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Addressing Tobacco Problems n Developing Countries

conomic Impact of Tobacco Use
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ulture, Employment and Agriculture: Between Tobacco Myth and Reality
obacco Use and Health
outh, Cigarettes, and Drugs

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conference and exhibition

Addressing Tobacco Problems In Developing Countries

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Abstract

LOZONGES FORMULATION FROM EXTRACT MIRACLE FRUIT WITH FREEZE DRYER METHODE: IMPROVEMENT HERBAL DOSAGE FROM ADDICTION SMOKER THERAPY

Yosi febrianti, Mutiara Herawati, Chyntia Paradhita

ABSTRACT

Smoking is widely has become one of the biggest causes of death in the world. The World Health Organization (World Health Organization or WHO) declared a billion people will die from tobacco in each country. The number of smokers worldwide is now at 1.2 billion people and 800 million of them are in developing countries. Indonesia is the third country with the largest number of smokers in the world after China and India. Several efforts have been taken by the government to reduce tobacco consumption such as increased cigarette taxes, as well as the application of non-smoking areas, but it has not had a significant impact in reducing tobacco consumption was proven that the high number of tobacco consumption in Indonesia. Efforts to prevent and control tobacco consumption, is the best option in addition to the increase in taxes on cigarettes, advertising bans as a whole, as well as the application of non-smoking areas, but many smokers who claim it is difficult to quit smoking due to the effects of cigarette addiction is very strong. Several therapies have been offered both medical and non-medical to help smokers quit smoking. The high cost of medical treatment incurred by patients for smoking cessation therapy being one of the obstacles in the control of tobacco consumption.

Traditional drug development has started in Indonesia in an attempt to obtain a safer drug therapy with minimal side effects. One of the plants has efficacy as a drug to treat addiction from cigarettes are miracle fruit (Synsepalumdulcificum).

Potential miracle fruit plant in Indonesia to serve as a traditional medicine against various diseases is enormous. This is due to the chemical content of the miracle fruit (Synsepalumdulcificum) is efficacious as a medicine miraculin. In Indonesia, the use of miracle fruit (Synsepalumdulcificum) for therapeutic treatment is still very limited. While in the United States and China miracle fruit plants have been widely used in the treatment of therapy specifically for the treatment of cancer and diabetes. The FDA has approved the miracle fruit as an alternative sweetener for diabetics. In addition to cancer therapy and diabetes, miracle fruit (Synsepalumdulcificum) is also believed to be used to overcome the effects of cigarette addiction.

The method used in the manufacture of lozenges is a method of freeze dryer. miracle fruitextraxion by maceration method, then the results of using the tool diserbuk extract spray dryer. The results obtained powder then formulated into lozenges. Testing was conducted on the test of time dissolve tablets in the mouth, weight uniformity, and hardness, friability, granule flow properties, tapp density. From the results obtained showed that the loxengesmiracle fruit extract has met several test requirements include: test weight uniformity, tablet hardness, friability tablet, soluble tablet time trial, and the flow rate of granules and granule silent corner, so that the product is stable farmasetis .

Keywords: smoking, lozenges, freeze dryer, miracle fruit

Full Paper

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CHAPTER-I
INTRODUCTION

Cigarette has been widely known as one of the world's biggest leading causes of death. World Health Organization declares that nearly one million people all over the world die due to the exposure of tobacco. The number of smokers around the world now are reaching 1,2 billion people, and 800 million of whom live in developing countries. Indonesia ranks as the third country with the biggest number of smokers after China and India1

Global Youth Tobacco Survey (GYTS) shows that the prevalence of teenagers who smoke in Jakarta during 2001 was 20,4% (Male 36,7%; Female 4.4%), and in 2004, the prevalence was 16,6% (Male 28,4%; Female 3,0%). The data GYTS used as the national scale in 2006 showed that the prevalence reached 12,6% (Male 24,5%; Female 2,3%). Three out of 10 students (30,9) smoked for the first time before they reached the age 10. Among those smoking students, 3,2% of them have suffered from tobacco addition, and this condition can be greatly indicated from their consumption of cigarette in the morning. In 2006, Indonesian GYTS stated that more than 14,4% students, consisting of 21,6% male and 7,4% female, have admitted that cigarette company had offered them 'free' cigarette

