



## Formulation and Evaluation of Tetanus Leaf (*Leea aequata* L.) Ethanol Extract on Tablet Preparation using Wet Granulation Method

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### Abstract

Degenerative diseases are currently widely suffered, especially in Indonesian society, as many as 30% of the population is detected with degenerative diseases. One alternative treatment that is widely consumed by Indonesian society is herbal or traditional medicine, one of the plants that is widely consumed by society, especially in Indonesia, namely Tetanus *Leea Aequata* L leaves. These leaves are often found, especially in the Karo area. The purpose of this study was to use ethanol extract of tetanus *Leea Aequata* leaves as tablets using the wet granulation method. The content contained in the leaves, such as Flavonoids, can be used as an alternative medicine to treat degenerative diseases by using a comparison of muchilago amyli used as a binder, namely f1 20%, f2 10% and F3 5% based on this study, a formula was obtained that can be used to make tablets, namely formula 1 20% muchilago amyli

### Abstrak

Penyakit degeneratif saat ini merupakan penyakit banyak diderita khususnya pada masyarakat Indonesia sebanyak 30 % populasi terdeteksi penyakit degeneratif. Salah satu alternatif pengobatan yang banyak dikonsumsi oleh masyarakat Indonesia yaitu pengobatan obat herbal atau tradisional salah satu tanaman yang banyak dikonsumsi oleh masyarakat khususnya pada Indonesia yaitu daun Tetanus *Leea Aequata* L daun ini banyak dijumpai khususnya pada daerah Karo. Tujuan dari penelitian ini ada menggunakan ekstrak etanol daun tetanus *Leea Aequata* sebagai tablet menggunakan metode granulasi basah kandungan yang terdapat pada daun tersebut seperti Flavonoid dapat digunakan sebagai obat alternatif untuk mengobati penyakit degeneratif dengan menggunakan perbandingan muchilago amyli yang digunakan sebagai bahan pengikat yaitu f1 20 %, f2 10% dan F3 5% berdasarkan penelitian tersebut di dapat formula yang dapat digunakan untuk membuat tablet yaitu pada formula 1 20% muchilago amyli

**Keywords:** Degenerative, Tetanus *Leea Aequata* L, Flavonoids, muchilago amyli, tablets.

**Kata kunci:** Degeneratif, Tetanus *Leea Aequata* L, Flavonoid, muchilago amyli, tablet.

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## INTRODUCTION

Degenerative diseases are a major health problem in Indonesia, with increasing risk factors due to unhealthy lifestyles<sup>1,2</sup>. Conventional drugs are still the main choice for treatment, but they have obstacles such as side effects and high costs<sup>3</sup>. On the other hand, herbal medicines made from natural ingredients are more popular because they are considered safer and more economical. Indonesia has great potential in phytopharmaceuticals<sup>4</sup>, including the use of tetanus leaf extract *Leea aequata* L. In previous research, research examined the contents of *Leea aequata* L. tetanus leaves and obtained the compounds contained, namely antioxidants and active

compounds such as alkaloids, saponins, tannins, flavonoids and phenols<sup>5</sup>.

Tetanus leaf extract is traditionally used to treat wounds and as an antiseptic. However, its use in traditional form is less practical and difficult to standardize. Therefore, this extract is formulated into tablets using the wet granulation method to increase stability, homogeneity and ease of consumption<sup>6</sup>. Tablets are a pharmaceutical dosage form that is easy to consume, has a more accurate dosage, and is more stable than other dosage forms<sup>7</sup>. This research aims to develop a tablet formulation based on ethanol extract of tetanus leaves and produce its physicochemical quality.



## METHODOLOGY

### *Tools and Materials*

The tools used in this research include analytical scales (ohaus), tapped density tester (Erweka SVM), analog caliper, hardness tester (YD-1), friabilator) friksibilator (FRC 2000), disintegrator tester (BTD-3), TDP 1 tablet printing machine (STH), UV vis spectrophotometry (B-one100 DA), granule sieve no. 14 and 16, oven, water bath, drying cabinet, porcelain cup, stirring rod. And a tool commonly used in pharmaceutical technology

laboratories and ethanol extract of tetanus leaves.

