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Anticancer mechanism of *Pisangulin angulata* through in silico as teaching material

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ABSTRACT

This study aims to reveal the anticancer mechanism of the bioactive compound of *Pisangulin angulata* and to assess the feasibility of that results as teaching material. This research includes descriptive explorations. In the first stage, an in silico analysis was performed by molecular docking method between physalin compounds and GLI1 protein. The second steps of this study aim to develop teaching materials based research using the Analysis, Reorganizing, Piloting Class, and Evaluating (ARPE models). Feasibility test was carried out by experts and practitioners. Think Pair Share was used in the pilot project. Student motivation and misconception were recorded using SMI and CRI instrument. This study reveals that physalin B has higher activities than controls. The type of chemical bond that is formed between GLI1 amino acids residues with physalin is hydrogen bonds and hydrophobic bonds. The visualization of the types of bonds in that molecular docking between GLI1 amino acid residues and physalin has a high degree of feasibility (89) and can be used to enrich Chemistry for Biology lectures. The visualization of these chemical bonds can increase learning motivation and can improve the understanding of the concept of chemical bonds.

INTRODUCTION

Preliminary studies have been carried out on remedial learning in Biology-Chemistry courses for Biology teacher candidates in one of LPTK in East Java. Data analysis revealed that students still had a chemical bond misconception. This course was a compulsory course that must be taken by

Biology teacher candidates in the first semester (Rafiuddin, Supriyanti, Nurrachman, & Liliasari, 2012; Rahmatan, Liliasari, & Redjeki, 2012). This course was the basic for mastering courses in Biochemistry, Cell Biology and Molecular Sciences, Plant Physiology, Animal and Human Physiology, Genetics, Evolution, and Modern Biology. A good understanding of chemical bonds is needed in the field of Biological studies (Santoso, 2017; Toy et al., 2018; Rafiuddin, et al., 2012). The physiological, cellular, and even molecular processes in cells are the mechanism of complex chemical bonds between one molecule and another (Azer, 2015; Roberts, Evans, Trivedi, & Menage, 2006; Blatch, Cliff, Beason-Abmayr, & Halpin, 2017). For example, the mechanism of interaction between enzyme molecules with the substrate and the folding mechanism (folding the polymer chain structure) hemoglobin. Included in the interaction between acif compounds of plants or drug molecules with body cells.

The preliminary study also revealed two main causes of misconception. Firstly, the presentation of chemical bonds has not been contextualized with daily activities. The concept of chemical bonds was still presented in the form of verbal in written language. Then, the example was used to contextualize the concept is a chemical bond in a chemical compound that cannot be observed directly by students. Secondly, the concept of chemical bonds has not been presented in a dynamic and interactive visualization. The concept of chemical bonds is still shown in two-dimensional visualization in the form of images contained in printed teaching materials and power points-such us in workshop sheet and just presented in two dimensional in textbooks.

Visualization of science concepts is crucial in learning (Ristanto, 2011; Ichsan, Rusdi, & Sartono, 2017; Fitriani, Adisyahputra, & Komala, 2018). Display in the form of animation, video, and the like is an essential part of pedagogy (O'day, 2006; Rosamsi, Miarsyah, & Ristanto, 2019). Molecular visualization in natural science is a vital tool for learning outcomes (Canning & Cox, 2001; Rosamsi et al., 2019). According to McClean et al. (2005) and O'day (2007), the visualization of science can help students maintain their knowledge for a more extended period. Santoso et al. (2017) also reported that the use of computational studies of biomolecular structures in Biochemistry class was able to reduce Biochemical misconceptions. Visualization of science concepts can clarify the process of change in molecular motion seen (Stith, 2004) so that students can observing in more detail the structure. Visualization of an object in science greatly influences students' perceptions. This is in line with Tanudjaja (2005) and Ferliyati, Kurniati, & Suryanda (2014) that there is a human tendency to organize stimuli which are separated into groups based on the closeness, similarity, closeness, continuity, and nature of the object actress. In silico analysis can model abstract concepts that needed by students to be able to understand a phenomenon.

