



Published in final edited form as:

*Cancer Epidemiol Biomarkers Prev.* 2009 December ; 18(12): 3497–3501. doi:  
10.1158/1055-9965.EPI-09-0620.

## Chinese “Herbal” Cigarettes are as Carcinogenic and Addictive as Regular Cigarettes

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### Abstract

**Objective**—To examine the Chinese tobacco industry's claim that herbal cigarettes are less harmful than regular cigarettes.

**Design**—Cross-sectional study.

**Participants**—135 herbal cigarette smokers and 143 regular smokers from one city in China completed a questionnaire on smoking behavior and provided a urine sample.

**Main Outcome Measures**—Cotinine and trans-3'-hydroxycotinine in all samples and polycyclic aromatic hydrocarbon metabolites (PAHs) (1-hydroxypyrene, naphthols, hydroxyfluorenes and hydroxyphenanthrenes) and the tobacco specific nitrosamine 4-(methylnitrosamino)-1-(3-pyridyl)-butanol (NNAL) and NNAL-glucuronide in randomly selected 98 samples (47 from the herbal smokers' group and 51 from the regular smokers' group). Values were normalized by creatinine to correct for possible variability introduced by dilution or concentration of the urine.

**Results**—Health concern was among the main reasons that smokers switched to herbal cigarettes from regular cigarettes. Smokers reported increased consumption after switching to herbal cigarettes from regular cigarettes. For all the four markers analyzed (cotinine, trans-3'-hydroxycotinine, total NNAL, total PAHs), we observed no significant difference in the levels ( $p=0.169$ ,  $p=0.146$ ,  $p=0.171$ ,  $p=0.554$ ) between smokers of herbal cigarettes and smokers of regular cigarettes. Both total NNAL and total PAHs were significantly correlated with cotinine and trans-3'-hydroxycotinine ( $p<0.001$  for all four correlations).

**Conclusions**—Our findings showed that herbal cigarettes did not deliver less carcinogens than regular cigarettes. The public needs to be aware of this fact and the Chinese tobacco industry should avoid misleading the public when promoting herbal cigarettes as safer products.

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**Conflicts of Interest Statement:** Dr. Benowitz has served as a paid expert witness in litigation against tobacco companies on issues related to addiction and light cigarettes. The other authors have no conflict of interest.

## Introduction

In Western countries, the term “herbal cigarettes” often refers to cigarettes that are made of a mixture of different herbs and that contain no tobacco or nicotine. In China, the China National Tobacco Corporation (CNTC) began in the late 1970s to develop tobacco cigarettes that also contain Chinese medicinal herbs, which it also calls “herbal cigarettes” (1). In the manufacture of these herbal cigarettes, extracts of Chinese medicinal herbs are mixed with or sprayed on leaf tobacco (2). A host of Chinese herbs have been used as cigarette additives, from the commonly known Ginseng to much less known ones such as *Jiaogulan* (2,3). Most of these herbs are common ingredients in traditional Chinese medicine and are used for therapeutic purposes or as dietary supplements. Since the first herbal cigarette brand in China, *Changle*, was marketed by the Beijing Cigarette Factory (affiliated with the CNTC) in 1979 (2), many herbal cigarette brands have been developed and marketed in China. In the 1990s herbal cigarettes began to gain popularity in China. The two brands that have achieved the most sales success in China were *Jinsheng* and *Wuyeshen*, which sold over 20 billion cigarettes in 2008, accounting for more than 1% of all the cigarettes produced in China (4-6). (For comparison, Lucky Strike had a 1.1% share of the US market in 1965 (7), Virginia Slims had 2.6% in 2000 (8).) Most herbal brands in China, including *Jinsheng* and *Wuyeshen*, have the same machine-determined yield of tar as regular cigarettes (15mg).

Although the market share of herbal cigarettes is still relatively small in China, herbal brands are quickly expanding their market there and into the global market. *Jinsheng*'s export markets in 2008 included the Philippines, Singapore, Indonesia, Malaysia, Cambodia, Myanmar, Canada and Taiwan (9). In 2003 *Jinsheng* was so successful in the Philippines that it accounted for 90% of imported cigarettes in Manila (10). *Zhongnanhai*, the first herbal brand with a low tar rating (at 1, 3, 5, 6, 8 mg) has achieved considerable success in Japan and can also be found in the markets of the United States, Singapore, Malaysia, Taiwan, Hong Kong and Macao (11).

