

# Detoxifying of Nicotine in Smokers with Consumption of Food Containing CYP 2A6 Enzyme from Beef Liver

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## ABSTRACT

**Background:** the addicted smoking nicotine levels in the blood have an average 12 mg/liter of blood, while the safe limit of nicotine in the blood is 2 mg/liter. Nicotine levels decreased can be done by using the food contains biotransformation enzymes i.e. CYP 2A6. The purpose of this study was to know the decrease in nicotine in the blood of smokers after the feeding of biotransformation enzyme containing nicotine CYP 2A6

**Method:** The research method was an experiment. The number of respondents active smokers 30 people which received rehabilitation at PHC Surabaya Hospital. Samples were taken by random sampling.

**Result:** Based on the results of the study, second inspection after consumption of food which contained enzyme CYP 2A6 from beef liver, there was an increased excretion of cotinine in urine. There were 80% of respondents have increased levels excretion of cotinine in urine.

**Conclusion:** The conclusion of this study was that food which contained nicotine biotransformation enzyme (CYP 2A6) decreased concentration of nicotine in the blood of smokers

**Keywords:** Nicotine, Detoxification, CYP 2A6 enzyme, Cotinine, Biotransformation

## INTRODUCTION

Nicotine is the main cause of addiction in smoking making smokers will continue to smoke<sup>1,2,3</sup>. The more often the smoking then the health impact arising diseases will be even greater. Disease control can be done by reducing and eliminating nicotine from the body of the smoker. The efforts are made by biotransformation of nicotine in the body<sup>4</sup>.

Metabolism of nicotine in the body was various, although the main route of nicotine metabolism is through cotinine (70-80%). Biotransformation of

nicotine is undertaken by the enzyme cytochrome P-450 (CYP 2A6) to become cotinine, biotransformation by the enzyme N-flavoprotein can be nicotine oxidase, biotransformation by glucuronate (UGT) becomes cotinine glucuronate so that the consumption of nicotine in the urine be found cotinine, nicotine, nicotine oxidase N-glucuronate and nicotine itself<sup>5,6</sup>.

Biotransformation process nicotine is change by CYP 2A6 is 75% cotinine, 8-10% nicotine glucuronide, nicotine N-oxide is 3-5%. When it's adding around 99.5% so enzymes that play a role in detoxifying nicotine is a Cytochrome P-450 CYP 2A6-, glucuronate, methylation, flavoprotein, and glutathione<sup>7</sup>.

Based on research before, foods contained ingredients for biotransformation such as<sup>8,9</sup>:

a. P 450 (CYP-2A6) cytochrome: vegetables and meat contained iron

Many foods contained iron have easily obtained

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ingredients. The food spread has ranged from vegetables, fruits, until the meat. Examples of foods that contain iron included potato peels, spinach, kale, corn, chard, Beet Greens, fruit apricots, citrus fruits, peanuts, green beans, soybeans, raisins, cereal, eggs, fish, and beef.

b. Flavoprotein : green tea, soy, hemp trunks arbei.

c. Glucuronate: cauliflower, broccoli, cabbage, celery, sprouts, apples, cherries, avocado .

Based on results of the other research, CYP 2A6 enzyme has an important role for change nicotine to cotinine<sup>10</sup>. This research has incorporated also with a relationship of metabolism of nicotine with immunodetectable hepatic CYP 2A6 (within = 31 human livers) and research on immuno-inhibition. Those research more to research experimentation by making use of culture in vitro and in vivo.

Other research also tends to be associated with this type of polymorphism of the enzyme CYP 2A6 such as of CYP2A6 \* 4. These allele types are believed to have ties with the smoking behavior even research according to result of Rao Y. et al research stated that the number of cigarettes that consumed per day with the CYP2A6 \* 4 alleles less on someone who does not have the CYP2A6 \*<sup>11</sup> .

Based on research in Japan, found that in the Japanese and Koreans, the formation of cotinine in the body will be reduced because of this allele (CYP2A6 \* 4) may inhibit the metabolism of nicotine<sup>12</sup>.

