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Original Article

GARLIC EXTRACT PHYTOSOME: PREPARATION AND PHYSICAL STABILITY

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ABSTRACT

Objective: Allicin is one of the components contained in garlic extract (*Allium sativum* L) and can easily be decomposed. To improve the chemical stability of allicin, a garlic extract was formulated in a phytosome system. Phytosomes, which are colloidal systems, are susceptible to ostwald ripening, which can result in an increase in particle size distribution. Changes in the size distribution indicate that the system is physically unstable. The aimed of the study was to test the physical stability of the garlic extract phytosome stored at three different temperatures for four weeks.

Methods: Garlic extract phytosomes (GEP) were prepared by the thin layer hydration method using garlic extract and lecithin at the same concentration of 4.5%. Furthermore, the phytosomes were stored at 4 °C, 25 °C, and 40 °C for four weeks. Every week, a physical evaluation was carried out (organoleptic, pH, density, particle size, polydispersity index, and zeta potential). The data obtained were analysed statistically using the Friedman test.

Results: The phytosome's organoleptic result showed separation at 4 °C and 40 °C, starting from the second week. The average particle size of phytosomes was 214.3 nm, the zeta potential value was -29.08 mV, and the polydispersity value was 0.46. The results of statistical analysis showed that the Asymp. Sig<0.05 indicated that the particle size, zeta potential, polydispersity index, pH values, and density were significantly different at each week and storage temperature.

Conclusion: Conclusion based on study indicated a decrease in the physical stability of phytosomes, especially those stored at extreme temperatures (4 °C and 40 °C).

Keywords: Allicin, Garlic extract, Phytosomes, Particle size, Zeta potential, Stability

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INTRODUCTION

A previous study showed that blood glucose levels in mice could be reduced by 400 mg/kgBB of garlic methanolic extract [1]. Garlic extract can lower blood sugar levels because it contains allicin [2]. To facilitate the use of this extract in treating diabetes, it is necessary to convert it into a dosage form. Other research has shown that garlic tablets containing 0.6% allicin can reduce fasting blood sugar in type 2 DM patients during 24 w of testing by 3.12% when combined with metformin [3]. That study also showed that the activity of lowering blood sugar was higher due to the combination compared to metformin alone.

Allicin is a compound that easily decomposes due to environmental factors, such as temperature and pH [4-6]. The decomposition takes time to form stable sulfur compounds [7]. Chemical stability and absorption of allicin contained in a garlic extract can be increased through the formation of phytosomes with the help of lecithin as a phospholipid-binding compound [8]. Compared with traditional herbal products, phytosomes can enhance the potency of the pharmacological effect because the medicinal ingredients are protected in the vesicle wall so that they are less likely to decompose [9, 10]. Cancer treatment research using an ethanol extract of garlic in phytosomes showed that 100% of the phytosomes at 108.5 µg/ml are toxic to cancer cell lines (MCF 7) [11]. With the potential of allicin contained in a methanolic garlic extract, it is essential to formulate garlic extract phytosome to optimize the use of allicin in treating diabetes.

Good physical stability is an important indicator of good-quality systems. A system or preparation that is physically stable during storage is indicated by the absence of changes in physical properties [12]. Nevertheless, phytosomes are susceptible to particle size changes because phytosome membranes tend to undergo degradation, fusion, and aggregation within vesicles. Studies on several other vesicle systems (transetosomes and transfersomes) showed that after several months of storage, the particle size of the vesicles increased progressively [13, 14].

For this reason, this study aimed to test the physical stability of garlic extract phytosomes stored at three different temperatures for four weeks to determine the storage temperature at which the physical stability of the phytosomes is sound.

MATERIALS AND METHODS

Materials

Garlic methanol extract (Lansida, Indonesia), soy lecithin (Lansida, Indonesia), S-Allyl-2-propane-1-sulfonic thioate (Sigma Aldrich, Singapore), ethanol 70% (Merck, Germany), dichloromethane (Merck, Germany), potassium dihydrogen phosphate (Merck, Germany), sodium hydroxide (Merck, Germany), hydrogen disodium phosphate (Merck, Germany), and aquadest. Further apparatus and analysis equipment used included a Spectrophotometer UV-Vis 1601 (Shimadzu, Japan), DelsaMax particle size analyser (Beckman Coulter, Singapore), transmission electron microscopy (Jeol JEM-1010, Singapore), and pH meter (LaMotte, USA).