Many claims of health benefits for smokers of herbal cigarettes were made by the Chinese tobacco industry. For example, *Jinsheng* claims a host of benefits, including less coughing and sputum, nourishment of the kidneys and the lungs, boosting of sexual drive (12). The health claims *Jinsheng* made can also be conveniently found in a card inserted in some cigarette packages (12). *Wuyeshen* claims over 60% reduction in cancer-causing nitrosamines, including tobacco specific nitrosamines, and the inhibition of benzo(a)pyrene's carcinogenicity (13).

Several studies have attempted to evaluate the health benefits of smoking herbal cigarettes by either measuring the yields of tobacco-specific nitrosamines in mainstream tobacco smoke with smoking machine or cellular response to tobacco smoke in *in vitro* experiments (14-17). No studies have directly measured the levels of carcinogens from herbal cigarettes in smokers' bodies. The present study examines, for the first time, the level of metabolites of several key tobacco constituents in herbal cigarette smokers' urine. In contrast to the claims made by the Chinese tobacco companies that herbal cigarettes are safer than regular cigarettes, we find no difference in the levels of nicotine or carcinogens in smokers' bodies between these two types of cigarettes.

## Methods

### Sampling protocol

All subjects were smokers smoking cigarettes of Chinese brands living in one city in China. 180 herbal cigarette smokers and 180 regular cigarette smokers were recruited through three district community centers. (Since all herbal brands are still very localized in China currently and all of the herbal smokers in our study smoked the same brand that was produced locally,

we chose not to disclose the name of brand to protect our local collaborators from the retaliation by the local tobacco company.) Regular cigarette smokers smoked cigarettes with 14 or 15 mg machine-measured tar yields per cigarette. Herbal cigarette smokers were smokers of a local popular herbal brand with 15mg of machine-measured tar yield. Several inclusion criteria were applied: (1) subjects had to be male smokers (because few women smoke in China); (2) subjects had to be between the ages of 18 and 65, with no diagnosis of cancer, heart disease or major respiratory diseases; (3) subjects had to smoke on average at least 5 cigarettes per day; and (4) subjects had to have been smoking the current brand for at least three months; (5) when brand-mixing was present, smokers had to smoke either regular or herbal brands at least 90% of the time.

Each subject signed a consent form and completed a questionnaire. At the end of the questionnaire, a 25 ml urine sample was collected.

The protocol was approved by the University of California San Francisco Committee on Human Research and the China Center for Disease Control and Prevention Committee on Human Subjects.

### Laboratory analysis of tobacco smoke compounds in smokers' urine

The urine samples were frozen and shipped to San Francisco General Hospital for analysis in the Tobacco Biomarker Core Facility of the UCSF Helen Diller Family Comprehensive Cancer Center. Cotinine and trans-3'-hydroxycotinine, both metabolites of nicotine, 4-(methylnitrosamino)-1-(3-pyridyl)-butanol (NNAL) and NNAL-glucuronide, metabolites of NNK, a tobacco specific nitrosamine and one of the most potent carcinogens in tobacco smoke (18), and metabolites of polycyclic aromatic hydrocarbons (PAHs), which represent a class of combustion products that include a number of carcinogens, were measured. All analytes, were measured using liquid chromatography by methods described previously: Cotinine and trans-3'-hydroxycotinine (19), NNAL and NNAL-glucuronide reported as total NNAL (20), metabolites of the PAHs including 1-hydroxypyrene, naphthols, hydroxyfluorenes and hydroxyphenanthrenes and reported as total PAHs (21). Concentrations of cotinine, trans-3'-hydroxycotinine, total PAHs and total NNALs were normalized by urine creatinine to correct for variations due to dilution or concentration of urine. Per cigarette level of normalized total PAHs, total NNAL, cotinine and trans-3'-hydroxycotinine were estimated by dividing the concentrations by the number of cigarettes the subject reported smoking per day.

Every sample was analyzed for the levels of cotinine and trans-3'-hydroxycotinine (for a total of 360 samples). A random sample of 60 samples from each group of smokers (for a total of 120 samples) was analyzed for PAHs and NNAL. Nine subjects were dropped because of incomplete demographic information in the questionnaire. Three samples were excluded from the results due to abnormally low levels of creatinine. Twenty-seven subjects who claimed to smoke herbal cigarettes and 19 who claimed to smoker regular cigarettes were dropped from the study because their urine samples indicated cotinine levels ( $< 50 \mu\text{g/liter}$  (22)) of a typical non-smoker. Seven smokers of regular cigarettes were dropped from the study because the main brand they smoked had a tar level of light cigarettes ( $< 14\text{mg}$ ). In sum, the results reported in this paper are based on 278 samples for cotinine and trans-3'-hydroxycotinine, 93 samples for PAHs and NNAL.

