



Aspirin Slow Release Tablet Formulation With Comparison Of HPMC And Pectin As Matrix

Kurnia Ambar Lestari^{1)*}, Desy Nawangsari²⁾, Sunarti³⁾

^{1,2,3)} Health Faculty, Universitas Harapan Bangsa Purwokerto

*Email: kurniambarlestari@gmail.com

ARTICLE INFO

Article history

Received : 22 November 2023

Revised : 15 Desember 2023

Accepted : 28 December 2023

Keywords

Aspirin

HPMC

Pectin

Slow Release

ABSTRACT

Aspirin is an antiplatelet drug that is used in the elderly as stroke therapy, while in elderly patients compliance with taking the drug often decreases. The aim was to determine the physical properties, dissolution, and stability of aspirin slow-release tablets with a comparison of HPMC and pectin as the matrix. Aspirin slow-release tablets were made in 3 formulas with HPMC and pectin ratios of 15%:10%, 12.5%:12.5%, and 10%:15%. Evaluation of slow-release tablets includes weight uniformity, size uniformity, hardness, friability, floating time, and dissolution tests. The data obtained was then analyzed using a one-way ANOVA. The results showed that in the physical properties test of the tablet, the results were F1, 2 and 3, including the weight uniformity test, the ANOVA results were $0.000 < 0.05$, the size uniformity test was $0.055 > 0.05$ in diameter and the thickness was $0.899 > 0.05$, the hardness test was $0.355 > 0.05$, fragility test $0.780 > 0.05$ and float time test at lag time F1 48 ± 3 , F2 49 ± 4.35 , F3 50 ± 1.52 at the duration time the results were 8 hours and in the F1 dissolution test 9, 20%, F2 10.14% and F3 8.14%. In physical stability, the results obtained were uniform tablet weight, uniform size, stable tablet hardness, stable tablet friability, and a stable floating time test, while in chemical stability, there was a change in the dissolution percentage, with the results on the 14th day of F1 stability being 11.79%, F2 11.05%, and F3 9.22%, and on the 28th day of stability, F1 10.55%, F2 10.51%, and F3 10.46%. Results that have significant differences ($p < 0.05$) include weight uniformity ($p = 0.000$).

This is an open-access article under the [CC-BY 4.0](https://creativecommons.org/licenses/by/4.0/) license.



INTRODUCTION

Stroke is the second leading cause of death worldwide. In low- and middle-income nations, the burden of impairment following a stroke is likewise significant and rising more quickly than in high-income nations. Stroke is becoming more common in young and middle-aged (i.e., younger than 55) adults, which is concerning. Worldwide. (Feigin et al., 2023) During the past three decades, in absolute terms, global stroke incidence increased by 70%, its prevalence increased by 85%, its mortality increased by 43%, and DALYs due to stroke increased by 32%, with a greater increase in stroke burden in low-income and middle-income countries (LMICs) than in high-income countries (HICs).¹ From 1990 to 2019, there was a 37% global increase in the total number of

stroke-related DALYs due to risk factors, with LMICs disproportionately affected.¹ Stroke-related DALYs attributable to risk factors increased by 48% in LMICs and declined by 25% in HICs between 1990 to 2019.¹ In 2019, the five leading risk factors of stroke were high systolic blood pressure, high body-mass index, high fasting plasma glucose concentrations, ambient particulate matter (PM_{2.5}) pollution, and smoking. (Feigin et al., 2021; Owolabi et al., 2022). Stroke is a local clinical manifestation of cerebral dysfunction that lasts more than a day. Based on the results of the 2018 Riskesdas, the number of elderly people suffering from stroke in Indonesia is increasing, with the age group >75 years having the highest incidence of stroke (50.2%) and the age group 65-74 years (45.3%) having the highest incidence of stroke. The second and third highest were 55-64 years (32.4%).

