

7. A CLINICAL INVESTIGATION OF PERILLA EXTRACT CREAM FOR ATOPIC DERMATITIS

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INTRODUCTION

Atopic Dermatitis

Atopic dermatitis is one kind of allergic disease. Allergies are very closely associated with an immune response. When the human body is invaded by a foreign substance (antigen), antibodies or sensitised lymphocytes will be produced as a result of the response of the immune system. Later when the same antigen invades the body again, it will soon be eliminated or become harmless to the body. This is an immune response which is an indispensable function to prevent infection and tumours. However, sometimes the immune reaction between antigen and antibodies or sensitised lymphocytes can cause harm to the body itself. This kind of immune reaction in which antigen comes from outside the body causes allergic disease, whereas antigen which comes from the body itself causes auto-immune disease.

According to the statistical investigation in 1992 by the Ministry of Welfare of Japan, 34% of the Japanese population suffer from some kind of allergy, and most of them are children between the age of 0 to 4. There is the tendency for allergic symptoms to appear as atopic dermatitis in childhood and to become asthma or rhinitis as they mature.

The word atopy is derived from Greek (Okabe, 1990) and means odd and thus atopic dermatitis is a disease unknown in its mechanism and its predisposition. It involves both the over-production of IgE antibody in reaction to environmental antigen as well as hereditary factors.

There are various criteria in the diagnosis of atopic dermatitis. In general, skin diseases with inveterate, chronic, and recurrent symptoms such as itchy, dry are diagnosed as atopic dermatitis or eczema. Atopic dermatitis was thought to be chronic eczema mainly occurring in infants or children. However, recently there has been a remarkable increase in the number of patients of all ages and the body takes a long time to recover. It is unknown why this is so, but it can be thought to be related to the living conditions, change in diet, air pollution, and contamination of water and food by chemical substances.

In Japan atopic dermatitis is becoming a serious problem; adult patients have increased in numbers and the disease has caused social problems such as discrimination at work and unsympathetic treatment by the family. Many methods are used to treat allergies: elimination of allergen, application of steroids and antihistamine, traditional Chinese medicine, folk remedies (mugwort, peach leaves, houttuynia), ultraviolet treatment as well as psychotherapy (Okabe, 1990). However, some cases of dystrophia are caused by

the elimination of allergen from the diet and adverse reactions often occur because of such medicine.

Background to How Perilla Extract came to be used for Atopic Dermatitis

Many cases of atopic dermatitis require considerable time and effort. The cause of the disease is complex, and the range of the patients' age bracket is widening, therefore, there are various remedies being used. For curative medicine, antihistamines and steroids are often used and have been shown to be effective in many cases. On the other hand, side effects caused by percutaneous absorption may decrease the effectivity of the medicine because of the repetitive use (Okuhira, 1993). More and more people have begun to worry and now refuse to use steroids since there has been so much exaggerated information given by the media. Psychological aspects, such as stress, are one of the primary causes of atopic dermatitis. Therefore, the patients' anxieties regarding the use of antihistamines and steroids cannot be ignored. This is why various treatments using naturally occurring substances have been examined.

Perilla extract cream was chosen for atopic dermatitis because of the reports from Dr. Yamazaki, at Teikyo University, that Perilla extract had an anti-inflammatory value inhibiting the production of Tumour Necrosis Factor (TNF). Perilla is eaten as a vegetable and in spices in Japan, and the patients can take it without any subsequent problem.

Perilla leaves contain perillaldehyde, an irritating substance, which was removed from the Perilla extract in the following clinical test.

CLINICAL TEST USING PERILLA EXTRACT CREAM

In investigations involving the usefulness of Perilla extract cream for the skin, it was shown to keep skin moist and to prevent dryness. Perilla extract is a natural substance and Perilla extract cream is not an ointment which is regarded as "medicine". Active surface agents were used as little as possible and any ingredient or compound considered to be an irritant was removed or omitted.