Data of the recent study show a quantitative relation between smoking and various diseases such as coronary heart disease, lung cancer, colon cancer, lung emphysema, periphery-vascular disease and neonatal mortality2. In 2002, it was assumed that 4,83 million of infant's premature death was resulted from smoking, and 50% of which happened in developing countries3.

Government has conducted several programs aiming at reducing the tobacco consumption such as the rise on cigarette tax, the overall ban of cigarette advertisement, and the establishment of free-smoking area. However, those efforts have not given any significant impacts on reducing tobacco consumption since the cigarette consumption in Indonesia remains high. Prevention and Cigarette Consumption Control Programs can be also considered as the best choice besides other programs, for example, the rise on cigarette tax, the overall ban of cigarette advertisement, and the establishment of free-smoking area; nevertheless, many smokers admit that stopping smoking is quite hard because cigarette has very strong addiction effect. Some medical and non-medical therapies have been promoted to help these smokers stop smoking. Unfortunately,the high cost of medical theraphy that the patient must take if they want to stop smoking becomes an obstacle in controlling tobacco consumption. Traditional treatment serves as an alternative that may help society besides medicine and other modern treatments.

Traditional medicines have been greatly developed in Indonesia in the attempt to provide safer treatment with minimum side effects. One of plants which is very effective in reducing cigarette addiction is Miracle Fruit (Synsepalumdulcificum). Miracle fruit has very great potential in Indonesia to be developed as traditional medicine that cures various diseases

because chemical compound in miracle fruit (Synsepalumdulcificum), miraculin, has function as medicine4. In Indonesia, the use ofmiracle fruit (Synsepalum dulcificum)for medical treatment is still very limited. Meanwhile, this plant has been greatly used in the United States and Chine as medical treatment, in particular for cancer therapy and diabetes5. FDA has approved that miracle fruit serves as alternative sweetener for diacbetics. In addition to cancer therapy and diabetes, miracle fruit (Synsepalum dulcificum)is believed to be useful for reducing addiction effect from tobacco.

This notion becomes an underlying principle for the use of miracle fruit (Synsepalum dulcificum) extract as one of natural ingredients for cigarette addiction therapy. The extract of miracle fruit (Synsepalum dulcificum) can be made into various pharmaceutical forms. One having been started to develop is the formulation and the making of lozenges. Lozenge can be defined as a solid medicated candy containing one or more medical ingredients intended to be dissolved slowly. Further, lozenge has high cohesiveness and hardness, and it is able to release slowly the drug. Lozenges has several advantages compared to other medicines, for example, it can be quickly absorbed and has better quality; therefore, it gives faster therapy effect, optimum compatibility and more practical uses6. In addition, lozenge is favorable due to its easy usage and storage.

B. PROBLEM FORMULATION

This research focuses on the formulation of miracle fruit (Synsepalum dulcificum) to be standardized lozenge. It is expected that the research is able to provide satisfying answer for following problems:

1. Can the extract of miracle fruit (Synsepalum dulcificum) be made into lozenges which is through further observation can be effectively used in cigarette addiction therapy?
2. How is the stability of lozenge formulated from miracle fruit(Synsepalum dulcificum)?

C. RESEARCH GOALS

This research has several goals as follow:

1. To produce lozenge from the extract of miracle fruit (Synsepalum dulcificum) which is through further observation is expected to be effectively used in the therapy of cigarette addiction.
2. To find out the stability of lozenges formulated from the extract of miracle fruit (Synsepalum dulcificum) after performing standardized feasibility test in the laboratory.

