Research Article

การกลบรสลูกกลอนด้วยสารเคลือบอิมัลชันจากไขใบคล้า

ชิษณุพงษ์ อนุกานนท์[1*], ไชยยง รุจจนเวท[1]

[1]สำนักวิชาแพทยศาสตร์ มหาวิทยาลัยแม่ฟ้าหลวง จังหวัดเชียงราย 57100

***ติดต่อผู้นิพนธ์:** ชิษณุพงษ์ อนุกานนท์ สำนักวิชาแพทยศาสตร์ มหาวิทยาลัยแม่ฟ้าหลวง จังหวัดเชียงราย 57100 อีเมล shisanupong.anu@mfu.ac.th

บทคัดย่อ

การกลบรสลูกกลอนด้วยสารเคลือบอิมัลชันจากไขใบคล้า

ชิษณุพงษ์ อนุกานนท์[1*], ไชยยง รุจจนเวท[1]

ว. เภสัชศาสตร์อีสาน 2565; 18(3) : 67-76

รับบทความ: 30 กรกฎาคม 2564 **แก้ไขบทความ:** 13 กันยายน 2564 **ตอบรับ:** 30 กันยายน 2565

ไขที่ได้มาจากธรรมชาติได้แก่ไขที่เคลือบใบคล้าสามารถเป็นแหล่งทรัพยากรที่สำคัญในการนำมาใช้ประโยชน์ต่าง ๆ แก่ท้องถิ่นนั้น ๆ ได้อย่างยั่งยืน การศึกษาครั้งนี้มีวัตถุประสงค์เพื่อพิจารณาค่าสัดส่วนระหว่างส่วนที่ชอบน้ำกับส่วนที่ชอบน้ำมันที่เหมาะสมที่สุดของไขจากใบคล้า และพัฒนาสูตรตำรับสารเคลือบอิมัลชันจากไขใบคล้าให้มีความคงตัว เพื่อกลบรสของลูกกลอนที่มีรสขม (ลูกกลอนฟ้าทะลายโจร) **วัสดุและวิธีการทดลอง:** นำไขจากใบคล้าเตรียมเป็นอิมัลชันที่มีค่าสัดส่วนระหว่างส่วนที่ชอบน้ำกับส่วนที่ชอบน้ำมันระหว่าง 9 ถึง 14 เตรียมโดยวิธีบิกเกอร์ และเลือกตำรับที่มีค่าสัดส่วนระหว่างส่วนที่ชอบน้ำกับส่วนที่ชอบน้ำมันที่เหมาะสมที่สุดจากการวัดขนาดของหยดอิมัลชันด้วยกล้องจุลทรรศ์ เมื่อได้ตำรับที่ดีที่สุดแล้วจึงนำมาเตรียมเป็นน้ำยาเคลือบลูกกลอนฟ้าทะลายโจร เพื่อนำไปทดสอบความสามารถในการกลบรสขมในอาสาสมัครสุขภาพดีต่อไป **ผลการศึกษา:** ตำรับสารเคลือบอิมัลชันจากใบคล้าที่มีความคงตัวที่ดีที่สุดจะต้องมีค่าสัดส่วนระหว่างส่วนที่ชอบน้ำกับส่วนที่ชอบน้ำมันเท่ากับ 12 และเมื่อนำลูกกลอนฟ้าทะลายโจรที่เคลือบด้วยสารเคลือบจากไขดังกล่าวทดลองกับอาสาสมัครเพื่อดูเวลาในการรับรสขมเมื่ออมลูกกลอนดังกล่าวพบว่าสารเคลือบจากไขใบคล้าสามารถป้องกันการรับรสขมได้อย่างมีประสิทธิภาพเมื่อเทียบกับลูกกลอนที่ไม่เคลือบ รวมไปถึงลักษณะทางกายภาพของชั้นเคลือบจากไขใบคล้า ได้แก่ ลักษณะภายนอก สี ความหนา และ น้ำหนักของชั้นเคลือบอยู่ในเกณฑ์ที่ดี **สรุปผล:** การศึกษาครั้งนี้สรุปว่าสารเคลือบจากไขใบคล้ามีประสิทธิภาพในการกลบรสขมจากลูกกลอนฟ้าทะลายโจรซึ่งมีความขมมากได้อย่างมีประสิทธิภาพ ซึ่งบ่งชี้ถึงประโยชน์ของไขชนิดนี้ในการเป็นไขทดแทนในทางเภสัชอุตสาหกรรมต่อไป

