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Use of *Vernonia cinerea* Jelly Candies for Smoking Cessation, Ubon Ratchathani Region, Thailand

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Abstract

Smoking cessation is difficult. Recently, there has been a traditional Thai herb called *Vernonia cinerea* to help quit smoking. The aim of the study was to determine using *Vernonia cinerea* (VC) candy use could improve smoking cessation success rates. It is a quasi-experimental study. We randomly recruited 50 smoking conscripts, and divided them into 2 groups of 25 participants each: the control group and the VC candy group. The VC participants received both some advice and VC jelly candy, whereas the control participants received only some advice. Both groups were followed up at 1-, 3-, and 6-month periods. At each follow-up date, all participants filled out the questionnaire and had their carbon-monoxide (CO) level measured at the military camps. The results showed there were 10 of 25 and 4 of 25 subjects from VC and control groups who gave up smoking at 6-month periods without the significance between groups ($p = 0.114$). Additionally, the differences of CO levels between groups were significantly decreased by 1.89 ppm at 2-month periods ($p = 0.043$). Noticeably, adding VC jelly candy into the cessation could possibly improve nicotine withdrawal symptoms than some regular advice alone. Some common side effects of VC were found including, dry mouth and throat, headache, and insomnia. Those taking VC jelly candy revealed they were overall satisfied with its taste and convenience. Finally, the finding revealed only VC candy and numbers of cigarettes (per day) factors that were significantly related to smoking cessation behavior ($p = 0.003$, 0.021, consecutively). Further evaluations of its long-tern side effects as well as the efficacy would be addressed.

Keywords: *Vernonia cinerea*; Jelly Candy; Innovation; Smoking Cessation

Introduction

Tobacco consumption is a risk health concern. Previous studies indicated the tobacco consumption is related to health problems, motor vehicle accidents, and other violent crimes (Jamison and Murray, 2006; Ezzati and Lopez, 2004; Mathers and Loncar, 2006; NHSO, 2004; Shafey *et al.,* 2003; Hornik, 2003; Mackay and Erikson, 2012; Gajalakshmi *et al.,* 2000). Recently, the National Statistics Office, Thailand, reported the first increase in the prevalence of Thai smokers compared to previous statistical reports (Pitayarangsarit, 2012). Additionally, it was reported that the majority of smokers were aged between 15 to 18 years, but a major concern is the decline in the ages of smokers over the past 20 years in different regions of the world (U.S. Surgeon General, 1989). The prevalence of smoking among young people represents a critical benchmark for tobacco control policy in Asia including Thailand. Youth smoking is also important given that those who begin smoking at an early age are more likely to become dependent and have greater difficulty quitting as adults (Fernandez *et al.,* 2000; Lando *et al.,* 1999; Breshan and Peterson, 1996; Cartwright, and Thompson, 1960). The previous research indicated that the school and military periods were the most critical time for the onset of smoking behavior and literature provided consistent support for friends' social norms as a predictor of adolescent smoking, making it difficult for young people to avoid cigarettes (NHSO, 1999). When focusing on the smoking prevalence by regions, the North-East region of Thailand has the second highest tobacco consumption behind the Southern region. Ubon Ratchathani region was the 13th in a list of provinces regarding the rate of tobacco consumption in 2010. There are current smokers approximately 27.09 percent (per 100,000 population) (Pongpit *et al.,* 2011). For those who wanted to quit might try different methods including, willpower, counseling, and pharmacotherapy (Wongwiwatthananuki, 2003). They might experience some disadvantages including, various responds, high cost, and some side effects which affect patient affordability, unpleasant outcome, resulting in underutilization of these cessation strategies (Fiore *et al.,* 2000; Fiore *et al.,* 2008; Prochazka, 2000). Thus, there is certainly a need to search for alternative or new treatment for smoking cessation to reach the diverse needs of smokers.

In Thailand, the plant of the genus *Vernonia cinerea* (VC) (Compositae) is widely distributed in most tropical and subtropical countries, and has long been used in traditional medicine to treat various types of diseases. This herb has been used to treat a number of disorders including inflammation, malaria, fever, worms, pain, diuresis, cancer, abortion, and various gastro-intestinal disorders (Madhava, 2005). Interestingly, this herb has been widely used to quit smoking in Thailand and other countries (Chaisawad and Makanuntachote, 1996; Wongwiwatthananukit *et al.,* 2009; Thiagarajan *et al.,* 2014; Lhieochaiphant, 1985; Boonyarikpunchai *et al.,* 2009). As the chemical substances inside VC called 'nitrate salt', potassium nitrates which induce tongue numbness, and cause less favor of cigarette smell and taste. Recently, there have been some VC products available for the seekers including, coffee, capsules, tea bags, and cookies (Thiagarajan *et al.,* 2004; Zmeili *et al.,* 1999; Triphubskul and Sithiphan, 2011; Jipukdeebpdintra and Jangwang, 2009). Recently, the authors underwent the efficacy of VC related to smoking cessation among

young smokers. The study was conducted late last year. The participants were divided into either study (VC) or control group. Overall, the percentages of quitters in the VC group were significantly higher than those in the control group ($p<0.001$). Additionally, average carbon-monoxide (CO) levels of the VC group from 1-month to 6-month periods were significantly different compared to the control group ($p<0.001$). Only minor side effects including, dry mouth and slightly increased high blood pressure were observed from the participants. Importantly, there was a significant relationship between VC products and cessation behavior (Chaikoolvatana *et al.,* 2017). Later this year, smoking cessation service has been served to those conscripts working in Ubon Ratchathani region. Some basic cessation strategies including, counseling regarding life style modification, 'go cold turkey' technique, and 0.5% sodium nitrate ($NaNO_3$) mouthwash were used. The overall results were favorable but no significant differences between groups ($p>0.05$). Despite the decrease in carbon monoxide (CO) levels, a number of quitters were still challengeable. Therefore, the development of a new innovation to enhance the efficacy of smoking cessation has been conducted. As the feasible reasons of the conscript smokers in the study including, working in the military bases, busy schedules, being regular smokers. The objectives for developing a new smoking cessation innovation are to help quitting cigarette more easy, convenient, and effective than the previous VC cookies (Chaikoolvatana *et al.,* 2017). Regarding the outcomes of VC cookies, the results were overall favorable related to the efficacy of its cessation activity. The findings showed the percentages of quitters in the study (VC) group were significantly higher than those in the control (non VC) group throughout 6 month periods ($p<0.001$, 0.001, and < 0.001, consecutively). Additionally, average carbon monoxide (CO) levels of the VC group from 1-month to *6*-month periods were significantly different compared to the non VC group ($p<0.001$) Common side effects of VC found, including; mouth and throat, high blood pressure. Finally, there was a significant relationship between VC cookies and cessation behavior (95% CI: 1.65, 251.60).