### *Tablet Formulation*

Tablets are solid preparations that are solid and compact, flat or round in shape, with a flat or convex surface. Wet granulation (WG) method is applied to achieve high drug loading, controlled release formulations, or to incorporate excipients in liquid form<sup>8</sup>. The tablet preparation formulation can be seen in **Table 1**.

**Table 1.** Formulation of Tablet Tetanus Leaf Extract

Material	Formula (%)		
	F1	F2	F3
Extrack Tetanus	200	200	200
Lactose	qs	Qs	qs
Muchilago amili	20%	20%	20%
Amylum	10%	10%	10%
Talk	1%	1%	1%
Mg Stearate	1%	1%	1%

### *Work procedures*

The ethanol extract of tetanus leaves and amylum were crushed in a mortar until homogeneous. Add the muchilago amyli that has been made into the preparation and lactose QS until the preparation becomes solid and compact. Sieve using Mush No. 14 sieve then dry in a drying cupboard for 24 hours<sup>9</sup>.

### *Granule evaluation*

#### *Flow time*

This testing process begins by weighing 100 grams of granules, then placing them in a funnel-shaped container with the bottom tightly closed. After that,

the funnel cover is removed so that the granules can flow completely, and the granule flow time is recorded when all the granules come out of the funnel (<10 seconds<sup>9</sup>.

#### *Silent corner*

Then the angle of repose is measured by calculating the diameter and height of the granule<sup>9</sup>.

#### *Tap index*

The tapped density tester is used by inserting 50 grams of granules into the tool, then tapping 500 times. After that, the resulting volume is recorded. Specific



gravity that is considered good ranges from 0.2–0.6 g/mL<sup>9</sup>.

### Tablet Evaluation

#### Weight uniformity test

A total of 20 tablets were weighed one by one and then averaged. The condition for good weight uniformity is that no more than 2 tablets have a greater deviation from column A and not a single tablet has a greater deviation than column B<sup>9</sup>.

#### Violence

A total of 20 tablets were taken at random, then tested for hardness using a hardness tester. The hardness requirement for a good lozenges is 7-14 kg/cm<sup>2</sup>.<sup>9</sup>

#### Fragility

Each of them took 20 tablets for the friability test and 20 tablets for the friability test, then weighed ( $W_1$ ) and then put them into the friabilator and friksibilator tool. The tool was run for 4 minutes at a speed of 25rpm. Once finished, the tablets were cleaned of dust and weighed ( $W_2$ )<sup>9</sup>.

#### Time is destroyed

Six tablets are placed in each tube in the basket, then another six tablets are placed on the guide disc before the device is run. The tubes were immersed in water at a temperature of  $37^{\circ}\text{C} \pm 1^{\circ}\text{C}$  with a minimum water height of 15 cm so that the tubes could move up and down regularly 30 times per minute. When they reached the highest position, the bottom of the basket remained on the water surface, while in the lowest position, the top of the basket was completely submerged<sup>8</sup>.

## RESULT AND DISCUSSION

### Flow time test (flow $t < 10$ seconds)

This flow time test is used to see whether the granules have good flow with the predetermined requirements, namely  $<10$  seconds. From the graph above, based on the research that has been carried out, it was found that everything meets the requirements. In f1, it has good flow properties, this is due to the use of muchilago amyli which is used as a binding agent so that it can influence the flow time, making the granules more moist, sticky and not free to flow<sup>10</sup>.

