CHAPTER IV

RESULTS

This chapter presents the study results, which include characterization of study products, results of eligibility and demographic data of subjects, efficacy of product, safety of product, and compliance of subject. Each issue is described individually below.

1. Characterization of test product and the placebo products

Table 7 Physical characteristics of the test and the placebo product

	Test product		Placebo product	
	Baseline	Week8	Baseline	Week8
Color	Brown	Brown	Brown	Brown
Texture	Smooth	Smooth	Smooth	Smooth
pH value	4.3	4.7 (0.14)	7.3	7.6 (0.10)

The test and placebo products were produced from the same formula except extract of tamarind's fruit pulp was added to the test product. Both products had brown color and smooth texture at the baseline and the end of study (Figure9). At baseline, pH values of test and placebo products were 4.3 and 7.3, respectively. These values were slightly increased at the end of study (Table7).

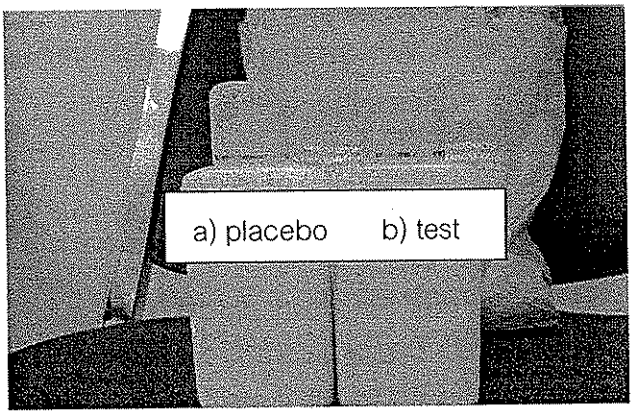


Figure 9 Placebo and test products

2. Result of eligibility and demographic data of subjects

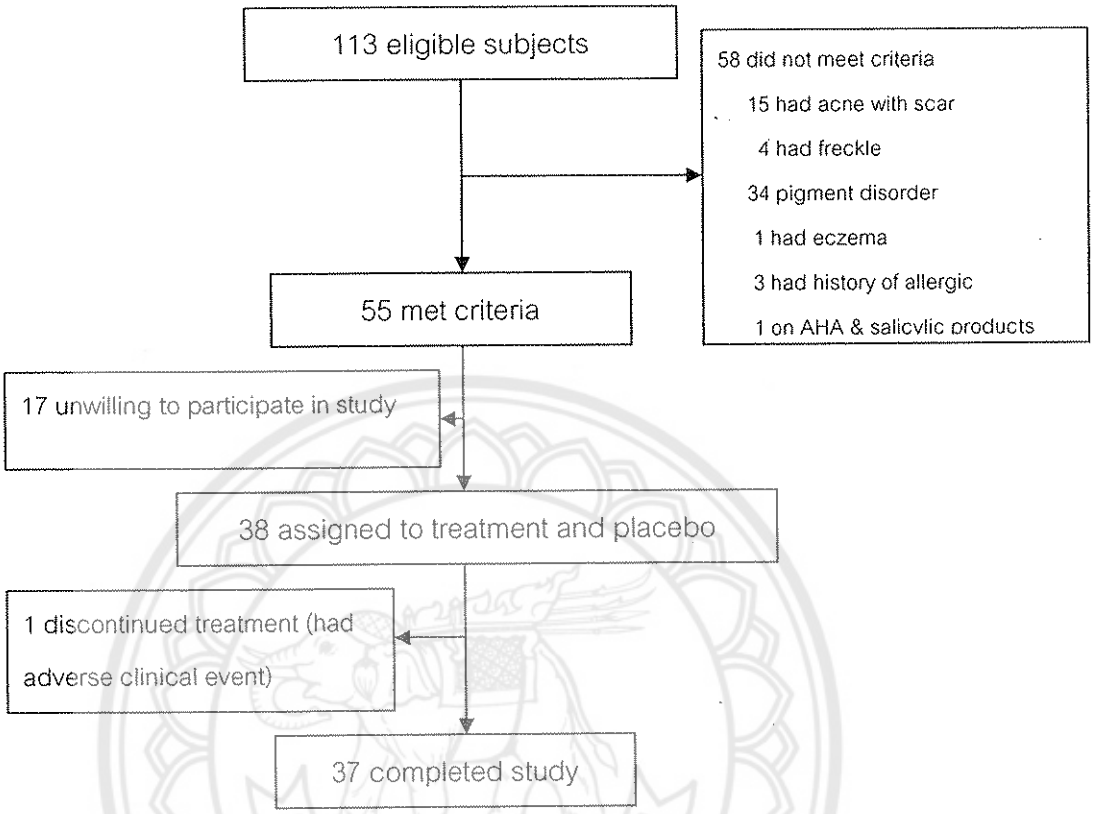


Figure 10 Result of eligible process

Subject recruitment process took approximately 3 months. One hundred and thirteen subjects were screened for eligibility. Fifty-eight subjects did not meet selection criteria, and 17 subjects unwilling to participate in study. Therefore, 38 Thai females were enrolled in the study. There was no lost follow-up but one subject was dropped out due to adverse clinical event. As a result, 37 subjects successfully completed study (Figure10).

The average age of subjects was 25.6 years with standard deviation of 4.3 years. Each subject received both the test and the control products. They were assigned to apply one product on one side of their face while the other product was applied on the other side of face. Demographic data of subjects were shown in table 8. In this study, subjects had various skin types including dry, normal, mixed, and oily type but more than haft of them had dry skin. All subject had education at least secondary school and most of them had income 5,000 to 15,000 baht/month.

Table 8 Demographic data of subjects

Characteristics	No. of subjects (%)	Characteristics	No. of subjects (%)
Type of skin*		Occupation	
Dry	21 (55.3)	Offices worker	22 (57.9)
Normal	8 (21.1)	Student	11 (28.9)
Mixed	7 (18.4)	Research assistant	4 (10.5)
Oily	2 (5.3)	Own business	1 (2.6)
Education		Concurrent product (on face)	