Cancer is one of a degenerative disease that causes death in the world - included in Indonesia. The uses of herbs by local people for cancer treatment is one of the wisdom of the community that must be should supporting by scientification. In Indonesia, *Physalis angulata* (L) (Solanaceae) is a traditional herbal plant that has been proven empirically to contain some bioactive compounds that were able to overcome the growth of cancer cells. Several previous studies have reported research on *P. angulata* to extract as an anticancer breast (Fitria et al., 2011), tongue cancer cells (Safitri et al., 2016), and several types of cancer cells such as MAD-MD 231, MCF-7, and HA22TKB (Fitria et al., 2011; Coelho, 2009; and Bourdi et al., 2000). However, research on the anticancer of the molecular action of *P. angula* extract has never been launched.

The study of the mechanism of molecular anticancer action have some best practices, such our methodologies, and research results. Both methods and research results can be used to improve the quality of learning. The contextualization of learning material can be done by integrating the results of scientific field research in learning in the form of cases, problem-solving, and examples of study objects. This also in line with the previous study that objects that are around students can be a contextual learning resource (Amin, 2010; 2015; & Mumpuni, Susilo, & Rohman, 2014; Lestari, Amelia, & Marianingsih, 2017). Contextual learning is needed in science learning so students can think concretely so students can understand difficult concepts and make students more active learning (Shan, 2011; Wuryaningrum et al., 2018). Contextual learning also can activate the thinking process

of students Glyn & Winter (2004). Visualizing abstract concepts and contextualizing material through research results can be used to help students understand abstract concepts, such as chemical bonds. This study aims to reveal the mechanism of the anticancer molecular action of *P. angulata* extract and examine its relevance as a promising material in developing lecture material to repair the student misconceptions.

METHOD

The First Research

The first steps of this study aim to reveal the molecular mechanism of physalin compounds through in silico approach. Devices needed: 4.00 GB RAM specification computer, Professional 64-bit Windows 8.1 2013 operating system, Intel (R) CoreTM i3-5005U CPU, internet installed. The computer has been installed the software: PyMol 1.3; PyRx Python Presciption 0.8; and LigPlot + v.1.4.5. In this study was carried out: preparation of physalin structures and control compounds, preparation of the GLI1 structure followed by protein structure validation, then molecular docking between target compounds (physalin and control) with GLI1 protein and visualization of interactions between molecules.

a. Preparation of Molecule Structures

The types of compounds physalin and vismodegib (controls) were downloaded from the online page on the PubChem (http://pubchem.ncbi.nlm.nih.gov). The structure was saved (in the form of .sdf), and the canonical smiles data of the compound was stored (in the form of .text) in notepad. Vismodegib compound was one of a synthetic compound commonly used widely in cancer treatment so that the compound was used as a positive control in this research.

b. Preparation of GLI1 Protein Molecules

The physalin structure was quite diverse. Therefore, the types of physalin to be used in the next stage are determined by analyzing the target molecules of every kind of physalin. This analysis was done by entering canonical smiles data on some online server database (the Swiss Target Prediction, PharmMapper, and SuperPred). Physalins that have the same target molecule are collected and stored (the form of .pdb). Validation was done by removing water molecules. This validation and changing the .sdf structure to .pdb is done using PyMol software.

c. Molecular Docking and its Visualization

Molecular docking between physalin, vismodegib, with GLI1 was carried out using PyRx software. The selected molecular are the results that have the lowest free energy and the lowest RMSD value (<2). The RMSD score can be used as a way to validate the molecular docking. Data tabulated and analyzed descriptively. The best molecular docking results were verified in three-dimensional structures and stored in the form of .pdb using PyMol. Then, the saved file was opened with LigPlot + software. The types of interactions between molecules (chemical bonds) are tabulated and analyzed descriptively.

The Second Research

The second phase of the study aims to improve Chemistry for Biology. This is done by accommodating the results of research Biology-related in learning variables. Therefore, this second research, researchers were used ARPE model. **ARPE model** is an acronym for the names of stages ***Analysis***, ***Reorganization***, ***Piloting***, and ***Evaluation***. The analysis aims to determine the level of feasibility of the results of research Biology-related that will be used to improve learning. Feasibility assessment was carried out using a rubric that had been validated by two experts in the field of Biology/Natural Sciences. This rubric gets an average value of 78.24, so it is valid and can be used as an instrument for the next (data not approved).