### Statistical Analysis

Survey questions were analyzed using chi-square. Levels of biomarkers were analyzed using a Mann-Whitney rank sum test. Calculations were done with Stata 10.1.

## Results

Demographic information for the subjects is presented in Table 1. Herbal cigarette smokers and regular cigarette smokers did not differ in age, number of cigarettes smoked per day, educational level, employment status or income.

### Urine levels of cotinine, trans-3'-hydroxycotinine total PAHs and total NNAL

Adjusted for creatinine, neither the levels of cotinine ( $p=0.169$ ) nor trans-3'-hydroxycotinine ( $p=0.146$ ) were significantly different between herbal smokers and regular smokers (Table 1 and Figure 1). (Unadjusted cotinine and trans-3'-hydroxycotinine (ng/ml) were lower in herbal cigarette smokers,  $p=0.047$  and  $p=0.058$ , respectively.) The levels of total PAHs ( $p=0.554$ ) and total NNAL were not statistically different between the two groups ( $p=0.171$ ) (Table 1 and Figure 2). Results per cigarette showed the same patterns (details not shown). Both NNAL and PAHs significantly correlated with cotinine (NNAL:  $r_s=0.535$ ,  $p<0.001$ ; PAHs:  $r_s=0.668$ ,  $p<0.001$ ) and trans-3'-hydroxycotinine (NNAL:  $r_s=0.539$ ,  $p<0.001$ ; PAHs:  $r_s=0.674$ ,  $p<0.001$ ) (scatter plots of cotinine vs NNAL and PAHs shown in Figure 3). Using a multiple regression model (results not shown), the relationships did not depend on the type of cigarettes the subjects smoked.

### Cigarette switching

There was no significant difference in daily cigarette consumption between regular and herbal smokers (Table 1). 106/135 (86%) of the herbal smokers had switched from regular cigarettes a median of 6.25 years earlier (IQR: 4-10 years). Smokers reported increased numbers of cigarettes smoked per day after switching to herbal cigarettes from regular cigarettes (Table 1). The most often cited reason for switching to herbal cigarettes was "better taste" compared to regular cigarettes (47%). Health concern was the second most popular reason reported for switching (24%) (Table 2). "Convenience of purchase" and "support for a local product and business" accounted for 21% and 15% of the responses, respectively. There are two opposite concerns about the price: some smokers switched because the current brand was more affordable, while others switched because the current brand was more expensive and "good for face" when offering cigarette to others, which is a common social etiquette in China. Additionally, "no fake cigarettes" was reported by 4% of the respondents as the reason for switching to herbal cigarettes.

## Discussion

The present study is the first that examines the level of tobacco toxins in the bodies of smokers of Chinese herbal cigarettes. We examined the major metabolites of nicotine and two groups of tobacco carcinogens among smokers of herbal cigarettes. There was no detectable difference in levels of nicotine or total NNAL, the metabolite of the main tobacco specific carcinogen NNK, or PAHs between herbal cigarette smokers and regular cigarette smokers.

Smokers of herbal cigarettes had lower concentrations of unadjusted cotinine and trans-3'-hydroxycotinine in the urine, but not after normalizing for creatinine. This result may suggest slightly lower intake of nicotine from their cigarettes, or more concentrated urine among herbal cigarette smokers. The reason for lower nicotine is unclear, as we did not measure the nicotine content of the various types of cigarettes. The primary toxicity of nicotine is sustaining addiction, and it is doubtful that very small differences in nicotine exposure, as were seen in our study, would have any meaningful effect on the addiction potential of the cigarettes. In any event, measures for tobacco smoke carcinogen biomarkers demonstrate no evidence whatsoever of lower exposure in herbal cigarette smokers, suggesting no less cancer risk.

While our results show that herbal cigarette smokers have similar levels of carcinogens in their bodies as regular cigarette smokers, we could not test the industry claim that the herbal additives inhibit the toxicity of these carcinogens. We could not locate any published studies that examined or supported such claims.

We found significant correlations between total NNAL/total PAHs and the metabolites of nicotine (cotinine and trans-3'-hydroxycotinine). The correlations persisted after stratifying for the type of cigarette smoked. Our findings support previous research that NNAL and cotinine are significantly correlated among smokers (23,24). This result suggests that cotinine and trans-3'-hydroxycotinine in smokers' urine are indicative of the levels of total NNAL and total PAHs in Chinese herbal and regular smokers due to smoking.

