGP is worth 1.63, because the drug is in capsule

form, there are several other criteria that must be met. In the Water Solubility aspect, all classes must show a 'Soluble' or easily soluble output. GI (Gastrointestinal) Absorption in Pharmacokinetics must show a 'High' output. Leadlikeness in the Medicinal Chemistry aspect must show an output of 'Yes' accompanied by Synthetic Accessibility close to number 1. The four specific criteria for oral drugs have been fully met starting from the output 'Soluble' on Water Solubility, 'High' on GI (Gastrointestinal) Absorption, 'Yes' on Leadlikeness and a score of 3.23 on Synthetic accessibility.

Toxicity Test of Drug Candidates

A toxicity test is needed to determine the level of toxic effect on the compounds contained in the drug preparation when taken orally. Toxicity prediction was obtained through analysis of the Protox-II webserver which iscomputer-based model adjusted for real data (in vitro or in vivo) to predict the toxic potential of the included compounds. The resulting output is a toxicity level prediction scheme such as oral toxicity (acute rodent toxicity), organ toxicity (hepatotoxicity), toxicological endpoints (such as mutagenicity, carcinogenicity, cytotoxicity, and immunotoxicity of B cell growth inhibition), toxicological pathways (AOPs) and toxicity targets (Novartis off-target) thereby providing insight into the possible molecular mechanisms behind such toxic responses.

The following is a schematic and detailed prediction of the toxicity of quercetin compounds in nanocapsule drug candidates.

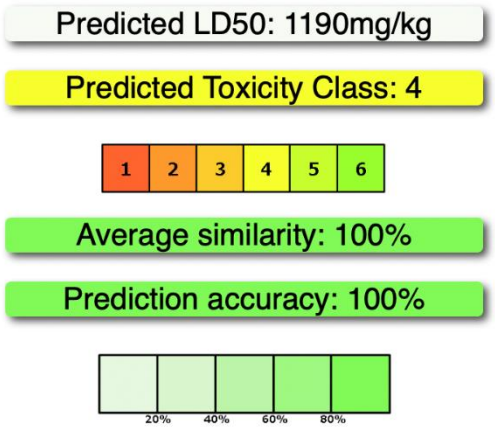

Figure 10 Results of LD50 and toxicity class

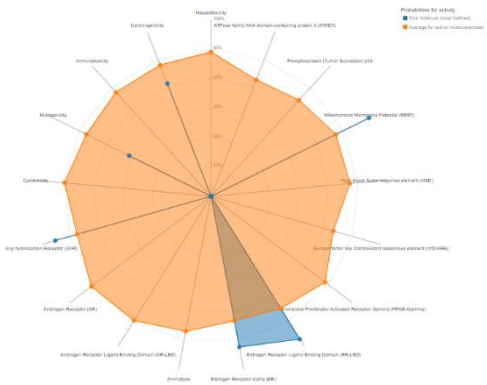

Figure 11 Scheme of the toxicityprediction from quercetin compounds

Classification	Target	Shorthand	Prediction
Organ toxicity	Hepatotoxicity	dili	Active
Toxicity end points	Carcinogenicity	carcino	Inactive
Toxicity end points	Immunotoxicity	immuno	Inactive
Toxicity end points	Mutagenicity	mutagen	Inactive
Toxicity end points	Cytotoxicity	cyto	Inactive
Tox21-Nuclear receptor signalling pathways	Aryl hydrocarbon Receptor (AhR)	nr_ahr	Inactive
Tox21-Nuclear receptor signalling pathways	Androgen Receptor (AR)	nr_ar	Inactive
Tox21-Nuclear receptor signalling pathways	Androgen Receptor Ligand Binding Domain (AR-LBD)	nr_ar_lbd	Inactive

Figure 12 Detailed table indicator of the toxicityprediction

The results of the analysis showed that a single drug dose (LD50) was at 1190 mg/kg, which means that the toxicity level of the drug candidate is in class 4 (safe), but has a small potential to cause respiratory or skin sensitization. Because the purpose of this drug is to heal the immune system, the Prediction table on Immunotoxicity should show the output column in green (inactive). The 'Inactive' criterion is proven in the results of the analysis, meaning that the quercetin

compound in the nanocapsules does not cause toxic side effects to the body when consumed orally.

4. Conclusion

Based on the tests that have been carried out, it was concluded that the quercetin content in shallot skin has potential as an alternative treatment for *SystemicLupusErytemathosus*. Quercetin has potential as an anti-inflammatory agent, antioxidant, immunosuppressant, T-cell inhibitor, and inhibitor of histamine secretion with an active potential that is higher than its inactive potential. Quercetin with a single dose of the drug1190 mg/kg known to be feasible as a drug substance with proven feasibility in various pharmaceutical aspects and a low level of toxicity to the body. It means that, nanocapsules based on shallot (*Allium ascalonicum*) skin extract have a relatively great potential when applied in SLE therapy orally.

5. Acknowledgements

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