Methods

Production of garlic extract

Garlic extract was made by maceration for 48 h using 1000 grams of garlic powder and 5000 ml of ethanol. Furthermore, it was filtered using Whatman No. 1 filter paper and evaporated at 40 °C to obtain a condensed extract [1].

Phytosome optimization

Optimization of the phytosomes in this study was done to determine the concentration (extract and lecithin) and preparation conditions (temperature and speed of stirring). In this study, the RSM (response surface methodology), together with the CCD (central composite design) was applied to simulate the phytosome characteristics. According to available studies on garlic extract activity and phytosome preparations, the four significant independent variables were selected to run RSM-CCD (table 1a), namely, concentration of garlic extract, concentration of lecithin,

temperature, and stirring speed were considered. All four independent variable parameters were considered at five levels (−α, −1, 0,+1,+α). Response variables (table 1b) used in formula optimization includes particle size, zeta potential, polydispersity index, entrapment efficiency, and density. Based on RSM-CCD, 30 experiments were obtained (table 2).

Table 1: Independent variables of GEP (a), and responses variable for RSM-CCD runs (b)

			Level				
Independent variables	**Symbol**	**Units**	**−α**	**−1**	**0**	**+1**	**+α**
Concentration of garlic extract	A	%	3	4.5	6	7.5	9
Concentration of lecithin	B	%	3	4.5	6	7.5	9
Stirring speed	C	rpm	50	75	100	125	150
Temperature	D	Celcius	25	30	35	40	45
					Constraints		
Response variables	Symbol	Units	Obs	Analysis	Goal	Lower limit	Upper limit
Entrapment efficiency	Y1	%	30	Polynomial	Maximize	37.2354	92.7226
Particle size	Y2	nm	30	Polynomial	Minimize	190.4	694
Polydispersity index	Y3	-	30	Polynomial	Minimize	0	0.571
Zetta potential	Y4	mV	30	Polynomial	Maximize	1.37	53.15
Density	Y5	g/ml	30	Polynomial	Is target = 1	1	1.0322

Table 2: The matrix of experimental values of response variables from RSM-CCD experimental design

Run	**Independent variables**				**Response variables**				
	A	**B**	**C**	**D**	**Y1**	**Y2**	**Y3**	**Y4**	**Y5**
1	7.5	4.5	125	40	69.494	212.9	0.571	18.12	1.0237
2	6	6	100	35	92.7226	190.4	0.571	4.33	1
3	4.5	7.5	75	30	71.3422	219.8	0.571	27.27	1.0188
4	7.5	4.5	75	30	43.6837	260.6	0.571	25.49	1.0271
5	4.5	7.5	125	40	59.4557	694	0.19	1.37	1.219
6	7.5	7.5	75	40	73.9598	624.3	0.19	4.73	1.0139
7	7.5	7.5	125	30	80.1088	434.9	0.571	3.51	1.0142
8	6	6	100	35	66.9369	303.3	0.571	15.88	1.013
9	4.5	4.5	125	30	64.4466	330.2	0.571	27.88	1.0034
10	4.5	4.5	75	40	64.3559	373.7	0.571	16.6	1.0081
11	4.5	4.5	75	30	69.3217	384.2	0	13.42	1.0133
12	7.5	4.5	125	30	75.2103	340.2	0.571	32.09	1.0233
13	7.5	7.5	75	30	66.2674	501.6	0	20.65	1.0258
14	7.5	4.5	75	40	63.5148	293.6	0.571	37.21	1.0322
15	7.5	7.5	125	40	53.3698	219.2	0.571	17.48	1.0228
16	4.5	4.5	125	40	49.4948	279.7	0.571	23.14	1.0199
17	6	6	100	35	50.4389	259.6	0.571	47.37	1.0229
18	6	6	100	35	37.2354	221.3	0.571	44.26	1.0109
19	4.5	7.5	125	30	59.0405	440.3	0	19.44	1.0206
20	4.5	7.5	75	40	68.688	424.7	0.571	36.1	1.0203
21	6	6	50	35	65.9282	328.8	0.571	39.21	1.0244
22	9	6	100	35	56.3523	386.2	0	20.8	1.0259
23	6	6	100	35	41.9372	449.1	0.571	47.68	1.0197
24	3	6	100	35	43.9952	211	0.571	51.5	1.0154
25	6	3	100	35	63.8584	223	0.571	53.15	1.0205
26	6	6	100	45	71.5393	433.4	0	45.04	1.0242
27	6	6	100	35	62.1885	399.3	0.571	45.79	1.0249
28	6	9	100	35	64.6292	389.4	0.571	39.77	1.0187
29	6	6	150	35	66.79	260.2	0.571	40.19	1.0196
30	6	6	100	25	61.7163	293	0.571	41.82	1.0122