คำสำคัญ: คล้า, ไขคออัสซู, การเคลือบเม็ดยา, อิมัลชัน, การกลบรส

Taste-masking of pills by coating with a wax emulsion made from *Calathea lutea*

Shisanupong Anukanon[1*], Chaiyong Rujjanawate[1]

[1]School of Medicine, Mae Fah Luang University, Chiang Rai, 57100, THAILAND

***Corresponding author:** Shisanupong Anukanon, School of Medicine, Mae Fah Luang University, Chiang Rai, 57100, THAILAND
E-mail : shisanupong.anu@mfu.ac.th

Abstract

Taste-masking of pills by coating with a wax emulsion made from *Calathea lutea*
Shisanupong Anukanon[1*], Chaiyong Rujjanawate[1]
IJPS, 2022; 18(3) **:** 67-76
Received: 30 July 2021 **Revised:** 13 September 2021 **Accepted:** 30 September 2021

The wax covering the leaf of *Calathea lutea* is a promising naturally resourced material and the use of this natural wax, as a pill coating, requires investigation. This study determined the required hydrophilic-lipophilic balance (HLB) values of this wax, to formulate both the most stable emulsion and the most effective taste-masking preparation for human use. **Materials and method:** The wax from *C. lutea* was prepared in a series of six emulsion formulations, with HLB values ranging from 9 to 14, using the beaker method. The optimal required HLB value was determined by using microscopic droplet size analysis. Bitter traditional herbal pills (made from *Andrographis paniculata*) were then coated with the optimal emulsion formulation in order to evaluate the masking of the bitter taste in healthy volunteers. **Results:** The results revealed that an emulsion formulation, with the required hydrophilic-lipophilic balance (HLB) of 12, was the most stable and was suitable for coating the bitter herbal pills. In a sensory evaluation in healthy participants in term of onset time exposed bitter taste, the formulation effectively masked the taste of bitter traditional herbal pills when compared to the uncoated pills. The physical characteristics of its coating layer were acceptable. **Conclusion:** This study suggests that an emulsion made from the wax of *C. lutea* can effectively mask the bitterness of the andrographis pill. This natural wax material can therefore be used as an alternative pill coating in pharmaceutical preparations.

Keywords: *Calathea lutea* (Aubl.) E.Mey. ex Schult, Cauassú wax, Pill coating, Emulsion, Taste-masking

1. Introduction

Solid medication dosage forms i.e. compressed tablets or capsules, are most frequently administered orally because of convenience of use, and to ease dose calculation (Sakr & Alanazi, 2013). This convenience can be double-edged sword, because there are both an advantages and disadvantages related to this dosage form. Offensive taste or odor of oral preparations, which release during the pass across the tongue, is one of the problems, leading to patient non compliance and a subsequent decrease in therapeutic efficacy of medications (Amita *et al.*, 2002 and

Sohi *et al*., 2004). Taste-masking techniques of this dosage form have been developed to resolve this problem, the most popular strategy is to create a barrier to the taste buds of the tongue (Nanda *et al*., 2002).

A natural wax, derived from a renewable resource such as a plant, insect or animal (Gurr *et al*., 2016), is a promising material which could be an option as a commercial wax or fat substitute. A report on the import value of agricultural products and their related products in Thailand from 2016 to 2017, reported that the import values of the category of other vegetable fat and oils was 195,960,000 and 185,824,000 baht, respectively. (Office of Agricultural Economics, 2018). These import values are not high when compared to all agricultural products but are high when compared to the usage of fat raw materials in the pharmaceutical industry. Although plant or animal fats used in the preparation or development of pharmaceutical products are less expensive nowadays, the importation of raw materials often results in high import duties. This may affect the cost of manufacturing pharmaceuticals and the price of pharmaceutical products (Kaevatana, 1998).