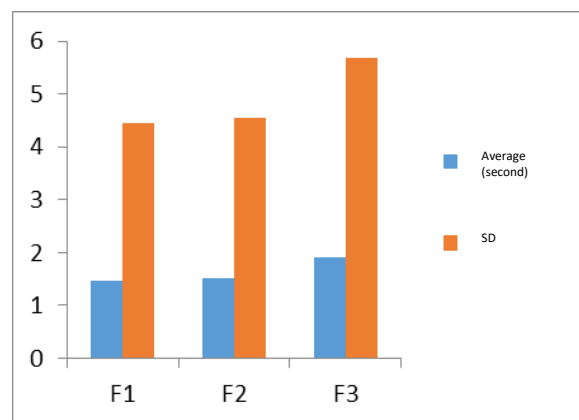
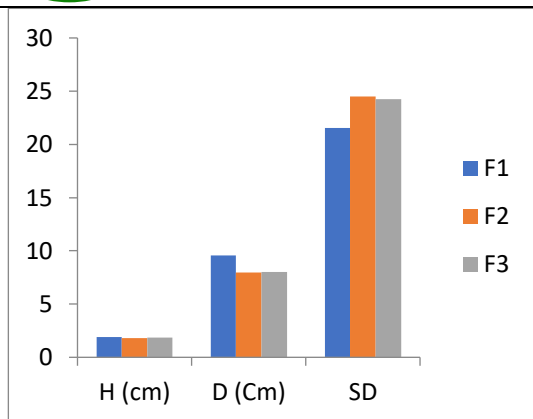


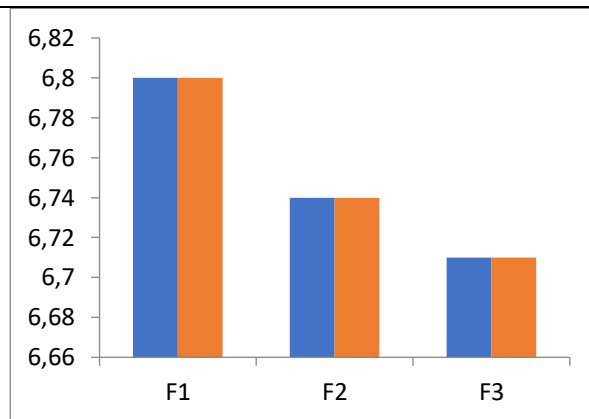
Figure 1. Graph of flow time test

### Repose angle test ( $20^{\circ} < 40^{\circ}$ )

The angle of repose test is to see the diameter obtained after carrying out a flow time test with the specified requirements, namely ( $20^{\circ} \geq 40^{\circ}$ ). The smaller the angle of repose formed, the better the flow properties of the granules so that it is easy to make them into tablets<sup>10</sup>.



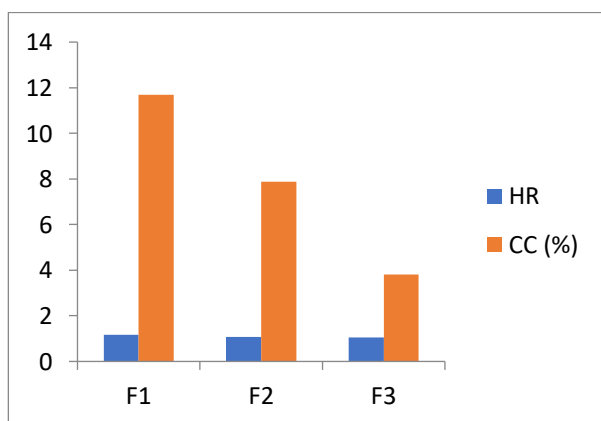
**Figure 2.** Graph of repose angle test



**Figure 4.** Graph of weight uniformity test

### **Tap index test (11.62 -18.18 %)**

The tap index test or density test is to see the density of the granules according to the requirements in accordance with the pharmacopoeia, namely (11.62-18.8%), the smaller the settling index or density produced, the better the flow properties. then the granules become denser and in the density test formula 1 is denser than formulas 2 and 3.