Production of GEP

First, dichloromethane was used to dissolve lecithin, while ethanol was used to dissolve garlic extract, and then the two solutions were mixed until homogeneous. Additionally, a thin layer was formed by evaporating dichloromethane at 30 °C and 125 rpm and stored at a temperature of 2-8 °C for 24 h. After that, hydrate the thin layer using a pH 5.5 buffer solution of 40 °C. Lastly, sonicate for 2 min [15].

Entrapment efficiency

Entrapment efficiency measurement [16] was done by separating the free active compound (supernatant) from 0.5 ml of the sample using centrifugation for 1,5 h at 14000 rpm. Then, the volume of the supernatant was made up to 10 ml with phosphate buffer pH 6.8. After that, the free allicin content was determined using a UV-Vis spectrophotometer. Finally, the allicin entrapment efficiency was calculated using Equation 1:

$$\% \text{ Entrapment efficiency} = \frac{\text{Total allicin in suspension} - \text{Free allicin concentration}}{\text{Total allisin in suspension}} \text{x } 100\%$$

Vesicle morphology

Morphological determination was performed by dissolving 1 ml of GEP optimal formula in 1 ml aqua pro injection. Then, 5µl of the solution was dripped onto a carbon copper-coated grid and allowed to dry. Next, 0.5% uranyl acetate (UA) was added and observed under a microscope with various magnifications.

Physical stability of GEP

The optimal formula obtained based on the RSM-CCD is then used in physical stability screening. Physical stability screening was done by storing the phytosomes for four weeks at 4 °C±2 °C, room temperature (25-30 °C±2 °C), and 40 °C±2 °C [17]. Organoleptic parameters observed in this study included odour, colour, and homogeneity. Measurement of pH [18] was done using a pH meter. Specifically, electrodes were calibrated using the standard buffer solution with pH 4 and 7, and then the pH value of the phytosome was determined. Further, density measurement was done using a pycnometer [18]. The average particle size, polydispersity index, and zeta potential were

determined by diluting the sample in distilled water (1:9), and then measurements were made using a particle size analyser instrument [19].

Data analysis

The data from physical stability were statistically analysed using the non-parametric Friedman test with Asymp. Sig 0.05 (*P<0.05).

RESULTS

Garlic extract

From the extraction results, 3,430 kg of extract was obtained, and the yield percentage was 15.9638%. The resulting garlic extract is a condensed liquid with a distinctive garlic odor, blackish-brown color, and bitter taste. Other physical parameters (table 3) determined are pH value, water content, total ash content, acid insoluble ash content, and determination of allicin content.

GEP optimization

Table 4 showed the suggested statistical analysis model for each response variable. Three response variables were suggested to be analyzed using the 2 FI (two factors interaction) model, and two other response variables were suggested to be analyzed statistically using the linear model.

Table 3: Characteristics of garlic extract

Parameters (units)	Result
Value of pH	6.6
Water content (%)	1.21
Total ash content (%)	3.43
Acid insoluble ash content (%)	0.15
Allicin content (%)	11.29

Table 4: Statistical analysis of response variables from RSM-CCD

	Response variables				
	Entrapment efficiency	Particle size	Polydispersity index	Zetta potential	Density
Model	2FI	Linier	2FI	Linier	2FI
Mean	62.6007	346.063	0.450433	28.7097	1.01872
Std. Dev.	12.46	119.39	0.26	10.19	5.055E-003
R2	0.2570	0.2283	0.2068	0.1969	0.6362
Adj. R2	-0.1800	0.0941	-0.2597	0.0573	0.4222
Equation	Y1 =+62.60+1.84*A+1.43*B-0.37*C-0.31*D+0.68*A*B+4.50*A*C+1.08*A*D-2.88*B*C-0.97*B*D-4.18*C*D	Y2 =+346.06+3.80*A+59.02*B-11.18*C+20.46*D	Y3 =+0.45-0.024*A-0.056*B+0.024*C-7.958E-003*D-0.036*A*B+0.083*A*C-0.036*A*D-0.036*B*C-0.012*B*D-0.036*C*D	Y4 =+28.71-2.81*A-3.76*B-1.52*C-0.36*D	Y5 =+1.02+3.237E-003*A+1.542E-004*B-8.042E-004*C+1.679E-003*D-4.156E-003*A*B-1.269E-003*A*C-7.437E-004*A*D+6.938E-004*B*C-1.081E-003*B*D+2.331E-003*C*D