The leaf of *Calathea lutea* (Aubl.) E.Mey. ex Schult (family Marantaceae) (Govaerts, 1999) is a potential source of wax, the plant being generally distributed throughout tropical region (Standley & Steyermark, 1952) (Figure 1). In Thailand, this plant is popular as an ornamental herb, because it has beautiful large leaves that grow in clumps. The wax covering the surface of this leaves is called Cauassú wax, and can be used for the same purposes as commercial wax or fat, such as food, cosmeceutical and pharmaceutical applications (National Academy of Sciences, 1979). The composition of cauassú wax has been reported, it consists of *n*-alkanes (C_{25}-C_{31}) and *n*-alkanols (C_{20}-C_{32}) (Malterud *et al*., 1979). The composition and melting point of this wax is similar to candelilla wax which can be used as a substitute in a wide range of medicinal applications. According to its ease of propagation and growth (National Academy of Sciences, 1979), it may be possible to use this wax in pharmaceutical applications, particularly as an herbal pill coating material for taste-masking purposes. It could be used as a coating material, to minimize the bitter or unpleasant tastes in solid medication dosage form (Mauger *et al*., 1998) especially herbal pills used in Thai traditional medicine, which are known to possess a bitter taste. More importantly its use could also encourage the use of this wax as an alternative to imported products.

Figure 1 *Calathea lutea* plant

2. Materials and Methods

2.1 Materials

Polyethylene glycol sorbitan monostearate (Tween 60, synthesis grade) and sorbitan monooleate (Span 80, synthesis grade) were purchased from Merck KGaA, Darmstadt, Germany. Hexane was purchased from VWR Chemicals Limited Liability Company, Ohio, United States. Andrographis powder, in capsule form (Andrographolide 12 mg/capsule), was purchased from Chaophya Abhaibhubejhr Hospital, Thailand (Reg. No G512/60). Honey was purchased from DoiKham Company Limited, Thailand.

2.2 Plant material and wax purification

A 1,000 mature leaves of *Calathea lutea* were collected from Chiang Rai province in January 2018. The plant was authenticated by one of the authors (Dr. Chaiyong Rujjanawate) and the voucher specimen (no. 168-F) was deposited at the school of Medicine, Mae Fah Luang University, Thailand.

After peeling the wax covering the surface of this leaves, the crude wax was dissolved in warm hexanes (about 60-70 °C) and then filtered while warm. The hexane was evaporated under reduced pressure using a vacuum rotary evaporator (Eyela, Tokyo, Japan) and then the purified wax, which from now on is referred as “CLW”, was used. The percent purity of CLW was calculated as follows; Percent purity = [Weight of CLW $\times$ 100]/Weight of crude wax. The average yield of CLW was calculated per leaf in order to compare with the average yield of this wax from that previously reported (National Academy of Sciences, 1979).

2.3 Required hydrophilic-lipophilic balance (HLB) determination of CLW

CLW was used to prepare a serie of 6 emulsions, with HLB values ranging from 9 to 14, and the average droplet diameter of each formulation was measured by using microscopic droplet size analysis. The required HLB is the amount of emulsifier required to make the most stable oil-in-water emulsion (Crowley, 2013). The most stable emulsion was prepared by blending two emulsifiers, with known HLB values, in order to produce HLB values close to the required HLB of the oil phase (Aulton, 2002). CLW was used to prepare a serie of 6 emulsions with HLB values ranging from 9 to 14 by blending together the emulsifiers (Span 80 and Tween 60) in different ratios, as shown in Table 1.

A hundred milliliters of each formulation was prepared, each containing 5% w/w of CLW, 5% w/w of blending emulsifiers (Span 80 and Tween 60) and distilled water. The HLB of each formulation was calculated using the alligation method (Schnaare & Prince, 2013). The method of preparation of emulsions was by using the beaker method (Griffin *et al*., 1967). Briefly, the required amount of Span 80 (HLB value is 4.3) was dissolved in melted CLW (oil phase) and that of the Tween 60 (HLB value is 14.9) in the distilled water (aqueous phase). The oil phase and water phase beakers were then heated to approximately 70-75 °C, over a water bath. The oil phase was then added to the aqueous phase, with continuous stirring, until the emulsion reached room temperature. The required HLB of CLW was calculated using the following formula (Gadhave., 2014);

$$\text{HLB of CLW} = \frac{W_{Tween} \times HLB_{Tween} + W_{Span} \times HLA_{Span}}{W_{Tween} + W_{Span}}$$

Where: W_{Tween} and W_{Span} were the weight of Tween 60 and Span 80, respectively

HLB_{Tween} and HLB_{Span} were HLB value for Tween 60 and Span 80, respectively

Table 1 Composition of different emulsions with HLB values ranging from 9 to 14.

