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# Optimization of Mucoadhesive Tablet Formulations of Papaya Leaf Extract (Carica Papaya L.) Using a Combination of Carbopol and Na. Cmc With Simplex Lattice Design Method

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**ABSTRACT**

Indonesia has natural wealth that is useful for researching all contents that have the potential to become herbal medicines that can be made into practical preparations as therapeutic agents for gastric ulcers, one of which is papaya plants which are useful for the treatment of protecting the gastric mucosa. Papaya leaf extract with a dose of 100 mg can prevent ulcers the same as conventional medicine. Controlled-release preparations aim of prolonging the residence time of the drug in the gastrointestinal tract and regulating the rate and amount of drug released. Papaya leaf extract mucoadhesive tablets were formulated using a variation of mucoadhesive polymer, namely Carbopol with Na. CMC is expected to increase the strength and duration of contact between the drug-containing polymer and the mucosal surface. The purpose of this research is to determine the most optimal formulation and the effect of the combination of Carbopol and Na matrices CMC on mucoadhesive tablet formulation of papaya leaf extract. The method used is a quasi-experimental design by comparing the results of the intervention with a control group from the evaluation of the formulation and based on the analysis of the simplex lattice design. Results: The results of the evaluation of the LOD test powder, the flow properties of all formulations met the requirements and the angle of repose in the formulation I, compressibility at FI and FIII met the requirements. The resulting tablets have a color, odor and shape. Weight uniformity, friability, in vitro were in accordance with the requirements and in the evaluation of hardness none of the formulations met the requirements. The most optimal formulation is formulation I based on simplex lattice design analysis with a combination concentration of Carbopol 30 mg and Na. CMC 40 mg and there is an effect of the combination of Carbopol matrix and Na. CMC is on the formulation of mucoadhesive tablets.

## INTRODUCTION

Indonesia, which has natural wealth, is useful for researching all the ingredients that have the potential to become herbal medicines that can be made into practical and economical preparations. Several Indonesian medicinal plants have the potential as therapeutic agents for gastric ulcers, one of which is papaya (Carica papaya L.). Many parts of papaya (Carica papaya L.) are useful for treatment but this time the part that is the focus is papaya leaf extract (Carica papaya L.) which is proven to be able to protect the gastric mucosa. Usually people use papaya leaf boiled water to overcome stomach problems [1].

Na. CMC is a polymer that is used as a mucoadhesive material because it increases the viscosity, the higher the viscosity, the slower the tablet release time so that it prolongs the drug stay in the stomach [2]. Carbopol can control drug release due to its strong binding properties. The requirements for polymers that are suitable for mucoadhesives are polymers that can adhere to the mucosa, and can release the active ingredient gradually. The mucoadhesive strength of carbopol can act as a mucosal agent that can help the tablet to adhere to the gastric wall [3]. Na. CMC is one of the polymers that can be used as a mucoadhesive material which has good stickiness as an ingredient and can increase the residence time of the drug [2].

Based on the description above, the researcher wants to make mucoadhesive tablets of papaya leaf extract (Carica papaya L) using Na. CMC and Carbopol polymers with the simplex lattice design method.

Tablet preparations with 3 different formulations were evaluated first using the Loss On Drying (LOD) and flow properties test. Then the tablet preparations were physically evaluated, namely by organoleptic test,

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weight uniformity test, friability test, hardness test and evaluation of mucoadhesive tablets by in-vitro test using the Parody method.