Table 5: Optimal formulation

Independent and response variables	Result of optimal formulation		
	1	2	3
Concentration of garlic extract (%)	4,50	4,50	4,50
Concentration of lecithin (%)	4,50	4,51	4,50
Temperature	30,00	30,01	30,01
Stirring speed	125,00	122,50	121,20
Entrapment efficiency (%)	62,6241	62,3947	62,2888
Particle size (nm)	251,605	253,04	253,329
Polydispersity index	0,466267	0,464897	0,464543
Zeta potential (mV)	-34,1088	-34,2422	-34,3376
Density (g/ml)	1,0051	1,0054	1,00551
Desirability	0,523	0,523	0,522
	Selected		

The results of the RSM-CCD analysis selected an optimal design, namely a concentration of garlic extract and lecithin of 4.5%, a temperature of 30 °C, and a stirring speed of 125 rpm (table 5 and fig. 1). The results of the optimal formula evaluation can be seen in table 6.

Table 6: The evaluation results of GEP

Parameters	Results
Organoleptic	Brown liquid has a distinctive garlic aroma and has a bitter taste
Density	1.0051 g/ml
Zeta potential	-32.55 mV
Polidispersity index	0.571
Particle size	270 nm
Entrapment efficiency	64.8798 %

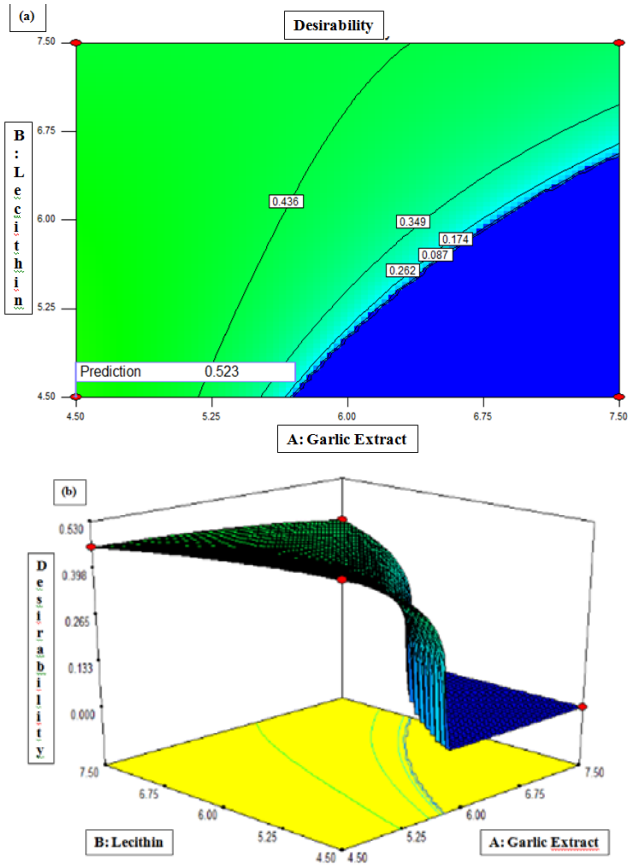

Fig. 1: Contour plot of the desirability value (a), and three-dimensional graph of the desirability value of the GEP optimal formula (b)

Vesicle morphology

Phytosomes obtained have a spherical shape with different sizes (fig. 2). This was in agreement with the results of polydispersity, which showed that phytosomes were a polydisperse system. Additionally, a white part was observed on the surface of the vesicle, which might be a garlic extract that was not entrapped and adhered to the surface of the vesicle. However, further research is needed to confirm this.