Formulation code	HLB value	Compositions			
		CLW (%w/w)	Tween 60 (%w/w)	Span 80 (%w/w)	Water (%w/w)
C1	9	5	2.22	2.78	90
C2	10	5	2.69	2.31	90
C3	11	5	3.16	1.84	90
C4	12	5	3.63	1.37	90
C5	13	5	4.20	0.90	90
C6	14	5	4.58	0.42	90

The droplet size analysis of each formulation was determined by optical microscope (Olympus CX 22 RFS1, Olympus Corp., Tokyo, Japan) (Sherman, 1968), using a calibrated ocular micrometer (Levius *et al.*, 1953). The droplets, in groups of 300 droplets, were measured, covering at least 8 fields of view, and the average droplet diameter was calculated. The emulsion formulation with the smallest average diameter of droplet size was considered as the most stable emulsion formulation (Jafari *et al.*, 2008). After standing for 24 hours, all emulsion formulations were checked and droplet sizes were measured again.

2.4 Preparation of coated bitter herbal pills

The bitter medicinal plant used in this study was andrographis [*Andrographis paniculata* (Burm.f.) Nees, family Acanthaceae], the king of bitterness (Subramanian *et al.*, 2012). The herbal pills from this plant were prepared, using refined honey to shape the andrographis powder into a pill form and these were dried in a hot-air oven (UM500, Memmret, Germany) at 40-50 °C for 24 hours.

The emulsion formulation, with the appropriate stability, using the above method, was prepared for coating the bitter herbal pills. The coating method in this study was the dipping method which is applicable to Thai traditional medicine practices. Dry herbal pills were randomly selected from the uncoated herbal pill batch and then dipped into the cool emulsion using forceps holding each pill. The pill coating process was repeated three times and each dipping cycle was followed by drying in a hot air oven set at 40-50 °C for 24 hours (Hussein *et al.*, 2013, Leon *et al.*, 1991). Rolling the dry coated pills before entering the next dipping cycle was performed in order to keep homogeneous coating thickness. The dry coated bitter herbal pills were kept in desiccators until used.

2.5 Evaluation of coated pills

2.5.1 Physical appearances

The appearances of all coated pills were determined visually to identify their color, shape and hardness.

2.5.2 Uniformity of thickness of coating layer

Thirty uncoated-herbal pills were measured individually using a micrometer caliper (Macoh, Thailand). After coating, the pills were re-measured and the thickness of the coating layer was calculated using the following formula;

Coating layer thickness = [Coated pill diameter – Uncoated pill diameter]/2

2.5.3 Uniformity of weight of coating layer

Thirty uncoated-herbal pills were weighed individually by using weighing macinie (Precision Balance ME403/M, Mettler Toledo, Ohio, United States). After coating, the pills were re-weighed and the weight of coating layer was calculated using the following formula;

Coating layer weight = Coated pill weight – Uncoated pill weight

2.6 Sensory evaluation

The protocol of this evaluation was approved by the Human Research Ethics Committee of Mae Fah Luang University (document no. 084/2560 dated on August 24, 2017) and each participant signed an informed consent before starting the study. Thirty participants (including both men and women) between 18 to 30 years old were enrolled.

The study was designed as a single-blind study to determine the taste-masking efficacy of the emulsion formulation containing CLW (adopted from Borodkin *et al*., 1991 and Nakamura *et al*., 2002). As the noticeable difference between the coated and uncoated pills was their visual appearance, participants were blindfolded during the tasting sessions. They randomly received the bitter herbal pills (a coated or uncoated pills) to hold in their mouth, then recorded the time to the perception of the bitter taste (onset time). Then, the participants spat out the pill and gargled with warm water to reset their taste sense. Twenty minutes later, they received another of the herbal pill formulations (a coated or uncoated pills) and recorded the time to notice the bitter taste in the same manner.

