Comparative study of sensitive skin in Chinese female population

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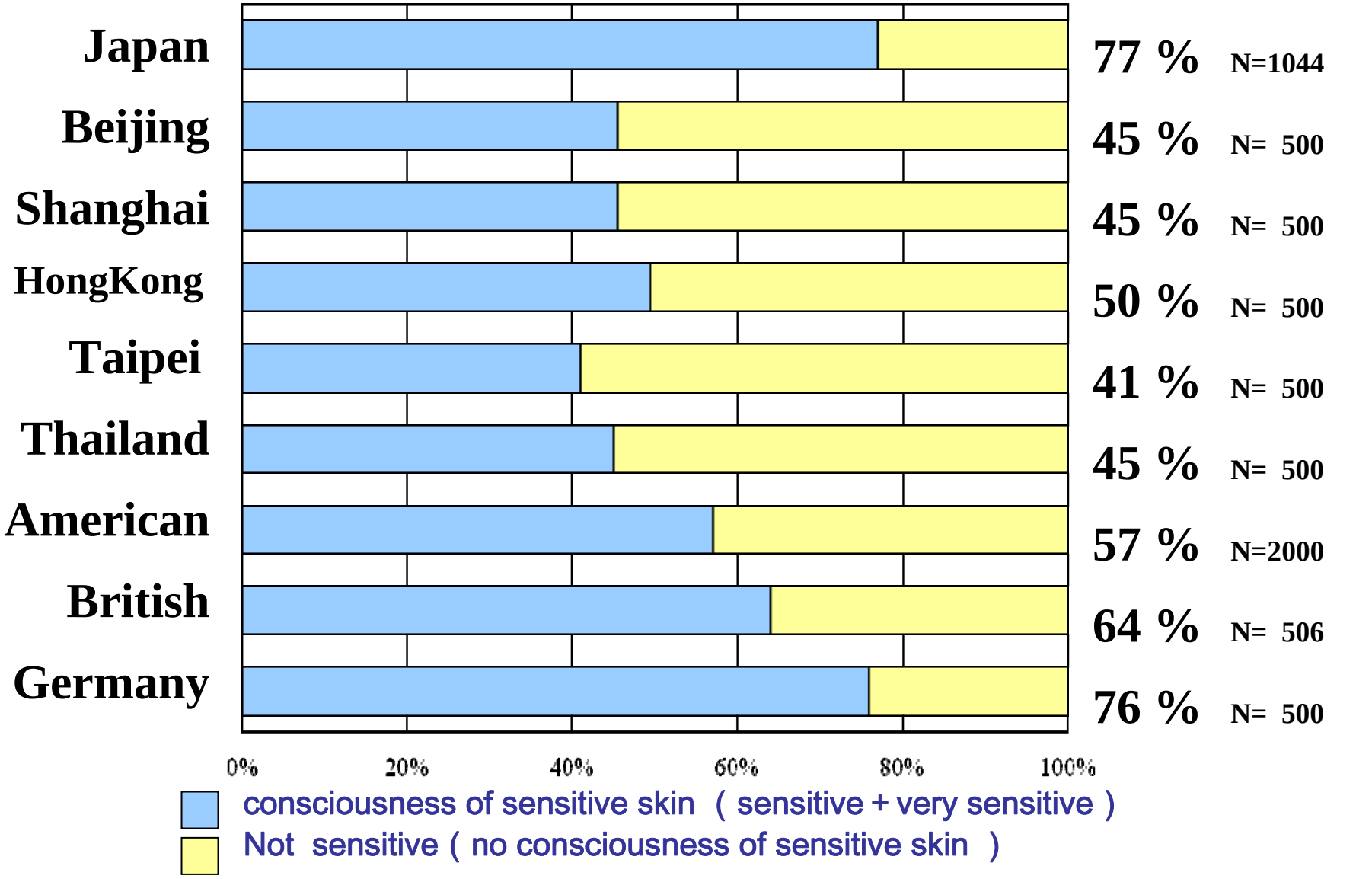
Self-consciousness of sensitive skin

Investigation in internet
Japan&asian：Sep,2007;
American&Europe: Jan,2010



Pathogenesis of Sensitive Skin (SS)

- **Skin barrier dysfunction**
- **Skin allergic condition**
- **Photosensitive reactions**
- **Neuronal irritancy**
- **Psychologic sensitivity**
- **Environmental pollutions**

Chemical probes used for evaluation of SS

- **Lactic acid**

  Frosch P, Kligman AM. Method for appraising the sting capacity of topically applied substances. J Soc Cosmetic Chem.1977;28:197-209

- **Balsam Peru**

  Bowman JP, Kligman AM,et al.The use of chemical probes to assess the facial reactivity of woman,comparing their self-perception of sensitive skin. J.Cosmet.Sci., 51,267-273

- **Chlroform/methanol**

  Bowman JP, Kligman AM,et al.The use of chemical probes to assess the facial reactivity of woman,comparing their self-perception of sensitive skin. J.Cosmet.Sci., 51,267-273

- **Sodium Lauryl Sulfate, SLS**

  Tupker RA, et al. Guidelines on sodium lauryl sulfate (SLS)exposure tests. A report from the Standardization Group of the European Society of Contact Dermatitis. Contact Dermatitis 1997: 37: 53-69.

- **Dimethyl Sulfoxide DMSO**

  Frosch P, et al. The response of human skin to dimethyl sulfoxide, British Journal of Dermatology 1980; 102: 263-274.

- **Capsaicin（TRPV1）**

  Szolcsány J. Forty years in capsaicin research for sensory pharmacology and physiology. Neuropeptides. 2004 Dec;38(6):377

- **Menthol**

  Kozyreva, et al.Agonist of TRPM8 channel, menthol, facilitates the initiation of thermoregulatory responses to external cooling. Journal of Thermal Biology 35 (2010):428

- **Ethanol and Benzolic acid**

  Farage et al. Sensory, clinical and physiological factors in sensitive skin: a review. Contact Dermatitis.2006;55:1-14

- **Phenoxyethanol**

  Effect of phenoxyethanol on inducing neuronal irritancy on skin as a marker for screening sensitive skin in asians

No consistence in methodologies

- Different signals and pathways
- Differences in recognition of sensory
- Complexity of sensitive skin
- Semi-objective methods

No gold standard for the evaluation of SS

Part I

Comparation of phenoxyethanol, lactic acid and capsaicin tests in evaluation of SS