One of the treatments used for stroke patients is antiplatelet therapy, for example, aspirin. The American College of Cardiology (ACC)/American Heart Association (AHA) and the European Society of Cardiology (ESC) Guideline recommendations on DAPT after PCI vary based on the clinical presentation (ACS or SIHD).^{3,4} In patient with SIHD undergoing PCI, a loading dose of aspirin (162–325 mg) followed by a maintenance dose of 75 to 100 mg daily is recommended. Initiation of P2Y₁₂ inhibitor is usually delayed until coronary anatomy is defined. (Akhtar & Baber, 2024; Dangas et al., 2012; Waksman et al., 2014). Aspirin remains the gold standard antiplatelet regimen following coronary artery bypass grafting (CABG), however, there is growing support for dual antiplatelet therapy (DAPT). (Hess et al., 2021) The dose of aspirin used as an antiplatelet aggregate is 75–150 mg/day. (Nurdianti et al., 2018) Sustained-release tablets are preparations that can be released over a longer period prolong the action of the drug. One type of slow-release modification is the floating system. One of the polymers in the floating system is hydroxypropyl methylcellulose (HPMC), which can be combined with pectin, which has an effect on fast floating lag times and long floating times. (Armadani et al., 2020) There are still no aspirin slow-release tablet preparations on the market in Indonesia. In addition, aspirin is made as a slow-release tablet to increase the compliance of elderly patients with taking their medication, reduce the duration of drug use, and maintain therapeutic levels of the drug in the blood or tissues for a long time. Based on this, researchers are interested in conducting research and making aspirin slow-release tablets using a comparison of HPMC and pectin as a matrix to determine the physical properties, dissolution and stability of aspirin slow-release tablets.

METHOD

The method used in this research is direct compression with aspirin as the active ingredient and HPMC and pectin as the matrix. The tools and materials needed are as follows:

1. Tool and Material

The tools used include: analytical balance (Kenko KK-Lab), glassware (pyrex®), printing machine (rotary single punch), hardness tester, friability tester, UV-VIS spectrophotometry (Biobase BK-D590). The ingredients used are aspirin, HPMC, pectin, advice PH 102, mg-stearate, sodium bicarbonate, HCL p.a, and Aquadest.



2. Composition

Table 1 Sustained release tablet formula

Name	Formula (%)		
	F1	F2	F3
Aspirin	37,5	37,5	37,5
HPMC	15	12,5	10
Pektin	10	12,5	15
Na-bikarbonat	12,5	12,5	12,5
Gelatin	2,5	2,5	2,5
Mg stearat	2,5	2,5	2,5
Avicel PH 102	20	20	20
Bobot tablet (mg)	200	200	200

Aspirin extended-release tablets are made by the direct compression method. Next, each ingredient is mixed, including aspirin (active substance), HPMC (matrix), pectin (matrix), Na-bikarbonat (gas producer), gelatin (binder), and Avicel PH 102 (filler), until homogeneous. Then add the lubricant, mg stearate. After that, it is compressed into tablets weighing 200 mg per tablet.

3. Evaluation of the Physical Properties.

Compressibility, moisture content, flow time and angle of repose tests are used to assess the physical characteristics of the printed mass. A closed test apparatus is used to accommodate a 25g printed mass after being weighed for the flow time test. After the funnel lid is opened, the flow time of the printed mass is recorded.(Appriliani & Oktavianoor, 2021). Less than 10 seconds per 100 grams is considered a good flow rate. The height and diameter of the flow time test results are then measured to determine the angle of repose. An angle of repose between 25-30° shows excellent results and is easy to flow (Aulton and Taylor, 2018). Moisture content is determined by weighing 500 grams of printed mass and placing it in an oven at a temperature of 105°C for 30 minutes.(Syahrina & Noval, 2021). Compressibility is determined using tapped density by weighing 25g of the printed mass and placing it in a 100mL measuring cup after which 500 taps are made. (Balfas & Nanda, 2019)

4. Evaluation of the Physical Properties of the Tablet

To ensure uniformity of weight, each tablet was weighed carefully and the average weight was determined. Tablet weight uniformity meets the requirements if there are no more than two tablets whose weight is different from column A and not a single tablet whose weight is different from column B (Ministry of Health of the Republic of Indonesia, 1979) Test size uniformity by measuring the thickness and diameter of the tablet. If the diameter of the tablet does not exceed three times the thickness, or less than one third, then the tablet is considered to meet size uniformity (Ministry of Health of the Republic of Indonesia, 1979). Hardness test equipment is used to test tablet hardness. Ten tablets are taken, and each is inserted sequentially between the press needle and the holder, and the apparatus is rotated until the tablet cracks or disintegrates. A good range for tablet hardness is 4-8kg. (Gopalan & Gozali, 2018)

Twenty tablets were cleaned and then weighed before being placed into the friability tester. The tool is then operated for four minutes, or one hundred times, to complete the test. If the friability percentage is less than 1%, the tablet is considered to meet the friability requirements. (Ayu & Devi, 2019) Prepare 0.1 N 100 mL HCL with a pH of 1.2 in a beaker glass and then insert the tablet for a float time test. Lag time is seen when the tablet appears on the surface. Floating time is determined by measuring the length of time the tablet floats after the tablet begins to surface.

