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RESEARCH

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Celery (*Apium graveolens* L.) Herba Extract Capsule Formulation as Anti-Ulcer

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Abstract

The use of medicinal plants for medicine has been prevalent since ancient times and various plants are used for public health. One of the plants that is often used in herbal medicine is celery, either directly in the form of vegetables or as an extract from the *Apium graveolens* L plant. Celery extract has previously been given to white mice, and can significantly protect the gastric mucosa and suppress gastric acid secretion. Traditional medicine derived from plant extracts is generally more desirable in tablet or capsule dosage forms. The objective of this study is to determine the best filler in the celery herb extract capsule formulation. This study used a pure experimental method using celery herb extracts which were formulated in capsule dosage forms. The powder fillers used in this formulation are Avicel 101, Avicel 102, and Amylum maydis. The extract capsules were then evaluated for uniformity of weight and disintegration time. Based on the evaluation results, the capsules formulated with Avicel 102 filler gave the best results with an average weight uniformity of 380.98 ± 4.41 mg and disintegration time of 2.64 ± 0.31 minutes. It is advisable to continue the evaluation of the dissolution test for the capsule preparation which gives the best result.

Keywords: Anti-Ulcer, Celery Herb Extract, Capsules

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1. INTRODUCTION

The use of medicinal plants for medicine has been prevalent since ancient times and various plants are used for public health. Medicinal plants have fewer side effects than chemical drugs (Kooti, et al., 2014). Currently, herbal medicines are used as an alternative to chemical drugs and the main reason is their low side effect rate compared to chemical drugs (Zaheer-Ud-Din, et al., 2012; Qusaj, et al., 2012).

One of the plants that is often used in herbal medicine is celery, either directly in the form of vegetables or as an extract from the *Apium graveolens* L. Thus, it has the potential to be developed as an alternative treatment that is safer and more affordable than synthetic drugs.

In a previous study conducted by Putri in 2015, testing on mice showed that celery extract provides antiulcer activity, which can significantly prevent gastric ulcers by decreasing the ulcer index (Putri, 2015). The content of celery (*Apium graveolens*) in the form of D-limonene and flavonoids which can act as antioxidants and anti-inflammatory and have an effect in reducing ulceration intensity in the stomach so that celery has the potential to be used to prevent damage to the stomach (Kooti, et al., 2014; Powanda, et al., 2015; Yu, et al., 2017; AlHowiriny, et al., 2015). Celery extract at a dose of 300 mg/kg showed a significant inhibitory effect on gastric lesions (91-95%), this is equivalent to the effect provided by omeprazole (94%) (Baananou, et al., 2013; Brankovic, et al., 2015).

Traditional medicine derived from plant extracts is generally in demand by the public in tablet or capsule dosage forms. Plant extracts that tend to have unpleasant tastes and odors can be overcome by formulating them in capsule dosage form (Al Tabakha, et al., 2015; Gulapalli & Mazetalli, 2017; Qusaj, et al., 2012; Patet & Amin, 2013; Lau, 2018; El, et al., 2012). But the problem is the consistency of the thick extract will affect the stability of the capsule preparation. In general, capsules can be powder or granule. To simplify the process of filling capsules, the contents of the capsules are made in powder form with the addition of fillers, lubricants, and glidants (Kemenkes, R.I., 2014; Amidon, et al., 2015; Darji, et al., 2018; Qusaj, et al., 2012, Stanzinger, et al., 2017).

The capsule formulation containing extracts with a thick consistency and high-water content requires special treatment to produce good capsules. Therefore, it is necessary to have excipients or additives capable of adsorbing or absorbing water and can improve the properties of powder flow. Avicel is an excipient that can be used as a filler which also functions as an adsorbent. The addition of Aerosil to the formulation is expected to maintain the hygroscopicity of capsules (Agoes, 2007; Gajdziok, et al., 2011; Darji, et al., 2018; Stanzinger, 2017; Qusaj, et al., 2012). To obtain a capsule mass with a good flow rate a suitable filler can be added, such as Avicel 101 and Avicel 102. Generally, Avicel is used in the pharmaceutical field, especially as a filler in tablet and capsule formulas. Avicel also has lubricant and disintegrate properties (Rowe, 2009; Barbosa, et al., 2019; Darji, et al., 2018; Stanzinger, 2017). Avicel 101 has a smaller particle size so that it is able to adsorb moisture. Avicel 102 has a larger particle size so it is useful for improving flow properties (Agoes, 2008; Darji, et al., 2018). Another filler used is starch. Starch maydis is widely used as a filler because of its small hygroscopicity. Magnesium stearate and talc can be used as a lubricant (Rowe, 2009; Barbosa, et al., 2019; Darji, et al., 2018; Stanzinger, 2017). This study aims to find the best filler in the thick capsule formulation of celery herb. The powder fillers used in this formulation are Avicel 101, Avicel 102 and starch maydis.