D. RESEARCH RESULTS

1. To obtain formula and techlogical package for standardized production process of lozenges, in particular for the cigarette addiction therapy.
2. To provide scientific articles widely published to society in national scale journal and presented in national seminar. It also entails an effort for patent right (HAKI) given to this research product.
3. The result of this research iscontinuously expected to enrich herbal alternatives used for local wisdom based-addiction therapy. Further, this research is expected to increase added value of miracle fruit farmers (Synsepalum dulcificum) in Indonesia.

E. RESEARCH USES

This research is expected to give benefits for many related parties such as:

1. For practitioners, this research becomes the fundamental and guideline in deciding which step undertaken for the optimal establishment of cigarette addiction therapy.
2. For decision makers, this research will be useful to decide strategic steps to formulate policies on comprehensive and integrated responses.

For society, the result of this research provides very useful information to actively participate in preventing and controlling cigarette consumption through the provision of herbal medicine extracted from miracle fruit (Synsepalum dulcificum) as the appropriate and effective therapy for cigarette addiction.

CHAPTER II
LITERATURE REVIEW

A. CIGARETTE

1. THE DEFINITION OF CIGARETTE

Cigaretteis a cylindrical roll of shredded tobacco wrapped in thin paper with the length of 70 mm to 120 mm (it varies depending on the country) and the diameter of 10 mm. Cigarette is ignited at one end and allowed to smolders so that its smoke is inhaled from the other end, which is held in mouth or to the mouth7.

2. THE PREVALENCE OF SMOKERS

Smoking period for teenagers is longer; moreover, teenagers and young adult start smoking earlier than before. Research of Basic Health conducted in 2007 and 2010 reveal that people start smoking in younger age. According to Basic Health Research in 2007, people who start smoking in the age of 5-9 years was 1,2 %; people who start smoking in the age of 10-14 years was 10,3% ; people who start smoking in the age of 15-19 years was 33,1%;people who start smoking in the age of 20-24 years was 12,1%, people who start smoking in the age of 25-29 years was 3,4%, and people who start smoking in the age of $\geq$ 30 years was 4%7.

3. THE CONTENT OF CIGARETTE

Every burnt cigarette contains 4000 dangerous and poisonous chemical substances. It is assumed that approximately 11.000 people die because of smoking. As the illustration, before burnt, cigarette contains 8-20 mg nicotine and after burnt, nicotine entering blood circulation is only 25 percent. Although only little content enters the body, it only needs 15 minutes to reach human brain. Cigarette smoke contains radioactive substance (polonium-201) and paint-maker substances (acetone), floor cleaner (ammonia), naphthalene, insect pesticide (DDT), arsenic, poisonous gas (hydrogen cyanide) used in death sentence and any other subtances9

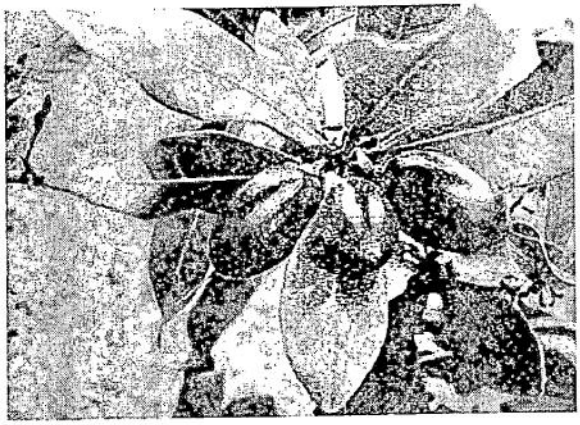
The most dangerous poisons contained in cigarette are tar, nicotine and carbon monoxide. Tar consists of 43 chemical substances which have been long known as carcinogens. Another substance like benzopyrene, a group of polycyclic aromatic hydrocarbon (PAH), has been known as cancer-triggering agent.