Test Method

The patients

The patients with atopic dermatitis who had agreed to this clinical test were examined. Those with an advanced disease were judged to be inappropriate for this study. Over 90 patients participated. Most of them were children under five years old. The sex, age and background of the patients are given in [Table 1](#).

The tests were performed using Perilla extract cream which contained 1% Perilla extract (Group A) or 5% extract (Group B) and later 3% extract (Group C) was used (Table 1).

Among the patients, about 26% of them also suffered from other complications such as allergic rhinitis, bronchial asthma, wheeze, hypophyseal dwarfism, and histidinemia.

Table 1 Background to patient symptoms (95 Cases)

<i>Observation Items</i>		<i>No of Cases (%)</i>		
		<i>Group A</i>	<i>Group B</i>	<i>Group C</i>
sex	male	14 (41.2%)	15 (50.0%)	19 (61.3%)
	female	20 (58.8%)	15 (50.0%)	12 (38.7%)
age group (years old)	0	0 (0.0%)	4 (13.3%)	0 (0.0%)
	1-2	15 (44.1%)	9 (30.0%)	10 (32.3%)
	3-5	12 (35.3%)	6 (20.0%)	15 (48.4%)
	>6	6 (17.7%)	11 (36.7%)	6 (19.3%)
	unknown	1 (2.9%)	0 (0.0%)	0 (0.0%)
diagnosis	atopic dermatitis	29 (85.3%)	30 (100.0%)	30 (96.8%)
	eczema	5 (14.7%)	0 (0.0%)	1 (3.2%)
severity				
eruption	very severe	4 (11.8%)	3 (10.0%)	5 (16.1%)
	severe	18 (52.9%)	20 (66.7%)	23 (74.2%)
	mild	4 (11.8%)	7 (23.3%)	1 (3.2%)
	slight or nil	0 (0.0%)	0 (0.0%)	0 (0.0%)
	unknown	8 (23.5%)	0 (0.0%)	2 (6.5%)
age symptoms started	0	21 (61.8%)	15 (50.0%)	19 (61.3%)
	1	7 (20.6%)	5 (16.7%)	4 (12.9%)
	2-6	4 (11.7%)	9 (30.0%)	5 (16.1%)
	unknown	2 (5.9%)	1 (3.3%)	3 (9.7%)

Investigation showed that in about 30% of the patients one or more of their family suffered from atopic dermatitis. More than 20% of all the patients complained that the occurrence of the allergy was associated with a change in the weather. More than 24% of the patients reported their allergy was diet related.

Most of the patients used such medicines as steroids, antiallergic agents and antihistamines before coming into this trial.

Those patients in Group B (receiving 5% extract cream) contained a higher percentage of patients with advanced disease than those in Group A (receiving 1% cream).

Side effects were recorded by the degree, symptoms, the relation of cause and effect, and the date of occurrence.

Application Method and Period

Perilla extract was applied two to three times daily onto skin at the affected part and judged every 2 weeks and 5 times in 8 weeks. Data was recorded on the designated cards. The average period of observation was 51.5 days in Group A, 35.1 days in Group B, and 61.4 days in Group C.

Table 2 Improvement of Symptoms

Group A (1% Cream, 32 cases)

<i>Observation Item</i>	<i>Non observed (case)</i>	<i>Observed (case)</i>	<i>Symptoms</i>				<i>Improvement aggravated%</i>
			<i>totally improved</i>	<i>improved</i>	<i>unchanged</i>	<i>aggravated%</i>	
itching eruption	0	32	3 9.4%	21 65.6%	8 25.0%	0 0.0%	75.0%
erythematous eruption	11	21	6 28.6%	8 38.1%	7 33.3%	0 0.0%	66.7%
papular eruption	19	13	4 30.8%	2 15.4%	7 53.8%	0 0.0%	46.2%
desquamative eruption	6	26	8 30.8%	10 38.4%	8 30.8%	0 0.0%	69.2%
infiltrating eruption	17	15	8 53.3%	1 6.7%	6 40.0%	0 0.0%	60.0%

Group B (5% Cream, 31 cases)