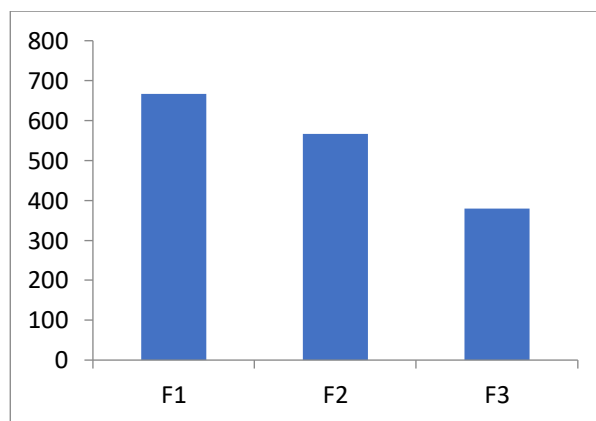
**Figure 3.** graph of tap index test

### **Weight uniformity test**

The robot uniformity test is to see whether the tablets being tested meet the standards and requirements, namely that if they are weighed one by one, no 2 tablets should deviate more than column A, no one tablet should be more than column B with column A: 5% and column B: 10%.

### **Test disintegration time (<15 minutes)**

The disintegration time test is used to see that the tablet disintegrates into small particles using a disintegration tester. The faster the tablet disintegrates, the better it is with the requirements needed for uncoated tablets, namely (<15 minutes). long crushed compared with formulations 2 and 3.



**Figure 5.** Graph of disintegration time test

### **Brittleness test time (< 0.8%)**

The brittleness time test is to see whether the tablet is easily brittle when rubbed or not. The smaller the brittleness of the tablet, the better the higher brittleness can affect the concentration or level of the active substance contained in the tablet. Based on the research that has been carried out, the results according to the graph above are that it is easily brittle in



formulation 3 and in formulation 1 the results are quite difficult for the tablet to be brittle but still within the specified requirements, namely ( $<0.8\%$ ). The high level of amyli used can strengthen the adhesion between the tablets.

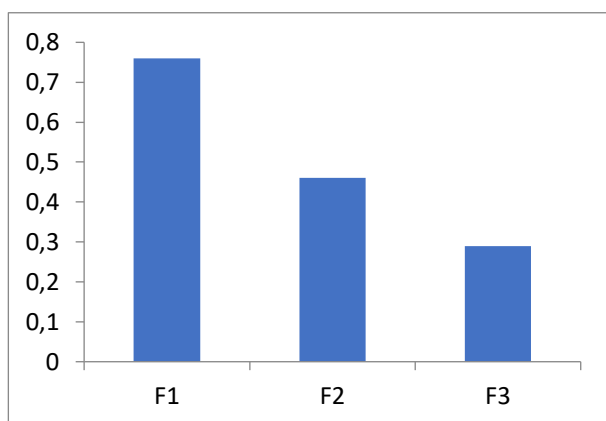


Figure 6. Graph of brittleness time test

#### Hardness test (4-8 kg)

The hardness test is carried out to determine whether the tablet has a hardness that is in accordance with the predetermined requirements, namely (4-8 kg) so that the tablet withstands transportation during transportation from harder shaking, the better the tablet, but it must comply with the predetermined requirements. Based on the results of the research that has been carried out, the results are in accordance with the graph above, namely with a formulation that provides high tablet hardness in formulation 1, namely 7.24, but in formulations 2 and 3 it does not meet the predetermined requirements, namely  $<4-8$  kg. This caused by the administration of muchilago amyli because the higher the binder used, the stronger the tablet.