Other substances containing in cigarette are heroine, amphetamine, and cocain which are able to stimulate human brain and to influence mesolimbic system leading to addiction. When having no cigarette with him, an addict is able to behave strangely as if he suffered from mind disorder; moreover, he experiences distressing situation. This explains why an addict seems unable to stop smoking unless he tries it hard and wholeheartedly.

B. MIRACLE FRUIT (Synsepalum dulcificum)

1. The Description of Miracle Fruit (Synsepalumdulcificum)

This plant, also well known as Miracle berry, Red Jelly-bean tree, is commonly found in Ghana-West Africa and still a family of SawoManila (Sapotaceae family). When ripe, its color turns into red. It grows well in soil with pH 4,5-5,8 within free-frozen dew environment and high humidity10.



Picture 1.miracle fruit

2. Plant Morphology

Miracle fruit (Synsepalumdulcificum) is small shrub with low-growth branches. For 10 year-old plant, its branch only reaches 120-150 cm. This plant starts producing fruit when reaching 30 cm in height, or reaching the age of 2-3 years if planted from its seed. The process of development from flower to be fruit only needs 30-45 days. If planted in calcareous alkaline soil, this plant will not survive since it prefers to grow in rather acidic soil, fertile, and well-drainaged8.

3. Chemical Substance

The fruit has unique characteristic since miracle fruit gives unusual taste after being consumed. If we eat lemon or other sour fruits after eating miracle fruit, this fruit binds to the tongue's taste buds, causing sour foods to taste sweet. It happens because miracle fruit contains long-trailing chain of glycoprotein substance called miraculin9.

III. RESEARCH METHOD

3.1 TOOLS AND MATERIALS

3.1.1. Tools

This research uses several tools such as blender, paper, waterbath, aluminium, refrigerator, stopwatch, freeze dryer, angle of repose tester, flow time tester, flow property tester, friability tester, hardness tester, electric scale, vacuum cleaner, blister tablet machine, electric stove, UV 254 and 366 nm lamps, pyrex glass tools.

3.1.2. Materials

Materials used in this research are miracle fruit extract, ethanol 70%, PVP, magnesium stearate, mannitol. Avicel PH 101, amylumsolanum.

IV. THE IMPLEMENTATION OF PROGRAM

4.1 TIME AND PLACE

Time : 5 month starting from 9 April to 5 August 2012

Place : Pharmaceutical Technology Laboratory Universitas Islam Indonesia.

4.2. IMPLEMENTATION STAGE / IMPLEMENTATION FACTUAL SCHEDULE

Table 1.Program Activities Schedule

No	Activity	March	April	May	Jun	Jul	Aug	Sep	Oct
1.	Proposal Submission	√							
2.	Proposal Presentation		√						
PREPARATION									
1.	Preparation of tools and operational material.		√						
2.	OperationalOrientation		√						
IMPLEMENTATION									
1.	Extract Making		√						
2.	Lozenge Making			√					
3.	Evaluation of tablet and granule's physical characteristics.				√				
4.	Stability Test					√	√		
REPORTING									
1.	Report Writing						√		
2.	Report Submission							√	
3.	Parallel Presentation								√

4.3. IMPLEMETATION INSTRUMENTS

4.3.1. Tools

This research uses several tools such as blender, paper, water bath, alloy, refrigerator, stopwatch, freezer, angle of repose tester, flow time tester, flow property tester, friability tester, hardness tester, electric scale, vacuum cleaner, blister tablet machine, electric stove, UV 254 and 366 nm lamps, Pyrex glass tools.