2.7 Statistical analysis

All values were expressed as mean ± standard deviations. The data was analyzed using SPSS version 16.0 (SPSS v16.0 for Windows, SPSS Inc., Chicago, IL, USA). One-way ANOVA and post hoc least-significant difference (LSD) were used to determine the statistical significance of mean droplet size difference among groups of emulsion formulation. Paired (dependent) *t*-test was used to compare the mean of droplet size differences between before and after standing 24 hours of each formulation. In addition, paired *t*-test also was used to compare the onset time to bitter taste between uncoated and coated herbal pills. Statistical significance was set at less than 0.05 of *p*-value.

3. Results

3.1 Plant material and wax purification

CLW from the leaves of *C. lutea* was a powdery, slightly greasy, white to yellowish solid and odorless. The crude of CLW yielded approximately 0.9 g/leaf and 91% purity of CLW after purification.

3.2 Required hydrophilic-lipophilic balance (HLB) determination of CLW

The average droplet diameter of each formulation against HLB values are displayed in Table 2. This finding showed that the smallest average droplet diameter was 3.28 ± 1.83 µm in formulation C4 with HLB value 12. It was statistically different from the other formulations indicating better retention of oil phase in this emulsion system. The relative standard deviation was also evaluated to determine the uniform distribution of its droplets in each formulation. The result demonstrated that the lowest RSD among these formulations was 40% in formulation C2 with an HLB value of 10.

Table 2 Average droplet size of CLW emulsion formulation with vary of HLB values (n = 300).

Formulation code	HLB value	Average droplet size (µm)		%RSD	
		Initiation	After 24 h standing	Initiation	After 24 h standing
C1	9	7.05 ± 3.13*	7.77 ± 3.80**	44	49
C2	10	5.38 ± 2.17*	9.94 ± 5.63**	40	57
C3	11	5.24 ± 3.30*	9.00 ± 5.46**	63	61
C4	12	3.28 ± 1.83	4.62 ± 1.91**	58	39
C5	13	6.00 ± 3.45*	7.22 ± 4.85**	57	67
C6	14	5.97 ± 3.02*	6.71 ± 2.66**	50	40

* Significantly different from the C4 formulation, $p < 0.05$ (One-way ANOVA and post hoc LSD)

** Significantly different from initiation of each formulation, $p < 0.05$ (Paired *t*-test)

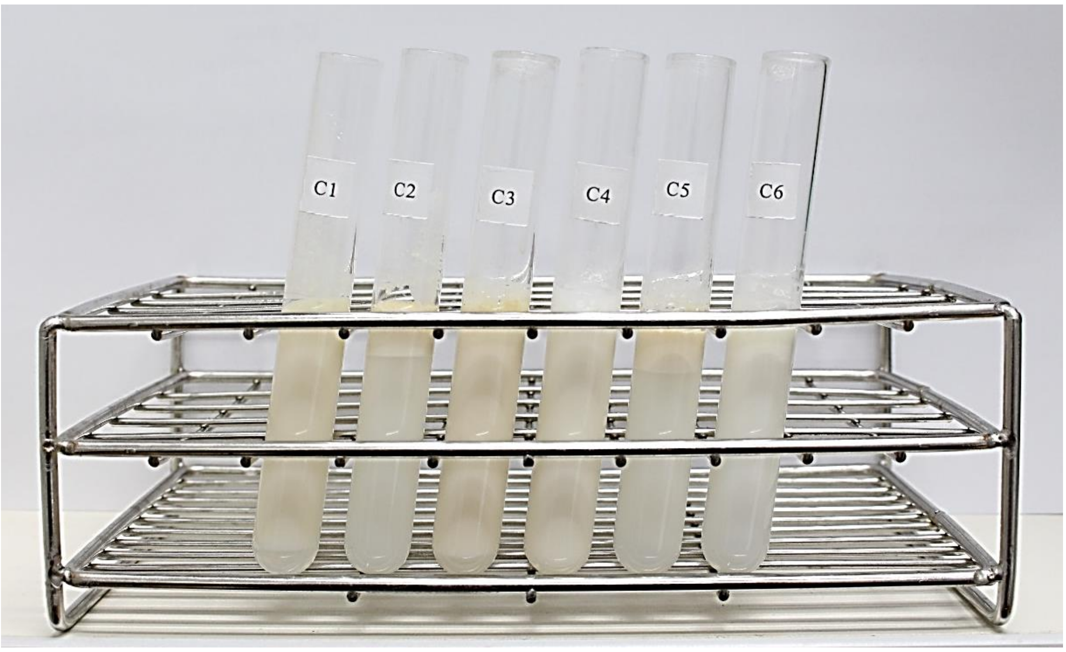

Figure 2 Emulsion formulations from the CLW at HLB 9-14 (C1-C6, from left to right) when left for 24 hours.