Herbal smokers who switched to herbal cigarettes from regular cigarettes reported increased cigarette consumption after switching. Because of the cross-sectional design, the current study was not able to examine the effect of this increased consumption on the nicotine and carcinogen intake from tobacco smoke. It would be of interest for future studies, especially with short or long-term switching experimental designs, to examine whether it was the health messages and/or the herbal additives that triggered this increased consumption.

Many of the herbal constituents in herbal cigarettes present therapeutic benefits if used alone (generally taken orally, rather than burned and smoked). When burned with processed tobacco and inhaled, these herbal constituents are likely to undergo complex physical and chemical changes. Of the three main herbal brands in China, *Wuyeshen*, *Jinsheng* and *Zhongnanhai*, we did not find any literature evaluating the health benefits of *Jinsheng* and *Zhongnanhai*. Three studies examined the safety claims of *Wuyeshen* (15-17). One study found reduction of tobacco-specific nitrosamines in mainstream smoke compared to regular cigarettes (17). The other two studies found lower toxicological effects from test animals smoking *Wuyeshen* and reduced deaths in mouse embryonic cells and human endothelial cells in *in vitro* experiments (14-16). None of these studies were conducted by independent researchers: one was by a researcher from the tobacco company that manufactured *Wuyeshen* (17) and the others by researchers with close ties with the tobacco industry (15,16). A full independent evaluation of the final products, which is yet to be undertaken, would be necessary before any conclusion can be reached to support claims of therapeutic effects of herbal cigarettes.

The marketing of herbal cigarettes as safer products by the Chinese tobacco industry, though unfounded, has been effective; we found health concern to be the second most reported reason for smokers to switch to herbal cigarettes (Table 2).

In 2001, *Jinsheng* and *Zhongnanhai* were among 36 most prestigious brands selected by CNTC out of hundreds of brands in China (25). With a strong foothold in several provinces in China, several herbal brands are being exported to Japan, Korea, countries in Southeast Asia and North America (1,9,11). Because of the health benefits the marketing implies and the fact that smokers in many of these countries are more health conscious, herbal cigarettes is, albeit slowly, gaining popularity in these countries. Local regulatory agencies should be aware of the unsubstantiated health claims and take measures to restrict the marketing of herbal cigarettes.