4.4. COST PLANNING AND REALIZATION

4.4.1. Cost Planning

Table 2.Cost Details

No	Resources	Unit	Cost Per Unit (Rp)	Total (Rp)
Living Cost and Transportation				
1.	Honorarium for Researcher	3 students	1.900.000,00	5.700.000,00
2.	Transportation			150.000,00
	Total			5.850.000,00
Research Cost				
1.	*Aquadest*	10 L	1.000,00	10.000,00
2.	Ethanol 70%	50 L	15.000,00	500.000,00
3.	*Miracle fruit*	20 kg	15.000,00	300.000,00
4.	Avicel PH 101	100 g	30.000,00	300.000,00
5.	PVP	50 g	3.000,00	150.000,00
6.	Amyilumsolanum	100 g	3.000,00	30.000,00
7.	Magnesium Stearate	100 g	3.000,00	300.000,00
8.	Mannitol	200 g	6.000,00	120.000,00
9.	Proposal Writing			
	a. Kuarto Paper	1 ream	30.000,00	30.000,00
	b. Printer Ink	2 units	30.000,00	60.000,00
	c. Proposal binding	3 units	20.000,00	60.000,00
10.	Instrument Cost Rent			
	a. Freeze dryer	1 month	300.000,00	300.000,00
	b. Friabilator	1 month	150.000,00	150.000,00
	c. Hardness Tester	1 month	150.000,00	150.000,00
	d. Freeze Dryer	1 month	100.000,00	100.000,00
	e. Disintegration tester	1 month	150.000,00	150.000,00
	f. Spectrophotometer UV VIS	1 month	150.000,00	150.000,00
	g. Tablet Blister Machine	1 month	200.000,00	200.000,00
11.	Laboratory Cost Rent	2 months	500.000,00	1.000.000,00
	Total			4.060.000,00
TOTAL COST				**9.910.000,00**

4.4.2. Cost Realization

Table 3.Cost Realization

No	Resources	Unit	Cost Per Unit (Rp)	Total (Rp)
Living Cost and Transportation				
1.	Honorarium for Researcher	3 students	1.450.000,00	4.350.000,00
2.	Transportation			150.000,00
	Total			4.500.000,00
Research Cost				
1.	*Aquadest*	10 L	1.000,00	10.000,00
2.	Ethanol 70%	50 L	15.000,00	500.000,00
3.	*Miracle fruit*	20 kg	50.000,00	500.000,00
4.	Avicel PH 101	100 g	30.000,00	300.000,00
5.	PVP	50 g	3.000,00	150.000,00
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	a. Freeze dryer	1 month	300.000,00	300.000,00
	b. Friabilator	1 month	150.000,00	150.000,00
	c. Hardness Tester	1 month	150.000,00	150.000,00
	d. Freeze Dryer	1 month	100.000,00	100.000,00
	e. Disintegration tester	1 month	150.000,00	150.000,00
	f. Spectrophotometer UV VIS	1 month	150.000,00	150.000,00
	g. Tablet Blister Machine	1 month	200.000,00	200.000,00
11.	Laboratory Cost Rent	2 months	500.000,00	1.000.000,00
	Total			4.260.000,00
TOTAL COST				**8.760.000,00**

V. RESULT AND DISCUSSION

Meticulous examination and evaluation on the physical characteristics of either granule or tablet is inevitably important in designing and monitoring product quality. Quality control of tablet produced must be conducted11. To find out whether tablets as the result of this research have met the criteria, it needs several tests including:

5.1. TABLET WEIGHT UNIFORMITY TEST

Uniformity of tablet weight serves as an initial indicator of the content uniformity of active substances. Assumed that mass mixture compressed into tablet is homogenous mixture, it can be concluded that the content of active substance will be uniform level as well. In the evaluation of tablet weight uniformity, the coefficient of variation price (CV) is less than 5%.

Table 5.Weight Uniformity Test

	Table Weight (mg)
Average	3,05
SD	0,06
CV%	1,97

Weight Uniformity Test Formula:

$$CV\% = \frac{SD}{bobot\ rata\text{-}rata} \times 100\%$$

The result of weight uniformity test shows that the formula contains good weight because its deviation is less than 5%12.

