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INTRODUCTION Indonesia is a maritime country with considerable potential as a producer of marine animals, primarily natural sources of chitin, such as shrimp and crab shells1. Shrimp shell contains 25-40% protein, 45-50% calcium carbonate, and 15-30% chitin, but the amount of the content depends on the type of shrimp2. In this study, chitin was extracted from whiteleg shrimp (Litopenaeus vannamei) because it was ranked first of the five primary commodities trafficked in the country (between provinces) as much as 72.81%.

This fact means that a lot of shrimp production has been distributed to regions between provinces. East Java is the second-highest province after Bengkulu (37.84%) as an L. vannamei supplier with 24.49%3. However, chitin is not soluble in water, so its use is limited. By using a strong base (deacetylation process) into chitosan, hydrolyzing chitin has better chemical properties4. Chitin can be transformed into chitosan, which has prospects in biomedical trends5. Besides being known as a drug carrier, chitosan is also known as an active agent for anticholesterol.

The previous research reported that in vitro, chitosan could bind cholesterol by 63.5% to prevent an increase in cholesterol levels6. A study stated that administering 30 chitosan tablets at a dose of 45 mg of chitosan/tablet three times a day can reduced cholesterol levels7. However, chitosan has poor solubility in water, but the permeability is high, so efforts are needed to increase the solubility so that chitosan can be used as an anticholesterol drug.

Solid dispersion is a method of making a dispersion system where drugs with low solubility in water will be dispersed into a water-soluble carrier to increase the solubility and dissolution of the drug8,9. The carrier used in this solid dispersion formulations is PVP K-30 because its polymer is hydrophilic, has very good water solubility, and can be used as a stabilizer10. The results of the chitosan solid dispersion formulation were hence made into direct compression tablets. The direct compression method was chosen because it is the most energy-efficient, fastest, and most economical way to produce tablets11.

Based on this background, research will be carried out to formulate and evaluate the solid dispersion tablet using chitosan extract from L. vannamei as an active agent with PVP K-30 as a carrier in the ratio of 1 : 1 and 1 : 3 (Chitosan : PVP K-30). Evaluation of solid dispersion tablets is weight and size uniformity, hardness, friability, and disintegration time. MATERIALS AND METHODS Materials The L. vannamei was obtained from Pasuruan, East Java. The reagents used include HCl (Merck), NaOH (Merck), ninhydrin solution, distilled water (Brataco), PVP K-30 (Merck), magnesium stearate, talk, and Avicel PH 102 (Mingtai). Methods Chitosan synthesis Pre-treatment:

The shell of L.

vannamei was washed with running water and boiled for 15 minutes. The clean shell dried in the sunlight for 2 x 24 hours or until dry. The dried shell was blended with a blender until smooth and sieved with 100 mesh12. Demineralization: 100 g of the sifted shell of L. vannamei powder was weighed. 1M HCl solution was added while stirring with a magnetic stirrer with a speed of 200 rpm at 75°C for an hour. The solution was filtered with filter paper, and rinse the residue with distilled water until neutral pH. The residue was dried in the oven at 60°C for 24 hours or until it dries12. Deproteination: The dry solids demineralized were dissolved in 3.5% NaOH while stirring with a magnetic stirrer speed of 450 rpm at 65°C for 2 hours. The mixed solution was filtered with filter paper, and the residue was rinsed with distilled water until neutral pH.

The residue was dried in the oven at 65°C for 24 hours or until it dries13. Deacetylation: Chitin from the deproteination was dissolved in 60% NaOH with ratio of 1 : 20 (w/v). The solution was stirred using a magnetic stirrer with 250 rpm at 100°C for 4 hours. The mixed solution was filtered with filter paper. The residue was rinsed with distilled water until neutral pH and dried in an oven at 65°C for 24 hours or until it dries13,14. Chitosan evaluation Chitosan from synthesis was evaluated by organoleptic, yield, ninhydrin, and deacetylation degrees15,16.

Solid dispersion procedure Chitosan and PVP K-30 was prepared in a ratio of 1 : 1 and 1 : 3 (w/w). Chitosan was dissolved in 2% acetic acid (1 : 50) and stirred until it dissolves. PVP K-30 as a carrier was dissolved in (1 : 5) of 2% acetic acid solvent. Both solutions were mixed and evaporated above the water bath in a fume hood at 50-60°C until a precipitate was formed. The evaporation results were dried in the oven at 50°C for 1-2 hours or until it dries. The masses were crusted and sieved with 100 mesh sieves17. Tablets formulation Chitosan and PVP K-30 solid dispersion were prepared as well as weighed magnesium stearate, talk, and Avicel PH 102 which was sieved with a mesh 100 sieve.

That ingredient was mixed until homogeneous. Therefore, the tablets were compressed by the direct compression method. The tablets were observed and evaluated (uniformity in tablet weight and size, hardness, friability, and disintegration time)18. Experimental design The dose of chitosan as an active pharmaceutical ingredient (API) was 45 mg/tablet by the study of Jing et al.7. The formulas were divided into three groups (n = 3). The division of groups was arranged based on different materials as follows: F1 (control): Pristine chitosan as an active agent F2: Chitosan : PVP K-30 solid dispersion (1 : 1) (w/w). F3: Chitosan : PVP K-30 solid dispersion (1 : 3) (w/w).