## Acknowledgments

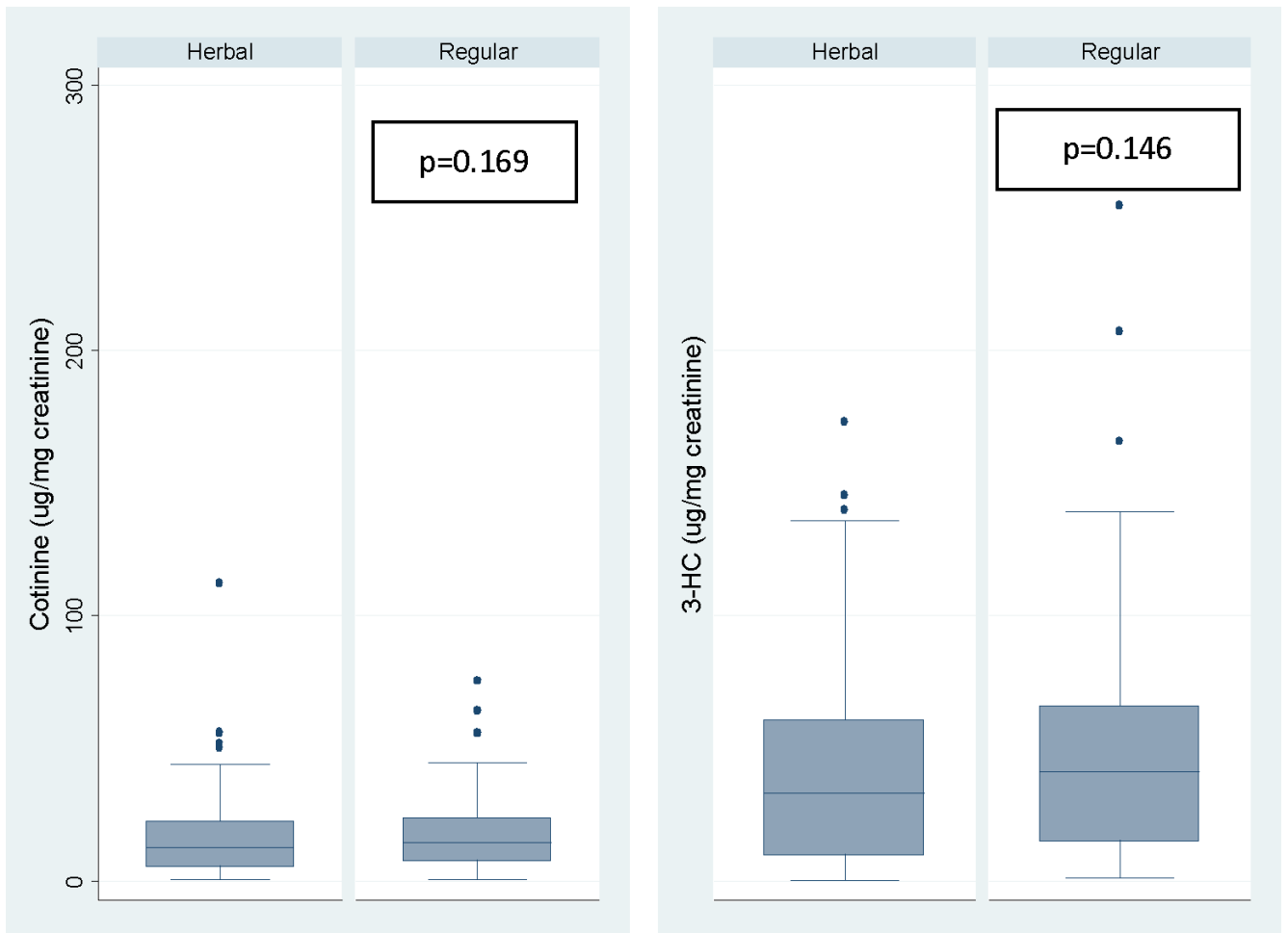
We express our deep appreciation to our local sampling collaborators in China, without whose help this project would not have been possible. We are also grateful to Margaret Peng and Lisa Yu for performing the analytical chemistry, and Drs Peyton Jacob III and Christopher Havel for supervised the laboratory analyses. This work was supported by National Cancer Institute Training Grant CA-113710, the William Cahan Endowment and the UCSF Bland Lane Center of Excellence on Secondhand Smoke funded by the Flight Attendants Medical Research Institute and the UCSF Helen Diller Family Comprehensive Cancer Center, and the China CDC. The external funding agencies played no role in the design of the project, collection and analysis of the data or preparation of the manuscript.