The dissolution test is carried out by making a series of solutions and determining the maximum wavelength. Series solutions were made in concentrations of 50, 60, 70, 80 and 90 ppm.

The dissolution test was carried out using a dissolution tester with a type 1 (basket) device for 480 minutes. 500 mL of acetate buffer, with a pH of 4.50 ± 0.05 , was used as a dissolution medium. Acetate buffer is made by mixing 1.66 mL of glacial acetic acid P and 2.99 grams of sodium acetate trihydrate with water to make 1000 mL. A total of 5.0 mL samples were collected at 5, 10, 15, 30, 60, 120, 180, 240, 300, 360, 420, and 480 minutes. To maintain the volume of the solvent medium, the sample taken was replaced with a new sample in the same volume. A spectrophotometer is used to measure the absorbance of samples at the highest wavelength.

Tablet stability tests were carried out for four weeks at weeks 0, 2, and 4 to ensure tablet stability at a temperature of $40 \pm 2^\circ\text{C}$ during storage. Tablet stability is determined chemically and physically. Two gram tablets were put into a two milliliter bottle and tightly closed to carry out a physical stability test. Vials were stored at $40 \pm 2^\circ\text{C}$ for 4 weeks. Physical stability tests are carried out using organoleptic tests (color, shape, and odor). (Nawang Sari & Sunarti, 2021) Next, tests were carried out on the uniformity of weight, size, brittleness, hardness, and floating time measurements. Aspirin dissolution is measured as part of a chemical stability test.

5. Analysis

SPSS tools were used to check the collected data. Next, homogeneity and normality tests were carried out. If the p value > 0.05 the data is considered homogeneous and normally distributed. Testing was then carried out using one-way ANOVA, and data analysis was carried out to determine whether the differences in HPMC: pectin in each formula were significantly different. (Ayuningtyas et al., 2021).

RESULT

Based on the research that has been carried out, the results obtained are:

1. Evaluation of the Physical Properties of the Printed Mass

The purpose of the flow time test is to measure variations in granule flow time. The results for F1, F2, and F3 were 5.20 ± 0.06 gram/s, 5.49 ± 0.07 gram/s, and 5.15 ± 0.12 gram/s, respectively. Based on the test results, results obtained according to the literature that a good flow rate is less than 10 seconds per 100 grams. (Rijal et al., 2022) The angle of repose test aim to assess the thickness and diameter of each tablet. F1, F2, and F3 obtained the following results for the angle of repose test: $27.92 \pm 0.45^\circ$, $27.17 \pm 0.69^\circ$, and $27.77 \pm 0.68^\circ$. Based on the test results, the angle of repose is produced according to the literature which states that the range of 25° - 30° is a very good category. (Syahrina & Noval, 2021)

The compressibility test aims to determine whether powder material that is forged at a certain pressure forms a compact mass. F1, F2, and F3 produced compressibility



test results of $13 \pm 2\%$, $12 \pm 3.06\%$, and $14 \pm 1.53\%$, in that order. The moisture content test aims to determine the water content in the granules. The results of the moisture content test were F1, F2 and F3 respectively, namely 2.25%, 2.40% and 2.50%.

Table 2 Results of printing mass evaluation

Evaluasi Massa Cetak	Formula		
	1	2	3
Waktu alir	5,20±0,06	5,49±0,07	5,15±0,12
Sudut diam	27,92±0,45	27,17±0,69	27,77±0,68
Kompresibilitas	13±2	12±3,06	14±1,53
Kadar lembab	2,25%	2,40%	2,50%

2. Evaluation of the Physical Properties of the Tablet

To ensure that the active component content is consistent, a tablet weight uniformity test is carried out. For formulas 1, 2, and 3, the weight uniformity results obtained were 213.48 ± 4.42 mg, 215.63 ± 2.69 mg, and 212.51 ± 2.57 mg. Each formula meets the weight uniformity test standards, namely 7.5% (column A) and 15% (column B).