Physical stability of GEP

Phytosomes had not shown changes in colour and odour during the storage period. However, regarding homogeneity, samples showed separation at 4 °C and 40 °C in the second week. The separation occurred because lecithin, one of the components that form the vesicle wall, was damaged, causing the vesicle wall to break and the phytosomes to release the entrapped active ingredients. Phase separation occurred at 4 °C due to the phase transition temperature of lecithin being below 10 °C and more than 160 °C [20]. While phase separation at 40 °C is caused by an increase in kinetic energy leading to a tendency of the particles to stretch. In addition, an increase in temperature can accelerate the decomposition of the compound compared to normal temperatures [12].

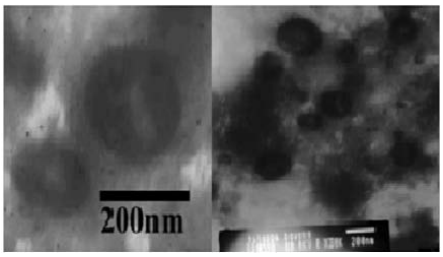

Fig. 2: TEM image of PGE at a magnification of 30,000

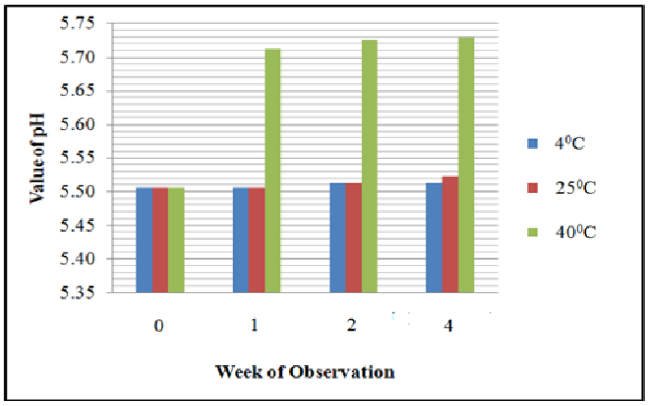

Fig. 3: Mena value of pH of GEP

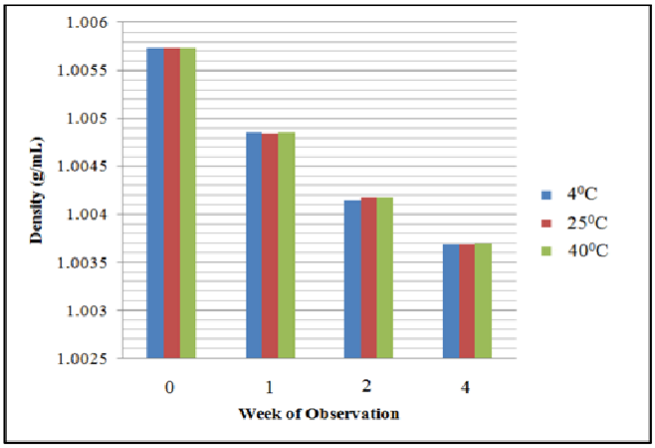

Fig. 4: Mean density of GEP

Table 7: Result of the physical stability test

Temperature	Evaluation	Week of observation			
		0	1	2	4
4 °C	Particle size (nm)*	214.3±1.32	217.86±0.51	242.8±15.88	307.36±10.55
	Zeta potential (mV)*	-29.08±0.85	-28.52±0.79	-28.45±2.61	-33.82±12.31
	Polidispersity*	0.46±0.12	0.45±0.04	0.56±0.02	0.57±0.0
25 °C	Particle size (nm)*	214.3±1.32	219.16±0.65	286.9±3.27	321.36±1.62
	Zeta potential (mV)*	-29.08±0.85	-27.98±0.99	-27.49±2.75	-34.96±11.15
	Polidispersity*	0.46±0.12	0.46±0.10	0.57±0.0	0.57±0.0
40 °C	Particle size (nm)*	214.3±1.32	227.33±3.57	292.8±2.07	358.6±45.5
	Zeta potential (mV)*	-29.08±0.85	-29.45±1.75	-24.84±4.08	-33.29±8.45
	Polidispersity*	0.46±0.12	0.46±0.08	0.57±0.0	0.57±0.0

*n=3

DISCUSSION

The water content of garlic extract meet the requirements as stated in the monograph, not more than 10% [21]. Based on these results, garlic extract does not quickly grow with microorganisms, so the extract's quality can be maintained during the storage period. The total ash content in the garlic extract is greater than the standard 2.7 [22], this indicates a high mineral content (carbon metal) in the extract so that the purity is low. Another study reported a total ash value of 3.5-3.7% using the gravimetric method, where the total ash value shows the mineral content which is influenced by the raw conditions of the garlic used and the planting area [23].