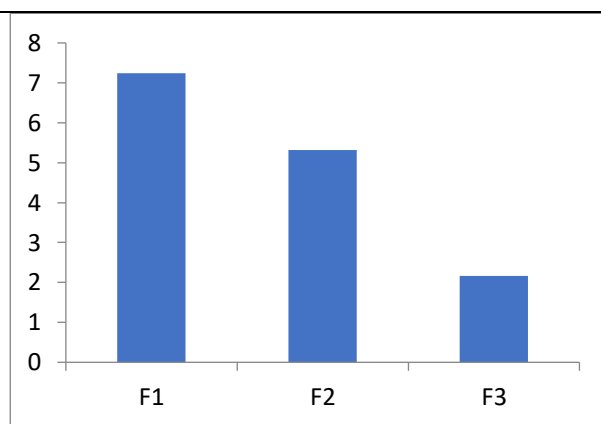


Figure 7. Graph of hardness test

#### CONCLUSION

This study successfully formulated tablets containing ethanol extract of *Leea aequata* L. leaves using the wet granulation method. Among the three formulas tested, Formula 1, which used 20% *mucilago amyli* as a binder, demonstrated the most optimal characteristics in both granule and tablet evaluations. The results showed that Formula 1 fulfilled the pharmacopeial requirements in flow time, angle of repose, tap index, hardness, friability, weight uniformity, and disintegration time. The higher concentration of *mucilago amyli* contributed to better granule flowability and tablet hardness, indicating its potential as an effective binder in herbal tablet formulations. Therefore, Formula 1 can be considered the best candidate for further development and standardization of herbal tablets containing *Leea aequata* L. leaf extract as a complementary treatment for degenerative diseases.

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## REFERENCES

1. Nasri, N., Silalahi, J., Kaban, V. E. & Satria, D. A Review on The Benefits of Probiotics as Fermented Food against Several Diseases. *J. Funct. Food Nutraceutical* 41–52 (2023).
2. Satria, D. *et al.* Synergistic Antibacterial Effect of Ethyl Acetate Fraction of Vernonia amygdalina Delile Leaves with Tetracycline against Clinical Isolate Methicillin-Resistant Staphylococcus aureus (MRSA) and Pseudomonas aeruginosa. *Adv. Pharmacol. Pharm. Sci.* **2023**, 1–11 (2023).
3. Kaban, V. E., Thomas, N. A. & Sholihah, I. PENGANTAR ILMU FARMASI.
4. Nasri, N., Kaban, V. E., Gurning, K., Syahputra, H. D. & Satria, D. Aktivitas Antibakteri Ekstrak Etanol Daun Pepaya (Carica papaya Linn.) Terhadap Bakteri Pseudomonas aeruginosa. *INSOLOGI J. Sains Dan Teknol.* **1**, 252–259 (2022).
5. Cook, T. M., Protheroe, R. T. & Handel, J. M. Tetanus: a review of the literature. *Br. J. Anaesth.* **87**, 477–487 (2001).
6. Fitri, R., Syahputra, H. D., Nasri, N., Kaban, V. E. & Rani, Z. Formulation of a biocellulose mask containing the essence of Aloe vera (L.) Burm. f combination with vitamin E as anti-aging. *Sci. Pharm. Sci.* 36–42 (2022).
7. Ginting, N., Suwarso, E., Rumapea, D. V. & Nerdy, N. Relaxation activity of tetanus (Leea aquata L.) leaf ethanolic extract on Guinea pig isolated trachea. *Asian J Pharm. Clin Res* **11**, 24–27 (2018).
8. Elisya, Y., Kardono, L. B. & Simanjuntak, P. Tablet formulation of the ethyl acetate soluble extract of soursop (Annona muricata L.) leaves. *Asian J. Appl. Sci.* **2**, (2014).
9. Mudrić, J. *et al.* Tablet and capsule formulations incorporating high doses of a dry optimized herbal extract: The case of Satureja kitaibelii. *J. Drug Deliv. Sci. Technol.* **66**, 102776 (2021).
10. Saryanti, D. Formulasi dan Uji Stabilitas Fisik Sediaan Tablet Ekstrak Buah Pare (Momordica charantia L.) secara Granulasi Basah. *Smart Med. J.* **2**, 25–31 (2019).