Secondary school	13 (34.2)	Sunscreen	38 (100)
Bachelor degree	19 (50.0)	*SPF 15*	*16 (42.1)*
Master degree	6 (15.8)	*SPF 16-25*	*8 (21.0)*
Income		*SPF > 25*	*14 (36.9)*
< 5,000 bath	9 (23.7)	Moisturizer	35 (92.1)
5,000 to 10,000 bath	17 (44.7)	Night cream	13 (34.2)
>10,000 -15,000 bath	11 (28.9)	Eye cream	6 (15.8)
> 15,000 bath	1 (2.6)	Toner	4 (10.5)
Frequency to go		Skin serum	2 (5.3)
to outdoor		Scar reducing cream	1 (2.6)
Some time	30 (78.9)		
Often	4 (10.5)		
Usually	4 (10.5)		

*Type of skin was classified by subjects themselves

Approximately 21% of subjects reported that they either often or usually go to the outdoor during day. Ninety-seven percentages of subjects worked or studied in office. All subjects applied sunscreen on both sides of their face. Ninety-two subjects used moisturizing product concurrent with sunscreen and study products. In addition, other current cosmetics of subject were allowed to use during study (Table8).

Each side of face was randomized to apply the test or the placebo product, and baseline skin characteristics of each group were measured at week 0 (baseline) before application. Six skin parameters including skin color, skin hydration, transepidermal

water loss (TEWL) of skin, skin redness, and skin elasticity were measured using biophysical instruments. All parameters were measured in arbitrary units of instrument except TEWL which was measured in g/m^2h. Erythema, scaling, and oedema of skin were assessed using visual scoring by the dermatologist. All baseline values were comparable in both groups (Table9).

Table 9 Baseline skin characteristics of each group

Characteristics	Mean (SD)	
	Test group	Control group
Skin color (Melanin)	228.60 (48.54)	230.47 (50.74)
Skin hydration (Water content)	47.97 (7.89)	48.65 (8.37)
TEWL of skin	12.11 (3.27)	11.59 (2.78)
Skin redness (Erythema)	220.22 (40.35)	222.00 (42.93)
Skin pH	4.63 (0.09)	4.75 (0.70)
Elasticity of skin		
Gross elasticity	0.036 (0.02)	0.033 (0.02)
Net elasticity	0.022 (0.02)	0.020 (0.02)
Visual scoring		
Erythema	0 (0)	0 (0)
Scaling	0 (0)	0 (0)
Oedema	0 (0)	0 (0)

3. Efficacy of product

The efficacy of product was measured using biophysical instruments at week 4 and week 8, and satisfaction questionnaire at week 8. Five skin parameters including melanin or skin color, water content, pH, gross elasticity, and net elasticity values were measured using Mexameter, Corneometer, pH meter, and Cutometer, respectively. Each parameter was provided below.