Therefore, health professionals at Pharsai Clinic, Ubon Ratchathani, Thailand under supervised by Dr. Chaikoolvatana have developed *Vernonia cinerea* jelly candies since October 2015. It contained similar amount of nitrate salts to the previous study and fulfilled the target satisfaction via the first survey (Chaikoolvatana *et al.,* 2017). This innovation is easy to use and carry for the conscripts guarding on the battle fields and need something to decrease their nicotine craving. Thus, the study aims to evaluate the efficacy of *Vernonia cinerea* jelly candy with lifestyle modification (LM) for smoking cessation via continuous abstinence rate (CAR), carbon monoxide (CO) levels as well as nicotine withdrawal symptoms during the cessation periods. This innovation is intentionally promising to be one of the smoking cessation strategies.

Methods

1. Design

It was a quasi-experimental study. The duration was started from October 2015 to June 2016 (9 months)

2. Participants

The participants were Thai conscripts working at the Sanpasithiprasong Military-Based, Ubon Ratchathani province. They were required for all inclusion criteria including; 1) aged between 18 and 40, 2) currently smoke at least 1 roll per day, 3) had no history of cardiovascular diseases, 4) no history of cessation therapy prior to the study, 5) signed the consent form, and 6) had good communication. If the participants experienced with any serious side effects including arrhythmias, gastrointestinal bleeding, showed hypersensitivity to VC during the treatment period, they would be asked to withdraw from the study. Also, if somehow the participants were missed any of the following visit, they were immediately excluded from the study. There were totally 50 military conscripts enrolled in the study. They were randomly selected into either study (VC) or control groups. Each group carried 25 participants. They were instructed to follow a 'go cold turkey' technique (stop immediately). VC participants received VC candy to encourage smokers to stop smoking, whereas those in control group used only that technique. The follow-up periods included *1*-, *3*-, and *6*-months. Prior to the study, the Ethic Approval from Mahidol University Institutional Review Board (MU-IRB) (COA.No 2014/011.401) was confirmed and all consent forms related to all personal information were requested.

3. Development of Vernonia cinerea (VC) Jelly Candy

The process of VC jelly candy development include, 1) Grinding dried *Vernonia cinerea* herb and boil at 75 ºC for 45 minutes as recommended (Wongwiwatthananukit *et al.,* 2009), then, 2) Mixing other ingredients together to form 'jelly', later 3) Adding favors and pour on the tray, 4) Putting the tray in the refrigerator with the temperature of 15 ºC and leave it overnight, 5) Cutting VC jelly into a small piece, and 6) Preparing packages. One piece of VC jelly candy contains nitrate salts equally to 1.2 grams (Wongwiwatthananukit *et al., 2009*). As it is recommended to take VC between 6 and 9 grams to optimize the cessation effects, thus the participants needed to take 5 to 8 pieces of VC jelly candy depended on the Fagerstrom scores and physician decision. For those in VC group, they received one pack of VC jelly candy containing 240 pieces for one month supply. In contrast, those in control group went for 'cold turkey' technique. Lifestyle modifications (LM) were advised in both groups.

4. Steps of data collection

All participants in both groups were given the information about the study objectives and steps by the authors. They were asked to stop smoking immediately at the first visit ('go cold turkey' techniques). Those in VC group were informed to take 5 to 8 pieces of VC jelly candy per day with LM, whereas those in control group received only lifestyle modifications (LM). Later both groups were followed up at *1*-, *3*-, and *6*-month periods. At each follow-up date, all participants filled out the questionnaire paper, contained continuous abstinence rate, CO levels, nicotine withdrawal symptoms, side effects, and VC satisfaction, and had their carbon monoxide (CO) level measured at the military camps.

5. Research tools

5.1 A questionnaire paper

The investigators followed a guideline of Thai Health Professional Alliance Against Tobacco for questionnaire items. It contained the following information related to smoking behaviors including: 1) Demographic data (e.g., age, alcohol consumption, marital status, 2) Smoking history (e.g., smoking duration (months), and number of rolls (per day), carbon-monoxide (CO) levels, 3) Cessation strategies (e.g., types of treatments either VC jelly candy with LM or 'go cold turkey' with LM, nicotine withdrawal symptom levels (nicotine craving) that the participants experienced during cessation periods. The participants were asked to range their craving symptoms from *low* (1) to *high* (10) levels, 4) quit results including, CAR, CO levels, side effects, nicotine withdrawal symptoms, VC jelly candy satisfaction, and the predicting factors related to smoking cessation).

5.2 Outcome Measurements

The study outcomes of both groups were all measured via some various measuring tools as described in Table 1.

Results

Totally, there were 50 participants enrolled into the study. Twenty-five participants were recruited in each group; VC and control. All were males (100%), an average age was 25, 27 years old consecutively. Alcohol consumptions were 48 percent in VC group and 68 percent in a control group. Both groups were single (68%). The majority were current smokers, except one case in the control group (quitter). VC participants smoked approximately 3 years, whereas those in the control group smoked less duration (1 year). Both groups smoked approximately 12 rolls of cigarettes per day (Table 2).

Table 1. Detail of Primary Outcomes and Measurements

Primary Outcomes	Groups	Measurements
Demographic data including, smoking history, common side effects, and nicotine withdrawal	*both groups*	Frequencies, percentages, standard deviation (SD). Regarding the nominal and ratio variables, χ^2 test and Mann-Whitney –test were utilized to assess the group differences
Continuous abstinence rate (CAR) month periods at *1-*, *3-*, and *6-*	*between groups*	- Numbers of participants (frequency, percentage, SD) - Data were investigated via χ^2 test
Co levels	*between groups*	1-3 ppm → Normal 4-6 ppm → Low 7-8 ppm → Moderate above 8 ppm → Severe - Data were investigated via mixed effects linear regression
Severities of nicotine withdrawal levels	*between groups*	1 →10 (low → high) Data were investigated via frequency, percentage, SD
Side effects of VC	*VC group only*	Frequency and percentage
VC jelly candy satisfaction	*VC group only*	Likert' scales (Strongly agreed (5) → Strongly disagreed (1))
The predicting factors related to smoking cessation at 6-month periods	*VC group only*	Smoking cessation behavior equation - Data were investigated via Multiple Logistic Regression and Hosmer & Lemeshow test

Continuous abstinence rate (CAR)

The results showed CAR at 1-, 3-, and 6-month periods between two groups. It revealed those received VC jelly candy had CARs equally to 0, 16, and 40 percent, respectively. For control group, CARs were 4, 16, and 16 percent, consecutively. Noticeably, there were no statistical differences of CARs between groups at the end of 6-month periods (p = 0.114) (Table 3).