Materials and Method

- 1.0% Phenoxyethanol/Carbapol
- 5% Lactic acid/Water
- 0.001% Capsaicin/water

Materials and Method

- 30 Chinese female subjects
- 18-50 years old
- Inclusion & Exclusion criteria
- Constant temperature and humidity
- 3 days interval

Sensory parameters

- Itching
- Burning
- Stinging

Grading standard

Score	Feeling
0	None
1	Weak
2	Moderately
3	Strong

Statistics

SPSS 11.5

-Total scores: Wilcoxon Signed Rank test

-Responsive subject numbers: Mc-Nemar test

-Mean starting time of subjects: T-test

Results

Of Itching

Table 1 Total Itching Score （N=30）

	Phenoxyethanol			Lactic acid			Capsaicin		
	2.5	5	cum	2.5	5	cum	2.5	5	cum
Test	5	4	**9**	7	5	**12**	1	1	**2**
Control	3	3	**6**	2	2	**4**	1	1	**2**
T-C	2	1	**3**	5	3	**8**	0	0	**0**

Statistics

- **Phenoxyethanol：**

  P2.5=0.157，P5=0.564，P2.5+5=0.257

- **Lactic acid：**

  P2.5=0.025，P5=0.180，P2.5+5=0.023

- **Capsaicin：**

  P2.5=1，P5=1，P2.5+5=1

Total Itching Scores

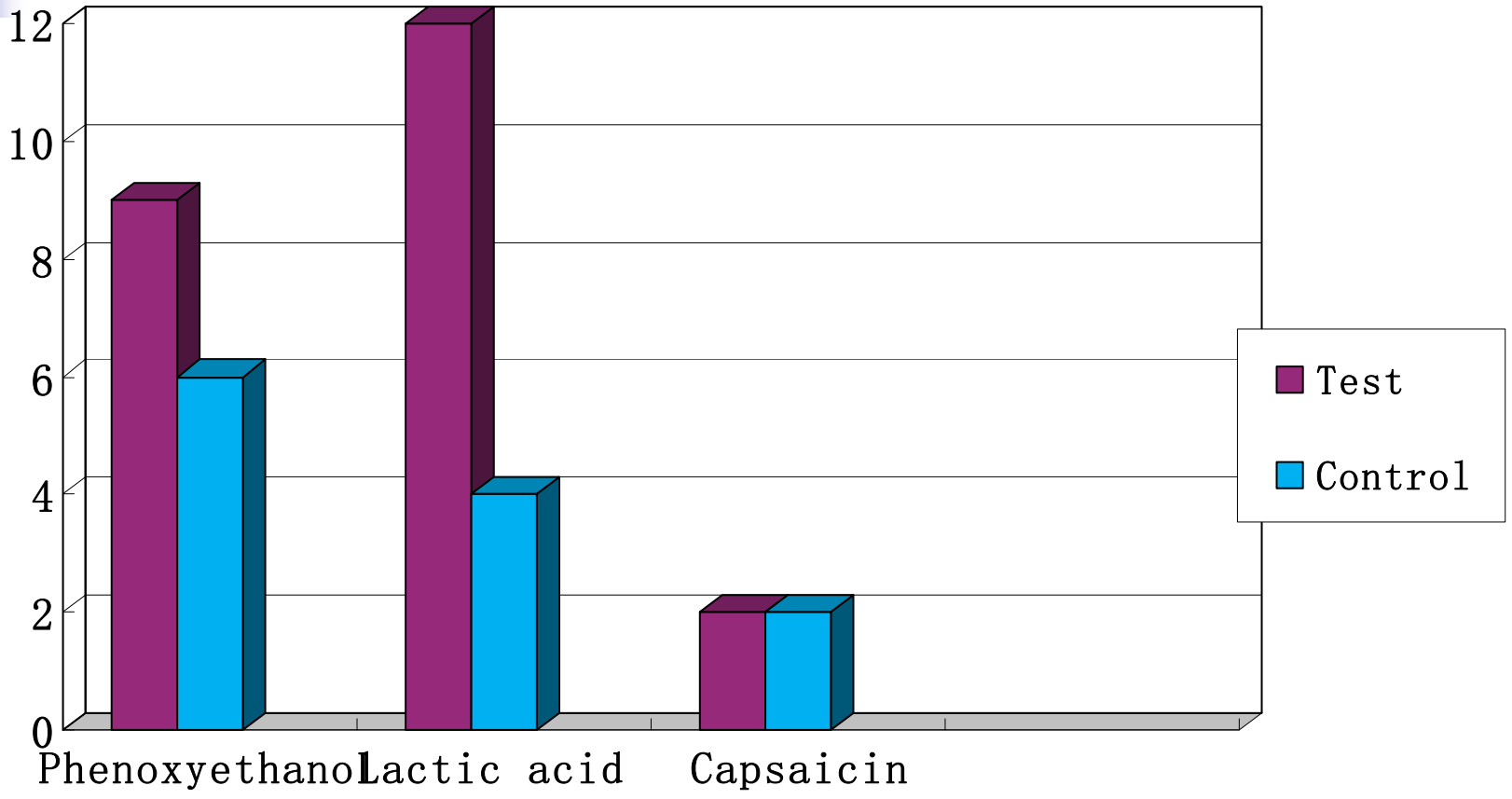


Table 2 Number of subjects feeling itching

	Phenoxyethanol	Lactic acid	Capsaicin
Test	5	9	4
Control	3	3	4

There is a significant difference in Lactic acid test (P=0.031)

Table 3 Mean starting times of subjects (s)

	Phenoxyethanol	Lactic acid	Capsaicin
Test	135	105	146

Results

Of Burning

Table 4 Total burning scores (N=30)

	Phenoxyethanol			Lactic acid			Capsaicin		
	2.5	5	**cum**	2.5	5	**cum**	2.5	5	**cum**
Test	6	7	**13**	5	4	**9**	7	5	**12**
Control	1	3	**4**	1	1	**2**	1	2	**3**
T-C	5	4	**9**	4	3	**7**	6	3	**9**