The rubric consists of three main aspects with several indicators in each aspect. The three elements in question include of: the relevance of the results of the research on the field of science, the relevance of the results of the study to support competency/learning outcomes, and the relevance of the results of the study to support the conceptualization of teaching material to be more contextual. The description of the indicators in each aspect is presented in Table 1. The feasibility assessment

was carried out by two experts (the field of Cell Biology and Learning Biology) and two practitioners (two lecturers). The average assessment results of two experts and two practitioners were used to determine the level of eligibility.

Reorganization, researchers rearrange learning variables so that researchers get a different learning design than before. Piloting class aims to apply learning design to small classes (minimum 10-15 students). The evaluation aims to determine the effectiveness of learning design. Researchers can compare learning outcomes, understanding concepts, high-level thinking skills, and other learning outcome variables.

Table 1.
The rubrics of feasibility assessment to assess the research results for developing teaching materials.

Num.	Assessment Aspect	Indicators
1	the relevance of the results of research on the development of science	a. The research background describes the urgency of problems solving currently in the field of biology/science.
		b. Problems raised are universal in some places.
		c. The method used follows the latest Biology/Natural Sciences field.
		d. The method used is supported by adequate literature in the field of Biology/Science.
		e. The instrument used is reliable and valid by the field of Biology/Science.
		f. The research results contain scientific information that supports/or can also conflict with previous findings*).
		g. The results of the study contain scientific information that can explain natural events/phenomena in the cellular system/organs/organs/individuals/populations/ecosystems*).
		h. The research results contain scientific information that can be used as a main for further development / research in the field of Biology/Science.
		i. The results of the study contain scientific information that can be used as a basic for policies making on issues related to the scientific field of Biology/Natural Sciences.
2	the relevance of research to support learning indicators/goals/outcomes	a. The research procedure is a science work (scientific) students can apply that in the elementary/junior/high school/college level curriculum*).
		b. Some/all stages of the research contain activities that can support civilizing attitudes of character and national values (Pancasila).
		c. Some/all stages of research contain activities that can support civilizing scientific attitudes.
		d. Some/all stages of research contain activities that can be carried out collaboratively.
		e. Some/all stages of research can be done quickly by students.
		f. Some/all stages of research contain activities that can support students' behavior to obey K3 (Occupational Safety and Health).
		g. The results of the study contain scientific information that can be used to add concepts to teaching material in the scientific field of Biology/Science.
		h. The results of the study contain scientific information that can be used to support the main theories contained in teaching material in the field of Biology/Science.
		i. Stages of research (methodology) contain work stages that can be visualized in the form of images (photos, graphics, tables, posters/leaflets, pocketbooks, atlases) or films (video/animation/moving picture) for the preparation of media/teaching materials.
		j. The results of the study contain scientific information that can be visualized in the form of images (photos, graphics, tables, posters/leaflets, pocketbooks, atlases) or films (video/animation/ moving picture) for the preparation of media/teaching materials.
3	the relevance of research to the curriculum	a. Some or all of the contents of the problem contained in the background of the study relate to the substance of the school curriculum (core competencies 1/2/3/4 curriculum)/college curriculum (learning outcomes of study programs/learning outcomes of courses*).
		b. Some or all stages of research contain activities related to substance.

Information:
1. *) choose one.
2. score = filled with number 1 (if not appropriate), 2 (not appropriate), 3 (appropriate), 4 (very appropriate).
3. the final score is determined by dividing the acquisition score by a total score (76) then multiplied by 100.
4. categorization of the feasibility level is done by using the reference: very feasible (80 <x <100), feasible (60 <x <80), feasible (50 <x <60), and inappropriate (x <50).

RESULTS AND DISCUSSION

1. Molecular mechanism of anticancer bioactive compounds of *P. Angulata*

There were six types of physalin compounds in the database (PubChem) that have been downloaded. The six types of physalin are collected in the form of .pdb with different compound identification numbers (CID) (presented in Table 2). Screening analysis of the molecular profile of the sixth physalin was carried out using Swiss Target Prediction, PharmMapper, and SuperPred. Recapitulation of profile profiles of target physalin molecules is presented in Table 3. Based on Table 2, there are three types of physalin which can act as anticancer targeting Glioma-associated Oncogene1 protein molecules (GLI1, CID: P0815). The three types of physalin include physalin F, physalin B, and physalin D.

Table 2.
The types of physalin in *P. angulata* along with CID.

No	Compounds	CID Number
1	*Physalin G*	42620981
2	*Physalin F*	49864133
3	*Physalin B*	11613161
4	*Physalin D*	72551426
5	*Physalin E*	101586381
6	*Physalin U*	44426450

Table 3.
Recapitulation about of molecular target of physalin molecules.