Table 3 Physical characteristic of coating layer of bitter herbal pills (n = 30)

Parameters	Coating layer of herbal pills
Physical appearance	Opaque in color, odorless and dry
Coating layer thickness (mm)	0.12 ± 0.02
Coating layer weight variation (mg)	15.83 ± 18.95

After standing for 24 hours, all formulations, except formulation C4, exhibited a slightly separated layer of wax layer on top of the emulsion (Figure 2), the average droplet size of these formulations are shown in Table 2. The formulation with the smallest average droplet size was still the C4 formulation (HLB value with 12) with a diameter of 4.62 ± 1.91 μm. All formulations were statistically different from the initiation of each formulation (before standing for 24 hours). The relative standard deviation of droplet size of these formulations was evaluated. The finding reveals that the lowest RSD among these formulations was 39% in formulation C4 with an HLB value of 12. This result strongly confirmed that the required HLB values for the most stable emulsion of CLW was determined as being approximately 12.

3.3 Preparation and evaluation of coated herbal pills

The formulation C4 was the most appropriate formulation which could be used as a pill coating material in this study. The emulsion was white to yellowish, creamy and consistent. After pill coating and drying, the coated herbal pills were investigated the various physical characteristics such as appearance, uniformity of thickness and uniformity of weight (Table 3). The visual appearance of the coated herbal pills was different from the uncoated pills, this being a difference in color. The average thickness and weight of the coating layer were 0.12 ± 0.02 mm and 15.83 ± 18.95 mg respectively.

3.4 Sensory evaluation

The study enrolled 30 healthy participants (2 men, 28 women) with a mean age of 20.4 ± 1.4 years old. After holding the pills in the mouth, the mean of onset time to bitter taste of the uncoated pills was 8.39 ± 6.80 seconds, whereas the mean of onset time to bitter taste of the CLW coated pills was 27.15 ± 20.44 seconds, statistically different from the uncoated pills (p-value < 0.05).

4. Discussion

Calathea lutea (Aubl.) E.Mey. ex Schult is easily propagated and grows with wet or saturated soil in unshaded areas. National Academy of Sciences (1979) reported that this plant can grow 75,000 plants on one hectare, result in an annual yield of 800 kg of crude wax. It is also readily accessible and its harvested leaves can be easily transported. This study revealed that the average yield of this wax was greater than the previous report which demonstrated that the average yield of this wax was 0.7 g/leaf (National Academy of Sciences, 1979). These differences may due to differences in harvesting location, weather, and leaf size. Chiang Rai province may be a location that isn't windy enough to blow the wax from the leaves, resulting in an increased yield of CLW. This may be a potential way to encourage to farm and harvest for a new source of commercial wax in Thailand.

The coating material formulation in this study was prepared in emulsion, a mixture of two liquids that are generally immiscible such as water and oil (Crowley, 2013). Because the physicochemical property of CLW is insoluble like natural waxes, pill coating with pure CLW might retard the dissolution of a drug in all parts of the gastrointestinal tract. An oil-in-water emulsion is preferred due to the oil phase in the emulsion system can easily be wetted by water when the coated pill is in contact with gastrointestinal liquid.

The required HLB values of natural waxes or fats depend on the composition and ratio of their fatty acids (ICI Americas Inc., 1984). There is a previous study that determined the chemical characteristics of CLW (Malterud *et al.*, 1979). It consists mainly of hydrocarbons such as *n*-alkanes (C_{25}-C_{31}) and *n*-alkanols (C_{20}-C_{32}) and has melting point at 75-78 °C. These chemical characteristics are more similar to candelilla wax (wax from *Euphorbia cerifera*) which is comprised predominately of *n*-alkanes (C_{29}-C_{33}) (Malterud *et al.*, 1979, and Toro-Vazquez *et al.*, 2007). Noticeably, the HLB value of CLW is rather different from that of candelilla wax, which has an HLB of about 14. This finding may due to differences in the amount and type of hydrocarbon compounds in both waxes which indicated the differences in required HLB values (ICI Americas Inc., 1984).