3.1 Skin parameter for efficacy assessment

Table 10 showed the result of each skin parameter at the middle (week 4) and the end of study (week 8). Skin color was represented in terms of melanin values. At

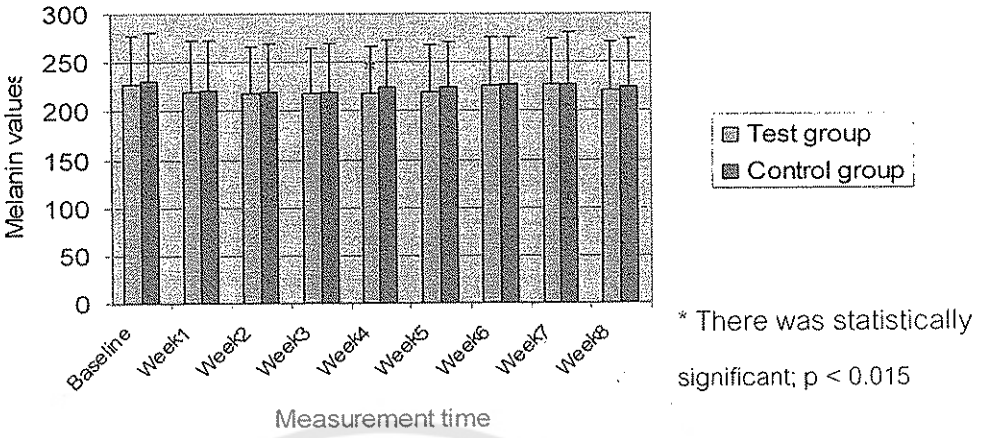
week 8, mean difference of melanin values between the test and the control group was not statistically significant ($p>0.05$). However, at week 4, mean difference of melanin value between the test and the control group was statistically significant ($p<0.015$). For other skin parameters including skin hydration, skin pH, and skin elasticity, mean differences between the test and the control group of all parameters were not statistically significant at both week 4 and week 8 ($p>0.05$) (Table10).

The melanin, pH, and elasticity values comparison of the test and the control groups for all measurements were shown in figure 11, 12, and 13, respectively. All skin parameters of the test group were comparable to that of the control group at all measurement times. Only melanin value at week4 was observed the significant difference between both groups (Figure11). The upper lines of mean values of all skin parameters presented the standard deviation of them

Table 10 Overall results at the middle and the end of study (week 4 & 8)

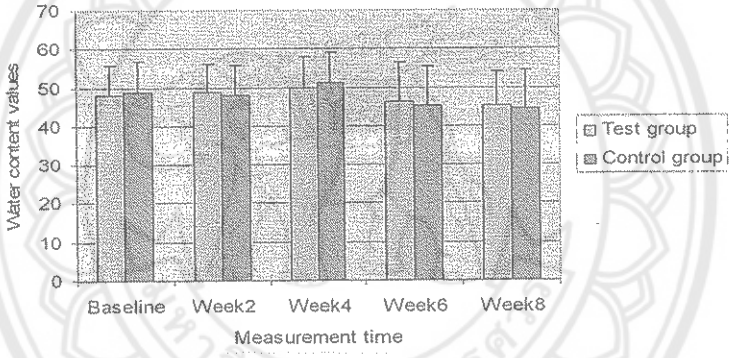
Skin parameter (Arbitrary units)	Mean (SD)		Mean difference (95%CI)	p-value
	Test group	Control group		
Week 4				
Skin color	218.55 (47.87)	225.10 (47.00)	-6.54 (-11.72, -1.37)	0.015**
Skin hydration	50.00 (8.06)	51.10 (7.81)	-1.10 (-2.36, 0.14)	0.082
pH	5.33 (0.62)	5.35 (0.64)	-0.02 (-0.24, 0.20)	0.848
Elasticity*				
Gross elasticity	0.034 (0.016)	0.034 (0.015)	-0.0005 (-0.004, 0.003)	0.792
Net elasticity	0.022 (0.013)	0.022 (0.011)	-0.0002 (-0.003, 0.003)	0.912
Week 8				
Skin color	222.02 (48.51)	224.46 (49.18)	-2.44 (-6.98, 2.10)	0.283
Skin hydration	45.32 (8.79)	44.54 (9.90)	0.78 (-0.40, 1.96)	0.188
pH	5.14 (0.72)	5.28 (0.57)	-0.14 (-0.34, 0.07)	0.180
Elasticity				
Gross elasticity	0.032 (0.02)	0.032 (0.02)	0.0001 (-0.004, 0.004)	0.948
Net elasticity	0.022 (0.02)	0.022 (0.01)	-0.0001 (-0.004, 0.004)	0.945