Compounds	Target Molecule	*page database*		
		STP	PM	SP
Physalin F	GLI1 protein	+	-	+
Physalin B	GLI1 protein	+	-	+
Physalin D	GLI1 protein	+	-	+

Description: (+) exists with a value of pa> 0.8 and (-) if it does not exist; STP (Swiss Target Prediction), PM (PharmMapper), and SP (SuperPred).

Molecular docking between physalin compounds, vismodegib (control) and GLI1 has been carried out and data obtained on binding affinity and RMSD values (Table 4). Both of the molecular docking RMSD values the upper (UB) and bottom (lb) values were less than 2. This indicates that the results of the molecular docking were valid, and the results can be used to interpret the interactions between ligands (physalin and vismodegib) and macromolecules (GLI1). Physalin B has the lowest binding affinity with GLI1 when compared to other ligands, which are -8.3 Kcal/mol. This revealed that physalin B, physalin F, and physalin D compounds found in *P. angulata* plants could more easily bind (interact) with GLI1 compared to the control ligand in the form of vismodegib. In cancer treatment, GLI1 activity can be inhibited using vismodegib compounds. The use of vismodegib compounds was reported to be able to suppress the proliferation of cancer cells. GLI1 is a human protein that is controlled by the GLI1 gene on the 12th chromosome of humans. This protein has several roles in the mechanism of regulation of gene expression. For example, the process of regulating the activity of RNA polymerase II transcription factors and binding of DNA sequences. Included in the mechanism of the proliferation of cancer cells through the Sonic Hedgehog (SHH) pathway (Che et al., 2012; Shida et al., 2006).

Table 4.
The binding affinity and RMSD of interaction several ligands with GLI1 macromolecules.

Molecules + Ligan	*Binding Affinity* (Kcal/mol)	RMSD (*ub*)	RMSD (*lb*)
GLI1 + *Physalin B*	-8.3	0,0	0,0
GLI1 + *Physalin F*	-8.0	0,0	0,0
GLI1 + *Physalin D*	-7.5	0,0	0,0
GLI1 + *vismodegib* (kontrol)	-7.2	0,0	0,0

Table 5.
Profile of amino acid residues from GLI1 that interact with ligands.

Ligans	Amino acid residues of GLI1
Physalin B	arg60*, arg61, lys66, **arg81**, asn84, ser80*
Physalin F	arg44, phe49**, met54**, val57**, **arg81***
Physalin D	phe49**, met54**, val57**, **arg81*,** leu82, glu83*
vismodegib	tyr79*, glu83, **arg81**, asn84, thr87, his88*, asn111

Description: * hydrogen bond, ** non-polar amino acid, without * sign = hydrophobic bond.

Visualization of chemical bonds formed in molecular docking was presented in Figure 1 and Table 4. The interaction pattern between Physalin F, physalin B, and physalin D with GLI1 is the same as the interaction pattern of cancer drugs, namely vismodegib (control) with GLI1 (Table 5). Arginin86 is a GLI1 amino acid residue which is always involved when there is an interaction between GLI1 and vismodegib and physalin F, physalin B, physalin D. The interaction between physalin and vismodegib with GLI1 can occur due to several chemical bonds formed between GLI1 molecules and ligands. For example, hydrogen bonds between amino acid arginine 81 GLI1 residues with C23 atoms physalin F. The hydrophobic structure interactions are also found between ligands and GLI1 molecules. Examples of amino acid residues Lisin 66 GLI1 with C6 atoms (carbon) physalin structure B. The number of hydrogen bonds and hydrophobic interactions between physalin and vismodegib with GLI1 are presented in Figure 2. The number of chemical bonds that occur between ligands and macromolecules is not the main factor affecting value binding affinity. The results of this study reiterate the report of Sharma, Bano, Dhaliwal, & Sharma, (2015) about the great potential of *P. angulata* as an herbal plant that has successfully cured cancer.