## LITERATURE REVIEW

**Table 1:** research authenticity

| No | Title | Design | Results |
|---|---|---|---|
| 1. | The Effect of Adding Avicel PH 102 on the Physical Properties of Papaya Leaf Extract Tablets (Carica papaya L.) By Direct Compression (Nofriyaaldi et al., 2020) | Experimental research using papaya leaf extract | Extract tablets Papaya leaves (Carica papaya L) made have good evaluation results based on the evaluations carried out. |
| 2. | Optimization of Glibenclamide Buccal Mucoadhesive Tablet Formula Using CMC Na Matrix and Oleic Acid as Enhachers (Falahi et al., 2021) | Experimental research using Glibenclamide and using CMC Na Matrix and oleic acid as enhachers | The mucoadhesive tablets made from Glibenclamide had good results based on the evaluations carried out. |
| 3. | Quality and Release Profile of Captopril From Mucoadhesive Gastroretensive Tablets Using Carboxymethyl Cellulose Sodium Matrix and Carbopol 934P (, 2019) | Experimental research on Captopril from Mucoadhesive Gastroretensive Tablets using Carboxymethyl Cellulose Sodium and Carbopol 934P. | Mucoadhesive tablets made have different characteristics for each formula. The best mucoadhesive tablets were shown by the MK4 and MK5 formula tablets. These formulas have a controlled drug release profile according to the Korsmeyer-Peppas and Higuchi kinetics model. |

## MATERIALS AND METHODS

### Materials

The research was conducted at the Pharmaceutical Technology Laboratory, Sari Mulia University, Banjarmasin. Jl. Scout No. 2 Pemurus Luar Village, East Banjarmasin District, Banjarmasin City, South Kalimantan. The target of this research was papaya leaf extract (Carica papaya L), which was to be made into mucoadhesive tablets using a combination of Na matrix. CMC and Carbopol.

### Methods

The research design method used in this research is experimental research or experiment (experimental research). The method used in this study was Quasi Experiment Design with a Non Equivalent Control Group design, namely comparing the results of interventions with a similar control group but not necessarily the same group. In this design, the grouping of sample members in the experimental group and control group was not done randomly or randomly [4]. Designs that do not select samples randomly but with a specific purpose, namely looking at the evaluation results of the Mucoadhesive tablet formulation or referring to the required conditions or standard provisions

### Formula / Equation

Mucoadhesive Tablet formulation of papaya leaf extract (Carica papaya L) as follows :

**Table 2:** Formulation Tablet Mukoadhesif

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| Ingredient | Formulation (mg) | | | Function |
|---|---|---|---|---|
| | F1 | F2 | F3 | |
| Ekstrak daun pepaya | 100 | 100 | 100 | Zat aktif |
| *Carbopol* | 30 | 35 | 40 | Polimer |
| Na CMC | 40 | 35 | 30 | Polimer |
| Asam oleat | 5 | 5 | 5 | Enhacer |
| Mg stearate | 5 | 5 | 5 | Pelicin |
| Manitol | 30 | 30 | 30 | Perasa |
| Talk | 2 | 2 | 2 | Plicin |
| Berat Tablet | 212 | 212 | 212 | |

**Tables**

The LOD test of a mixture of papaya leaf extract powder (Carica papaya L.) can be seen in the table below:

**Table 3:** Loss On Drying (LOD) Test Results

| Hasil Uji *Loss On Drying* (LOD) | | |
|---|---|---|
| Formula I | Formula II | Formula III |
| 3,1 % | 3,4 % | 3,0 % |

The results of the flow properties test of a mixture of papaya leaf extract powder (Carica papaya L.) can be seen in the table below:

**Table 4:** Flow Properties Test Results

| Uji | F I (detik) | F II (detik) | F III (detik) |
|---|---|---|---|
| Replikasi I | 2 | 2 | 2 |
| Replikasi II | 2 | 2 | 3 |
| Replikasi III | 2 | 2 | 3 |
| Rata-rata ±SD | 2±0 | 2±0 | 2,6±0,5 |

The results of the organoleptic test of papaya leaf extract tablets (Carica papaya L.) can be seen in the table below:

**Table 5:** Organoleptic Test Results

| | F I | F II | F III |
|---|---|---|---|
| Warna | Coklat | Coklat | Coklat |
| Rasa | Pahit | Pahit | Pahit |
| Bau | Berbau ekstrak pepaya | Berbau ekstrak pepaya | Berbau ekstrak pepaya |
| Bentuk | Bulat | Bulat | Bulat |