Average CO levels

Figure 1 revealed that CO levels in VC group were higher than those in the control group between 1- and 5-month periods. As we know cigarette smoking results in the accumulation of carbon monoxide (CO) gas in lungs. Thus, it implied that VC jelly candy could possibly reduce cigarette smoking. As a result, CO levels were declined over periods of time.

The findings also revealed the average CO levels of VC group from 1-month to 6-month periods was not significantly different compared to the control group at any periods (p > 0.05). However, when some confounding variables were controlled including, alcohol consumption, duration of smoking, number of cigarettes, the similar results were shown as $Meandiff_{adj}$. The differences of CO levels between groups were significantly decreased by 1.89 ppm at 2-month periods only (p = 0.043) (Table 4).

Nicotine withdrawal symptoms

Figure 2 revealed nicotine withdrawal symptom (craving) levels in both groups were sharply increased during the first 3 months, then dropped through the end of the periods. It was also reported there were no significant differences of nicotine withdrawal levels between groups (p > 0.05), except 2-month periods (p = 0.001) that Meandiff values of VC group were lower than those in the control group by 1.32 points. When some confounding variables were controlled including, alcohol consumption, duration of smoking, number of cigarettes, the similar finding was shown. $Meandiff_{adj}$ values between groups at 2-month periods were significantly different (p = 0.004), and the values of VC group were lower than the control group by 1.18 points (Table 5).

Table 2 Demographic Information (n = 50)

Demographic information	VC group (n=25)		Control group (n=25)		*p*-value
	f	%	f	%	
Age (years)					0.537 [b]
Mean (S.D.)	25.3 (10.4)		27.96 (12.8)		
Median (IQR)	21 (2)		21 (6)		
Alcohol consumptions					0.306 [a]
Never	1	4.0	1	4.0	
Sometimes	12	48.0	7	28.0	
Regularly	12	48.0	17	68.0	
Marital status					>0.05 [a]
Single	17	68.0	17	68.0	
Married	7	28.0	8	32.0	
Widow/ divorce	1	4.0	-	-	
Smoking history					>0.05 [a]
Current smoker	25	100.0	24	96.0	
Non-smoker	-	-	-	-	
Quitter	-	-	1	4.0	
Smoking duration (month)					0.002 [b]
Mean (S.D.)	35.0 (31.0)		11.4 (9.6)		
Median (IQR)	24 (49)		7 (13)		
Numbers of cigarette rolls (per day)					0.682 [b]
Mean (S.D)	12.5 (6.2)		12.2 (8.3)		
Median (IQR)	10 (11)		10 (12)		

Note: *[a] Fisher exact test, [b] Mann-Whitney test*

Table 3 Frequency, percentage of CAR between groups (1-, 3-, and 6- months)

Cessation	*1*-month		p-value	*2*-month		p-value	*3*-month		p-valu
behavior	VC	Control		VC	Control		VC	Control	
No quit	25(100.0)	24(96.0)		21(84.0)	21(84.0)		15(60.0)	21(84.0)	
			>0.05[a]			>0.05[a]			0.114[c]
Quit	-	1(4.0)		4(16.0)	4(16.0)		10(40.0)	4(16.0)	