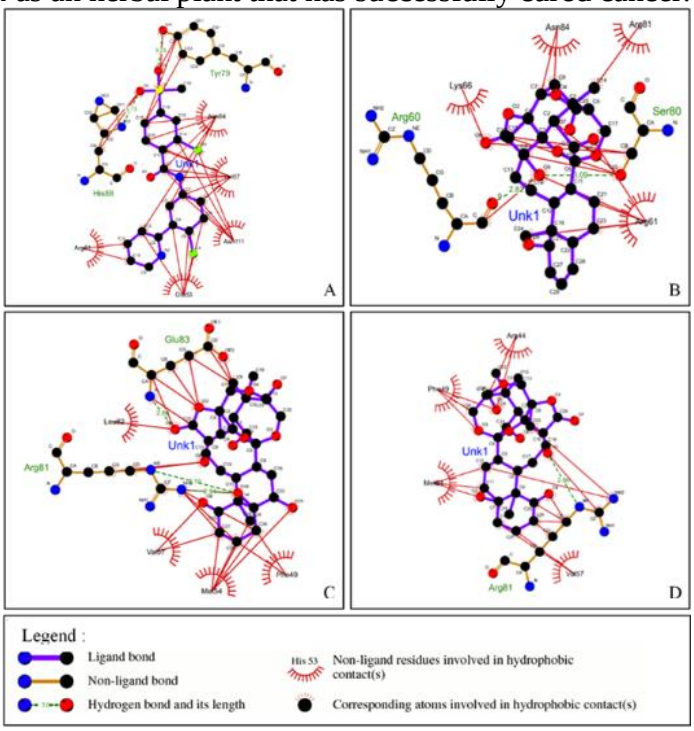

Figure 1. The results of molecular docking visualization with LigPLot +. The profile of the chemical bond pattern between the target ligands is vismodegib (A), physalin B (B), physalin D (C), physalin F (D) with macromolecules GLI1

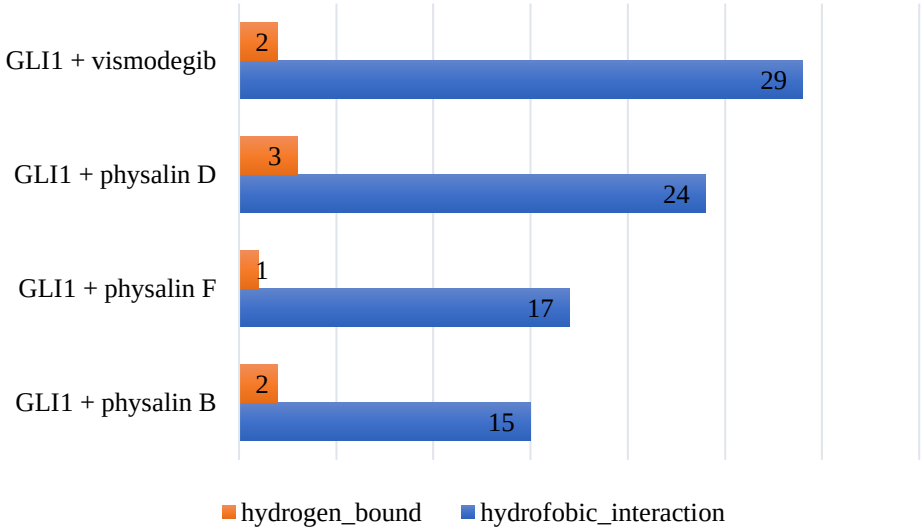

Figure 2. The profile of the number of chemical bonds between the target ligands is vismodegib (A), physalin B (B), physalin D (C), physalin F (D) with macromolecules GLI1.

This research has some of the scientific information. Scientific information includes exploration of the database physalin structure and structure of GLI1 protein, molecular docking, interaction patterns between ligands and macromolecules, binding affinity, profile types and the number of chemical bonds that can be formed during molecular belaying. Scientific information from the results of this study can explain the phenomena that occur in everyday life about herbs made from *P. angulata*, which can treat cancer. Disclosure of this phenomenon is a form of interpretation of local wisdom in using *P. angulata* extract as a promising cancer drug.

2. Improving Learning through ARPE Model

Analyzing

This analysis was conducted to determine the level of development needs of teaching materials enriched with the results of research Biology-related. Needs analysis is carried out in two stages. Firstly, the feasibility test of the results of research Biology-related. At this stage, the feasibility test is carried out by four experts and two practitioners to assess the feasibility level of the anticancer mechanism.

Table 6.
Feasibility assessment of the results of molecular docking for enriching teaching material.