Tabel 1 Hasil evaluasi tablet

Evaluasi tablet	Formula		
	1	2	3
Keseragaman bobot	213,48±4,42	215,63±2,69	212,51±2,57
Keseragaman ukuran			
Diameter	0,83±0,004	0,83±0,005	0,83±0,005
Tebal	0,43±0,004	0,43±0,004	0,43±0,004
Kekerasan	4,9±0,10	5,06±0,15	4,93±0,15
Kerapuhan	0,43±0,15	0,46±0,15	0,36±0,20
Uji waktu mengapung			
Lagtime	48±3	49±4,35	50±1,52
Duration time	8 jam	8 jam	8 jam
Disolusi	9,20%	10,14%	8,14%

The purpose of the float time test is to increase the duration of the drug in the stomach. In formulas 1, 2, and 3, the lag time test results were 48 ± 3 , 49 ± 4.35 , and 50.33 ± 1.52 , respectively; in formulas 1, 2, and 3, the duration time test results are 8 hours. It can be concluded from these test results that they are in accordance with the literature, which shows that the faster the tablet floating time, the higher the amount of HPMC. (Armadani et al., 2020)

The dissolution test begins by determining the maximum wavelength, which is carried out with a solution of 50 ppm concentration producing a wavelength of 268 nm. Furthermore, at a maximum wavelength of 268 nm, the absorbance of series solutions of concentrations of 50, 60, 70, 80, and 90 ppm was measured and the respective absorbance values were 0.274; 0.3115; 0.341; 0.405; and 0.427. The equation obtained is $y = 0.0396(x) + 0.0752$ with $r = 0.9897$. The tablet dissolution test produced F1, F2, and F3 values, namely 9.20%, 10.14%, and 8.14%.

Aspirin dissolution was measured to perform a chemical stability test. In the dissolution test there was a change in the dissolution percentage results on the 14th day stability of F1 11.79%, F2 11.05% and F3 9.22%, on the 28th day stability of F1 10.55%, F2 10.51% and F3 10.46%. The dissolution rate is influenced by the nature and characteristics of the dissolution medium, temperature, pH and mixing speed. The physical stability test was carried out using organoleptic tests and tablet physical properties tests. Physical stability test results include consistent tablet hardness, consistent tablet brittleness, consistent weight uniformity, consistent size uniformity, and consistent floating time.

The dissolution test begins by determining the maximum wavelength, which is carried out with a solution of 50 ppm concentration producing a wavelength of 268 nm.

DISCUSSION

1. Evaluation of the Physical Properties of the Printed Mass

Based on the test results, results obtained according to the literature that a good flow rate is less than 10 seconds per 100 grams. (Rijal et al., 2022) The angle of repose test aim to assess the thickness and diameter of each tablet. F1, F2, and F3 obtained the following results for the angle of repose test: $27.92 \pm 0.45^\circ$, $27.17 \pm 0.69^\circ$, and $27.77 \pm 0.68^\circ$. Based on the test results, the angle of repose is produced according to the literature which states that the range of 25° - 30° is a very good category. (Syahrina & Noval, 2021)

The compressibility test aims to determine whether powder material that is forged at a certain pressure forms a compact mass. F1, F2, and F3 produced compressibility test results of $13 \pm 2\%$, $12 \pm 3.06\%$, and $14 \pm 1.53\%$, in that order. The moisture content test aims to determine the water content in the granules. The results of the moisture content test were F1, F2 and F3 respectively, namely 2.25%, 2.40% and 2.50%. Based on the test results, the three formulas have good compressibility because according to the literature it is defined as a range between 11 and 15%. (Rijal et al., 2022) The moisture content test aims to determine the water content in the granules Based on the test results, it is in the good water content category because it meets the water content standard, namely less than 5%, as stated in the literature. (Syahrina & Noval, 2021)

2. Evaluation of the Physical Properties of the Tablet

To ensure that the active component content is consistent, a tablet weight uniformity test is carried out. For formulas 1, 2, and 3, the weight uniformity results obtained were 213.48 ± 4.42 mg, 215.63 ± 2.69 mg, and 212.51 ± 2.57 mg. Each formula meets the weight uniformity test standards, namely 7.5% (column A) and 15% (column B). The purpose of the size uniformity test is to ensure that each tablet has the same size (Depkes, 2014). The results obtained for F1, F2, and F3 are in accordance with the literature, namely the diameter of the tablet is no more than three times or less than four thirds of its thickness, so the tablet is said to have met the size uniformity standard.