Note: [a] Fisher exact test, [c] Chi-square test

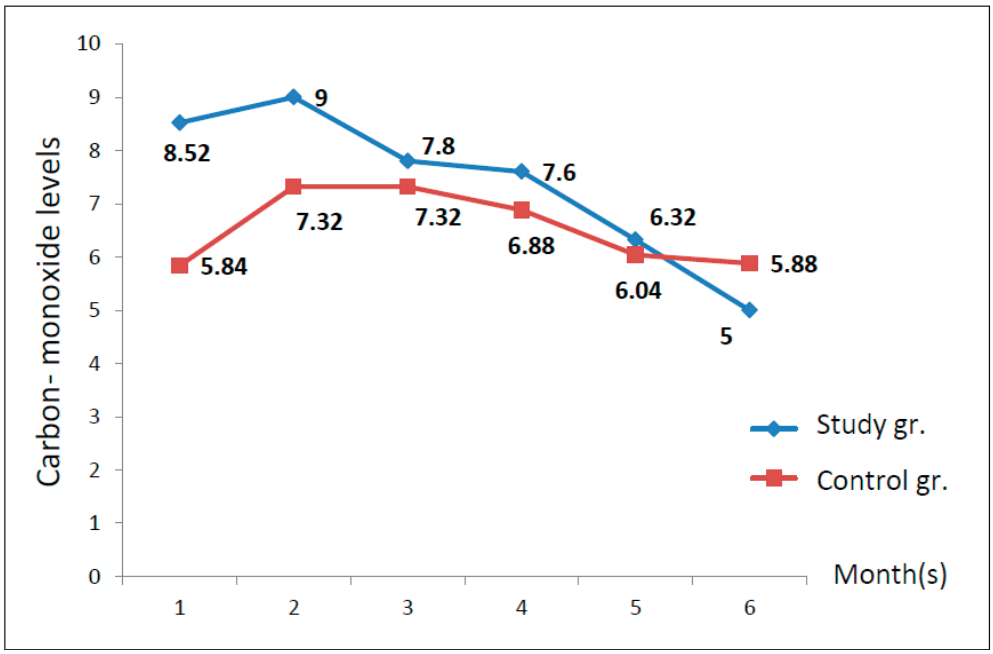

Figure 1 CO levels between VC (study) and control groups

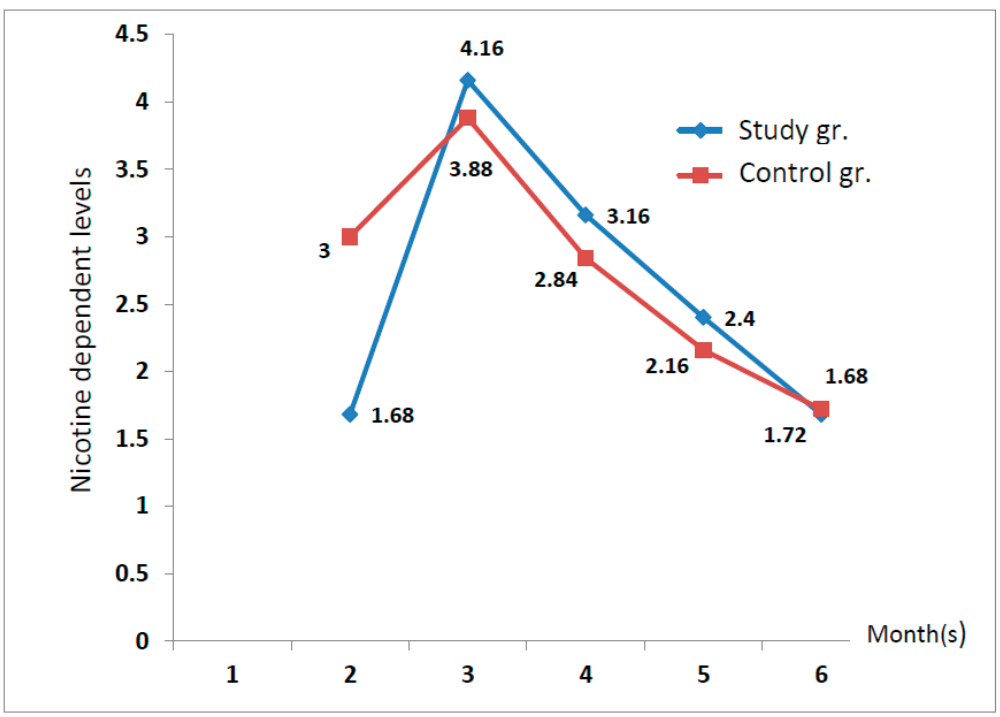

Figure 2 Nicotine withdrawal symptom levels between VC (study) and control groups

Table 4 Comparison of CO levels between groups (1- to 6-month periods)

Duration	Meandiff	95% CI diff	*p*-value	$Meandiff_{adj.}$	95% CI diff	*p*-value
1-month	ref			ref		
2-month	1.68	-0.32, 3.68	0.100	1.89	0.06, 3.74	0.043*
3-month	0.48	-1.53, 2.49	0.640	0.70	-1.14, 2.54	0.458
4-month	0.72	-1.31, 2.75	0.487	0.94	-0.90, 2.78	0.318
5-month	0.28	-1.78, 2.34	0.790	0.50	-1.34, 2.34	0.597
6-month	-0.88	-2.97, 1.21	0.410	-0.66	-2.50, 1.18	0.479

Note: $Meandiff_{adj}$: The differences of CO levels between groups when controlling some confounding variables

Common side effects of VC jelly candy

During 1- , 3-, and 6-month periods, the most common side effects of VC included dry mouth and throat, especially in 1-month period (72%), followed by headache (28%), and insomnia (20%) respectively. However, those symptoms were relieved when the time passed. Regarding dry mouth and throat, the subjects were informed to drink plenty of water for symptom relief.

VC Satisfaction

Overall, the participants taking VC jelly candy agreed that VC could possibly help them to quit smoking. Also, they satisfied with its taste and convenience. Some common side effects including, dry mouth and throat and high blood pressure were less concerned (Table 6). A further evaluation of satisfaction of VC product needs to be addressed to enhance the user compliance which helps smoking cessation become successful.

The relationship between the predicting factors related to smoking cessation at 6-month periods

There were some factors significantly related to smoking cessation behavior at 6-month periods ($p < 0.05$) including numbers of cigarettes per day as well as VC jelly candy cessation strategy via multiple logistic regression ($p = 0.003, 0.021$, consecutively) (Table 7). These factors could possibly predict smoking cessation behavior by 30.8% (as the equation below). Therefore, if a smoker receives VC jelly candy and smokes less, he will tend to quit smoking successfully.

Smoking cessation behavior equation is equal to

[0.611 + 2.007 (VC jelly candy strategy) - 0.261 (Numbers of cigarettes per day)]

Table 5 Comparison of nicotine withdrawal levels between groups from 1-to 6-month periods

Duration	Meandiff	95% CI diff	*p*-value	$Meandiff_{adj.}$	95% CI diff	*p*-value
1-month	ref			ref		
2-month	-1.32	-2.08, -0.56	0.001*	-1.18	-1.97, -0.38	0.004*
3-month	0.28	-0.48, 1.03	0.467	0.42	-0.37, 1.22	0.297
4-month	0.32	-0.44, 1.08	0.406	0.46	-0.33, 1.26	0.253
5-month	0.24	-0.52, 1.00	0.533	0.38	-0.41, 1.18	0.345
6-month	-0.04	-0.80, 0.72	0.917	0.10	-0.69, 0.90	0.799

Note: $Meandiff_{adj}$: The differences of nicotine withdrawal levels between groups when controlling some confounding variables

Table 6 Frequency, percentage of VC jelly candy satisfaction (6-month periods)

Questionnaire items	Strongly agree(5)	Agree (4)	Fairly agree (3)	Disagree (2)	Strongly disagree(1)	Average scores ( )
1. You like the taste of VC jelly candies	0	19 (76)	4 (16)	2 (8)	0	3.68
2. You think it is con venient to take VC jelly candies with you	12 (48)	3 (12)	8 (32)	2 (8)	0	4
3. You think you will use VC jelly candies next time	0	14 (56)	7 (28)	3 (12)	1 (4)	3.36
4. You think VC jelly candies help you to decrease your smoking	4 (16)	7 (28)	10 (40)	1 (4)	3 (12)	3.32
5. You think VC jelly candies help you to quit smoking	9 (36)	3 (12)	9 (36)	4 (16)	0	3.68
6. You concern about side effects of VC such as dry throat and mouth	0	4 (16)	3 (12)	11 (44)	7 (8)	2.16
7. You concern about side effects of VC such as high blood pressure	0	2 (8)	10 (40)	11 (44)	7 (8)	2.68
Average score						**3.41**

Table 7 The predicting factors related to smoking cessation-6-month periods

Variable(s)	Beta	OR	95%CI OR	p-value
VC jelly candy cessation strategy	2.007	7.45	1.35, 41.17	0.021
Numbers of cigarettes (per day)	-0.261	0.77	0.65, 0.91	0.003
Constant value(s)	0.611	1.84	0.36, 9.54	0.467

Adjusted R^2 = .308 , Hosmer and Lemeshow test *p*-value= .503

Discussion

As we know, set up an effective referral system for smoking cessation is one of the policy goal is to quit tobacco use (Bureau of Tobacco Control, 2012). There are three major methods of smoking cessation: go cold turkey techniques, behavior and social treatment and drug treatments (Zillich *et al.*, 2002). Some medications are associated with unwanted side effects such as weight gain, nausea, dry mouth and sedation. Nowadays natural products are alternative treatment for smoking cessation. One of the herbs popularly studied in Thailand for periods of time is Vernonia cinerea. (VC) (Wongwiwatthananukit *et al.,* 2009; Jipukdeebpdintra and Jangwang, 2009). The other names of this plant are little iron weed or Ya-Dok-Koa in Thais (Figure 3).