Appraisal and Expertise Categories		Final Score	Average	Category
Experts	Biochemistry	79	87,00 ± 7,53	feasible
	Biology	83		very feasible
	Biology Education	96		very feasible
	Learning technologies	90		very feasible
Practitioners	Biology	92	90,50 ± 2,12	very feasible
	Biology Education	89		very feasible
Average			88,17 ± 6,18	very feasible

Starting from the description of the characteristics of the scientific information of the study above, the results of this study have the potential to be used as the primary material to enrich the lecture material, especially in Chemistry for Biology. The feasibility test of scientific information has been carried out by four experts and two practitioners. The results of the feasibility test are presented in Table 6. The average score of the feasibility test is good in the very feasible category (88.17 ± 6.18). This revealed that scientific information about the molecular mechanism of physalin

compounds from *P. angulata* extract as an anticancer can be used as material to enrich teaching material in Chemistry lectures for Biochemistry.

Secondly, an analysis of the suitability of learning outcomes with the results of research in the field of Biology was carried out by researchers with experts and practitioners through the Forum Group Discussion (FGD). The FGD aims to map patterns of conformity between the learning outcomes of Chemistry for Biology lecturing to the results research in Biology-related on the mechanism of anticancer.

Both of the experts and practitioners are provide recommendations that the results of research on the disclosure of the anticancer molecular mechanism of the active compounds of *P. angulata* can be used as material to enrich teaching material in Chemistry for Biology. Especially in aspects: interactions between ligands and macromolecules, binding affinity, type profiles and the number of chemical bonds that can be formed during molecular belaying between physalin and vismodegib with GLI1. This can be seen from the conformity of scientific information from the research results with the formulation of the learning outcomes of the course. Conformity can be mapped and presented in Table 7.

Table 7.
The conformity between the results of research with learning outcomes in Chemistry for Biology lecturing.

LO Code	National Learning Outcome (LO)	Code			
	Learning outcome of Biology Education charged to Chemistry for Biology lecturing	**A**	**B**	**C**	**D**
S1	Fear the Almighty God and be able to show religious attitudes				
S10	Demonstrate an attitude of responsibility for work in his area of expertise independently				
P2	Mastering the concepts of statistics, biophysics, chemistry, and biochemistry	v	v	v	v
KU1	Applying logical, critical, systematic, and innovative thinking in the context of developing or implementing science and technology by their fields of expertise	v	v	v	v
KU2	Able to demonstrate independent, quality and measurable performance				
KK2	Being able to apply biological science to be beneficial for themselves and society in everyday life				
LO Code	**Learning outcome of Chemistry for Biology lecturing**	**A**	**B**	**C**	**D**
M1	Students can describe the development of atomic theory and the discovery of elements				
M2	Skilled students determine the electron configuration of an element and its impact on the nature of the element and its grouping				
M3	Students can describe the characteristics of the types of chemical bonds and functional groups		v	v	v
M4	Students are able to describe characteristics reduction, oxidation, and redox				
M5	Students are skilled in basic chemical solutions (basic chemical calculations, chemical solutions, pH measurement techniques, and separation techniques)				
M6	Students can describe the characteristics of organic and aromatic compounds and their potential identification techniques	v			
M7	Students can describe polymer characteristics and their uses				

Description: A = exploration of physalin structures and database GLI1 molecules, B = interactions between ligands and macromolecules, C = binding affinity, D = profile type and number of chemical bonds that can be formed during molecular belaying between physalin and vismodegib with GLI1.

Reorganizing

This stage aims to reorganize learning variables, which include conditions, methods, and learning outcomes. Reorganization of learning variables is needed so that recommendations obtained at the analysis stage can be accommodated so that they can be used to improve the quality of learning. This stage is carried out collaboratively by researchers with colleagues in the form of FGDs so that the products produced do not need to be validated. FGD results: (1) the form of teaching material developed is power point. The power point that the lecturer already has is enriched with the results

of research on the anticancer mechanism of physalin compounds, (2) the TPS learning strategy is used by lecturers because the TPS has been used at the previous meeting, (3) The Science Motivation Inventory (SMI) instrument from Santoso (2017) was used to measure students' learning motivation. The CRI instruments from Primandiri (2017) was used to measure the level of understanding (misconception) of students. Both instruments are used before and after learning using research-based teaching materials. Both of student motivation and concept understanding were analyzed by descriptive. Data were analyzed descriptively and determined the value of Gain on changes in scores between before and after learning.

