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The 5th ICETIA: New Submission Received. Contribution ID: 171

1 message

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Wed, Oct 31, 2018 at 11:45 PM

Reply-To: icetia@ums.ac.id

To: wenny_i_s@ukwms.ac.id

Dear Ms. Wenny Irawaty,

We have received your submission. Thank you.

Submission Details

=====

ID : 171

Title : Design of Kaffir Lime Peel Extract-Containing Tablets by Direct

Compression: Effects of Filler-Binder on Rheological Properties

Author(s): Wenny Irawaty

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With best regards,

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Wenny Irawaty <wenny_i_s@ukwms.ac.id>

LoA paper ID 171

11 messages

ICETIA ICETIA <icetia@ums.ac.id>

Mon, Nov 12, 2018 at 8:56 AM

To: wenny_i_s@ukwms.ac.id

Dear Wenny Irawaty

This is to inform you that your full paper entitled: **Design of Kaffir Lime Peel Extract Containing Tablets by Direct Compression: Effects of Filler-Binder on Rheological Properties (paper ID 171)** has been accepted for oral presentation at:

The 5th International Conference on Engineering, Technology, and Industrial Application (ICETIA 5 2018)

Hotel Alila Solo, Wednesday, 12 - 13 December 2018

Jl. Slamet Riyadi No.562, Jajar, Laweyan, Kota Surakarta, Jawa Tengah 57144

Please login into your account in submission website to find out the detail (<http://icetia.ums.ac.id/2018/submit/>). We would like also to inform you that the scientific committee is still undertaking a thorough review for the full paper. Author will be notified the comments from reviewers later on to have the final revised version prior to the paper publication. Please be aware that there will be no standalone ICETIA 2018 proceeding since all accepted papers will be published in a Scopus Indexed Proceeding (American Institute of Physics (AIP) (ISSN: 0094-243X/E-ISSN: 1551-7616, +additional publication fee)).

(Please ignore it if you already made a payment). To ensure the presentation remains in the programme, all authors are kindly requested to register online and make the payment for registration. Please be informed that deadline for

Early Bird Registration: extended to October, 5th 2018

Regular Registration: November, 11th 2018

Please recheck that your paper should be no more than 8 pages. If your paper is more than 8 pages, you need to pay additional payment IDR 150,000 or USD 25/page.



Wenny Irawaty <wenny_i_s@ukwms.ac.id>

Invitation letter

1 message

ICETIA ICETIA <icetia@ums.ac.id>

Tue, Dec 4, 2018 at 8:03 AM

To: Koko Suryawan <iwayankokosuryawan@gmail.com>, Jazaul Ikhsan <jazaul.ikhsan@umy.ac.id>, Imam Alfianto <imam.alfianto.ft@um.ac.id>, Wahyuda Wahyuda <wahyuda@gmail.com>, Herry Purnama <hp269@ums.ac.id>, Subroto Subroto <sub224@ums.ac.id>, Irham Sya'bani <irhamsb@gmail.com>, "Sudarmilah, Endah" <Endah.Sudarmilah@ums.ac.id>, Umar Umar <umar@ums.ac.id>, wenny_i_s@ukwms.ac.id

Dear Mr/Mrs/Ms

Presenter The 5th International Conference ICETIA 2018,

We would like to invite you to present your contribution which had been accepted for oral presentation at:

The 5th International Conference on Engineering, Technology, and Industrial Application (the 5th ICETIA 2018)**Hotel Alila Solo, Wednesday 12th December 2018**

Jl. Slamet Riyadi No.562 Jajar Laweyan, Surakarta, Jawa Tengah 57144

All presenters are kindly requested to register online by filling in the form link below:

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Please be aware that there will be no standalone ICETIA 2018 proceeding since all accepted papers will be published in **AIP (American Institute of Physics)** - a Scopus Indexed Proceeding (ISSN: 0094-243X/E-ISSN: 1551-7616) + **additional publication fee which will be charged later.**

We also offer a **free City Tour on Thursday 13th December 2018**. The tentative agenda of City Tour will be visiting Mangkunegaran Palace, Kampung Batik Kauman, and visiting D'Tjolomadoe. If you would like to join the tour, please fill in the form link below: <http://bit.ly/ICETIA2018-CityTour>.

For further information please visit the conference website at <http://icetia.ums.ac.id>. If you wish to obtain more information, please do not hesitate to contact the Conference Committee on telephone/*WhatsApp*: [+62-812-2790-9919](tel:+62-812-2790-9919) or [+62-896-7981-7735](tel:+62-896-7981-7735) or e-mail to: icetia@ums.ac.id.

