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Vernonia cinerea pastilles is effective for smoking cessation

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ABSTRACT

Background and aim: *Vernonia cinerea* (VC) is a herb that can alleviate nicotine addiction, potentially aiding in smoking cessation. Previous studies have examined four-to eight-week treatments using VC, but have found it to be ineffective. This study aimed to evaluate the smoking cessation effects of VC in addicted smokers over a longer treatment duration with pastilles.
Experimental procedure: This was a randomized double-blinded controlled trial conducted at a community pharmacy. The inclusion criteria were age between 18 and 60 years, intention to quit smoking, and low to moderate level of nicotine addiction. All eligible participants were stratified according to nicotine addiction level and then randomly assigned either VC treatment or placebo. The VC group received two pastilles three times daily, while the control group received a placebo for 12 weeks. The outcomes were continuous abstinence rate (CAR) and point abstinence rate (PAR) at four and 12 weeks.
Results: There were 121 eligible participants; 10 participants were not willing to participate. In total, there were 111 eligible participants, 54 of whom were treated with VC (48.65%) and 57 of whom were given a placebo (51.35%). Baseline characteristics were comparable between the two groups. The VC group had a significantly higher chance of smoking cessation at 2.01 (95% CI of 1.03, 3.92) compared with the placebo group at the end of the study. There were no significant side effects in either group.
Conclusion: The VC pastille group had significantly higher CAR than the placebo group at week 12.

1. Introduction

Cigarette smoking is a major risk factor for chronic obstructive airway disease (COPD) and lung cancer. A retrospective cohort study from Denmark showed that smoking increased the risk of COPD by 6.3 times with a 95% confidence interval (CI) of 4.2, 9.5.[1] In 2010, there was an estimated global COPD prevalence of 328 million people.[2] A meta-analysis showed that smoking is related to lung cancer in both men and women, with relative risks of 7.33 and 6.99, respectively.[3] Smoking cessation is, thus, strongly encouraged.

Some herbs, such as *Vernonia cinerea* (VC), have been shown to aid in smoking cessation.[4] The advantages of using herbs for smoking cessation include their relative safety and low cost. VC extract and its metabolites can reduce nicotine addiction by inhibiting MAOs. Of the five studies to date that have evaluated the efficacy of VC on smoking cessation,[5–9] all have found VC may be an effective alternative therapy. For example, a 2-week course of VC tea had higher smoking cessation at two weeks higher than placebo at week 12 (43.8% vs 21.9%; p value 0.06).[5] However, these studies administered VC through tea, juice, lozenge, or capsule, and the intervention periods were between two to eight weeks. A pastille may be a better choice for smoking cessation because it can be chewed, allowing for longer duration of contact, added artificial

Abbreviations: *Vernonia cinerea*, VC; Continuous abstinence rate, CAR; Point abstinence rate, PAR; Chronic obstructive airway disease, COPD; Confidence interval, CI; Monoamine oxidases, MAO; Fagerstrom Test for Nicotine Dependence, FTND.

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flavors, greater portability. A longer treatment duration may also be necessary for VC to exhibit any effect. This study, therefore, aimed to evaluate the smoking cessation effects of VC pastilles in addictive smokers over a longer treatment duration.

2. Materials and methods

This was a randomized double-blinded controlled trial conducted at (Blind) University Faculty of Pharmaceutical Science's community pharmacy. The study period was between July 2016 and June 2017. The inclusion criteria were age between 18 and 60 years, intention to quit smoking, and low to moderate level of nicotine addiction. Patients' nicotine addiction level was defined by the Fagerstrom Test for Nicotine Dependence (FTND). An FTND score of less than four and between four and six were defined as mild and moderate nicotine addiction, respectively. Patients were excluded if they had underlying diseases, such as cancer, stroke, neurological malfunction, depression, or abnormal liver or kidney function; were using other addictive substances, such as cannabis or heroin; were receiving treatment for smoking cessation via other drugs, for instance, alternative nicotine replacement, bupropion, clonidine, nortriptyline, or other herbs; or were pregnant or breast feeding.