Statistics

- **Phenoxyethanol：**

  P2.5=0.025，P5=0.206，P2.5+5=0.058

- **Lactic acid：**

  P2.5=0.046，P5=0.180，P2.5+5=0.053

- **Capsaicin：**

  P2.5=0.034，P5=0.180，P2.5+5=0.083

Total Burning Scores

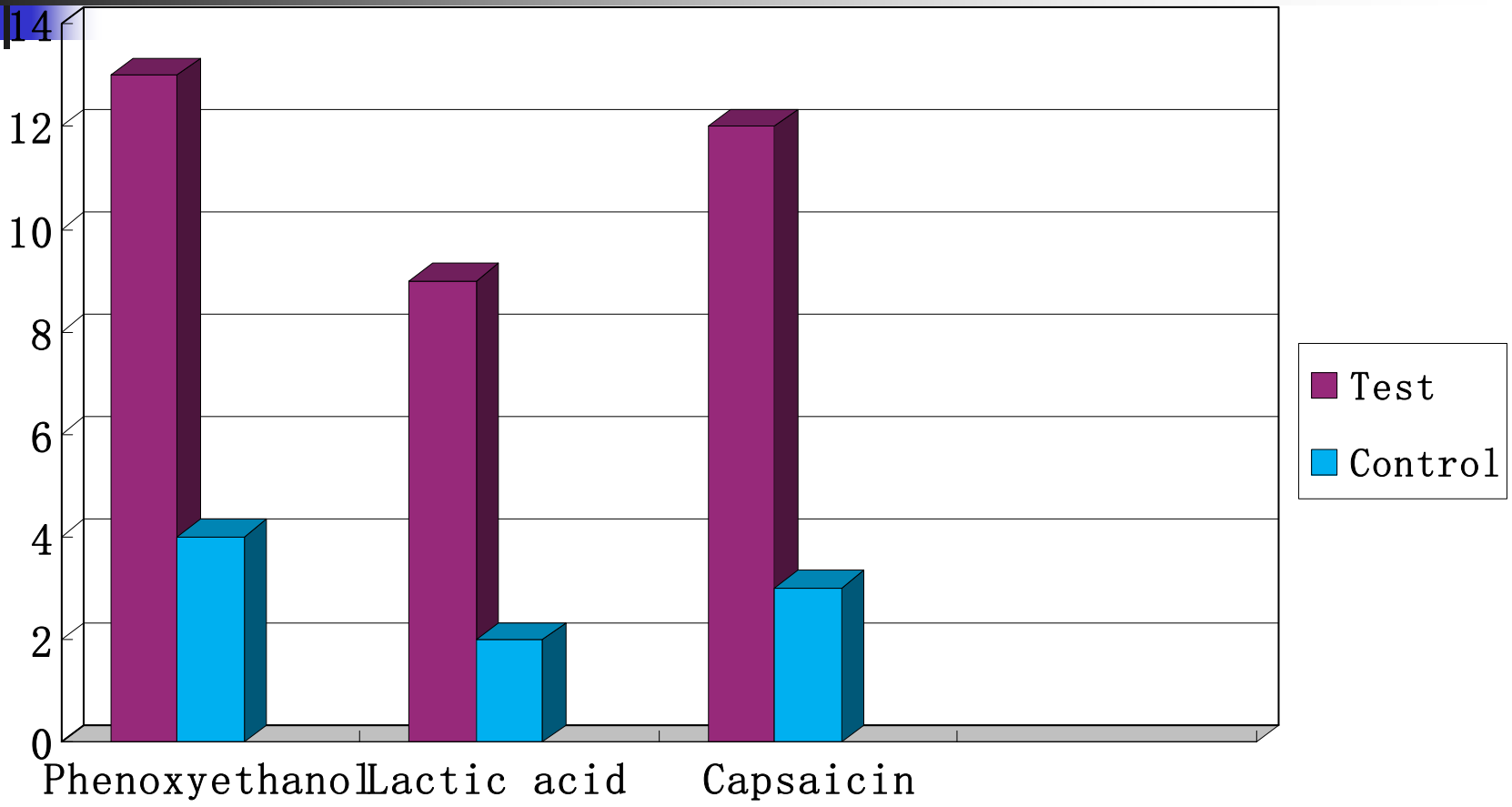


Table 5 Number of subjects feeling burning

	Phenoxyethanol	Lactic acid	Capsaicin
Test	6	8	9
Control	4	4	2

There is a significant difference in group capsaicin test(P=0.039)

Table 6 Mean starting time of subjects

	Phenoxyethanol	Lactic acid	Capsaicin
Test	101.7	102.4	101

Results

Of Stinging

Table 7 Total score of stinging (N=30)

	Phenoxyethanol			Lactic acid			Capsaicin		
	2.5	5	**cum**	2.5	5	**cum**	2.5	5	**cum**
Test	3	5	**8**	3	1	**4**	1	1	**2**
Control	1	0	**1**	0	0	**0**	2	2	**4**
T-C	2	5	**7**	3	1	**4**	-1	-1	**-2**

P=0.066

There is no significant difference between test sample to control of three groups