Phytosomes are heterogeneous systems that belong to colloidal dispersions. Factors that influence the formation of heterogeneous systems vary greatly, including stirring time, stirring speed, oil phase concentration, surfactant concentration, ratio between oil and surfactant phases [24, 25]. In this study, extract concentration (active ingredient), lecithin (surfactant) concentration, stirring temperature, and stirring speed were used as independent variables that could affect the formation of phytosomes. In many studies, RSM is used to investigate various factors that can affect the quality of preparations so that optimal conditions can be obtained that can produce preparations with good characteristics [24-28]. The advantage of RMS is that it can reduce the number of experiments that take time and money [29].

In the statistical analysis equation in table 4, it can be seen that there are positive and negative coefficients. A synergistic effect on the response will be seen if the coefficient is positive. On the other hand, those with negative coefficients have an antagonistic effect, thus showing an inverse relationship between the independent variable and the response variable [30, 31]. Based on the equation resulting from statistical analysis, it is known that particle size is greatly influenced by the stirring speed because it has a negative coefficient value with a p-value<0.01. This can also be seen in the formation of other colloidal systems, namely nanoemulsions, and nanophytosomes, that the greater the stirring speed used will reduce the size of particles in the system [25, 32]. Meanwhile, zeta potential is influenced by all independent variables (a p-value<0.01), in the order of the largest to the smallest influence, namely lecithin concentration>extract concentration>stirring temperature>stirring speed. Several factors that can influence zeta potential were the physicochemical properties of compounds (drug, polymer, carrier, emulsifiers), the presence of electrolyte, and adsorption on surface areas [33].

Meanwhile, the response variable using the 2FI model shows that each independent variable and the interaction of the two independent variables can influence the response variable. In the response variable of entrapment efficiency, it can be seen that the most influencing factor was the interaction between stirring speed and temperature (a p-value<0.01). Phytosomes are a vesicle system, the increasing rate of stirring used in the thin layer hydration method made the walls of the vesicles that have been formed damaged, resulting in smaller vesicle sizes and releasing allicin previously entrapped in the system. Both lecithin and allicin are known to be materials that are sensitive to temperature [6, 20]; increasing the temperature used in producing phytosomes can also result in the destruction of these two materials so that the amount of allicin trapped in the vesicle walls will decrease. Whereas the response variables of the polydispersity index and density showed that the independent variables and the interactions that occur between the independent variables have the same magnitude of influence.

The entrapment efficiency describes the level of allicin that is entrapped in phytosomes. The results of the phytosome entrapment efficiency obtained were 64.8798%, where the phytosome suspension was made by mixing garlic extract with lecithin in the same % ratio of 4.5%. Generally, a phytosome suspension is prepared with a specific molar ratio (usually 1:1 to 1:3) between the phytoconstituents and phosphatidylcholine, resulting in a complex with stronger bonds because one molecule of phytoconstituent will be bound by one molecule of phosphatidylcholine [34, 35]. The low-efficiency results can be influenced by several factors, including

those that affect the formation of a thin layer (speed, temperature, and duration), the hydration process, and the lack of lecithin concentration to bind the entire active substance [36]. Another study made quercetin phytosomes using the same method (thin layer hydration) but with a quercetin: phosphatidylcholine ratio of 1:2, resulting in a higher entrapment efficiency value of 97.67% [37]. Other research shows that the entrapment efficiency of liposomes containing garlic extract is 47.5±7.3%, which shows that phytosome can increase the entrapment of active ingredients in the vesicle system [38]. Other studies have shown that the method of producing phytosome can produce different entrapment efficiency values even though the ratio used is the same [32]. Nazeer *et al.*, 2017 reported that garlic extract phytosomes made using the solvent evaporation method with a ratio of 1:1 produced an entrapment efficiency of 97.306% [11].

The phytosome system has a pH value of 5.5 (fig. 3), so it can be given orally or topically. The advised pH value of the system should be 5.5-7.5 when given orally and 4.5-6.5 when given topically [39]. Results showed the most significant change in pH value at 40 ˚C compared to other temperatures. In addition, lecithin is an amphoteric surfactant that can function both as an acid (releasing hydrogen ions) and as a base (giving hydroxyl ions), which can cause changes in pH values [12]. An increase in temperature also indicates a tendency to increase the degree of basicity possessed by lecithin. Statistical analysis showed that the Asymp. Sig<0.05 indicated that storage duration and temperature could affect the pH value.