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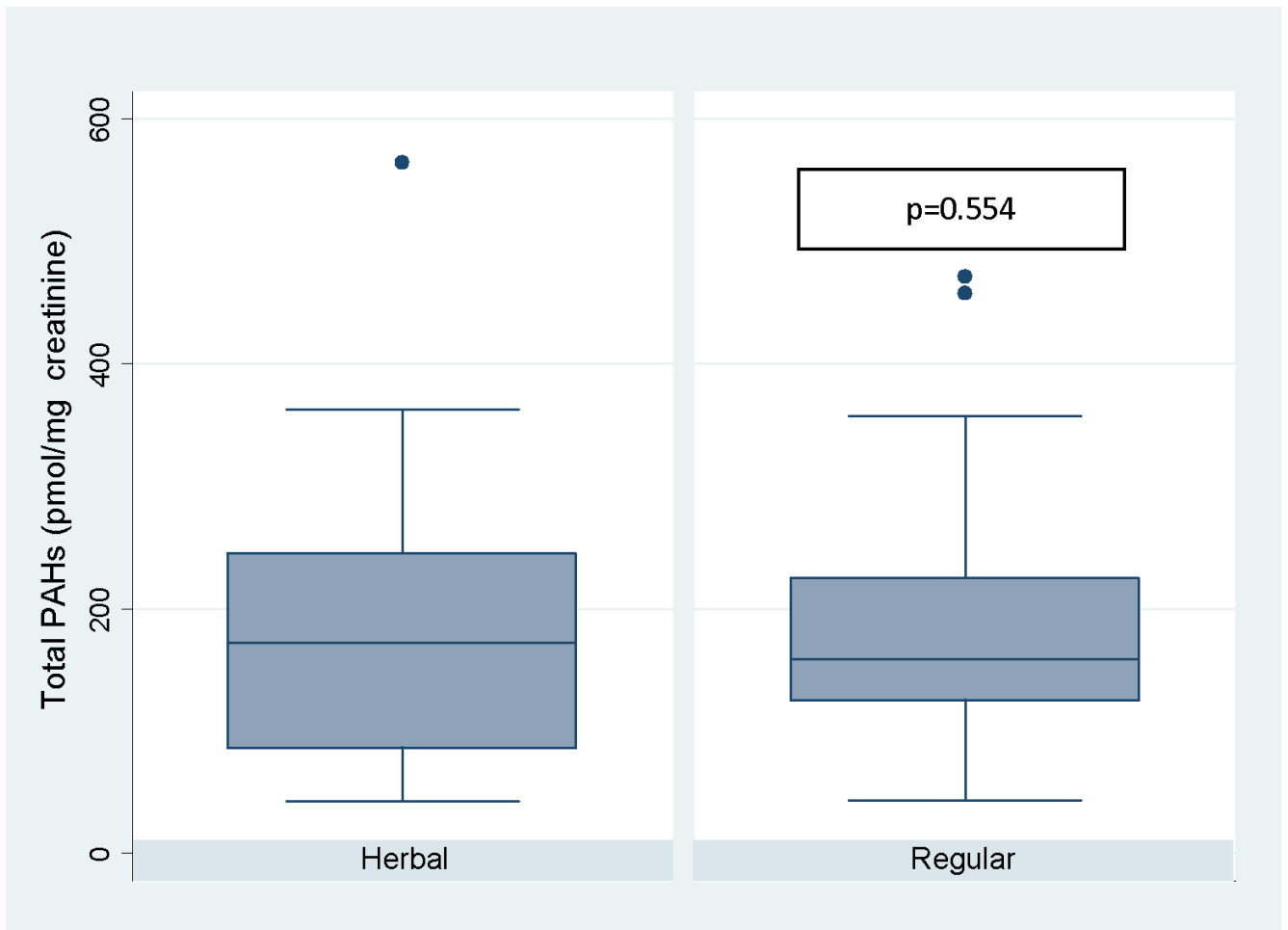