Total Stinging Scores

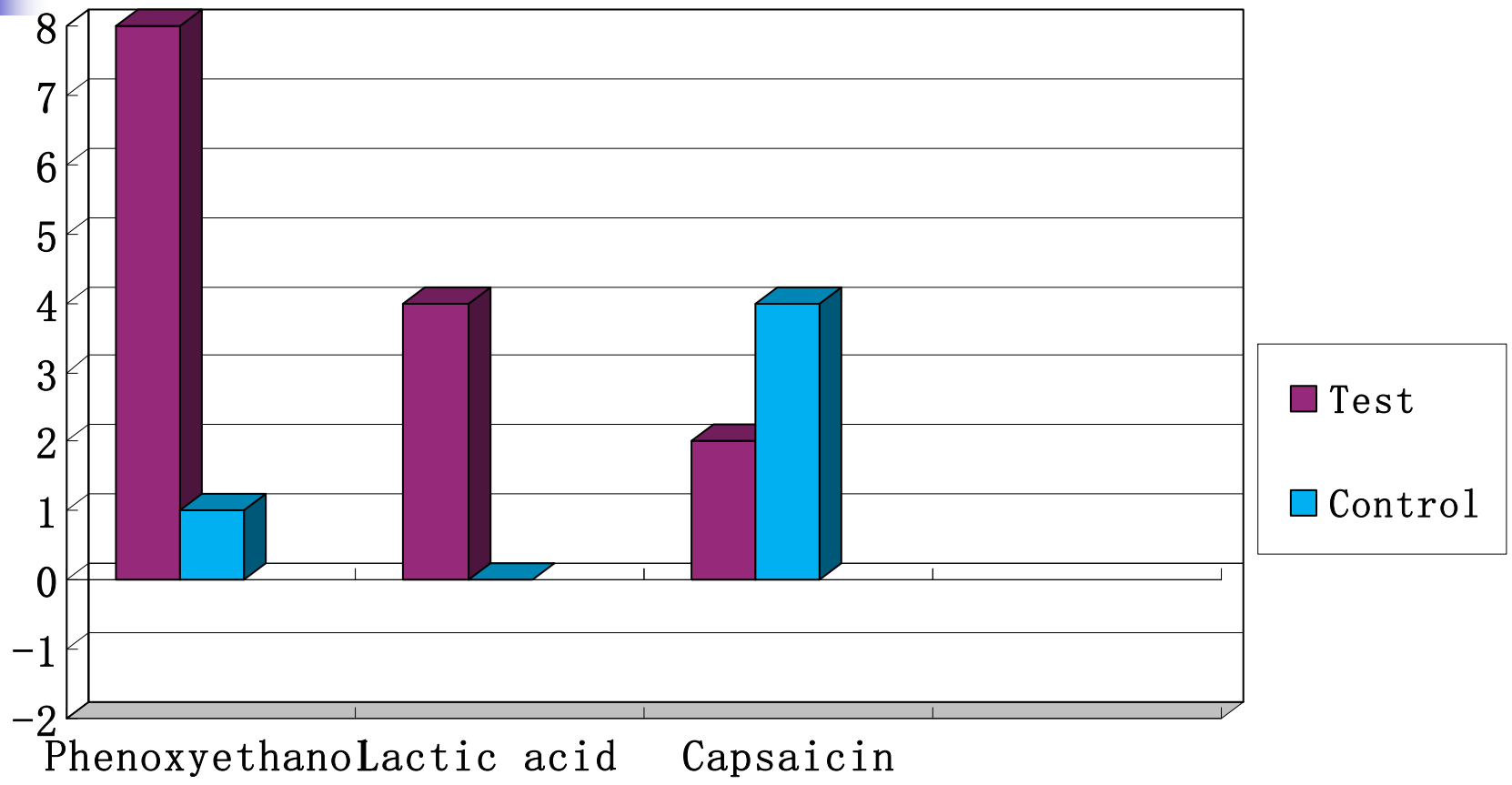


Table 8 Number of subjects feeling stinging

	Phenoxyethanol	Lactic acid	Capsaicin
Test	5	10	8
Control	2	3	3

There is no significant difference between test sample to control in three groups (Lactic acid :P=0.065 Capsaicin:P=0.227)

Table 9 Means starting time of subjects

	Phenoxyethanol	Lactic acid	Capsaicin
Test	159	71	29.3

There is significant difference between group phenoxyethanol and capsaicin(P=0.007) P&L:P=0.060, L&C:P=0.141

Mean starting time

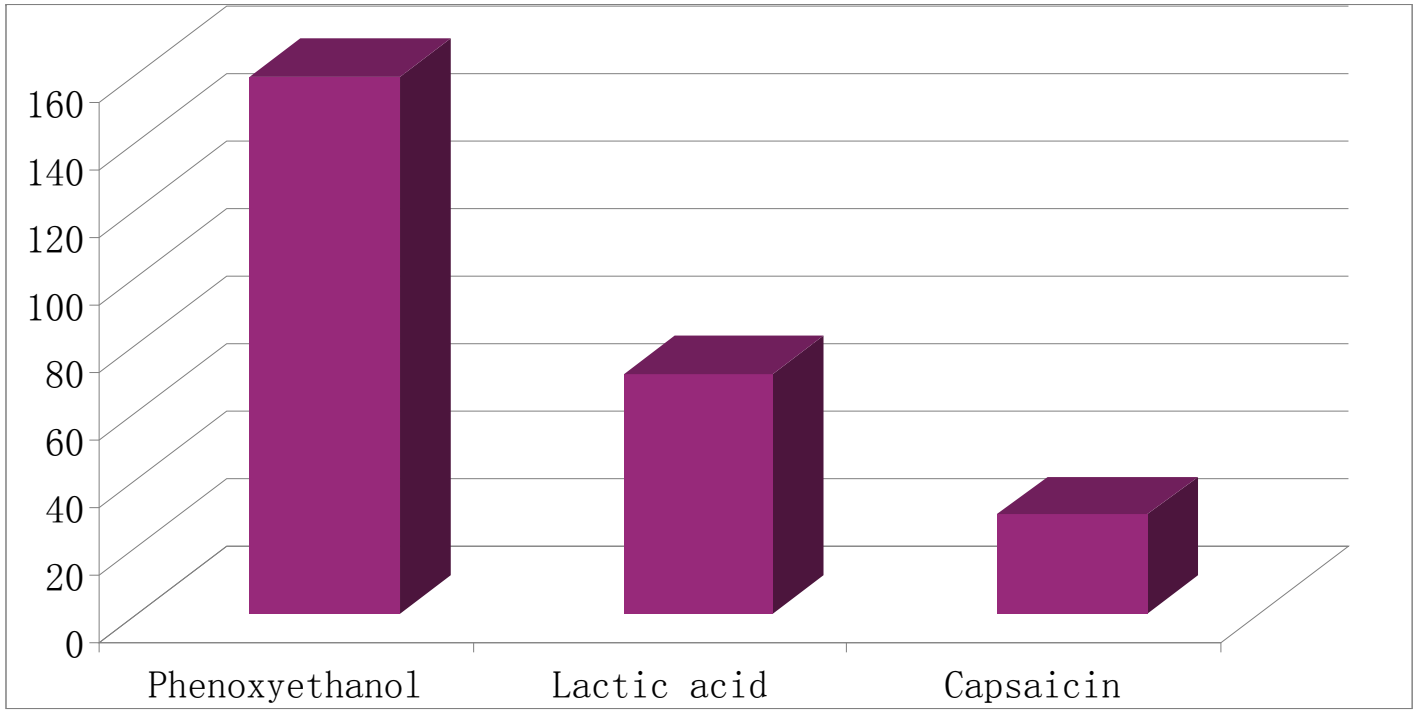


Table 10 Total Stinging scores during 0-2.5 and 2.5-5 Min.（N=30）

	Phenoxyethanol			Lactic acid			Capsaicin		
	0-2.5	5	Cum	0-2.5	5	Cum	0-2.5	5	Cum
Test	3	5	8	9	2	11	10	1	11
Control	2	0	2	1	2	3	2	2	4
T-C	1	5	6	8	0	8	8	-1	7

Lactic acid: P2.5+5=0.035, Capsaicin: P2.5=0.046

Table 7 Total score of stinging (N=30)

	Phenoxyethanol			Lactic acid			Capsaicin		
	2.5	5	**cum**	2.5	5	**cum**	2.5	5	**cum**
Test	3	5	**8**	3	1	**4**	1	1	**2**
Control	1	0	**1**	0	0	**0**	2	2	**4**
T-C	2	5	**7**	3	1	**4**	-1	-1	**-2**

P=0.066

There is no significant difference between test sample to control of three groups

Finding conceals in details

Better way to evaluate stinging sensory of SS should record the feeling from the application of samples, not at 2.5 and 5 Minutes described in traditional method.