VC has been documented and widely used as a Thai traditional medicine and in other countries for relieving cigarette craving, asthma, cough, fever, malaria, arthritis and urinary calculi (Lin, 2005; Chea et al., 2006; Starr and Starr, 2008). It is a perennial herbaceous plant distributed in the tropical regions which are commonly found in South-East Asia and Hawaii (Bunyapraphatsara, 2000; Lin, 2005; Chea *et al.,* 2006; Starr and Starr, 2008). It is also official in Herbal List of National List of Essential Medicine 2011 for smoking cessation. Normally, this herb is used for smoking cessation with 2 g in 120-200 ml boiling water, after meal, for 3-4 times daily (National List of Essential Medicine, 2011). It was found that potassium nitrate obtained from the stems and roots of VC is the main substance caused tongue

Figure 3 *Vernonia cinerea*

numbness and facilitated smokers to give-up smoking (Zmeili *et al.,* 1999). Another available form of VC is a mouthwash preparation which has been investigated and used as anti-smoking (Lhieochaiphant, 1985; Local-Manager Online, 2012). The other VC products included, coffee, capsules, and tea bags (Thiagarajan *et al.,* 2014; Zmeili et al., 1999; Thiagarajan *et al.,* 2004; Jipukdeebpdintra and Jangwang, 2009). Each product had various results which depended on its research method. Despite some benefits of VC products have been documented, there were still some limitations reported including, middle aged participants, lack of randomization, and short term follow-up (Wongwiwatthananukit, 2003; Zmeili *et al.,* 1999; Thiagarajan *et al.,* 2004; Chaikoolvatana *et al.,* 2015). Recently, the author developed an innovation for smoking cessation called "VC cookies". The overall results indicated VC cookies could possibly be an alternative for mild to moderate nicotine dependent smokers. It helped to quit smoking significantly compared to the control group. Noticeably, the smokers preferred to comply with this strategy, had some minor side effects including, dry mouth and throat (Jipukdeebpdintra and Jangwang, 2009). Nevertheless, VC cookies are suitable for young smokers to enjoy delicious, edible herbs as dessert. However, they might not be appropriate for grown-up smokers who tend to look for something convenient, easy-to-use and carry, good taste, and effective. For these reasons, VC jelly candy was eventually developed and investigated in this study (Figure 4, 5).

Figure 4 *Vernonia cinerea* (VC) Jelly Candies

Figure 5 VC Label

Regarding CAR results, even the overall CARs between groups at different periods were not significantly different (Table 2). However, a number of quitters in VC group were increased from 0 → 4 → 10 by the end of 6-month periods. It might imply those who took VC jelly candy could possibly decrease a number of cigarette rolls. Some previous findings provided the results of the VC benefit related to mild-to-moderate nicotine addicted smokers (Triphubskul, and Sithiphan, 2011; (Chaikoolvatana *et al.,* 2017; Chaikoolvatana, et al., 2015; Leelarungrayub *et al.,* 2010). Similarly, VC participants in this study were moderate, nicotine-addicted due to some evidences (e.g., number of cigarettes, and duration of smoking). To succeed quit smoking, VC should be recommended for mild nicotine-addicted smokers (Choudhary *et al.,* 2015). Further investigations of long-term efficacy and toxicity of VC innovations are strongly recommended to see whether this herbal product could possibly enhance quit results with some minor side effects.

Interestingly, even VC group had a longer duration of smoking than the control group (Table 2). However, Figure 2 showed nicotine withdrawal levels of VC were lower than the control group during the periods. It might be some other factors involved in coping with nicotine withdrawal among VC participants. Some previous studies confirmed the moderate levels of physical activity (MLPA) with intensity between 60 and 90 percent lasting for 30 to 40 minutes could relieve nicotine withdrawal symptoms (craving), especially for the first few weeks of cessation (Chaikoolvatana *et al.,* 2010; Chaikoolvatana, and Anansuchatkul, 2010). Additionally, if the quitter works out as described 3 times per week at least 3 consecutive months, quit rate would be more successful, and a quit duration would be longer (Chaikoolvatana and Prawittana, 2009; Chaikoolvatana, and Thairiwong, 2008; Chanakit *et al.,* 2008; Chaikoolvatana *et al.,* 2008). This evidence could be the explanation for the study, as participants in both groups were Thai military conscripts. They have regularly engaged in physical activity to improve body strength and prepare for the ground battle during the quit process. As a result, nicotine withdrawal symptoms (e.g., shaking, sweating, losing of concentration) were closed between groups by the end of 6-month periods (Figure 2).

Even VC participants had a history of heavy smoking compared to those in the control groups (Table 2). Nevertheless, when we focus on CO levels (Table 4), it revealed VC group tended to improve their CO levels, especially at 2-month periods. It might have implied VC could be potentially effective after quitting shortly. However, it still needs to be scientifically proved. Noticeably, some previous evidences revealed the physical activities could increase CO elimination from lungs (Arent *et al.,* 2000; Elibero *et al.,* 2011; Turankar *et al.,* 2013). Theoretically, the physical activities are more effective in accelerating CO elimination than air breathing, because it increased isocapnic ventilation, thereby decreasing the half-life of CO elimination. As a result, it scientifically showed after quit smoking, CO levels were gradually (Ussher *et al.,* 2009). From these evidences, it is recommended for persons, who want to quit smoking effectively, should undergo some moderate level physical activities including, football, track and field, basketball while quitting cigarettes (West *et al.,* 2005; Zavorsky *et al.,* 2012; Zhou *et al.,* 2009).

Normally, nicotine withdrawal symptoms usually reach their peaks at day-2 or -3 after quitting cigarettes. Most people start to feel better after one week, then it takes at least 2 to 3 months for your brain chemistry to return to normal (Ward *et al.,* 2001; Kenford *et al.,* 1994). Interestingly, it is similar in the study as described in figure 2.

At present, CO measurement is one of the precise indicators to investigate the quit success. Exhaled carbon monoxide is a readily available, simple and affordable marker that can be assessed using a noninvasive technique that produces immediate and reliable results (Middleton and Morice, 2000). It will be very encouraging for smokers to see the difference after working their way through the first few days without cigarettes. Thus, CO monitoring could be a motivational tool (Chatkin *et al.,* 2007).

Regarding toxicity of VC, the results showed only some minor side effects including, dry mouth and throat, increased blood pressure, headache, and insomnia. Some previous reports indicated there were no serious toxic effects related to VC (Latha *et al.,* 2010; Aruna *et al.,* 2012). So far, this herb has still been used safely as following the instructions.