All eligible participants were randomly assigned to either placebo or VC treatment and stratified by nicotine addiction level. The VC group received six 575.34 mg VC pastilles extracted from VC powder per day, or two pastilles three times daily. The control group received a placebo with a size, dose, and method of ingestion similar to those of the VC pastilles. The duration of treatment was 12 weeks.

The baseline characteristics, smoking history, and nicotine addiction level of all eligible participants were recorded. The primary outcome of this study was smoking abstinence rate, defined by self-reporting and an exhaled CO confirmation test result of less than or equal to 6 ppm [8]. There were two smoking abstinence rates examined in this study: continuous abstinence rate (CAR) and point abstinence rate (PAR). Both rates were evaluated at weeks four and 12. Self-reported side effects were documented at week 12 in both groups.

2.1. Sample size

Based on a previous report,[9] the CARs of the VC and control groups were 75% and 43%, respectively. The required sample size for this comparison with 95% confidence and a 5% margin of error was 59 subjects in each arm.

2.2. Statistical analyse

The analysis was performed by using the intention to treat protocol. Descriptive statistics were used to compare factors between the placebo and VC group. Comparisons of proportions between the two treatment groups were executed using a Fisher Exact test or Chi-square test as appropriate. A student *t*-test or

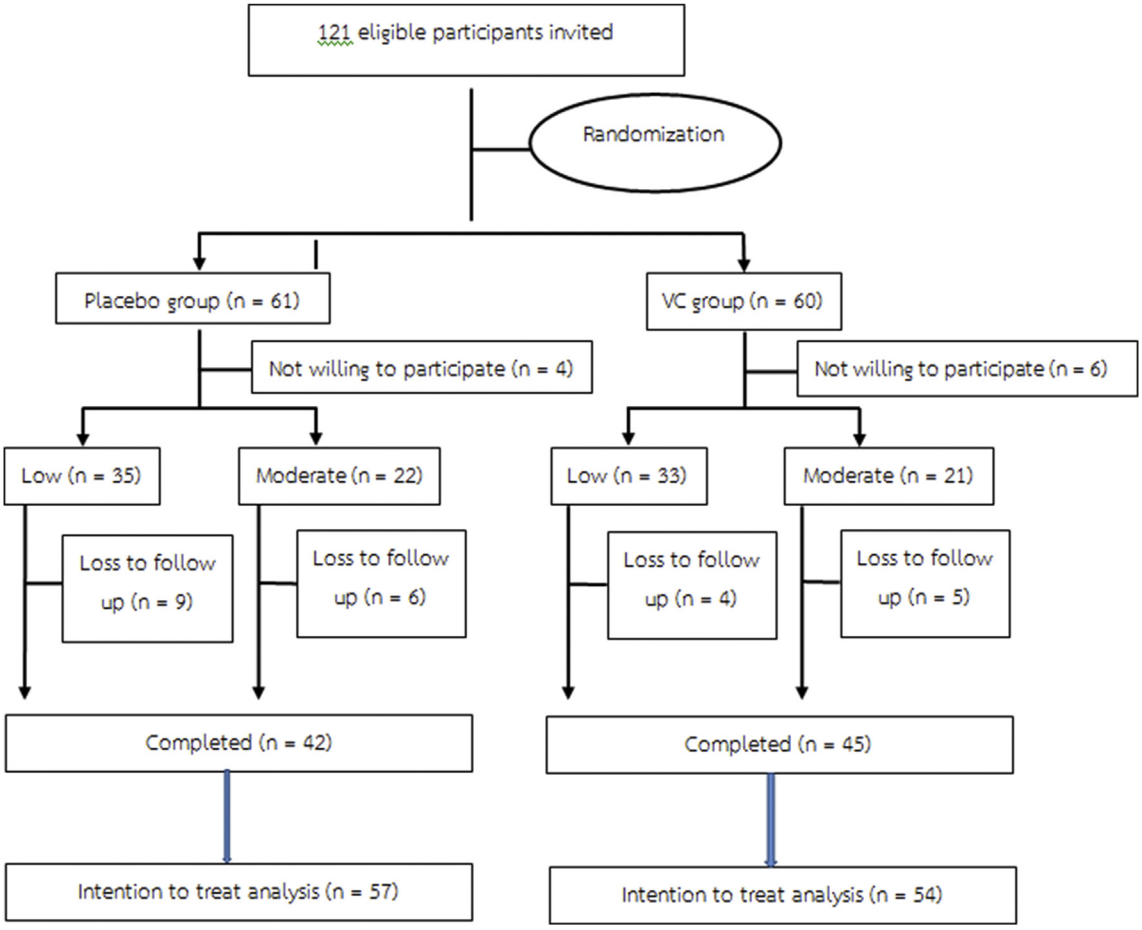


Fig. 1. Study flow of a 12-week treatment of either placebo or *Vernonia cinerea* (VC) for smoking cessation in mild and moderate nicotine addiction.
Note. CI: confidence interval.

Wilcoxon rank sum test was used to compare numerical data between the two groups. The CAR and PAR at each time point were also compared between the two groups using a Fisher Exact or Chi-square test. The relative risk and 95% confidence interval (CI) were calculated. All analyses were performed using STATA software version 14.0 (College Station, Texas, USA).

3. Results