RESULTS AND DISCUSSION The formulation of solid dispersion tablets of chitosan extract from L. vannamei shell with PVP K-30 as a carrier of solid dispersion started with chitosan synthesis. From these stages, the chitosan obtained was then evaluated. The evaluation results were presented in Table I, while the chitosan powder appearance was presented in Figure 1. Table I. Result of chitosan characterization from L. vannamei shell Parameter _Chitosan characterization _Result _Interpretation _ _Shape _Flakes to powder _Powder _Good _ _Color _Light brown to white _Creamy white _Good _ _Deacetylation degree _<70% _74.02% _Good _ _Ninhydrin _(+) Changes to purple _(+) Changes to purple _Good _ _Yield _- _16.21 % _- _ _ / Figure 1.

Chitosan powder F1 From the evaluation of chitosan, it could be stated that chitosan had fulfilled all the evaluation requirements that exist from organoleptic (shape and color) which was creamy white19, deacetylation degree with 74.02% (>70%)20, and ninhydrin test with positive purple6. The yield test was a chitosan recovery test compared to the amount of shrimp shell used. The yield test result was 16.21%, which was higher than the previous research result which was 15.26%.21. Hence, the chitosan was made into a solid dispersion system to increase chitosan solubility, except for F1 as control, and then formulated into tablet preparations as showed in Table II.

The direct compression method carried out the tablet formulation and used additional ingredients to formulate the direct compression tablet method with good flow and compactibility, as shown in Figure 2. Table II. Formulation of solid dispersion tablet chitosan Material _Use _F1 (control) _F2 (1 : 1) _F3 (1 : 3) _ _Chitosan _Active agent _45 mg _45 mg _45 mg _ _PVP K-30 _Carrier _- _45 mg _135 mg _ _Mg Stearate _Lubricant _1% _1% _1% _ _Talk _Glidant _2% _2% _2% _ _Avicel PH 102 _Diluent _ad 350 mg _ad 350 mg _ad 350 mg _ _ / Figure 2. Solid dispersion of F2 (left) and F3 (right) Evaluation of dispersion tablet started with weight uniformity.

The result from this evaluation was all three formulas had good uniformity and none of the tablets out from A and B column18. The statistical analysis with one-way ANOVA shows that sig. 0,000. Moreover, the LSD (Least Significant Difference) shows that F2 and F3 significantly different from F1. Therefore, a solid dispersion tablet made an impact on chitosan without solid dispersion making. The uniformity size from F1, F2, and F3 fulfill the requirements18, which was ? T < D < 3T. T was the thickness, and D was the diameter. F1 was 1.25 < 11.14 < 11.25; F2 was 1.27 < 11.29 < 11.40; and F3 was 1.27 < 11.09 < 11.40.

The statistical analysis with Kruskal-Wallis from diameter shows that asymp. Sig. 0.000. Furthermore, Mann-Whitney Test shows that all the formulas had significantly different from each other. However, the Levene Test's statistical analysis from tablet thickness

shows that the result was not significantly different from each other. The tablets were also tested using the hardness tester. The requirement for tablet hardness was 4-8 kg22. The average hardness from F1 was 1.975 ± 0.444 kg; F2 was 1.175 ± 0.494 kg; and F3 was 4.275 ± 1.482 kg. It shows that F3 was the best hardness character and the one hardness that fills requirements22. F3 was chitosan without made solid dispersion.

Development formula from direct compression tablets was required to generate good hardness tablet quality. The statistical analysis with Kruskal-Wallis from the hardness test shows that asymp. Sig. 0.000. Moreover, Mann-Whitney Test shows that all the formulas had significantly different from each other. The tablet friability from all formulas was not too good. The requirements were <1%23, while F1 friability was 6.05%, F2 was 46.25%, and F3 was 1.44%. Necessarily, formula development made the tablet more compact and had a good binding, so it was not too weak and brittle.

Wet granulation could be considered to made better compactibility because the wet granulation method made intragranular bonding (formed during granule drying) that did not seem broken during compression, the cohesion of particles and binders carrier-binding adhesion was a type of bond that contributes to the strength of the tablet11. The last evaluation was disintegration time. The requirement of disintegration time was no more than 15 minutes18. The result for F1 was 4.33 ± 0.819 s; F2 was 20.67 ± 2.33 s; and F3 was 33.17 ± 9.43 s. The tablets had so fast disintegration time because the friability was weak and did not fill the requirements. Necessarily, formula development made the tablet more compact and had a good binding, not too weak and brittle.

The statistical analysis with Kruskal-Wallis from disintegration time shows that asymp. Sig. 0.001. Furthermore, by Mann-Whitney Test show that all the formulas had significantly different from each other. The overall results of the evaluation and characterization were presented in Table III. Table III. Result of solid dispersion chitosan tablet characterization Characteristic tablet _F 1 _F2 _F3 _ _Diameter (mm) _11.14± 0.046 _11.29± 0.255 _11.09± 0.040 _ _Thickness (mm) _3.75±0.415 _3.80±0.474 _3.80±0.394 _ _Weight variation (g) _0.3575± 0.010 _0.3435± 0.007 _0.3480± 0.006 _ _Hardness (kg) _1.98±0.44 _1.18±0.49 _4.28±1.48 _ _Friability (%) _6.05 _46.26 _1.44 _ _Disintegration time (s) _4.33±0.82 _20.67±2.34 _33.17±9.43 _ _The direct compression method had the limitation that could ensue segregation and poor compressibility compared to the wet granulation method. Differences in density between materials could cause segregation24.

That could also cause the evaluation of hardness and friability in this study to be unfavorable. Further method development was needed to provide better research, such

as using the wet granulation method. CONCLUSION In conclusion, Formula F1, F2, and F3 meet the requirements for uniformity of weight and size as well as disintegration time. The hardness of F3 is better than F1 and F2. Statistical analysis from weight uniformity, hardness, and disintegration time give a significant difference—obligatory formulation developing to make better tablet's compactibility.

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