Conclusions

- **Lactic acid test is superior than phenoxyethanol and capsaicin when evaluating itching by traditional method with 2.5 and 5 minutes' scores,**
- **Phenoxyethanol, Lactic acid and capsaicin tests are all sensitively to evaluate burning sensory of SS.**

- **Lactic acid and capsaicin tests are more sensitive to evaluate stinging with the method of recording 0-2.5 and 2.5-5 minutes' highest scores.**
- **Sensitive skin has a late response to Phenoxyethanol at around 2.5 minute, Therefore, phenoxyethanol test should be conducted in traditional way of evaluating SS.**

Part II

The screening test of sensitive skin with phenoxyethanol

Materials and Method

- 1%phenoxyethanol – glycol
  (GS12AK010-F)
- Control: glycol
  (GS12AK010-E)

Materials and Method

- 239 Chinese female subjects
- 18-50 years old
- Inclusion & Exclusion criteria
- Constant temperature and humidity

Sensory parameters

- Itching
- Tingling
- Burning
- Stinging

Grading standard

Score	Feeling
0	None
1	Very Weak
2	Weak
3	Moderate
4	Strong
5	Very Strong

Statistics

SPSS 11.5

-Total scores: Wilcoxon Signed Rank test

-Responsive subject numbers: Mc-Nemar test

-Mean starting time of subjects: T-test

Results

Table 11：Total Sensory Scores (N=239)

	Itching			Tingling			Burning			Stinging		
	2.5	5	2.5 +5	2.5	5	2.5+ 5	2.5	5	2.5+ 5	2.5	5	2.5 +5
Test	31	57	88	100	96	196	59	60	119	22	32	54
Control	33	57	90	69	80	149	23	31	54	22	28	50

Statistics

Itching: $P_{2.5}=0.792$, $P_5=0.891$, $P_{2.5+5}=0.770$

Tingling: $P_{2.5}=0.022$, $P_5=0.144$, $P_{2.5+5}=0.030$

Burning: $P_{2.5}=0.001$, $P_5=0.010$, $P_{2.5+5}=0.001$

Stinging: $P_{2.5}=0.911$, $P_5=0.710$, $P_{2.5+5}=0.884$

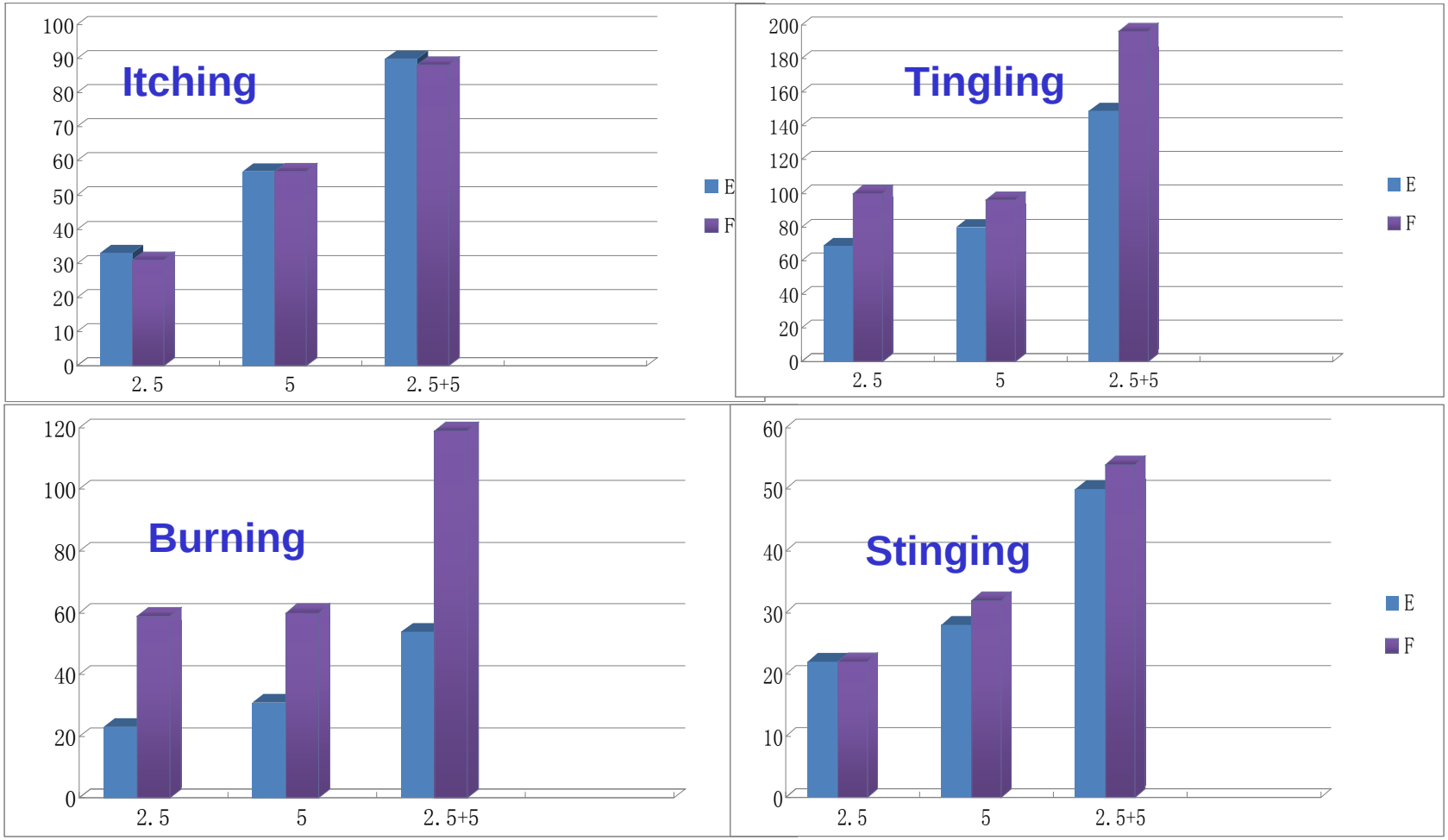

Itching
100
90
80
70
60
50
40
30
20
10
0
2. 5
5
2. 5+5
E
F
Tingling
200
180
160
140
120
100
80
60
40
20
0
2. 5
5
2. 5+5
E
F
Burning
120
100
80
60
40
20
0
2. 5
5
2. 5+5
Stinging
60
50
40
30
20
10
0
2. 5
5
2. 5+5
E
F