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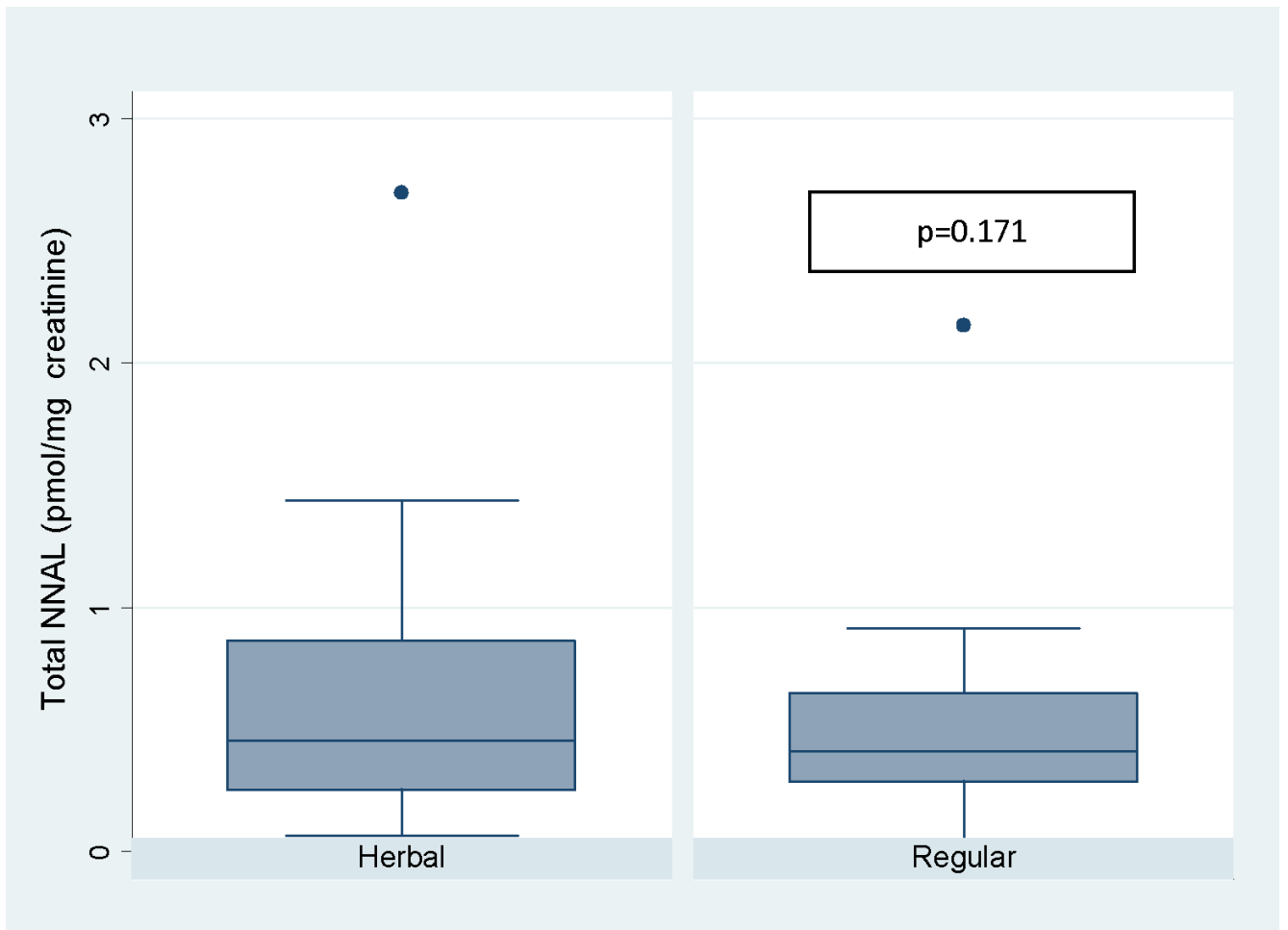
**Figure 1.**