Interestingly, only two variables including type of cessation strategy; VC jelly candy, and number of cigarettes (per day) are related to smoking cessation behavior. Some similar results were found (Kim and Cho, 2014; Dale *et al.,* 2001; Stapleton *et al.,* 1995). Nevertheless, the other findings found health concerns, education background, age, and side effects were influenced smoking cessation behavior (Lee and Kahende, 2007; Vahidi *et al.,* 2014; Dale, 2001; Stapleton *et al.,* 1995).

Nowadays, new innovations have been developed for quitting cigarettes (Boromarajonani College of Nursing, 2014). For example, local villagers adapted Thai herbs to get rid of craving symptoms including, *Murraya simensis Craib, Phyllanthus emblica, Syzygium aromaticum, Myristica fragrans* Houtt (Smoke-Free School, 2016). Also, there was quit smoking spray made from mixtures of *Vernonia cinerea, Glycyrrhiza glabra,* peppermint, *Cassia fistula* L. ("Banana lip balm could help relief dark lips from cigarette smoking as well as lipstick-allergy", 2016). Interestingly, a 'Pisang Awak banana' lip balm helps to minimize dark lips from heavy smoking (Kitikannakorn *et al.,* 2013). Another work by Nantawan mentioned about meta-analysis of seven articles written about the use of herbs for smoking cessation including, St.John's wort, mixed herbal tea, and inhale black peper (Baccetti *et al.,* 2015). The efficacy of quit smoking among these herbs were varied. Acupuncture was also investigated to help smokers quit smoking by combining with acupressure (Das *et al.,* 2016). Recently, information technology such as computer program, mobile phone applications, or even games have been implemented as supplements for smoking cessation (Das *et al.,* 2016; One-leg standing rabbit for new face smoker project, 2015; 'Dewals: Decrease-Deny-Don't smoke', 2014). Further evaluations of its efficacy are required.

Study limitations

As the similarity of demographic data was statistically different between groups, it could bias the results. Therefore, increasing the population size by expanding the study sites should be addressed. Another issue is the further

investigations of long term side effects of VC. More research should be conducted, especially in those with some chronic diseases such as hypertensive conditions.

Conclusion

A new innovation for smoking cessation has been developed 'VC jelly candy'. It has been investigated both efficacy and toxicity. The overall results were well-performed, despite no difference of abstinence rates between VC and control groups. Nevertheless, trends of number of quitters and CO levels were well promising with only minor side effects occurred (e.g., dry mouth and throat). Finally, the attitudes towards VC products were satisfied. Further investigations of VC efficacy and toxicity are favorably recommended.

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Conflicts of Interest

There is no conflict of interest related to the trial. The research was for academic and research purposes only. It was funded via Thai Governmental organizations including, Thai Health Promotion Organization, National Health Security Office, Region 10, and Provincial Public Health Office, Ubon Ratchathani province.

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References

A guidebook of Thai traditional herbs for smoking cessation. A textbook of smoking cessation via herbal plants. Boromarajonani College of Nursing, Saraburi. Praboromarajchanok. Office of the Permanent Secretary, Ministry of Public Health, Thailand 2014: 1-17.

Arent S, Landers M, Etnier JL. The effects of exercise on mood in older adults: a meta-analytic. Journal of Aging and Physical Activity 2000; 8: 407–30.

Aruna GP, Reddy J, Prabhakaran V. Safety evaluation of ethanol extract of *Vernonia cinerea* L. in experimental animals. International Journal of Pharmaceutics 2012; 2(1): 34-38.

Baccetti S, Monechi M, Fre M, Conti M, Faedda M, Panti P et al. Smoking cessation with counseling and Traditional Chinese Medicine: A randomized controlled trial. Acupuncture and Related Therapies 2015; 3: 48-54.

"Banana lip balm could help relief dark lips from cigarette smoking as well as lipstick-allergy" [Internet]. 2016 [cited 2559 10th September 2016]. Available from: http://manaer.co.th/QOL/ViewNews.aspx?NewsID=9590000088763

Boonyarikpunchai W, Wattanasa- ringkhan S, Aroonwong S, Chitvanich O, Sardsangchan C. "Formulation of *Vernonia cinerea* (Linn) Less. extract flimstrip for smoking cessation", senior project, Huachiew Chalermprakiat University, Thailand. (in Thai) 2009.

Breshan N, Peterson EL. Smoking cessation in young adults: age at initiation of cigarettes and other suspected influences. American Journal of Public Health 1996; 86: 214-20.

Bunyapraphatsara N. Medicinal plants indigenous to Thailand volume 5, Bangkok: Department of Pharmacognosy, Faculty of Pharmacy, Mahidol University 2000: 72-4.

Bureau of Tobacco Control, Department of Disease Control, Ministry of Public Health, "Global Adult Tobacco Survey": 2011 GATS, Thailand 28 May 2012", Thammasart University Publishing, 2012.

Cartwright A, Thompson JG. Young.smoker s: an attitude study among schoolchildren, touching also on parental influence. British Journal of Preventive and Social Medicine 1960; 13: 1.

Chaikoolvatana A, Anansuchatkul J. The effectiveness of interventions on basic knowledge and skills in the preparation of cytotoxic drugs at a hospital in northeastern Thailand. Isan Journal of Pharmaceutical Sciences 2010; 6(1): 66-76.

Chaikoolvatana A, Anansuchatkul J, Wattanapong W, Chanakit T. Modified Quality of Life (QOL) Questionnaire for Breast Cancer Patients: a phase of pilot study. Khon Kaen Medical Journal 2010; 34(2): 7-16.

Chaikoolvatana A, Chanakit T, Ulman R. The development of a high alert intravenous medication database system (HAIMDS) for health care professionals, Thailand. Songklanagarind Medical Journal 2010; 28(4): 191-204.

Chaikoolvatana A, Chandee S, Chaikoolvatana C, Sithibutra C. A Comparison of smoking cessation drug therapies related quality of life between *Vernonia cinerea* tea and 0.5% sodium nitrate mouthwash. Nurse Journal 2015; 43: 94-104.

Chaikoolvatana A, D Ayuthaya N, Suthipinittharm P, Chaikoolvatana C, Saisingh N. Development and evaluation of the effectiveness of *Vernonia cinerea* (VC) cookies for smoking cessation. Journal of Health Research 2017; 31(1): 1-10.

Chaisawad S, Makanuntachote M. 1996. A study of smoking cessation therapy model using *Vernonia cinerea* Less and natural cure at Theng Hospital, Chiangrai. Nonthaburi, Thailand: Office of the alcohol beverage and tobacco committee, Department of Diseases Control. Ministry of Public Health, 1999. Thailand.

Chaikoolvatana A, Prawittana J. The development of a multimedia interactive learning (MIL) program in diabetes care for health care professionals in northeastern Thailand. Siriraj Medical Journal 2009; 60(2), Mar-Apr: 203-7.