<i>Observation Item</i>	<i>Non observed (case)</i>	<i>Observed (case)</i>	<i>Symptoms</i>				<i>Improvement %</i>
			<i>totally improved</i>	<i>improved</i>	<i>unchanged</i>	<i>aggravated</i>	
itching eruption	0	31	3 9.7%	21 67.8%	6 19.3%	1 3.2%	77.5%
erythematous eruption	0	25	2 8%	10 40.0%	12 48.0%	1 4%	48.0%
papular eruption	10	21	4 19.0%	3 14.3%	13 61.9%	1 4.8%	33.3%
desquamative eruption	0	31	6 19.4%	12 38.7%	11 35.5%	2 6.4%	58.1%
infiltrating eruption	20	11	3 27.3%	2 18.2%	6 54.5%	0 0.0%	45.5%

Group C (3% Cream, 30 cases)

<i>Observation Item</i>	<i>Non observed (case)</i>	<i>Observed (case)</i>	<i>Symptoms</i>				<i>Improvement %</i>
			<i>totally improved</i>	<i>improved</i>	<i>unchanged</i>	<i>aggravated</i>	
itching eruption	0	30	7 23.3%	19 63.3%	3 10.0%	1 3.3%	86.7%
erythematous eruption	0	30	8 26.7%	15 50.0%	6 20.0%	1 3.3%	76.7%
papular eruption	21	9	4 44.4%	2 22.2%	3 33.3%	0 0.0%	66.7%
desquamative eruption	7	23	6 26.1%	11 47.8%	6 26.1%	0 0.0%	73.9%
infiltrating eruption	5	25	8 32.0%	11 44.0%	6 24.0%	0 0.0%	76.0%

Evaluation and Improvement of Symptoms (Table 2)

Symptoms were divided into 5 types: itching eruption, erythematous eruption, papular eruption, desquamative eruption, and infiltrating eruption. They were evaluated at five levels: high degree, middle degree, low degree, slight degree, and none. Two weeks after the treatment with Perilla cream, the above symptoms and also redness were evaluated. The improvement of individual symptom was evaluated at four levels (totally improved, improved, unchanged and aggravated). The general improvement was evaluated at five levels (highly improved, improved, slightly improved, unchanged, and aggravated).

As a whole, effectiveness of Perilla cream was evaluated collectively from the skin symptom, the general improvement, and its side effects after treatment by following four levels: highly effective, effective, slightly effective, and ineffective.

Results of the Treatment*Symptoms improvement*

Table 2 shows the improvement in the symptoms in all the three groups. In each group symptom itching eruption was improved very well. In Group A and B symptom papular eruption was less improved and Group C showed the most satisfying improvement for all the symptoms.

General improvement

General improvement using 1% (Group A), 5% (Group B), and 3% (Group C) Perilla cream are shown in [Figure 1](#). The improvement was recognised in each group: 73.5% in Group A, 80.6% in Group B, and 83.4% in Group C.

Effectiveness

In every case, no side effect was found. The effectiveness percentages of Perilla cream for the treatment of atopic dermatitis is shown in [Figure 2](#). The effectiveness were 70.6%, 80.6%, and 80.0% in the three groups after using 1%, 5%, 3% Perilla cream respectively.

Furthermore effectiveness was evaluated according to the patients conditions such as effectiveness whilst using other medicines ([Figure 3](#)), effectiveness on pruritus ([Figure 4](#)), effectiveness on different types of eruption ([Figure 5](#)), and effectiveness after the use of steroids had been discontinued ([Figure 6](#)).

For the effectiveness of Perilla cream in the absence of other medicine ([Figure 3](#)) there was not much difference between Group A and Group B, 60% and 68% effectiveness, respectively.

When comparing the effectiveness of 1%, 5% and 3% creams, for pruritus ([Figure 4](#)) 5% cream had a higher effectiveness than 1% cream but in mild cases 3% cream appeared even better. Concerning the dry type of infantile eczema ([Figure 5](#)) both 5% and 3% creams had a high effectiveness but there was insufficient data to say which strength cream was to be preferred and likewise for other types of eruptions.