There were 121 eligible participants and randomly assigned to either placebo (n = 61) and VC group (n = 60). There were 10 participants were not willing to participate. In total, 111 remaining participants, 54 of whom were treated with VC (48.65%) and 57 of whom were given a placebo (51.35%) as shown in Fig. 1. Baseline characteristics were comparable between the two groups in terms of age, sex, body mass index, duration of smoking, and nicotine addiction level (Table 1).

The CAR of the VC group was higher than that of the placebo group at weeks four (40.74 vs 20.32) and 12 (35.19 vs 17.54) as shown in Fig. 2. The CARs of both groups at week 12 were lower than those at week four. The VC group had a significant relative risk for smoking cessation at 2.01 (95% CI of 1.03, 3.92) compared with the placebo group at the end of the study. Although there was no statistically significant difference between the PARs of the two groups, the VC group had a higher PAR than the placebo group at all time periods (Fig. 3). There were nine side effects reported by the participants, with numb tongue being the most common in both treatment groups (Table 2). There was no significant difference in terms of side effects between the two groups.

4. Discussion

This randomized placebo-controlled trial showed that VC pastilles led to a significantly higher smoking cessation rate than

Table 1
Volunteer baseline data participated in the study categorized by treatment group; placebo or *Vernonia cinerea* (VC) treatment.

Factors	Placebo group (n = 57)	VC group (n = 54)	p value
Male, n (%)	55 (96.5)	52 (96.3)	0.999
Age, years	39.5 ± 14.7	41.1 ± 15.3	0.584
Body mass index, kg/m^2	23.4 ± 5.2	23.7 ± 3.9	0.733
Duration of smoking, years	20 (9–30)	20 (7–32)	0.485
Number of cigarette smoked, cigarettes	7 (4–15)	10 (5–15)	
Number of cigarettes smoked (0–10 cigarettes/day)	42 (73.7)	39 (72.2)	0.688
Nicotine addiction level, n (%)			0.999
Low (FTND < 4)	35 (61.4)	33 (61.1)	
Moderate (FTND 4–6)	22 (38.6)	21 (38.9)	

Note. Data presented as mean ± SD unless indicated otherwise; FTND: Fagerstrom Test for Nicotine Dependence.