There is no significant difference in levels of cotinine and trans-3'-hydroxycotinine (normalized by creatinine to account for differences in urine concentration) between herbal smokers and regular smokers.

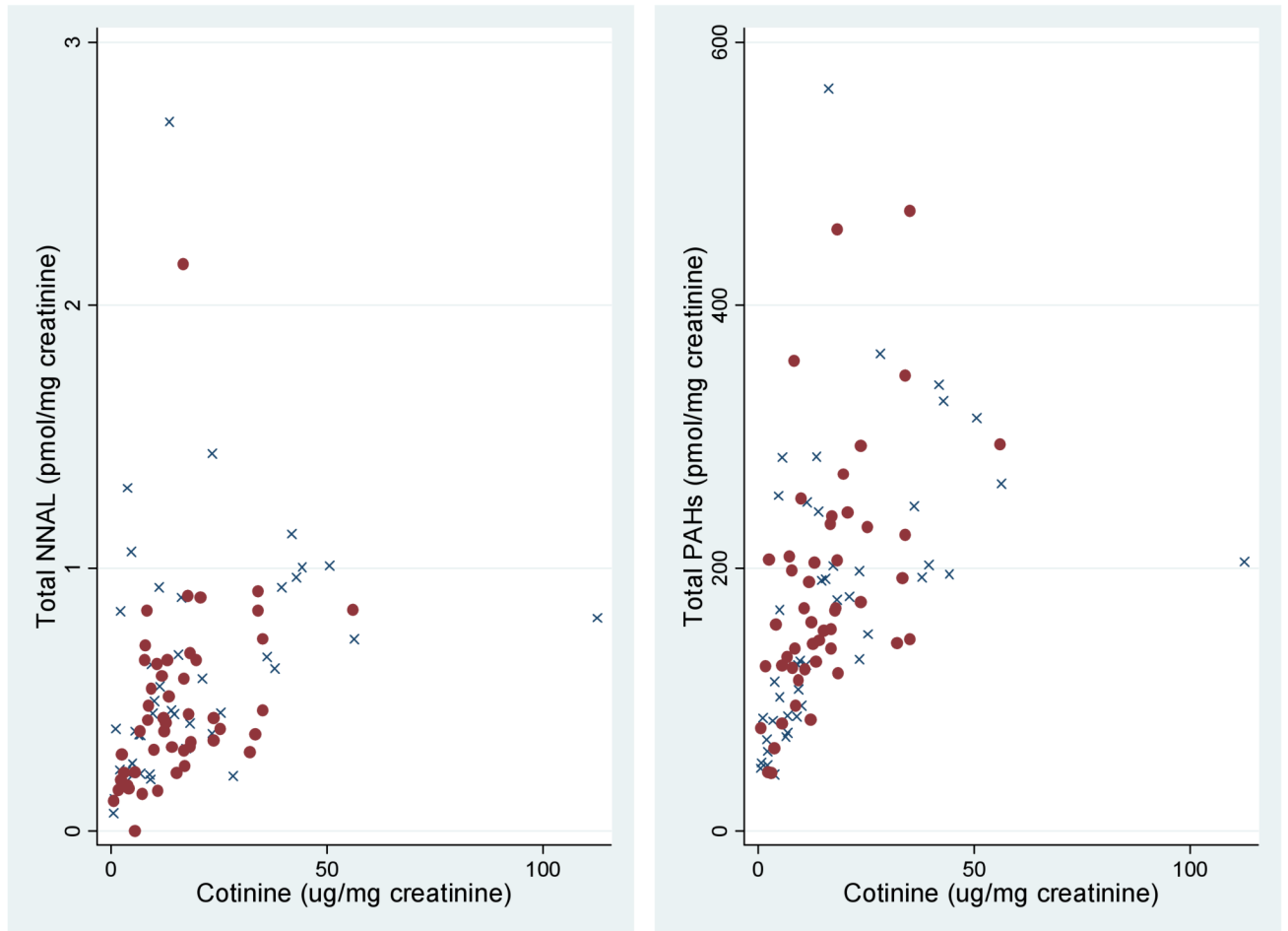




**Figure 2.**  
There is no significant difference in PAHs between herbal smokers and regular smokers.



**Figure 3.**  
There is no significant difference in NNAL between herbal smokers and regular smokers.



**Figure 4.**

Scatterplots of cotinine vs total NNAL ( $r_s=0.535$ ,  $p<0.001$ ) and total PAHs ( $r_s=0.668$ ,  $p<0.001$ ) show that higher levels of cotinine are associated with higher levels of carcinogens. (Crosses: herbal smokers; dots: regular smokers.)

Table 1

Demographic characteristics of the subjects.

	Smokers of herbal cigarettes	Smokers of regular cigarettes	p-value
Sample size, N	135	143	
Age (yrs), Median (IQR)	48 (38-56)	48 (39-54)	p=0.567*
Cigarettes per day on average			
Median (Interquartile range)	20 (15-20)	20 (15-20)	p=0.962*
Education, N (%)			
Junior high school and below	70 (52%)	77(54%)	
Secondary technical school	41 (30%)	42 (29%)	
Junior college	20 (15%)	18 (12%)	
College and above	4 (3%)	6 (4%)	p=0.621 <sup>†</sup>
Employment status, N (%)			
Employed	81 (60%)	94 (66%)	
Unemployed	54 (40%)	49 (34%)	p=0.979 <sup>†</sup>
Monthly income, N(%)			
<500 yuan	19 (14%)	30 (21%)	
500-999 yuan	40 (30%)	41 (29%)	
1000-1999 yuan	58 (43%)	52 (36%)	
2000-4999 yuan	17 (12%)	18 (12%)	
>=5000 yuan	1 (1%)	2 (1%)	p=0.567 <sup>†</sup>
Change in daily consumption after switching from regular cigarettes (14-15mg) to herbal cigarettes			
Increased daily consumption	47%	-	
Decreased daily consumption	30%	-	
No change in daily consumption	23%	-	
Cotinine and trans-3'-hydroxycotinine (Median and Interquartile range)			
Sample size	134	142	
Cotinine (µg/mg creatinine)	12.8 (5.57-22.2)	14.3 (8.00-23.7)	p=0.169*
Cotinine (ng/ml)	1142 (476-2175)	1538 (666-2463)	p=0.047*
trans-3'-hydroxycotinine (µg/mg creatinine)	33.0 (9.88-61.4)	41.1 (15.6-65.7)	p=0.146*
trans-3'-hydroxycotinine (ng/ml)	2799 (732-6346)	3732 (1518-7230)	p=0.058*
Total PAHs and total NNAL (Median and Interquartile range)			
Sample size	44	49	
Total PAHs (pmol/mg creatinine)	172 (87.1-245)	159 (126-225)	p=0.554*
Total NNAL (pmol/mg creatinine)	0.454 (0.256-0.862)	0.410 (0.291-0.649)	p=0.171*

\* Based on Mann-Whitney signed rank test;

<sup>†</sup> Based on chi-square test.

**Table 2**

Reasons for herbal cigarette smokers to switch from regular cigarettes (14-15mg tar) to current herbal brands.\*

Ranking of reasons	Specific reasons	Response (%)
1	Better taste	50 (47%)
2	Health concerns	26 (24%)
3	Convenience of purchase	22 (21%)
4	Support for local product & business	15 (15%)
5	Price	10(9%)
6	No fake cigarettes of current brand	4 (4%)

\* 106 out of 135 subjects who smoked herbal cigarettes answered this multiple-choice question. Percentages do not add to 100% because respondents were allowed to report more than one reason.