Apart from the types of emulsifiers to indicate the stability of oil-in-water emulsions, the environmental temperature also is a characteristic needed to monitor the stability of an emulsion (Crowley, 2013). The instability of an emulsion represents the separated layers, consisting of an oil-in-water emulsion part and an excess fat part at low temperatures (Forgiarini *et al.*, 2001). Our results demonstrated that unstable emulsion formulations tended to separate into 2 layers within 24 hours of standing (formulas C1-C3, and C5-6, Figure 1). This finding correlated with the change in droplet size after standing for 24 hours (environmental temperature during research was about 15-25 °C).

The coating of the herbal pills using the dipping method was used in this study even though is a traditional and classic method. This method provided a broad range of uniformity of thickness and weight with high relative standard deviation. It could be an acceptable way to apply this coating method in Thai traditional medicine practice, for taste-masking of their pungent and bitter herbal medicines. After the pill coating process, the physical properties of coated pills i.e. physical appearance, uniformity of thickness, and weight were acceptable, which indicated that the process of preparation is fairly reproducible.

The sensory evaluation or organoleptic test is a process to evaluate a product's characteristics by using the human sense of sight, smell, taste, touch, and hearing of this product (Institute of Food Technologists-Sensory

Evaluation Division, 1975). This study used a time-intensity method (Lawless, 2013) to measure the onset time to experience the bitter taste of the coated pills compare with uncoated pills. These results suggest that CLW emulsion can effectively delay a bitter taste perception when holding the pill within the mouth. Because of its water-insoluble properties, it can reduce drug solubility in saliva and produce a barrier between the drug and the taste buds of the tongue (Bettman *et al*., 1998). Although the standard variation of onset time to the bitter taste of the coated pills was high, it may caused by genetic variations in taste sensation between individuals (Garcia-Bailo *et al.*, 2009) or because the sample size is inadequate.

Because of the limitation of accessibility to modern pharmaceutical instruments in this study, these findings may provide the initial concept of the development of natural products available in Thailand, using simple and non-complicated methods. Therefore, both pilot and production scales of solid dosage form coating will need to be performed to explore the efficacy of this coating emulsion derived from CLW.

5. Conclusions

This research work revealed that an emulsion made from the wax of *Calathea lutea*'s leaves, with the required HLB of 12, showed the most stability with smallest droplet size, and was suitable for coating the bitter traditional herbal pills. The physical characteristic evaluation of the coating layer i.e. appearance, uniformity of thickness, and uniformity of weight, was fairly acceptable. It can effectively mask the bitter taste of bitter herbal pills when holding within the mouth, and so this locally produced natural wax can be used as an alternative source of commercial wax.

Acknowledgments

This study was financially supported by Mae Fah Luang University, Chiang Rai, THAILAND. English language support was kindly provided by Dr. Roger Callaghan (MD), School of Medicine, Mae Fah Luang University.

References

Amita N, Kandarapu R, Garg S. An update on taste masking technologies for oral pharmaceuticals. *Ind J Pharm Sci* 2002; 64(1):10-7.

Aulton ME, editor. Pharmaceutics: The science of dosage form design. 2nd ed. London, England: Churchill Livingstone; 2001.

Bettman MJ, Percel PJ, Powell TC. Effervescent microcapsules. US Patent. Patent No. 5,709,886., 1998.

Borodkin S, Sundberg DP. Polycarboxylic acid ion-exchange resin adsorbates for taste coverage in chewable tablets. *J Pharm Sci* 1971; 60(10):1523–7.

Dubois V. Reverse vesicle containing a hydrophobic phase. Patent. European Patent No. EP1905425 A1, 2008.

Felton LA, editor. Remington: Essentials of pharmaceutics. London, England: Pharmaceutical Press; 2013.