The results of the weight uniformity test of papaya leaf extract tablets (Carica papaya L.) can be seen in the table below:

**Table 6:** Results of Weight Uniformity Test

| Formulasi I | | Formulasi II | | Formulasi III | |
|---|---|---|---|---|---|
| Bobot 20 Tablet (mg) | | Bobot 20 Tablet (mg) | | Bobot 20 Tablet (mg) | |
| 300 | 300 | 303 | 308 | 329 | 307 |
| 305 | 301 | 304 | 307 | 304 | 305 |
| 302 | 302 | 307 | 302 | 299 | 300 |
| 302 | 304 | 308 | 301 | 303 | 302 |

| | | | | | |
|---|---|---|---|---|---|
| | | : | | | |
| 300 | 306 | 309 | 303 | 300 | 299 |
| 304 | 303 | 302 | 300 | 296 | 300 |
| 305 | 313 | 301 | 306 | 296 | 300 |
| 307 | 309 | 304 | 303 | 300 | 300 |
| 308 | 302 | 307 | 301 | 302 | 302 |
| 302 | 301 | 306 | 303 | 305 | 306 |
| Jumlah bobot : 6.076 mg | | Jumlah bobot : 5.985 mg | | Jumlah bobot : 6.055 mg | |
| Rata – rata bobot ±SD: 303,8±3,47 | | Rata – rata bobot ±SD : 299±2,76 | | Rata – rata bobot ±SD: 302 mg±6,86 | |

The results of the hardness test of papaya leaf extract tablets (Carica papaya L.) can be seen in the table below:

**Table 7:** Hardness Test Results

| Uji | F I | F II | F III |
|---|---|---|---|
| Replikasi I | 3 kg | 2,5 kg | 2,5 kg |
| Replikasi II | 4 kg | 3 kg | 2 kg |
| Replikasi III | 3 kg | 3,5 kg | 4 kg |
| Rata-rata±SD | 3,3 kg ±0,57 | 3 kg ±0,57 | 3,16 kg ±1,41 |

The results of the friability test of papaya leaf extract tablets (Carica papaya L.) can be seen in the table below:

**Table 8:** Fragility Test Results

| Uji | F I | F II | F III |
|---|---|---|---|
| Percobaan I | 0,3 % | 0,2 % | 0,6 % |
| Percobaan II | 0,4 % | 0,6 % | 0,6 % |
| Percobaan III | 0,2 % | 0,4 % | 0,6 % |
| Rata-rata±SD | 0,3%±1 | 0,4%±2 | 0,6%±0 |

The results of the in-vitro test of papaya leaf extract tablets (Carica papaya L.) can be seen in the table below:

**Table 9:** In-Vitro Test Results

| Uji | F I | F II | F III |
|---|---|---|---|
| Hasil | 32 Menit | 28 Menit | 21 Menit |

## RESULTS AND DISCUSSION

Based on the results of the LOD test, the powder mixture in all formulations met the requirements for good moisture content from the test results on the three formulations, namely all formulations with an average range of 3% of these results. The results of this study are also supported by a research, the study of tomato juice lozenges, the results of the loss in drying (LOD) test were 3% for the three formulations, which results were in the range of requirements for a good granule moisture content of 2-5% [5]. The tablet formulations showed that all papaya extract tablets had a physical quality of moisture content in accordance with the required specifications.

In this study to test the flow time using 100 grams of powder for each formulation. The results showed that all formulations met the requirements for a good flow rate in the range of 2 – 2.6 seconds at 100 grams

of powder. This research is in line with research [6]. In the study of green gedi leaf extract tablets, the results of the flow properties test obtained results for both formulations that met the flow time requirements, which were under 10 seconds for 100 gr granules [7]. The flow properties of powders are influenced by particle size, particle shape, particle surface texture and moisture content. The more Na-CMC added will increase the density resulting in better ganul flow properties.