Chaikoolvatana A, Thairiwong P. Personal and environmental factors related to both amphetamine addiction and quitting of traffickers in south-eastern, Thailand. Siriraj Med J 2008; 60(5) Sept-Oct: 254-58.

Chaikoolvatana A, Wongbutdee J, Boonlue P. Factors related to HIV preventive behaviors of prostitutes in Muang District, Ubon Ratchathani. Siriraj Medical Journal 2008; 60(1): 69-73.

Chanakit T, Chaikoolvatana A, Unlamam R, Sawatwongchai R, Wong-A-Nan W. The development of web-based intravenous admixture database. Thai Pharmaceutical and Health Science Journal 2008; 2(3): 221-30.

Chatkin J, Fritscher L, de Abreu C, *et al.* Exhaled carbon monoxide as a marker for evaluating smoking abstinence in a Brazilian population sample. Primary Care and Respiratory Journal 2007; 16: 36–40.

Chea A, Hout S, Long C, Marcourt L, Faure R, Azas N, et al. Antimalarial activity of sesquiterpine lactones from *Vernonia cinerea*. Chemical and Pharmaceutical Bulletin 2006; 54: 1437-39.

Choudhary S, Sharma M, Tripathi J, Mishra P. Antihyperglycemic activity of *Prabha/ Therapeutic Uses of Vernonia cinerea*. IJPCR, July 2015 – August 2015, Volume 7, Issue 4 Page 325 Vernonia cinerea L. on alloxan-induced diabetic mice; ISSN NO 2320-5407 Int J Adv Res 2015; 1(2): 35-42 35.

Dale LC, Glover ED, Sachs DP, Schroeder DR, Offord KP, Croghan IT, Hurt RD. Bupropion for smoking cessation: predictors of successful outcome. Chest 2001; 119(5): 1357-64.

Das S, Tonelli M, Ziedonis D. Update on Smoking Cessation: E-Cigarettes, Emerging Tobacco Products Trends, and New Technology-Based Interventions. Current Psychiatry Report 2016; 18: 1-15.

'Dewals: Decrease-Deny-Don't smoke. The community innovation strategy for the knowledge of cigarette danger. [Internet]. 2014 [cited 2016 June 16th 2016]. Available from: http://www.riskcomthai.org/news/detail.php?id=23133.

Elibero A, Janse Van Rensburg K, Drobes DJ. Acute effects of aerobic exercise and Hatha yoga on craving to smoke. Nicotine & Tobacco Research 2011; 13(11): 1140–1148. doi:10.1093/ntr/ntr163.

Ezzati M, Lopez AD. Smoking and oral tobacco use. In Comparative quantification of health risks: Global and regional burden of disease attributable to selected major risk factors edited by Ezzati M, Lopez AD, Rodger A, Murray CJL. Geneva: WHO 2004; 959-1108.

Fernandez E, Schiaffino A, La Vecchia C. Age at starting smoking and number of cigarettes smoked in Catalonia, Spain. La Presse Medicale 1999; 28: 361-66.

Fiore MC, Bailey WC, Cohen SJ, Dorfman SF, Goldstein MG, Gritz ER, *et al.* Treating tobacco use and dependence: clinical practice guideline. Rockville, MD: U.S. Department of Health and Human Services. 2000.

Fiore MC, Jaen CR, Baker TB, Bailey WC, Benowitz NL, Curry SJ, *et al.* Treating tobacco use and dependence: 2008 update clinical practice guideline. U.S. Department of Health and Human Services. 2008.

Food and Drug Administration (FDA) 101. Smoking Cessation Products. FDA Consumer Health Information. US Food and Drug Administration. 2015; Jan: 1-2.

Gajalakshmi CK, Jha P, Ranson K, Nguyen S. Global patterns of smoking and okingattributable mortality. In: Jha P, Chaloupka FJ, eds. Tobacco control in developing countries. Oxford, England: Oxford University Press. 2000: 11-39.

Hornik R. Alcohol, tobacco, and marijuana use among youth. Same-time and lagged and simultaneous change associations in a nationally representative sample of 9-to-18-year-olds. In reducing adolescent risk: toward an integrated approach, edited by: Romer D. Thousand Oaks, California, United State: Sage Journal. 2003: 335-43.

Jamison DT, Murray CJL. Global and regional burden of disease and risk factors, 2001: Systematic analysis of population health data. Lancet 2006; 367: 1747-57.

Jipukdeebpdintra S, Jangwang A. Coffee for smoking cessation. Journal of Food Agriculture and Environment 2009; 7(4): 130-33.

Kenford SL, Fiore MC, Jorenby DE, Smith SS, *et al.* Predicting smoking cessation. Who will quit with and without the nicotine patch. The Journal of American Medical Association1994; 271(8): 589-94.

Kim Y, Cho WK. Factors Associated with Successful Smoking Cessation in Korean Adult Males: Findings from a National Survey. Iranian Journal of Public Health 2014; 43(11): 1486-96.

Kitikannakorn N, Chaiyakunapruk N, Nimpitakpong P, Dilokthornsakul P, Meepoo E, Kerdpeng W. An overview of the evidences of herbals for smoking cessation. Complementary Therapies in Medicine 2013; 21: 557-64.

Lando HA, Thai DT, Murray DM. Age of initiation, smoking patterns, and risk in a population of working adults. La Presse Medicale 1999; 29: 590-98.

Latha LY, Darah I, Jain K, Sasidharan S. Toxicity study of *Vernonia cinerea*. Pharmaceutical Biology 2010; 48(1): 101-4.

Lee CW, Kahende J. Factors Associated With Successful Smoking Cessation in the United States, 2000. American Journal of Public Health 2007; 97(8): 1503-1509.

Leelarungrayub D, Pratanaphon S, Pothongsunun P, Sriboonreung T, Yankai A, Bloomer RJ. *Vernonia cinerea* Less. supplementation and strenuous exercise reduce smoking rate: relation to oxidative stress status and beta-endorphin release in active smokers. Journal of International Society Sports Nutrition 2010; 7: 21. doi: 10.1186/1550-2783-7-21.

Lhieochaiphant SA, "A phytochemical study of *Vernonia cinerea* Less. (Compositae)", M.S. Thesis, Chiang Mai University, Thailand. 1985.

Lin KW. Ethnobotanical study of medicinal plants used by the Jah Hut people in Malaysia. Indian Journal of Medical Science 2005; 59: 156-61.

Local-Manager Online, Thailand, [updated 2012 August 24; cited 2012Sept 9], Available from:http://www.manager.co.th/local/viewnews.aspx?NewsID=9550000104183.