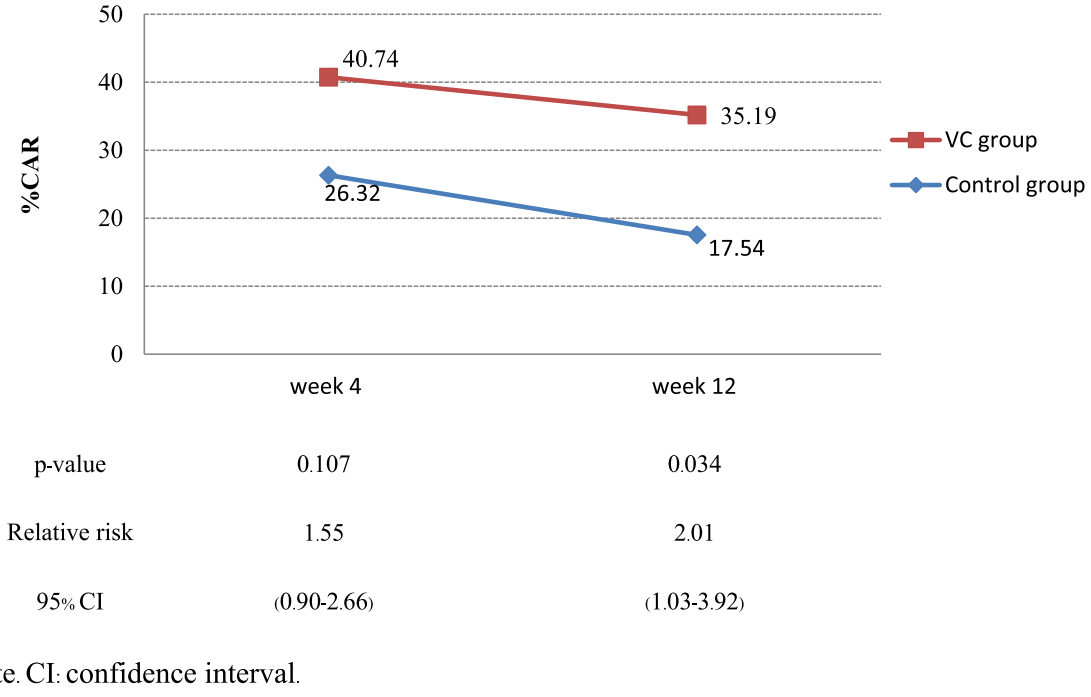
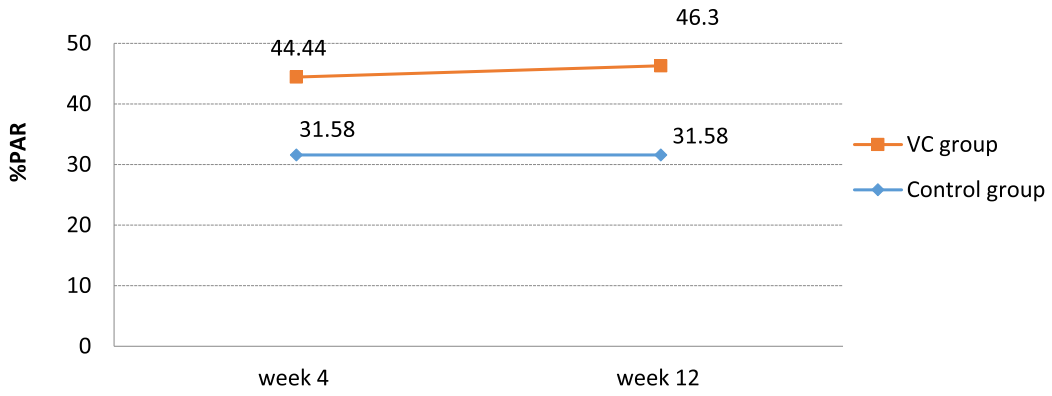


Fig. 2. Continuous abstinence rates (CAR) defined by self-reported and exhaled CO confirmation test at weeks four and 12 in cigarette-addicted participants by treatment type: placebo or *Vernonia cinerea* (VC
. Note. CI: confidence interval.



p-value	0.162	0.112
Relative risk	1.41	1.47
95% CI	(0.87-2.28)	(0.91-2.36)

Note. CI: confidence interval.