The results of the organoleptic test on tablets for all formulations are brownish tablets, have a bitter taste, smell of extract and are round in shape. The results of this study are in line with the results of previous research, in the study of water spinach extract tablets which showed the results of the organoleptic test, the extract had a distinctive smell and tasted slightly bitter.

Weight uniformity test showed that all formulations had an average weight of 151 mg to more than 300 mg. The standard deviation of the average weight of tablets which has an average weight of 151 mg-300 mg, namely column A is 7.5% and column B is 15% and more than 300 mg then column A is 5% and column B is 10%, meaning no there may be more than 2 tablets whose weight deviates from column A and not 1 tablet whose weight deviates from column B [7]. The results of the calculation of the weight uniformity showed that the tablets in all formulations did not deviate from the specified requirements. This research is in line with previous research, on the manufacture of mucoadhesive shows that the tablets made have a uniform weight or meet the specified requirements. Based on the results obtained in the weight uniformity test, all formulations met the requirements because none of the tablets deviated from column A and column B. Based on the results of the weight uniformity test, the most optimal formulations were formulation I and formulation III, namely 303.8 and 302 mg because the ideal weight is 300 mg. As for the tests carried out, the weight of each tablet before printing has been weighed first, so the cause of the deviation of tablet weight from the research results is due to the non-uniformity of tablet weight during the tablet printing process, where some of the tablet weight sticks to the hole causing the resulting tablet weight to not meet requirements [8].

Hardness test of each formulation showed an average of 3-4 kg. The requirements for a good tablet hardness test are in the range of 4-8 kg [7]. The test results showed that the formulation that met the hardness requirements was in formulation I. The addition of high Carbopol with low levels of Na-CMC had low tablet hardness and high levels of Na-CMC resulted in increased tablet hardness. The antagonistic interaction is shown by the opposite graph, the more Na-CMC is added, the tablet hardness decreases, while at low carbopol, the addition of Na-CMC increases the tablet hardness. Na-CMC is hygroscopic so that in moist conditions it can absorb water up to >50%. As the concentration of Na-CMC used increases, the cohesion force produced between particles is getting stronger so that the tablet hardness value is high. Carbopol has the potential to reduce hardness, so the higher the level of carbopol, the more it releases binding power so that the hardness value decreases.

Factors that affect tablet hardness are the pressure at the time of tablet molding and the concentration of the binder. The stronger the pressure during tablet printing, the harder the tablet will be. The tablet factor does not meet the hardness requirements because of the lack of pressure force during tablet printing, if the pressure is increased, the tablet hardness value will increase[7].

The hardness in the results of the study, in the manufacture of tablets is also not suitable, namely 3.15 kg, this occurs due to the lack of pressure during the tablet compression process. The results show that the optimal formulation is in formulation I with a hardness of 3.3 kg [9].

The tablet friability test showed an average of 0.3% of formulation I, formulation II of 0.4%, formulation III of 0.6% according to the friability test requirements, namely the loss of tablet weight after testing was less than 0.5% to 1 % [7]. The effect of compression pressure at the time of printing can also affect, the higher the pressure, the harder the tablet will be so that the tablet friability will be low [10]. The thing that can increase the brittleness of a tablet is the use of a tablet printer punch that is not good enough[10]. Furthermore, another factor that can cause a small friability of a tablet is the moisture content. The drier the tablet or the less moisture it contains, the more brittle the tablet will be [11].

## CONCLUSION

The conclusion from this research is that the most optimal formulation is formulation I based on the analysis of simplex lattice design formula I with a combination concentration of Carbopol 30 mg and Na. CMC 40 mg with a desirabability value of 1, has the effect of a combination of

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Carbopol and Na matrices. CMC on the mucoadhesive tablet formulation of papaya leaf extract (Carica papaya L) on the evaluation of flow properties, friability, hardness and in vitro.

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