Mackay J, Erikson M. The tobacco atlas. Geneva, IL: World Health Organization 2010. http://www.who.int/tobacco/statistics/tobacco_atlas/en/. Accessed on November10th 2012.

Madhava Chetty K. *Vernonia cinerea* L. Chittoor medicinal plants, Himalaya Book Publications, Tirupati, 2005.

Mathers D, Loncar D. Protection of global mortality and burden of disease from 2002 to 2030. Plos Medicine 2006; 3: e442.

Middleton ET, Morice AH. Breath carbon monoxide as an indication of smoking habit. Chest 2000; 117: 758–63.

National Health Statistical Office (NHSO). Tobacco information among Thai people. Bangkok: Action on Smoking and Health Foundation (ASH Thailand). 1999.

National Health Statistical Office (NHSO). The cigarette smoking and alcoholic drinking behavior survey. Thai Ministry of Information and Communication Technology. Bangkok, Thailand. 2004.

National List of Essential Medicine, "Herb List", Drug division, Ministry of Health, Thailand. 2011: 84 (in Thai).

One-leg standing rabbit for new face smoker project. Thai Dentist Alliance Against Tobacco. [Internet]. 2015 [cited September 2nd, 2016]. Available from: http://thaidentistagainsttobacco. org/

Phanmuang W. The use of alternative medicine in smoking cessation, Thawong hospital. An abstract for an annual academic meeting of alternative and community medicine. National Alternative Medicine Meeting, August 31st – September 3rd 2006, Maung-Thongthani Convetion Hall. 2006: 61.

Pitayarangsarit S. Current situation of tobacco control, Thailand 2012. Charoen-Dee-Mankong Press. Tobacco Control Research and Knowledge Management Center (TRC). 2012.

Pongpit K, Chankamkum S, Kraiwisej R, Chaikoolvatana A. A survey of general knowledge, attitude and belief related to cigarette smoking of Ubon Ratchathani University students. Isan Journal of Pharmaceutical Sciences 2011; 7: 36-46.

Prochazka AV. New developments in smoking cessation. Chest 2000; 117: 169-75.

Shafey O, Dolwick S, Guindon GE. Tobacco control country profiles. American Cancer Society: Atlanta, Georgia, United States of America. 2003.

Smoke-Free School: ThaiHealth Organization adding council, spray and book. [Internet]. 2557 [cited 2559 6th September 2016] Available from: http://www.oknation.net/blog/happysyndrome/2014/09/28/entry-1

Stapleton JA, Russel MA, Feyerabend C, Wiseman SM, Gustavsson G, Sawe W, et al. Dose effects and predictors of outcome in a randomized trial of transdermal nicotine .patches in general practice. Addiction 1995; 90: 31e42.

Starr F and Starr K. Plants of Hawaii. 2008. Available at: http://www.hear.org/starr/plant s/images/species/?q=cyanthillium+cinereum (accessed 5 August 2016).

Thiagarajan VR, Shanmugam P, Krishnan UM, Muthuraman A. Ameliorative potential of *Vernonia cinerea* on chronic constriction injury of sciatic nerve induced neuropathic pain in rats. Anais da Academia Brasileira de Ciências 2014; 29; 0: 0.S.

Triphubskul W, Sithiphan C. Efficacy of *Vernonia cinerea* for smoking cessation in Thai active smokers. A final report. Tobacco Control Research and Knowledge Management Center (TRC). Thai Health Promotion Foundation. 2011.

Turankar AV, Jain S, Patel SB, Sinha SR, Joshi AD, Vallish BN, et al. Effects of slow breathing exercise on cardiovascular functions, pulmonary functions & galvanic skin resistance in healthy human volunteers—a pilot study. Indian Journal of Medical Research 2013; 137(5): 916–921.

Ussher M, Cropley M, Playle S, Mohidin R, West R. Effect of isometric exercise and body scanning on cigarette cravings and withdrawal symptoms. Addict 2009; 104(7): 1251–57. doi:10.1111/j.1360-0443.2009.02605.x.

U.S. Surgeon General. Reducing the health consequences of smoking: 25 years of progress. A reprint of the Surgeon General, Executive Summary, Rockville MD. Department of Health and Human Services, Center for Chronic Disease Prevention and Health Promotion, Office on Smoking and Health. 1989. Department of Health and Human Services Publication no. (CDC) 89-8411.

Vahidi RG, Lezadi S, Mojahed F, Shokri A, Gholipour K, Imanparvar R. Factors Affecting Successful Smoking Cessation: Patient Views Regarding Determinants of Successful Smoking Cessation- A study from East Azerbaijan, Tabriz–Iran. Journal of Pioneering Medical Sciences 2014; 4(2): 89-93.

Ward MM, Swan GE, Jack LM. Self-reported abstinence effects in the first month after smoking cessation. Addictive Behaviors 2001; 26(3): 311-27.

West R, Hajek P, Stead L, Stapleton J. Outcome criteria in smoking cessation trials: proposal for a common standard. Addiction 2005; 100(3): 299–303. doi:10.1111/j.1360-0443.2004.00995.x

Wongwiwatthananukit S, Benjanakaskul P, Songsak T, Suwanamajo S, Verachai V, "Efficacy of *Vernonia cinerea* for smoking cessation". Journal of Health Research 2009; 23(1): 31-36.

Wongwiwatthananukit S. Role of pharmacists in smoking cessation program. In: Jindavijag B, ed. Ambulatory pharmaceutical care. 1st ed. Bangkok. Journal of Thai Hospital and Pharmaceutical Association 2003: 153-74.

Zavorsky GS, Beck KC, Cass LM, Artal R, Wagner PD. Dynamic vs. fixed bag filling: impact on cardiac output rebreathing protocol. Respir Physiol Neurobiol 2010; 171(1): 22–30.

Erratum in: Respiratory Physiology & Neurobiology 2012; 80(2–3): 353–54.

Zhou X, Nonnemaker J, Sherrill B, Gilsenan AW, Coste F, West R. Attempts to quit smoking and relapse: factors associated with success or failure from the ATTEMPT cohort study. Addictive Behaviors 2009; 34(4): 365–373. doi:10.1016/j.addbeh.2008.11.013.

Zillich AJ, Ryan M, Admas A, Yeager B, Farris K. "Effectiveness of a pharmacist-based smoking cessation program and its impact on quality of life". Pharmacotherapy 2002; 26(6): 759-65.

Zmeili S, Salhab A, Shubair K, Gharaibeh M, Suliman N, Kayed Al-A, *et al,* "Clinical evaluation of a new A.S. mouth wash 881010 as an antismoking agent: a placebo-controlled double-blind trial". International Journal of Clinical Pharmacology and Therapeutics 1999; 37(1): 41-50.