Previous research was still associated genetic relationship such as polymorphism CYP 2A6 type with the smoking behavior of the smoker and seldom to explain how to reduce nicotine level in workers blood. But other research stated that decrease levels of nicotine in the body of the smoker can be using a food contains biotransformator enzymes i.e. CYP2A6 with nicotine level in the blood i.e. 2 mg/L in blood (for smoker, nicotine in blood averages 12 mg/liter)<sup>13</sup>. But, this research still requires other research evidence. So, it is needed to research on the relationship of foods consumption containing CYP 2A6 enzyme from the liver of beef with decrease level of nicotine.

The study will assess to know the decrease in nicotine in the blood of smokers after the feeding food containing nicotine biotransformation enzyme

(CYP2A6).

## MATERIAL AND METHOD

This study used experiment method. This experiment such as giving food containing P-450 (CYP 2A6) cytochrome.

Research conducted in experimental against smokers. Smokers are fed every day 3 times, i.e., morning, noon and night. Feeding for 6 days. The given food contains cytochrome P-450. Consecutive meals to be provided are: spinach, corn, kale, chard, beet greens, apricots, oranges, peanuts, green beans, soybeans, raisins, cereal, eggs, fish, and beef, green tea, soy, hemp trunks arbei, cauliflower, broccoli, cabbage, celery, sprouts, apples, cherries, avocado. The types of food that are made in the form of vegetables and fish and milk with the same weight on each of the respondents.

Before feeding on day one, firstly, measured the levels of nicotine in the urine. After feeding the sixth-day smokers also measured the levels of nicotine in the urine, and also the nicotine glucuronate, nicotine N-oxides, and cotinine.

The number of respondents as many as 30 people active smokers who got treatment at the rehab place smoker in PHC hospital Surabaya. Samples were taken in random sampling. Independent variables were the mass of the enzyme cytochrome P450 enzymes i.e. biotransformator or PYC 2A6 with units of mg/liter. Dependent variables were nicotine levels and cotinine in the urine with units of mg/l. Nicotine and cotinine in the urine measured by QRMA (Quantum Resonance Magnetic Analyzer). To test the difference in the levels of nicotine and cotinine in the urine before and after the awarding of the food contains biotransformator of nicotine on smokers used t-test are not paired.

## FINDINGS/RESULT

**Table 1 Distribution of Respondent Smoking Habit**

Smoking Habit	Quantity	Percentage
Smoking	20	100 %
No Smoking Habit	0	0 %
<b>Total</b>	<b>20</b>	<b>100.00 %</b>

Based on the above table shows that all respondents have a smoking habit

**Tabel 2. Distribution of Respondent First Age Smoking**

First Time Smoking	Quantity	Percentage
Elementary school (6-13 years old)	5	25,00 %
Junior high school (14-16 years old)	5	25,00 %
Senior high school (17-19 years old)	8	40,00 %
Recently	1	5,00 %
Other	1	5,00%
<b>Total</b>	<b>20</b>	<b>100.00 %</b>

Based on the table above shows that the distribution of the first age respondents do smoking is since senior high school during of 17-19 years old with the percentage of 40.00%.

**Tabel 3. Distribution of Smoking duration**

Duration smoking	Quantity	Percentage
1-20 years	9	45,00 %
11-20 years	3	15,00 %
>20 years	8	40,00 %
<b>Total</b>	<b>20</b>	<b>100.00 %</b>

Based on the table above shows that most respondents smoking during 1-20 years old with the latest smoking is 2 years old.