Table 12 Numbers of Responding Subjects

	Itching	Tingling	Burning	Stinging
Test	46	98	57	28
Control	48	76	26	26

Tingling: P=0.004
Burning: P=0.000

Table 13： Mean Starting times of Subjects (S)

	Itching	Tingling	Burning	Stinging
Test	165.3	114.7	138.9	145.4
Control	171.2	124.5	186.4	162.0

Burning： P=0.044

Summary

- **Burning and Tingling: Both the total scores and the responding subject numbers in Phenoxyethanol group are significantly higher than Glycol control.**
- **Itching : Both Phenoxyethanol and Glycol groups give similar results in inducing itching.**

Part III

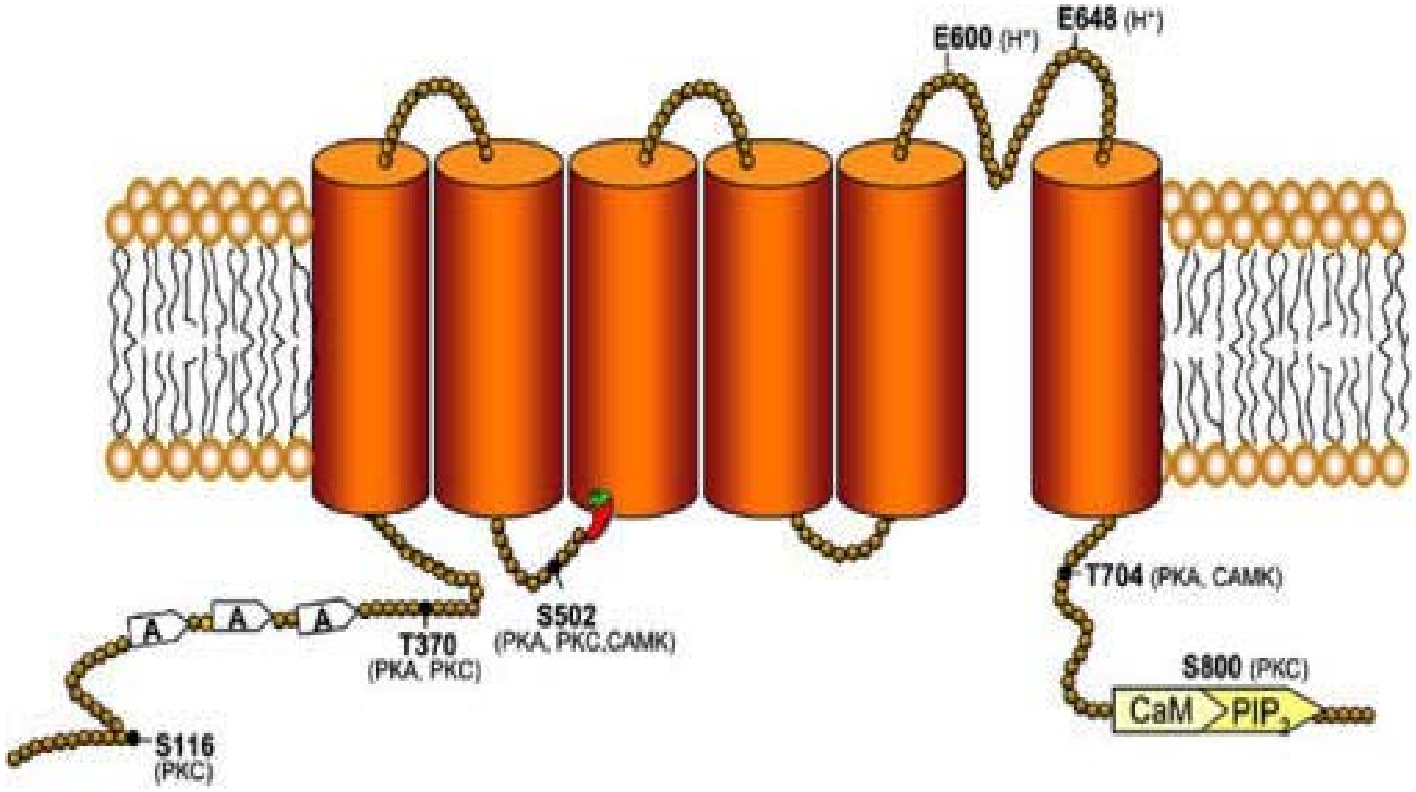
The inhibiting effect of TRPV-1 antagonist on Phenoxyethanol in inducing skin irritancy

TRPV1

Transient receptor potential channel, vanilloid subfamily member 1

瞬时受体电位香草素亚型 I

TRPV1


E600 (H+)
E648 (H+)
A
A
A
T370
(PKA, PKC)
S502
(PKA, PKC,CAMK)
S116
(PKC)
T704 (PKA, CAMK)
S800 (PKC)
CaM
PIP2

Materials and Method

- 1% Phenoxyethanol +TRPV1 antagonist (trans-tert-Butylcyclohexanol) in Glycol

  (GS12AK010-H)

- 1% Phenoxyethanol in Glycol

  (GS12AK010-G) (control)

Materials and Method

- 60 Chinese female subjects
- All responsive to Phenoxyethanol in Part II
- 18-50 years old
- Inclusion & Exclusion criteria
- Constant temperature and humidity

- **Sensory parameters**
- **Grading standard**
- **Statistics**

Results

Table 14 Total scores of two groups (N=60)

	Itching			Tingling			Burning			Stinging		
	2.5	5	2.5 +5	2.5	5	2.5+ 5	2.5	5	2.5 +5	2.5	5	2.5 +5
Test	1	16	17	16	12	28	11	5	16	8	2	10
Control	20	20	40	25	22	47	18	15	33	9	4	13