We look forward to welcoming you at the conference.

Best Regards,

Anto Budi Listyawan, MSc

Conference Chair

 **EVENT PROGRAM TENTATIVE.pdf**
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Design of kaffir lime peel extract tablets by direct compression: Effects of filler-binder on rheological properties

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Wenny Irawaty, Lannie Hadisoewignyo, Jenifer Wijaya, Shindy Saera Sababalat, and Andy Sebastian Tanjaya



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Design of Kaffir Lime Peel Extract Tablets by Direct Compression: Effects of Filler-Binder on Rheological Properties

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Abstract. Dried kaffir lime peels from *Citrus hystrix* were extracted with ethanol by maceration method, followed by solvent evaporation to obtain dry extract. Due to economical aspect and good flow properties of the extract, a direct compression method was applied in making the tablets. The main objective of this study was to study the influence of filler-binder (Avicel PH 102, Emcompress and Lactose) on rheological properties of kaffir lime peel extract tablet dough. *Firstly*, kaffir lime peel extract was prepared by peeling, cutting and drying kaffir lime peels prior to soaking them to ethanol. After separating the solid part, the extract was subsequently concentrated and filler was added into the crude extract to obtain dry product. *Secondly*, dry extract was then combined with filler-binder, sweetener and lubricant prior to the compression. Rheological properties evaluated in this study were density, flow time, the Carr index and the Hausner ratio. *Thirdly*, the best formulation dough was compressed to produce tablets. From the results, it can be concluded that ethanol is the best solvent to extract polyphenols from kaffir lime peels. In addition, the use of a mixture of lactose and Avicel PH 102 as the filler-binder agent exhibited the best formulation.

INTRODUCTION

Natural antioxidants from fruits offer an alternative source of dietary ingredients to promote healthy life. *In vivo* studies show that epigallocatechin gallate contained in green tea is able to inhibit memory deficits in Alzheimer case [1], hesperidin isolated from citrus peels allows the regeneration of ulcerated tissue and prevents hemorrhagic injury of gastric mucosa [2], polyphenols in cocoa bean can reduce the risk of atherosclerosis [3], anthocyanins isolated from blueberry exhibits protection on liver [4], xanthonenes in mangosteen can protect nervous system [5], flavonoids of polymethoxylated flavones, procyanidins and isoflavones tyrosinase in several extracts (tangerine peels, cocoa and red clover) is potent to treat Parkinson's disease [6], and so forth. Basically, the assessment on antioxidant activity of plant extracts has lately received great attention. Kaffir lime (*Citrus hystrix*) is selected in this study since the utilization of this fruit is still limited hence further investigation is required.

Kaffir lime peels have been claimed to exhibit several activities, such as neutralize free radicals [7], antidiabetic performance [8], anti-inflammation action [9], and anti-microbial activity [10]. However, the use of kaffir lime peels is still limited, for instance, a certain amount of kaffir lime peel added in tea-based commercial drink to obtain citrus flavor. Therefore, further investigation to develop kaffir lime peels as advanced products becomes a challenge. Here, we investigate a possibility of kaffir lime peels extract to be processed as a tablet. Considering the benefits shown by kaffir lime peels, it is expected that the tablet can be a potential supplement to improve stamina and as an anti-degenerative agent.

Nowadays, tablet is still among the favorite forms of commercial drugs for treating diseases [11-13]. It has used Carr's plant extract to be used as an anti-microbial agent, supplement and even as an anti-cancer agent [14-16]. Tablets are obtained from the aggregation of powder by applying pressure during the process. Direct compression method offers several advantages compared to other methods, e.g., granulation technique, since the method requires less cost, labor and time. Accordingly, direct compression method is widely applied in pharmaceutical industries. Efforts have been made to optimize the tablet formulation [17, 18]. Proper flowability of the materials is an important element to ensure rapid flow and dose uniformity during die-filling. In addition, compactability is also required to obtain satisfactory result since the materials must remain in compact form after the compression force is removed. The tablet generally consists of plant extract, filler, binder, sweetener, flavor, color, preservative and lubricant. Plant extract usually exhibits poor flowability in which this characteristic frequently becomes a problem during the preparation phase. Another factor is the hygroscopic property of tablet-forming materials since plant extract tends to be hygroscopic due to high affinity of the plant phytochemicals to water vapor present in the environment. Common sweetener added during tablet preparation is mannitol, sucrose, dextrose, saccharin, and so forth. However, some sweeteners exhibit hygroscopic characteristic, lack of stability in the presence of water, and bitter after taste. Therefore, this study aimed to formulate kaffir lime peels extract tablet by evaluating the effect of filler-binder on the rheological properties of the tablet dough, followed by tablet preparation through direct compression method.