* This parameter was measured at week 5, ** There was statistically significant

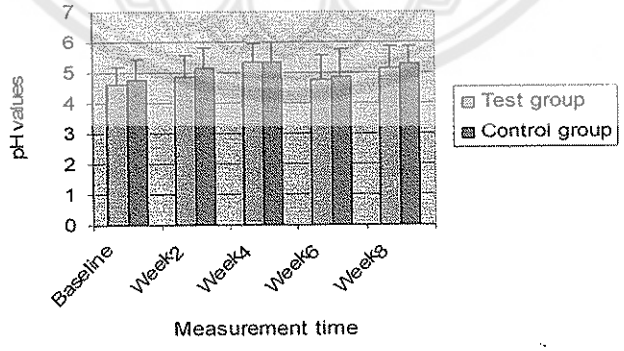


* There was statistically significant; $p < 0.015$

Figure 11 The melanin values of each group

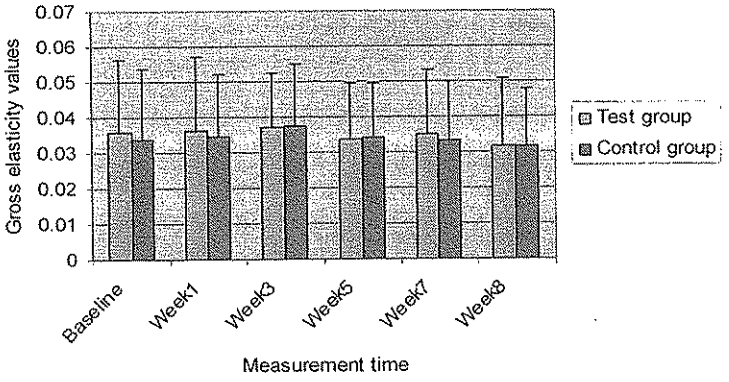


a. Skin hydration

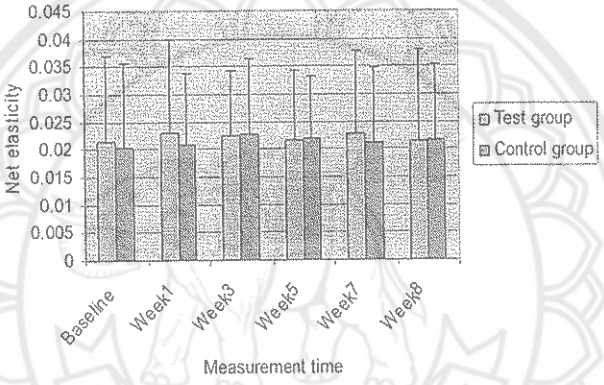


b. Skin pH

Figure 12 The skin hydration and skin pH of each group



a. Gross elasticity



b. Net elasticity

Figure 13 The gross and net elasticity of skin of each group

3.2 The satisfaction of subjects

Approximately two-thirds (67.6%) of subjects preferred the test product while only one-third (32.4%) of subject preferred the placebo product. Approximately 65% of subjects preferred to continue use, purchase, and advice the test product for their friends while subjects preferred to continue use, and advice the placebo product for their friends were 29.7%. In addition, only 27% of subject preferred to purchase the placebo product if it launch in the market.

Subject's satisfactions to physical characteristics including color, odor, packaging, size, and overall physical characteristics of product were comparable between the test and the placebo product. In addition, subject's satisfaction to properties of product during application such as viscosity, product removal, spread

ability, mildness to skin of test product were the same as the placebo products (Table11).

Table 11 Mean of satisfaction value.