The resistance of tablets to mechanical stress, the potential for tablet damage in packaging is described by hardness test parameters. For formulations 1, 2 and 3, the tablet hardness results were 4.9 ± 0.10 kg, 5.06 ± 0.15 kg, and 4.93 ± 0.15 kg,



respectively. The hardness results are in accordance with the literature, namely good tablet hardness in the range of 4 to 8 kg. (Gopalan & Gozali, 2018)

Tablet resistance to surface abrasion is demonstrated for the tablet friability test. For formulas 1, 2, and 3, the tablet friability test results were $0.43 \pm 0.15\%$, $0.46 \pm 0.15\%$, and $0.36 \pm 0.20\%$. Based on the test results, the three formulas are in accordance with the literature which shows that tablets have good friability if the friability percentage is less than 1%. (Gopalan & Gozali, 2018). The tablet dissolution test produced F1, F2, and F3 values, namely 9.20%, 10.14%, and 8.14%. Each formula meets the dissolution test requirements that the active ingredient is released from the matrix by 30% in less than 8 hours. The dissolution rate is in accordance with the literature which shows that the dissolution rate decreases with increasing HPMC content and decreasing pectin concentration (Armadani et al., 2020)

CONCLUSION

Based on the research results, it can be concluded as follows:

1. In the physical properties test for tablets F1, 2 and 3, including the weight uniformity test, the ANOVA results were $0.000 < 0.05$, the size uniformity test was $0.055 > 0.05$ in diameter and $0.899 > 0.05$ in thickness, and the hardness test was $0.355 > 0.05$, fragility test $0.780 > 0.05$ and float time test at lag time F1 48 ± 3 , F2 49 ± 4.35 , F3 50 ± 1.52 and at duration time the results were 8 hours.
2. In the dissolution test, the results obtained were F1 9.20%, F2 10.14% and F3 8.14%. The higher the HPMC concentration and the lower the pectin concentration, the lower the dissolution rate.
3. Testing the chemical stability of the dissolution test, there was a change in the dissolution percentage results on the 14th day stability of F1 11.79%, F2 11.05% and F3 9.22%, on the 28th day stability of F1 10.55%, F2 10.51% and F3 10.46%. The dissolution rate is influenced by the nature and characteristics of the dissolution medium, temperature, pH and stirring speed. In terms of physical stability, the results obtained were uniform weight uniformity, uniform size uniformity, stable hardness, tablet friability and stable floating time test.

SUGGESTION

Based on the research that has been carried out, further research needs to be carried out for antiplatelet tests to determine the antiplatelet effect of drugs in preventing blood clots. Antiplatelet testing can be done in vitro and in vivo.

REFERENCES

- Akhtar, K. H., & Baber, U. (2024). Antiplatelet Therapy for Patients Who Have Undergone Revascularization Within the Past Year: Which Agents and for How Long? *Medical Clinics of North America*. <https://doi.org/10.1016/J.MCNA.2023.12.003>
- Appriyani, R., & Oktavianoor, H. (2021). Evaluation of the Effect of Variation in Cempedak Seed (Arthocarpus Champeden) Starch Concentration as a Filler in