MATERIALS AND METHODS

Materials

Kaffir lime fruits were purchased from a local market in Surabaya, East Java. Different solvents (ethanol solution with concentrations of 96% and 41%) were employed to extract polyphenols compounds from kaffir lime peels. Magnesium aluminometasilicate (Neusilin US2) was added to the extract to obtain dry extract.

Filler-binders used were α -lactose monohydrate (Lactose), dicalcium phosphate dehydrate (Emcompress), microcrystalline cellulose (Avicel PH 102). Distilled water and ethanol (96%) from commercial source were also used. The sweetener was mannitol.

Methods

The methods include extract preparation, tablet powder characterization, tablet preparation and tablet characterization.

Extract Preparation

Fresh fruits were washed and rinsed with water to remove dirt and soil. Subsequently, they were peeled and cut into a size of 0.5 x 0.5cm. After that, the peels were dried under forced draft fan for 48 h. The peels were then soaked in ethanol (1: 40^{w/v}) for 8 h at room temperature. After separating the solid part, the extract was concentrated by using a rotary vacuum evaporator (IKA, RV10) at 50°C followed by the addition of neusilin to obtain dry extract.

Tablet Preparation

The composition of tablet is shown in Table 1. Extract, filler-binder and mannitol were blended for 5 min by tumbling at 100 rpm (Erweka). Subsequently, magnesium stearate was added and blended for another 2 min. After that, the mixture was compressed to obtain the kaffir lime peel extract tablet.

Characterization

Prior to tablet preparation, the powder was characterized by measuring its moisture content, flow time, the Carr index and the Hausner ratio. The moisture content was measured by using moisture analyzer balance. Flow-time data were assessed by the bulk, and tapped densities were determined in a 100-mL graduated cylinder mounted on a mechanical tapping device (Erweka SVM12). *Firstly*, the sample was introduced into the cylinder until the reading

reaches the 100 mL-mark and the total weigh was recorded. Then, it was tamped until a constant volume was obtained (around 500 times) and the final volume was documented. The bulk density was calculated as the ratio between the sample weight and the initial volume. The tapped density was obtained from the ratio between the sample weight and the final volume. The evaluated rheological properties of powder are density, flow time and compressibility which the latter is expressed as the Carr index and the Hausner ratio.

RESULTS AND DISCUSSION

Tablet manufacturing by direct compression offers benefits compared to other methods. However, it is necessary to consider the properties of plant extracts added in the tablet mixture since it will determine the product characteristics, including flowability, compactability and compressibility. For the present study, kaffir lime peels extract was prepared by different solvents, followed by an evaluation prior to the compression method for tablet preparation. Previous study [19] shows the best solvent to extract polyphenols from kaffir lime peels is ethanol 41%, therefore, it was firstly selected as the extraction solvent in the present experiment. To investigate any possibility to use other solvents, ethanol solution with different concentrations, i.e. 70 and 96% were used and examined. After the concentration phase, kaffir lime peels extracts were obtained from different extraction solvents are shown in Fig. 1.

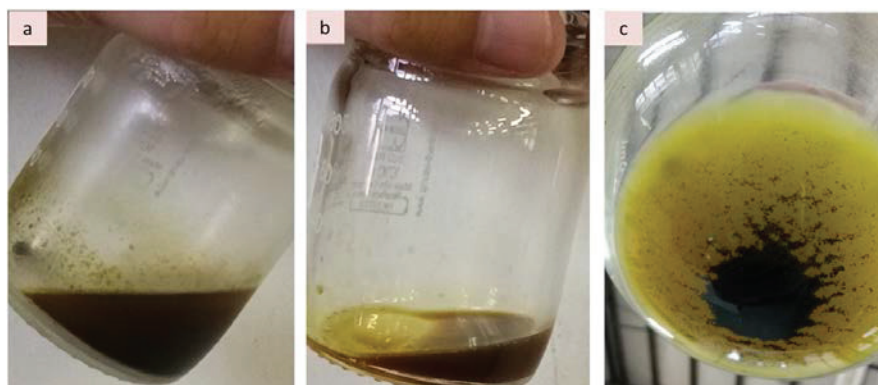


FIGURE 1. The effect of solvent on the appearance of kaffir lime peel extract: (a) 41% ethanol, (b) 70% ethanol, and (c) 96% ethanol