The phytosome system has a low-density value of 1.0057 (fig. 4), indicating that the phytosome can flow properly and is easily pourable. Changes in density values showed that, at all temperatures and times of storage, phytosomes tended to decrease in density. The decrease in density indicated a decrease in the viscosity of the system so that vesicles could move more readily in the system. This can lead to higher collisions between vesicles and could cause vesicles to coalesce into larger particles [40]. Changes in temperature will affect the kinetic energy possessed by the particles, causing spaces between the particles to vary and particles to be further apart or closer together, which will change the particle density [12]. Based on statistical analysis (Asymp. Sig<0.05), storage duration and temperature can affect the density value.

Phytosomes are nanoparticles because they have a small vesicle size to improve the penetration of active compounds [41]. Based on the results, phytosome vesicles have a particle size of 214.3 nm, indicating that garlic extract phytosomes are nanoparticles. Other research has also shown that 246.1 nm of phytosome evodiamine played a significant role in the sustained release and enhancement of evodiamine's oral absorption efficiency [42]. In another study, phytosomes of garlic extract had a particle size of 270 nm, indicating that the rate of diffusion of allicin was greater than in the form of extract alone [43]. Based on the particle size, the phytosome of garlic extract was appropriate for oral and topical drug delivery. Moreover, the most significant increase in particle size was seen after four weeks of storage at all storage conditions. This could be due to a greater attractive force between particles, causing nano-sized particles to join together to form aggregates so that they tend to become larger [12]. Several other studies also reported an increase in the particle size and polydispersity index of phytosomes after being stored for 1 mo at 25°C due to the low zeta potential value [32].

The distance between particles and the surface charge of particles can be revealed by zeta potential. The possibility of particles forming aggregates is low if the zeta potential is higher, and the system can be said to be stable [44]. More specifically, the stability of the nanoparticles is indicated by a zeta potential value greater than 30 [44]. The higher zeta potential value can prevent similar particles from approaching each other because of the high charge contained in each, resulting in a more stable system [45]. Furthermore, it was previously shown as a characteristic property of particles for attraction followed by flocculation to exceed repulsive forces if the zeta potential was in the range of-20 to 30 mV [46, 47]. The results showed a zeta value of-29,08 mV, indicating that the phytosome has poor stability due to a zeta potential lower than 30 mV. In table 7, it can be seen that in the fourth week, the phytosomes showed a zeta potential of more than-30 mV at all temperatures, indicating that the GEP vesicles took up to four weeks to attain stable conditions. Further research is needed to confirm this.

The polydispersity index provides information about the distribution of particle size in the systems. The homogeneity of the particle size can also be evaluated based on the polydispersity (PD) value. A system can be classified as monodispersed if it has a small PD value. The monodispersed or homogeneous system has a PD value of less than 0.15, while the polydisperse or heterogeneous system has a PD value greater than 0.35 [48]. Therefore, garlic extract phytosome is a polydisperse system because it has a PD value of 0.458. In addition, the statistical analysis resulted in Asymp. Sig<0.05, indicating that the particle size, zeta potential and polydispersity index were significantly affected by temperature and storage time.

The garlic extract can also be trapped in phytosome vesicles by showing a rounded vesicle shape. However, phytosome vesicle walls could not maintain particle size and zeta potential for four weeks of storage, and extreme temperatures could increase these changes. Changes in particle size and zeta potential in colloidal dispersion systems such as phytosomes can be minimized by increasing consistency through the addition of thickening or gelling agents. Mixing a thickening or gelling agent with phytosomes will create barriers between vesicles that inhibit them from agglomerating or coalescing, thereby increasing stability and extending the shelf life of garlic extract phytosomes.

CONCLUSION

There is a decrease in the physical stability of phytosomes, especially those stored at extreme temperatures(4 and 40˚C) cause by lecithin's phase transition temperature and phytosomes's kinetic energy.

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AUTHORS CONTRIBUTIONS

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CONFLICT OF INTERESTS

"The authors declare that there is no real, potential, or perceived conflict of interest for this article."

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