**Tabel 4: The Amount Spent on Cigarettes**

The number of cigarettes that is spent every day	Quantity	Percentage
1-10 cigarettes	15	75,00 %
11-20 cigarettes	2	10,00 %
21-30 cigarettes	2	10,00 %
Other	1	5,00 %
<b>Total</b>	<b>20</b>	<b>100.00 %</b>

Based on the above table shows that the majority of the respondents spent smoking as much as 1-10 cigarettes per day with the percentage of 75%

## The Result of Cotinine Examination

**Tabel 5 Result of Before and After Cotinine Examination**

ID Responden	Hasil Pemeriksaan 1	Hasil Pemeriksaan 2
1	529.95	3143
2	1314.73	475
3	2624.88	3484
4	441.61	1690
5	934.35	446
6	520.37	1111
7	2776.52	4224
8	1258.12	2310
9	400.64	3236
10	84.44	469

(Source: Primary Data, 2016)

Table above shows that the results of the examination of the second against respondents after the giving of food contain CYP 2A6 enzyme, glucuronate, and flavoprotein, there is an increase in cotinine level in the urine. There are 8 respondents occurred increased levels of cotinine in the urine while 2 respondents experienced a decrease in the levels of cotinine.

## DISCUSSION

### Smoking Habit

The results showed that 100.00% of the respondents have a habit of smoking. This shows that someone who smoked did not immediately feel the consequences that arise from the harm of smoking. Based on Susenas data in 2001, stated the prevalence of former male smokers and women relative small at such a young age, this can be attributed to the effects of smoking that occurred approximately 20 years. This situation can be seen in people who have quit smoking mostly in the elderly.

### Distribution of Respondent First Age Smoking

Results of the study stated the largest percentage the distribution first age smoking is since senior

high school during 17-19 years old. This suggests that this age is the age of teenagers with high a sense of curiosity is high, including trying to smoke.

Data Riskesdas and Health Research Agencies noted that the trend of the age of smoke rises in the age of the adolescents in the age group 10-14 years and 15-19 years of age. Results of data Riskesdas in the year 2007, 2010 and 2013, shows that the highest number of age start smoking at age group 15-17 years.

According to the Smet explained the age of first smoking generally ranges between 11-13 years. It can be said that someone started smoking at a time when children or teens. In general, according to Kurt Lewin, the smoking behavior is affected by individual factors and environmental factors<sup>14</sup>. Individual factors coming from within a teenager. Teenagers start smoking is associated with the presence of psychosocial crisis during its development namely “ identity search”. In this time the teen feels there is a mismatch between social development with a psychic. Teenagers will know that efforts to find an identity, not all correspond to the environment.

#### **Duration and The Amount Spent on Cigarettes**

A majority of respondents have smoked for a long-range 1-20 years. The reasons respondents liked the smoke can be a pleasant feeling of smoking, reducing anxiety, anger, and agitation. While the distribution of cigarettes spent 10-20 pieces per day. This shows that smoking can cause addiction and create a habit for users.

#### **The Result of Cotinine Examination**

Results of the study stated the presence of increased levels of cotinine in the urine of second inspection results against respondents after the giving of food contain CYP 2A6 enzyme, 8 respondents occurred increased levels of cotinine with a percentage of 80%. This shows that the nicotine has been converted into a form of cotinine have been expelled through the urine. Cotinine issued through the urine can reduce the levels of nicotine in the body of the respondents, so the level of dependency against nicotine can be reduced.

While the test of Paired t-test produces showed that significance  $0.028 < 0,005$ , then  $H_0$  is rejected. So,

there is relation between decline nicotine level in the blood against the giving of food containing CYP 2A6 enzyme.

### **CONCLUSION**

The characteristics of the respondents such as smoking habit, first age smoking, duration and amount spent of cigarettes affects a decrease of concentration of nicotine in the blood of smokers after feeding food containing nicotine biotransformator enzyme (CYP 2A6), and there is a relation between decrease concentration of nicotine in the blood of smokers after feeding food containing nicotine biotransformator enzyme CYP 2A6

### **RECOMMENDATION**

Further research is needed, especially in involving the nicotine detoxification by using food that is nutritious. Awareness is also needed for a healthy living mainly by involving family support nearby to reduce the consumption of cigarettes and cultivate a nutritious food ingredient.

**Conflict of Interest:** All authors have no conflicts of interest to declare.

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