As demonstrated in Fig. 1, the solvents employed to extract polyphenols from kaffir lime peels influences the characteristics of the extracts. Figure 1(a) is the extract obtained from ethanol 41%. It was expected that the use of 41% ethanol will offer more benefits for tablet manufacturing since the extract contains the optimum polyphenols compounds of kaffir lime peels. Since 41% ethanol is used as the solvent, the extract solution contains a lot of water. Due to the restriction in the laboratory, in this experiment, the water cannot be removed completely. Even after the concentration period is prolonged, total duration for concentration phase is around 6 h, the extract cannot be further concentrated. After 6 h of heating process at 40°C, the citrus aroma on the extract cannot be identified. It indicates that the essential oil or compounds that were originally extracted from kaffir lime peels were vanished during the heating process even at low temperature. From the examination on the extract, it is obvious that it would be difficult to dry the extract and therefore, it cannot be further processed tablet preparation. Furthermore, 70% ethanol was selected as the solvent and the extraction steps were similar as before. Since the ethanol concentration was higher, it is easier to evaporate the ethanol. Similar to the case of 41% ethanol, the extract still contains water, but in lesser amount (Fig. 1(b)). Accordingly, the extract cannot be added to tablet ingredients since the tablet powder will be wet and cannot be pressed in the press machine. The use of 96% ethanol is another option to obtain dry extract regardless the type and composition of polyphenols being extracted from the peels. Since 96% ethanol is used as the solvent, it can be easily removed until it is almost dry and the color of the solution does not change during the process. However, it is noticeable that the concentrated extract is present in black tiny particles in the solution (Fig. 1(c)). We found those particles are polyphenols which initially dissolves in ethanol but later, some polyphenols cannot dissolve due to the availability of limited ethanol in the system. Subsequently, heating process is done on the

solution, resulting dry extract of pure kaffir lime peels with a darker color final result.

For the preparation of kaffir lime peels extract tablet, the extract as shown in Fig. 1(c) is added to the tablet ingredients due to the color extract, and the result is examined. Therefore, another effort has been tried by applying short heating to the solution obtained by maceration method. Just before the black tiny particles formed in the solution, neusilin was added and the heating process was further continued until dry extract was obtained. The yield of extract was around 25%. Furthermore, dry and yellow yield was obtained as expected (Fig. 2).

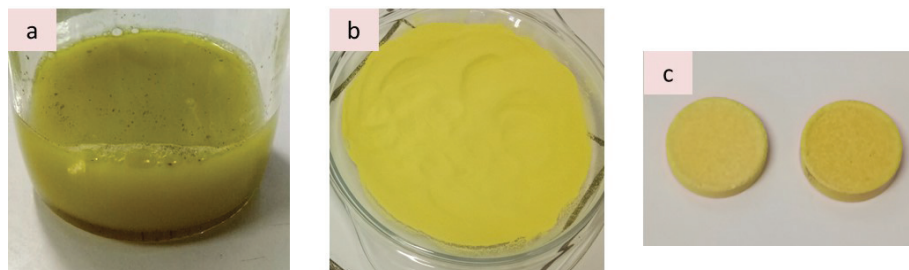


FIGURE 2. Kaffir lime peels in different forms: (a) crude extract solution, (b) dry extract, and (c) tablet

Dry extract may not exhibit the good rheology and compressibility required for tablet preparation by direct compression. Several attempts have been proposed to improve the rheology properties of plant extracts and their dough tablets, such as extract drying method [20], the selection of suitable excipients during formulation [17, 21], operating conditions [21], and so forth. During the extract preparation, neusilin was added to obtain dry extract. It can be observed that the dry extract demonstrated suitable flowability (data is not provided). Dry extract of kaffir lime peels was further processed into tablet after they are mixed with other ingredients. The compositions of tablet have been investigated and the results are shown in Table 1. The rheological properties of tablet powder were evaluated, including moisture, flow time, density, the Carr index, and the Hausner ratio. The results are tabulated in Table 2.