- Paracetamol Tablet Formulation. *Jurnal Surya Medika*, 6(2).
<https://doi.org/10.33084/jsm.vxix.xxx>
- Armadani, V. A., Aisiyah, S., & Kuncahyo, I. (2020). DESIGN THE EFFECT OF PECTIN AND HPMC K15 M MATRIX ON FLOATATION BEHAVIOUR, SWELLING AND DISOLUTION OF VERAPAMIL HCL FLOATING TABLET USING FACTORIAL DESIGN METHOD. In *Journal of Pharmacy* (Vol. 9, Issue 1).
- Ayu, I., & Devi, S. (2019). *Optimasi Konsentrasi Polivinil Pirolidon (PVP) sebagai Bahan Pengikat terhadap Sifat Fisik Tablet Ekstrak Etanol Rimpang Bangle (Zingiber cassumunar Roxb)*.
- Ayuningtyas, N. D., Febrianto, Y., & Lutfi, T. (2021). Orally Disintegration Tablet (ODT) Formulation of Candesartan Cilexetil With Croscarmellose Sodium and Crospovidone as Superdisintegrant. *Jurnal Farmasi & Sains Indonesia*, 4(1), 21–28.
<https://doi.org/10.52216/jfsi.v4i1.64>
- Balfas, R. F., & Nanda, M. De. (2019). Uji Waktu Alir dan Uji Kompresibilitas Granul Pati Kentang dengan Metode Granulasi Basah. *Snytax Idea*, 1(5).
- Dangas, G. D., Claessen, B. E., Mehran, R., Xu, K., Fahy, M., Parise, H., Henriques, J. P. S., Ohman, E. M., White, H. D., & Stone, G. W. (2012). Development and Validation of a Stent Thrombosis Risk Score in Patients With Acute Coronary Syndromes. *JACC: Cardiovascular Interventions*, 5(11), 1097–1105.
<https://doi.org/10.1016/J.JCIN.2012.07.012>
- Feigin, V. L., Owolabi, M. O., Owolabi, M. O., Owolabi, M. O., Feigin, V. L., Abd-Allah, F., Akinyemi, R. O., Bhattacharjee, N. V., Brainin, M., Cao, J., Caso, V., Dalton, B., Davis, A., Dempsey, R., Duprey, J., Feng, W., Ford, G. A., Gall, S., Gandhi, D., ... Zagozdzon, P. (2023). Pragmatic solutions to reduce the global burden of stroke: a World Stroke Organization–Lancet Neurology Commission. *The Lancet Neurology*, 22(12), 1160–1206. [https://doi.org/10.1016/S1474-4422\(23\)00277-6](https://doi.org/10.1016/S1474-4422(23)00277-6)
- Feigin, V. L., Stark, B. A., Johnson, C. O., Roth, G. A., Bisignano, C., Abady, G. G., Abbasifard, M., Abbasi-Kangevari, M., Abd-Allah, F., Abedi, V., Abualhasan, A., Abu-Rmeileh, N. M., Abushouk, A. I., Adebayo, O. M., Agarwal, G., Agasthi, P., Ahinkorah, B. O., Ahmad, S., Ahmadi, S., ... Murray, C. J. L. (2021). Global, regional, and national burden of stroke and its risk factors, 1990–2019: a systematic analysis for the Global Burden of Disease Study 2019. *The Lancet Neurology*, 20(10), 795–820. [https://doi.org/10.1016/S1474-4422\(21\)00252-0](https://doi.org/10.1016/S1474-4422(21)00252-0)
- Gopalan, S. V., & Gozali, D. (2018). Review Artikel : Formulasi Dan Evaluasi Sediaan Granul Effervescent Dan Sediaan Tablet Dengan Metode Granulasi Basah. *Farmaka*, 16(1).
- Nawangsari, D., & Sunarti. (2021). Uji Stabilitas Sediaan Salep Ekstrak Etanol Rimpang *Kencurempferiae galanga L.) Dalam Berbagai Basis*. In *Journal of Pharmacopolium* (Vol. 4, Issue 2).
- Nurdianti, L., Nurdiansyah, D., Aryani, R., S1, P., Stikes, F., Tunas, B., & Tasikmalaya, H. (2018). *Prosiding Seminar Nasional dan Diseminasi Penelitian Kesehatan STIKes Bakti Tunas Husada Tasikmalaya*.
- Owolabi, M. O., Thrift, A. G., Mahal, A., Ishida, M., Martins, S., Johnson, W. D., Pandian, J., Abd-Allah, F., Yaria, J., Phan, H. T., Roth, G., Gall, S. L., Beare, R., Phan, T. G., Mikulik, R., Akinyemi, R. O., Norrving, B., Brainin, M., Feigin, V. L., ... Zhang, P. (2022). Primary stroke prevention worldwide: translating evidence into



- action. *The Lancet Public Health*, 7(1), e74–e85. [https://doi.org/10.1016/S2468-2667\(21\)00230-9](https://doi.org/10.1016/S2468-2667(21)00230-9)
- Rijal, M., Buang, A., & Prayitno, S. (2022). PENGARUH KONSENTRASI PVP K-30 SEBAGAI BAHAN PENGIKAT TERHADAP MUTU FISIK TABLET EKSTRAK DAUN TEKELAN (*Chromolaena Odorata*. (L.). *Journal Kesehatan Yamas Makasar*, 6(1), 98–111. <http://journal.yamasi.ac.id>
- Syahrina, D., & Noval. (2021). Optimization of the Combination of Citric Acid and Tartaric Acid as an Acidifying Agent in Effervescent Tablets of Purple Sweet Potato Extract (*Ipomoea batatas* L). *Jurnal Surya Medika*, 7(1). <https://doi.org/10.33084/jsm.vxix.xxx>
- Waksman, R., Kirtane, A. J., Torguson, R., Cohen, D. J., Ryan, T., Räber, L., Applegate, R., Waxman, S., Gordon, P., Kaneshige, K., & Leon, M. B. (2014). Correlates and Outcomes of Late and Very Late Drug-Eluting Stent Thrombosis: Results From DESERT (International Drug-Eluting Stent Event Registry of Thrombosis). *JACC: Cardiovascular Interventions*, 7(10), 1093–1102. <https://doi.org/10.1016/J.JCIN.2014.04.017>