Characteristic evaluated	Mean of satisfaction scales* (SD)	
	Test product	Placebo product
Physical characteristics of products		
Color	3.43 (0.73)	3.68 (0.71)
Odor	3.43 (0.80)	3.51 (0.73)
Packaging	3.16 (0.76)	3.13 (0.79)
Size	3.78 (0.48)	3.78 (0.48)
Overall liking of physical characteristics	3.76 (0.43)	3.84 (0.50)
Properties of products during application		
Viscosity	3.65 (0.82)	3.35 (0.95)
Product removals	3.78 (0.67)	3.78 (0.85)
Spread ability	4.03 (0.55)	3.81 (0.74)
Mildness to skin	4.19 (0.52)	4.05 (0.66)
Easy to rinse	3.98 (0.72)	3.94 (0.70)
Overall liking products during application	4.05 (0.57)	4.00 (0.53)
Product effect to skin		
Cleansing effect**	4.38 (0.59)	4.08 (0.72)
Whitening effect**	3.90 (0.77)	3.49 (0.80)
Moisturizing effect	4.08 (0.72)	3.92 (0.68)
Elasticity effect	4.00 (0.67)	3.94 (0.62)
Overall liking of product effect**	4.11 (0.56)	3.86 (0.54)
Rating scales (0= hate, 10 = love)**	8.22 (1.06)	7.72 (1.03)
Cost of product	107.43 (48.35)	60 (20.86)

*; Scaling system: 5 = like very much, 4 = like moderately, 3 = neither like nor dislike, 2 = dislike moderate, 1 = dislike very much

**; Using wilcoxon signed rank test, difference of satisfaction values between test product and placebo product was statistically significant

However, subjects' satisfactions to cleansing effect, whitening effect, overall of product effect, and rating scales of the test product were higher than that of the placebo product ($p<0.05$). Moreover, cost of the test product, which subject willing to buy was higher than that of the placebo product (Table11). Ranges of product cost for the test and the placebo product were 35-250 and 35-100 baht, respectively.

4. Safety of products

4.1 Skin parameters for irritation assessment

Safety of product was measured using biophysical instruments, visual scoring by dermatologist, and self-report by subjects themselves. Each issue was described below.

Table 12 Each skin parameter at the middle and the end of study (week 4 & 8)

Skin parameter	Mean (SD)		Mean difference (95%CI)	p-value
	Test group	Control group		
Week 4				
Erythema (unit)	223.58 (41.89)	220.56 (41.51)	3.02 (-4.68, 10.71)	0.432
TEWL (g/m^2h)	12.10 (3.25)	11.84 (2.49)	0.25 (-0.51, 1.02)	0.507
Week 8				
Erythema (unit)	218.39 (43.28)	220.24 (46.32)	-1.84 (-9.99, 6.30)	0.650
TEWL (g/m^2h)	11.26 (3.01)	11.16 (2.46)	0.10 (-0.75, 0.95)	0.811

Mean differences of erythma index (arbitrary unit), and TEWL (g/m^2h) between the test and the control group were not statistically significant at both week 4, and week 8 (Table12). The results of TEWL (g/m^2h), and erythema index (arbitrary unit) at all measurement times were presented in figure 6, and 7, respectively. Both values of the test group were comparable to that of the control group (Figure14 &15).