TABLE 1. The composition of kaffir lime peels extract tablet

Composition (%)	Formula					
	I	II	III	IV	V	VI
Extract	24	19	15	15	15	15
	60	60	54	54	54	54
Filler-binder	(Avicel PH 102)	(Avicel PH 102)	(Avicel PH 102)	(Emcompress)	(Emcompress & Lactose 1:1)	(Avicel PH 102 & Lactose 1:1)
Mannitol	15	20	30	30	30	30
Magnesium stearate	1	1	1	1	1	1

TABLE 2. The rheological properties of tablet dough

Characteristic	Formula					
	I	II	III	IV	V	VI
Moisture (%)	6.1	6.2	6.1	2.1	1.8	4.0
Flow time	ok	ok	ok	x	x	ok
Bulk density (g/mL)	0.4095	0.3812	0.3943	0.4536	0.4406	0.4072
Tapped density (g/mL)	0.4914	0.4530	0.4868	0.6630	0.6330	0.5312
Carr index (%)	16.7	15.8	19.00	31.6	30.4	23.3
Hausner ratio	1.20	1.19	1.23	1.46	1.44	1.30

As demonstrated in Table 2, the rheological properties of tablet powder are significantly affected by ingredients added into the mixture. The bulk and tapped density of the mixture added with Avicel PH 102 as the filler-binder were 0.40 and 0.45 g/mL, respectively. Accordingly, the values of Carr index and Hausner ratio are in the range of 16-19% and 1.2, respectively. The Carr index greater than 25 is considered to possess poor flowability. Therefore, the formula I to III of the tablet powders have good flowability. Mannitol is selected in the present study since it has a relatively low-calorie sweetener and poorly adsorbed in the small intestine, as well as it contains glycemic index of zero [23]. Therefore, the product will be suitable for people with diabetes. In addition, mannitol provides cooling effect to improve the taste and thus, enhance the acceptance level of the tablet by customers. However, mannitol is hygroscopic and the presence of mannitol may reduce the flowability property of the powder. Data presented in Table 1 shows formula I to III, which exhibit the good flowability of the powder. The comparison between formula III and IV indicates that the use of emcompress as the filler-binder increases both bulk and tapped density by 15% and 36%, respectively. Emcompress consists of dicalcium phosphate dihydrate, high density material, making the mixture possesses a higher density compared to microcrystalline cellulose (Avicel PH 102) [17]. The moisture content, however, decreased by 67%. Meanwhile, α -lactose monohydrate is a relatively dry filler-binder compound. Therefore, the addition of lactose to Avicel PH 102 (1:1) has decreased the tapped density from 0.6630 to 0.6330 g/mL (compared to emcompress alone). Similar trend was observed for the bulk density as shown in Table 2. However, the parameter of Carr index of both formula IV and V, which is in the range of 30 and 32, indicates a poor flowability of the mixture. When emcompress (formula V) is replaced with Avicel PH 102 (formula VI), the density of the mixture is lower than the previous one. This finding verifies previous result that emcompress exhibits higher density material. Thus, the use of Avicel PH 102 decreased the tapped density in greater extent than the bulk density, as indicated by the decrease in the Hausner ratio from 1.44 to 1.3 or from 30 to 23 for the parameter of Carr index. Moreover, the moisture content decreased from 6.1% (filler-binder of pure Avicel PH 102; formula III) to 4.0 % (filler-binder of a mixture of Avicel PH 102 and lactose; formula VI), which is consistent with previous result. The Carr index has decreased to below 25, showing a good flowability of the powder in the system. Considering several parameters were observed during the preparation of kaffir lime peels extract tablet, the combination of Avicel PH 102 and lactose is the best filler-binder added during solid form formulation. Kaffir lime peels extract tablet prepared by direct compression method is shown in Fig. 2(c).

CONCLUSION

In the formulation of tablet from kaffir lime peels extract, there are several main conclusions. *Firstly*, the importance of solvent employed to extract polyphenols from the peels to accommodate the property of the produced extract. Since the tablet is prepared by direct compression method, thus the plant extract must be dry perfectly and it can be achieved by the use of ethanol as the solvent, followed by the addition of neusilin as the drying agent. The solid extract exhibits good flowability property. *Secondly*, filler-binder provides significant effect on the characteristics of the produced tablet. The best filler-binder evaluated in the present study is a combination of Avicel PH 102 and lactose.

ACKNOWLEDGMENT

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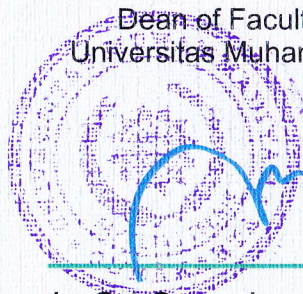
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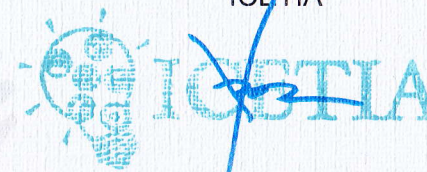
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