Fig. 3. Point abstinence rates (PAR) defined based on self-reporting and exhaled CO confirmation test at weeks four and 12 by treatment in cigarette-addicted participants by treatment type: placebo or *Vernonia cinerea* (VC).

Table 2
Adverse events during the 12 weeks of the treatment with either placebo or *Vernonia cinerea* (VC).

Symptoms	Placebo group n = 57	VC group n = 54	p value
Numb tongue	14 (24.56)	20 (37.04)	0.216
Stomachache	3 (5.26)	2 (3.70)	1.000
Drowsiness	4 (7.02)	1 (1.85)	0.364
Nausea and vomiting	7 (12.28)	4 (7.41)	0.529
Dizziness	3 (5.26)	3 (5.56)	1.000
Giddiness	2 (3.51)	2 (3.70)	1.000
Dry mouth	7 (12.28)	2 (3.70)	0.163
Not wanting to smoke	8 (14.04)	8 (14.81)	1.000
Feeling offended by the smell of smoke	9 (15.79)	5 (9.26)	0.395

Note. Data presented as number (percentage).

placebo at week 12 (35.19 vs 17.54) with no serious side effects. The relative risk for smoking cessation of VC at week 12 was 2.01 (p value 0.034).

Unlike the previous five studies that have evaluated the efficacy of VC on smoking cessation, this study showed that VC had a significant effect on CAR. There are several factors may explain these findings. First, this study had a longer duration of treatment than previous studies (12 weeks vs two to eight weeks). Second, the fact that the VC was in pastille form meant that it was in contact with the tongue for a longer duration. Previous studies conducted using *Vernonia cinerea* administered as infusion tea and capsules found continuous abstinence rates to be 28.1, and 22.9%, respectively.[5,8] However, a study carried out using hard VC in lozenge form found the continuous abstinence rate at Week 12 to be 29.4% [9], which is closer to that found in this study (35.19%). Third, the chewing of VC may increase the smoking cessation rate,[10] as sodium nitrite in the VC may cause tongue numbness resulting in reduction of cigarette craving.[6] Finally, the number of participants in the study may affect the CAR. The five previous studies did not show significant CAR results. However, these results are significant when analyzed together. A recent meta-analysis of the five studies (three included CAR analyses) showed that VC led two a 2.18 times greater average chance of smoking cessation after 12 weeks of treatment.[11]

As with the previous reports,[5,9] the PAR in this study did not differ between the VC and placebo group. However, PAR only evaluates the past seven days, possibly making it less reliable than CAR, which evaluates smoking behavior over a longer duration (14 days). This means that the PAR of a given group is likely to be higher than its CAR (Figs. 2 and 3). The meta-analysis discussed above also found higher PARs than CARs.[11] Note that in the meta-analysis, both PAR and CAR of the VC and control groups only differed significantly after week eight of treatment. These findings may suggest that smoking cessation may require a long treatment duration.

The strengths of this study were 1) the study design (placebo controlled) and 2) the location. The five previous studies discussed above compared VC with either counseling or exercise. This study showed that smoking cessation may be performed at a community pharmacy by pharmacists, rather than in the hospital or by physicians. The main limitation of this study is that only participants

with low to moderate levels of nicotine addiction were enrolled. The severe nicotine addiction participants are required standard treatment for smoking cessation. Therefore, it may be unethical to enroll these participants into the study. However, further studies in smokers with high levels of nicotine addiction are needed. It might be beneficial effects of other herbs or even VC in terms of molecular benefits but were not evaluated in this study.[12–14]

5. Conclusion

Administration of VC pastels resulted in significantly higher CARs than placebo at week 12.

Footnotes

None.

Ethical statement

All subjects given informed consent prior to study participation and the study protocol was approved by the ethic committee in human research, Khon Kaen University.

Declaration of competing interest

The authors declare no conflicts of interest.

Acknowledgement

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jtcme.2019.09.006.

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