5.2. TABLET HARDNESS TEST

Tablet hardness test can be defined as overall tablet strength testing which is conducted by giving pressure for the tablet diameter. USP has provided requirement regarding tablet hardness, in which it is stated that good tablet has hardness approximately between 4-8 kg. This test is performed by crushing 20 tablets one by one into hardness tester which detects the level of hardness12.

Table 6. Tablet Hardness Test.

	Tablet Hardness (mg)
Average	9,04
SD	0,14
CV%	1,6

The test resultshowsthatthe formulahas the average hardness value of 9,04 mg. Tablet hardness greatly depends on compression pressure and binder amount used. The greater the pressure and the amount of binder used, the higher the tablet hardness will be. Moreover, tablet hardness is directly related to soluble time since hard tablets usually have longer soluble time11.

5.2. TABLET FRIABILITY TEST

Friability serves as a parameter which describes the strength of tablet surface against friction and shock leading to abrasion on its surface. An apparatus used in this testing is friabilator. This test uses 20 tablets are wighed and and placed in friabilator (100 revolutions/4 minutes). Then, the tablets are weighed and the weight is compared with the initial weight before treatment. The value is expresses as a percentage. A maximum weight loss of not more than 1 % is considered generally good 13.

Table 7. Tablet Friability Test

Formula	Initial Tablet Weight (mg)	Final Tablet Weight (mg)	Weight Difference (mg)	Friability %
Average	61,775	61,650	0,125	0,202

$$F = \frac{a - b}{a} \times 100\%$$

Note :
a = Weight before testing
b = Weight after testing
F= (friability)

The result shows that every formula has different tablet weight due to the amount of binders and compression strength during tableting process. The greater the amount of binders and compression strength, the smaller the friability value. The formula has acceptable friability value since it is less than 1%.

5.3. FLOW RATEAND ANGLE OF REPOSE TESTS

Flow characteristic test covers granule flow rate and angle of repose. Good flow characteristic is characterized by flow rate less than 10s13.

Table 8. Granule Flow Characteristic Test

	Flow Time (s)
Average	4
SD	0,022
CV %	0,55

Data above show that the formula has fast flow time because of the little amount of binders; therefore, adhesion and cohesion among particles are also low. The more the amount of binders, the higher adhesion and cohesion among particles. As a result, the resistance of flow rate is greater leading to longer flow time.

Angle of repose measurement (α) is performed by measuring the steepest angle of bulk granule materials relative to the horizontal plane gained from flow characteristic test.

Table 9. Granule angle of repose test

	α
Average	12,45
SD	0,49
CV %	3,93

Based on data above, angle of repose is resulted from the high amount of binders in formula; thus, the greater the adhesion and cohesion, the bigger the angle of repose. This formula has good angle of repose since it ranges between 25o- 40o.

5.4. FLOW PROPERTY TEST

Flow Property Test is performed by inserting 100 ml granule in the measuring cup which is then placed in flow properties tester (scale 100 taps). Tap value is used to find out whether the formulation needs improvement of flow characteristics.

This flow property test results in formula with acceptable flow property percentage less than 20%; therefore, the tablet formula does not need the improvement of flow characteristics12.

Table 10. Flow Characteristics Test

Taps	Formula
0	100
100	94,67
200	93,33
300	93
400	92,67
500	92,67
600	92,67
Compresibility C (%)	8%

VI. CONCLUSION AND SUGGESTION

6.1. CONCLUSION

1. Lozenge resulted from keen observation is effective for cigarette addiction therapy.
2. Stable lozenges are gained from standardized laboratory feasibility test.

6.2. SUGGESTION

1. Following research is expected to perform content uniformity test and active substance test probably remaining in lozenge after several tests are performed.
2. It is strongly encouraged that other research will further observe whether lozenge made from the extract of miracle fruit (Synsepalum dulcificum)is effective for cigarette addiction therapy.

   It also performs microbial contamination test of lozenge from the extract of miracle fruit (Synsepalum dulcificum) .

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