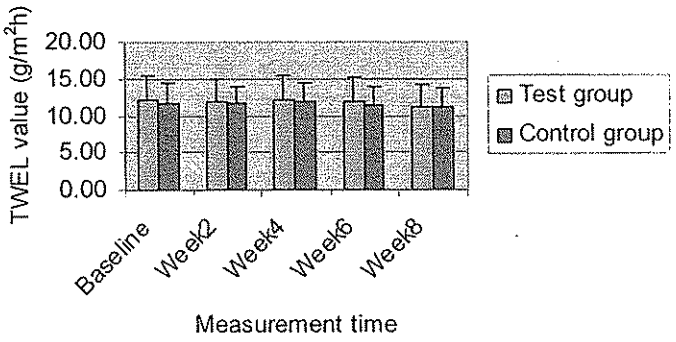


Figure 14 The TEWL in each group

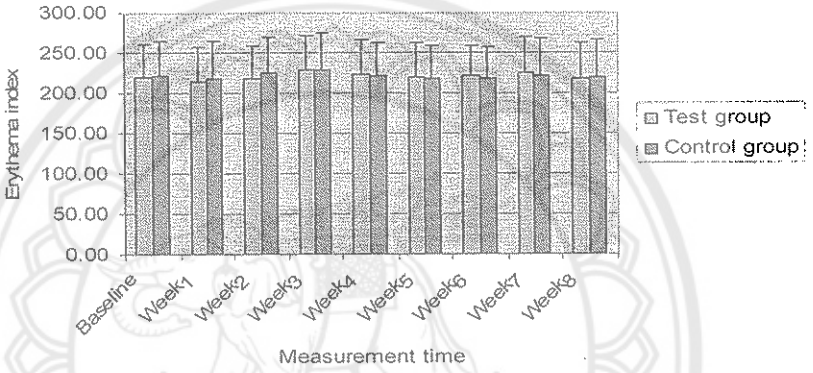


Figure 15 The erythema index in each group

4.2 Clinical evaluation of adverse events

Based on questionnaire, two subjects (5.4%) reported having an adverse event. One subject reported that she had moderate skin redness, and mild rash and scaling on the control side of face while had mild skin redness, rash, and scaling on the test side of face at week 3. Another subject reported that she had adverse event on only the test side of face including slight itching immediately after the first use of product, mild skin redness and stinging at both week 1, and week 2. In addition, she had mild rash at week 2. She did not sure about these adverse events on control side of face. However, in her diary she reported having mild skin redness on both sides of face. In addition, dermatologist reported that this subject had mild skin redness on both side of face at week 2. Based on recording of diaried, 6 subjects reported having acne during study.

5. Quality control of study

We used the results of assessment subject compliance, stability of study product, and the ability of production to blind subject to represent the quality of study. The results of them were provided below.

5.1 Compliance of subject

The compliance of subjects was verified by weighing the products before and after study, evaluation of product application of subjects, and checking the frequency of application product during study period.

On an average 102.78 g of test product, and 102.48 g of placebo product were used (Table13). Appropriated dose of product used was defined as 0.5-1.5 g/time. Overall, 100% of subjects used product twice daily with appropriated dose (Table14). Only one subject had mistake of use product at week1 of assessment. There was no subject missing use of product over study period.

5.2 Other procedures to control the quality of study

The stability of study products had been showed in part of characterization of product. The pH of both test and control products at baseline and the end of study were comparable. The ability of production to blind subject was evaluated using questionnaire at the end of study. Fourteen (37.8%) subjects can identify which one was test product. All evaluators and subjects were trained before start study.

Table 13 Product weight and total amount of using product

Measurement time	Mean of product weight; g (SD)	
	Test group	Control group
Baseline	137.28 (4.80)	137.30 (4.00)
Week 2	107.66 (8.99)	107.39 (10.57)
Week 4	81.80 (11.80)	82.68 (12.08)
Week 6	58.06 (12.31)	59.53 (12.77)
Week 8	34.52 (8.28)	34.85 (9.04)
Overall use (Week8-Baseline)	102.78 (9.71)	102.48 (9.84)

Table 14 Number of subjects use appropriate or inappropriate dose

	Analysis time				
	Subgroup analysis for every 2 weeks				Overall use
	Week2	Week4	Week6	Week8	
% Use appropriate dose (No. of subjects)					
Test group	92.11 (35)	94.59 (35)	94.59 (35)	94.60 (35)	100.00 (38)
0.50- 0.99 g	50.00 (19)	54.05 (20)	83.78 (31)	67.57 (25)	84.21 (32)
1.00-1.50 g	42.11 (16)	40.54 (15)	10.81 (4)	27.03 (10)	15.79 (6)
Control group	86.84 (33)	89.19 (33)	94.60 (35)	94.59 (35)	100.00 (38)
0.50- 0.99 g	50.00 (19)	48.65 (18)	89.19 (33)	62.16 (23)	84.21 (32)
1.00-1.50 g	36.84 (14)	40.54 (15)	5.41 (2)	32.43 (12)	15.79 (6)
% Use inappropriate dose (No. of subjects)					
Test group	7.89 (3)	5.41 (2)	5.40 (2)	5.41 (2)	0 (0)
< 0.5 g	0 (0)	5.41 (2)	2.70 (1)	5.41 (2)	0 (0)
> 1.5 g	7.89 (3)	0 (0)	2.70 (1)	0 (0)	0 (0)
Control group	13.15 (5)	10.81 (4)	5.40 (2)	5.41 (2)	0 (0)
< 0.5 g	5.26 (2)	10.81 (4)	2.70 (1)	5.41 (2)	0 (0)
> 1.5 g	7.89 (3)	0 (0)	2.70 (1)	0 (0)	0 (0)