2. RESEARCH METHOD

The method used is a pure experimental method using celery herb extract as an antiulcer drug at a dose of 336 mg/70 kg BB obtained from the research of Baananou, et al, 2013. The extract is made in capsules with fillers Avicel 101, Avicel 102 and starch maydis which is mixed in the thick extract of celery herbs in a ratio of 1:1. The complete capsule formula is as shown in Table 1. The study has received Ethical Approval from the Health Research Ethics Commission of the Health Polytechnic of the Ministry of Health of Tasikmalaya No. 2019/KEPK/PE/VII/0008.

Table 1. Formulations for capsules made

Component	Formula		
	F1	F2	F3
Celery herb extract	336 mg	336 mg	336 mg
Avicel 101	336 mg	-	-
Avicel 102	-	336 mg	-
Amilum maydis	-	-	336 mg
Lactosa	33 mg	33 mg	33 mg
Aerosil	3 %	3 %	3 %
Talk	2 %	2 %	2 %
Mg Stearat	1 %	1 %	1 %
Capsule weight	750 mg	750 mg	750 mg

The formulation of celery herb extract capsules was made in 3 formulas, which were formula 1 with Avicel 101 filler, formula 2 with Avicel 102 filler and formula 3 with starch maydis filler. Formulations were made with a variety of fillers and other additives used are fixed (Augsburger, 2000; Barbosa, et al., 2019; Darji, et al., 2018; Gullapalli & Mazzitelli, 2017; Stanzinger, et al., 2017).

3. RESULTS AND DISCUSSION

a. Celery Extract Making

Celery herb comes from agricultural areas in Lembang, West Bandung Regency. Herba Celery has been determined at the University of Siliwangi, Tasikmalaya. Celery was extracted using the maceration method with 96% ethanol solvent for three times 24 hours with occasional stirring at each solvent change. The choice of this maceration method was used because of the secondary metabolites that were not heat resistant, which were flavonoids because flavonoid compounds are easily oxidized at high temperatures. Cold extraction allows many compounds to be extracted, although some compounds cannot use the maceration method. Celery extract was concentrated using a rotary evaporator. Concentration was done to separate the solvent, so that a thick extract was obtained. The yield obtained from the extraction and concentration was 3.56%. The size of the yield shows whether or not the extraction is effective. The effectiveness of extraction can be influenced by several things, namely the type of solvent, the extraction method used, the particle size of the *dadap* leaf powder and the length of the extraction time (Baananou, et al., 2013).

Phytochemical screening tests on concentrated extracts were carried out to determine what secondary metabolites were present in the extract. The test method and secondary metabolite reagents are in accordance with the book from the Indonesian Ministry of Health, 2000 (Departemen Kesehatan, R.I., 2000).

Table 2. Results of Phytochemical Screening Test

Phytochemical Test	Reactor	Test results
Alkaloid	Meyer	-
	Dragendroff	-
Flavonoid	Mg+ HCl pekat	+
Tanin	FeCl ₃ 1%	+
Saponin	Aquadest + HCl	+
Steroid	Liebermann	-

Information : + = There are secondary metabolites

- = There are no secondary metabolites

The results of phytochemical screening of celery herb extracts showed that celery extract contained secondary metabolites of flavonoids, tannins and saponins.

b. Celery Extract Capsule Formulation

In making celery extract capsules, it begins with a literature study to calculate the dosage of celery extract used for anti-ulcer treatment in humans. In addition, to therapeutic doses, a toxic dose literature study was also conducted to clarify that the therapeutic dose of celery extract as an anti-ulcer to be formulated in capsule form does not exceed the toxic dose, where it is known that the toxic dose of celery extract is 2500 mg/kg BW (Aini, L.N, 2017).

After determining the dosage, 3 formulas of celery extract powder were made using Avicel 101, Avicel 102 and Amylum maydis fillers with a ratio of 1: 1 for each extract and filler.

Capsules are made conventionally in all formulas both with Avicel 101, Avicel 102 and Amylum maydis fillers. The conventional method was chosen because it has the advantage of being more economical, increasing the optimization of capsule disintegration because it immediately becomes fine particles so that the disintegration time is faster, the absorption rate increases and increases bioavailability (BPOM, 2010; El, et al., 2012; Charoo, et al., 2017). The excipient used was selected based on the properties of the excipient which had good flow and compressibility properties and was able to absorb a lot of water (Nugroho, 2012; Darji, et al., 2018; Stranzinger, et al., 2017). The weight of the capsules as in table 1 is made of 750 mg per capsule of 200 capsules.