Statistics

Itching: $P_{2.5}=0.004$, $P_5=0.386$, $P_{2.5+5}=0.040$

Tingling: $P_{2.5}=0.098$, $P_5=0.054$, $P_{2.5+5}=0.041$

Burning: $P_{2.5}=0.107$, $P_5=0.034$, $P_{2.5+5}=0.023$

Stinging: $P_{2.5}=0.887$, $P_5=0.480$, $P_{2.5+5}=0.876$

Comparation of different sensory scores in Two groups

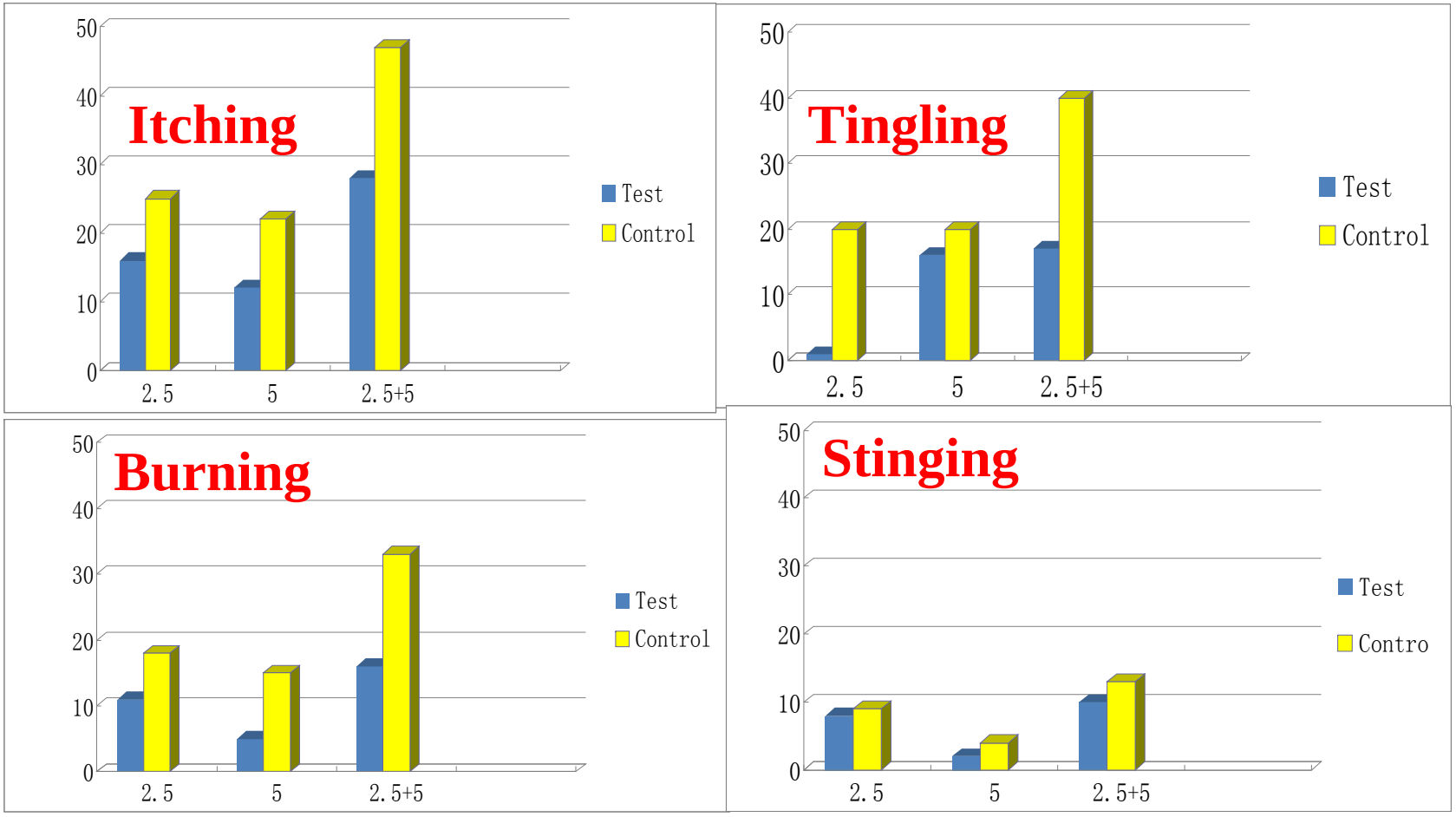


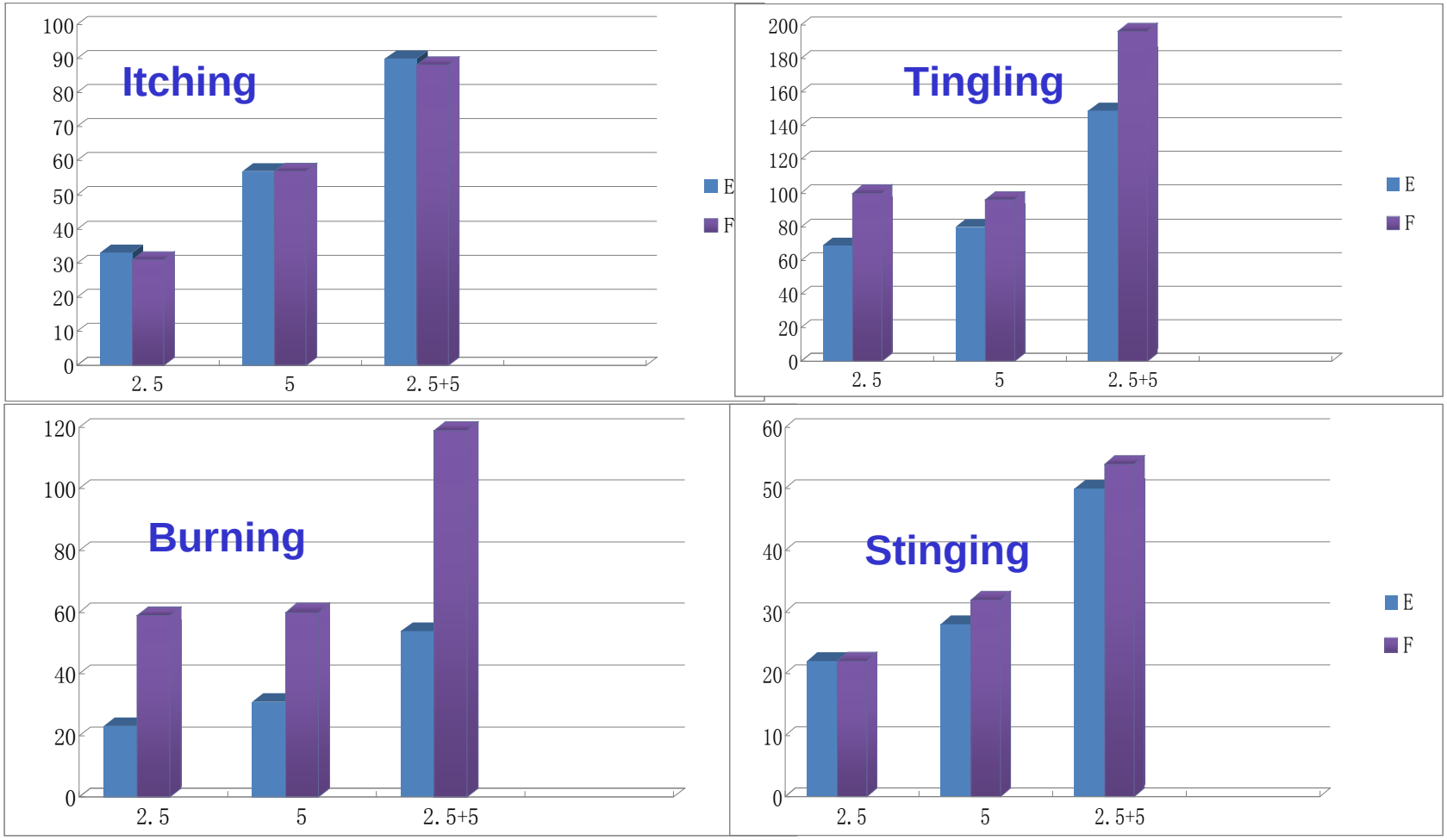
Table 15 Numbers of responding subjects

	Itching	Tingling	Burning	Stinging
Test	13	23	10	6
Control	13	20	13	7

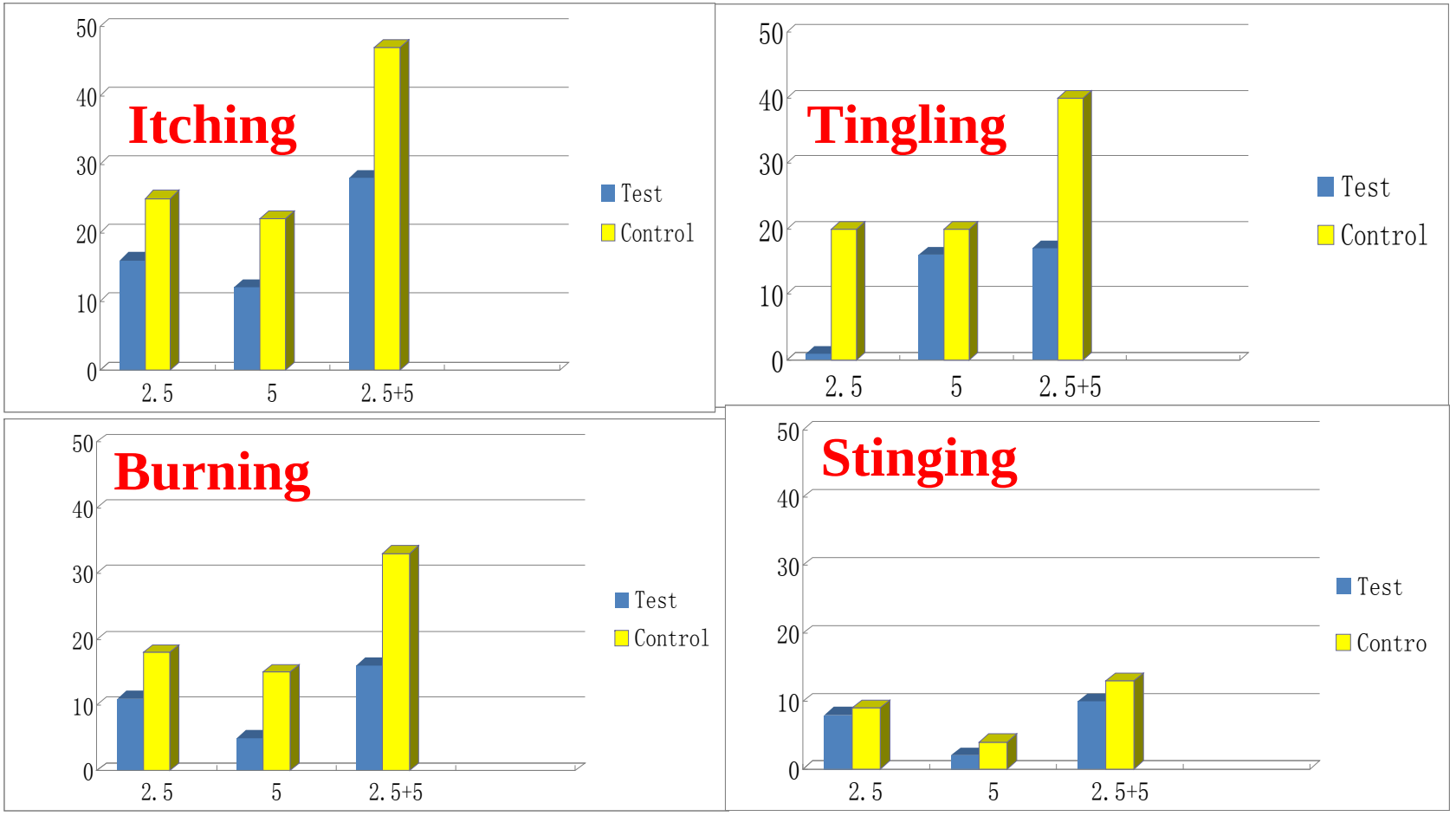
Table 16 Mean starting times of subjects (S)

	Itching	Tingling	Burning	Stinging
Test	214.5	117.1	67.9	127.7
Control	136.4	113.5	98.3	131.0

PART II：Phenoxyethanol and Itching sensory



PART III: Phenoxyethanol inducing Itching



Phenoxyethanol in inducing itching

PART Ⅱ: Glycol

PART Ⅲ: Trans-tert-utylcyclohexanol

Glycol as a Matrix in Part II may induce itching as much as phenoxyethanol, while trans-tert-utylcyclohexanol may be better in study of phenoxyethanol.

Conclusions

TRPV1 antagonist can inhibit the sensory stimulation induced by phenoxyethanol in sensitive skin

THANKS