Gadhave A. Determination of hydrophilic-lipophilic balance value. *IJSR* 2014; 3(4): 573–575.

Garcia-Bailo B, Toguri C, Eny KM, El-Sohemy A. Genetic variation in taste and its influence on food selection. *OMICS* 2009; 13(1):69–80.

Govaerts R. World checklist of seed plants. MIM; 1999.

Griffin WC, Lynch MJ, Lathrop LB. Emulsions, part one. *Drug Cosmet Ind* 1967; 101(4):41.

Gurr MI, Harwood JL, Frayn KN, *et al*. Lipids: Biochemistry, biotechnology and health. 6th ed. Nashville, TN: John Wiley & Sons; 2016.

Hussein AA, Ghareeb MM, Hussain RAA. Preparation and characterization of meloxicam colon targeted coated tablets. *Int j pharm* 2013; 5(1):338–342.

ICI Americas, Inc. The HLB system: a time-saving guide to emulsifier selection. New York: ICI Americas Inc.; 1994.

Institute of food technologists-sensory evaluation division. Minutes of division business meeting. Chicago, US: Institute of Food Technologists; 1975.

Jafari SM, Assadpoor E, He Y, *et al.* Re-coalescence of emulsion droplets during high-energy emulsification. *Food Hydrocoll* 2008; 22(7):1191–1202.

Kaevatana Y. Pharmaceutical industry and export development Guidelines. Bangkok, Thailand: Department of international trade promotion, Ministry of commerce; 1998.

Lawless HT. Quantitative sensory analysis: psychophysics, models and intelligent design. Hoboken, NJ: Wiley-Blackwell; 2013.

Leon L, Herbert AL, editors. The theory and practice of industrial pharmacy. 2nd ed., Bombay, India: Varghese Publishing house; 1991.

Levius HP, Drommond FG. Elevated temperature as an artificial breakdown stress in the evaluation of emulsion stability. *J Pharm Pharmacol* 1953; 5(10):743–56.

Malterud KE, Wollenweber E, Gómez LD. Notizen: The wax of *Calathea lutea* (Marantaceae). *Z Naturforsch C* 1979; 34(1–2):157–8.

Mauger JW, Robinson DH. Coating technology for taste masking orally administered bitter drugs. Patent. U.S. Patent No.5,728,403, 1998.

Nakamura T, Tanigake A, Miyanaga Y, *et al*. The effect of various substances on the suppression of the bitterness of quinine-human gustatory sensation, binding, and taste sensor studies. *Chem Pharm Bull* (Tokyo) 2002; 50(12):1589–93.

National Academy of Sciences. Underexploited tropical plants with promising economic value. Washington, DC: National Academy of Sciences; 1979.

Office of Agricultural Economics. Agricultural statistics of Thailand crop year 2019. Bangkok, Thailand: Ministry of Agriculture and Cooperatives; 2018.

Sakr AD, Alanazi FK. Oral solid dosage forms. In: Felton L, editor. *Remington-essentials of pharmaceutics*. London: Pharmaceutical Press; 2013. 581–610.

Schnaare RL, Prince SJ. Metrology and pharmaceutical calculations. In: Felton L, editor. *Remington-essentials of pharmaceutics*. London: Pharmaceutical Press; 2013. 101–132.

Sherman P. General properties of emulsions and their constituents. In: Sherman P, editor. *Emulsion Science*. London: Academic Press; 1968. 157–162.

Sohi H, Sultana Y, Khar RK. Taste masking technologies in oral pharmaceuticals: recent developments and approaches. *Drug Dev Ind Pharm* 2004; 30(5):429–48.

Standley PC, Steyermark JA. Marantaceae. In: *Flora of Guatemala- volume 24, part III*. Chicago: Chicago natural history museum press; 1952.

Subramanian R, Zaini Asmawi M, Sadikun A. A bitter plant with a sweet future? a comprehensive review of an oriental medicinal plant: *Andrographis paniculata*. *Phytochem Rev* 2012; 11(1):39–75.

Toro-Vazquez JF, Morales-Rueda JA, Dibildox-Alvarado E, *et al*. Thermal and textural properties of organogels developed by candelilla wax in safflower oil. *J Am Oil Chem Soc* 2007; 84(11):989–1000.