Table 3. Results of Mass Evaluation of Celery Extract Capsules

Formula	Flow properties (g/sec)	Real BJ (g/mL)	BJ incompressible (g/mL)	Compressibility (%)	Angle of Rest (α°)
F1	2,03 ± 0,17	0,38	0,45	13,92	33,33
F2	2,17 ± 0,17	0,41	0,45	10,29	25,00
F3	1,95 ± 0,18	0,37	0,44	15,85	45,54

Information: F1 = capsules with Avicel 101 fillers

F2 = capsules with Avicel 102 fillers

F3 = capsules filled with Amylum maydis

In the process of making celery extract capsules, the mass of the capsules is evaluated. From the results of the evaluation, the flow properties, compressibility index and angle of rest of the capsule mass with Avicel 102 (F2) filler were 10.29% and 25.00 α° had better values compared to the mass of other celery extract capsules with Avicel 101 fillers (F1) of 13.92% and 33.33 α° and fillers of amyllum maydis (F3) of 15.85% and

45.54 α° . This can be caused by differences in the types and properties of fillers. For the mass of the F2 celery extract capsule, Avicel 102 filler in the form of granules was used, while for the mass of the F1 and F3 celery extract capsules, Avicel 101 and amylum maydis were used respectively.

To see the mass homogeneity of the capsule, a microscope was tested. The homogeneity of the capsule mass is important because it will affect the dosage per capsule.

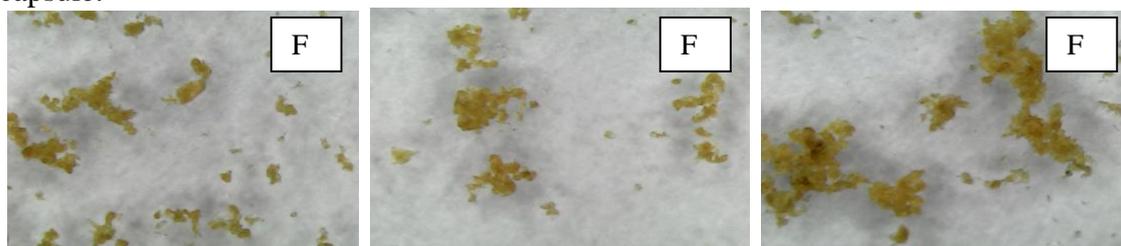


Figure 1. Homogeneity test results using a 500X magnification microscope

After evaluating the mass of the capsule, the capsule mass is inserted into the capsule shell using the capsule shell number that corresponds to the compressed density value of each formula, which is the capsule shell number 0 with a volume capacity of 0.68 mL and an compressive density of 0.544 g/mL. Furthermore, the quality of the celery extract capsules was evaluated.

Table 4. Evaluation Results of Celery Extract Capsules with Avicel 101, Avicel 102 and Amylum Maydis Fillers

Formula	Uniformity of weight (mg) n=20	Variation of weights (mg) n=20	Time destroyed (seconds)	Hygroscopic Test 25°C, RH 70% (Day)
F1	376,68 ± 13,60	472,44 ± 13,60	3,62 ± 0,40	90
F2	380,98 ± 4,41	476,74 ± 4,41	2,64 ± 0,31	90
F3	377,42 ± 10,56	473,18 ± 10,56	2,88 ± 0,42	90

Table 4 shows that the capsules made with Avicel 101 fillers have a higher weight variation (376.68 ± 13.60 mg) than the weight of celery extract capsules with Avicel 102 fillers and celery extract capsules with Amylum maydis filler with an average weight of each. the capsules were 380.98 ± 4.41 mg and 377.42 ± 10.56 mg respectively. The variation in capsule weight was caused by the poor mass flow properties of the capsules with Avicel 101 fillers and the unfavorable mass of the capsules with Amylum maydis as the filler, which are 2.03 g/sec and 1.95 g/sec, while the best flow properties were seen in the mass of the capsules of celery extract with Avicel 102 filler is 2.17 g/minute (Hadisoewignyo & Fudholi, 2013; Gajdziok, et al., 2011; Stranzinger, et al., 2017). Celery extract capsules with Avicel 102 fillers have good flow properties and small weight variations because the shape of Avicel 102 is granular so that it has high porosity which absorbs moisture well and has high compressibility properties compared to Avicel 101 and Amylum maydis which are in powder form (Narang & Boddu, 2015; Gajdziok, et al., 2011; Stranzinger, et al., 2017). Flow properties will affect the uniformity of capsule contents where uniformity of capsule contents will affect the accuracy of the dosage.



Figure 2. Result of Hygroscopicity Test for 3 months of storage

Figure 1 shows the hygroscopicity test applied on celery extract capsules of all formulas, where the capsules are stored in containers and packages used for storage and stored under controlled room conditions with a temperature of 25°C and 70% humidity. This hygroscopicity test was performed to determine how long the celery extract capsules were stable on storage. The results of the hygroscopicity test carried out for 3 months showed that all of the capsule formulas of celery extract were stable in tightly closed containers at 25°C and 70% humidity.

4. CONCLUSION

The capsule formulation of thick celery herb extracts made with Avicel 101, Avicel 102 and Amilum maydis fillers produces good and stable capsules. Based on the evaluation results, the capsules formulated with Avicel 102 filler gave the best results with an average weight uniformity of 380.98 ± 4.41 mg and disintegration time of 2.64 ± 0.31 minutes.

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