Piloting Class

Teaching materials that have been developed are tested on students who take Chemistry for Biology. Students who take part in this piloting were students who have misconceptions about the topic of chemical bonds (n = 12 students). At this stage, the lecturer uses the *Think Pair Share* (TPS) learning strategy for two meetings (4 x 50 minutes). Learning on Chemistry for Biology has been carried out according to the learning plan. The level of implementation of the learning stages by using TPS was carried out reached 98%.

Evaluating

The results of molecular docking research are integrated into the topic of chemical structures and bonds-scientific information from research results. The results of the trial revealed that the integration of the results of the research into teaching materials could increase student learning motivation (medium category) (Table 8). This reveals that the visualization of hydrogen bonding models and hydrophobic interactions between GLI1 and physalin compounds can attract students' attention. Visualization is done with the Pymol program. Chemical bonds can be visualized attractively (colored, three-dimensional, and dynamic). Students are also motivated to learn because the model used is a chemical bond model of compounds obtained from plants that are easily found around them, namely *P. angulata* or ceplukan (Java). This was revealed by the results of respondents with DN students who stated that *"it is more interesting because it answers my sense of enlargement why concomitant can be anti-cancer. It turns out that chemical bonds play an important role in the body"* (respondents' expression was paraphrased).

Table 8.
Profile of Student Response to Teaching Materials that Integrate Research Results.

Students Responses		Score	Gain Score	Category
Learning motivation	Before	68,08% ± 0,61	0,52	middle
	After	84,61% ± 0,68		
Understanding of concepts	Before	50,56% ± 8,64	0,48	middle
	After	74,44% ± 3,14		

Tested teaching materials are also able to improve understanding of the student's concepts about the structure of compounds and chemical bonds (medium category) (Table 8). Modeling the three-dimensional visualization of chemical bonds between physalin and GLI1 can help students learn more about the characteristics of hydrogen bonds. This is also in line with the statement of the AD students that "*I just found out that hydrogen bonds do not have to be formed from H atoms with H atoms and the color is exciting*" (the phrase has been paraphrased). The BL student also revealed that "*it turns out that hydrophobic interactions can be formed between C atoms and GLI1 amino acid residues*" (the student expression has been paraphrased).

Student learning motivation is very dynamic and can be increased if students find unusual behavior or rarely encountered (Moos & Honkomp, 2011; Ahn et al., 2016; Azrai et al., 2016) also visualization of concepts can also encourage students to become self-regulated learner (Maree et al., 2013; Rosamsi, et al., 2019). The use of media is also able to improve students academic abilities (Aloraini, 2010; Ristanto, 2011; Sartono et al., 2017) and participation in class (Acha et al., 2009; Ali et al., 2010; Abdullah et al., 2012). The contextualization of lecture material is very helpful for

students in understanding concepts (Primandiri; 2017; Santoso, 2017; Mahanal, Zubaidah, Sumiati, Sari, & Ismirawati, 2019). In organizational learning variables, research results can be used as case studies, problem-solving, and representative examples of knowledge (in the form of facts) (Pratama, 2018). Contextual learning is also able to motivate students to learn because students have a description of the object being studied more clearly and real by everyday life (Pintrich et al., 1993; Wuryaningrum; Sartono, & Dewahrani, 2014; Bustami, Syafruddin, & Afriani, 2018). The other hand, this research has also shown that lecturer must be able to design their learning for teacher candidate (Ristanto, Zubaidah, Amin., & Rohman, 2018). Teachers can make meaningful learning by linking concepts that will be taught to aspects of human life (Emenike et al., 2011) - stated that teachers need to think about how students can maintain their learning motivation in class so they can achieve achievement (Ames,1990; Fitriani et al., 2018; Ismirawati, Corebima, Zubaidah, & Syamsuri, 2018).

CONCLUSION

The mechanism of anticancer molecular action of *P. angulata* extracts can occur because *P. angulata* extract contains physain which can interact with GLI1. Interactions between physalin and GLI1 can be formed due to the existence of two types of chemical bonds, namely hydrogen bonds and hydrophobic interactions. Scientific information is very feasible to use as material for developing Chemistry teaching materials for Biology. The results of the trial revealed that visualization of chemical bond models based on research results could increase student learning motivation and can improve the student's concept understanding up to 0.48 (middle category).

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