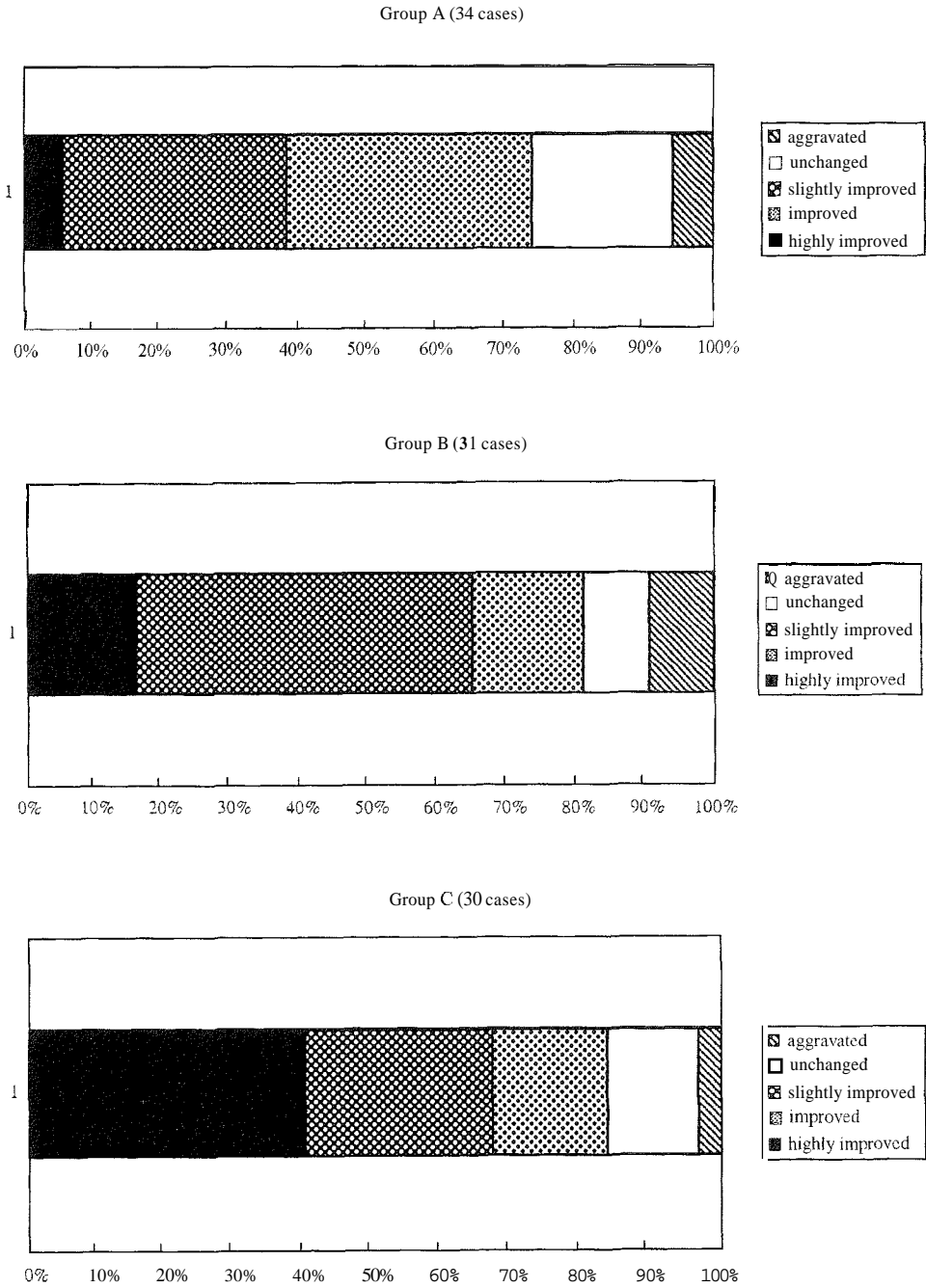


Figure 1 General improvement

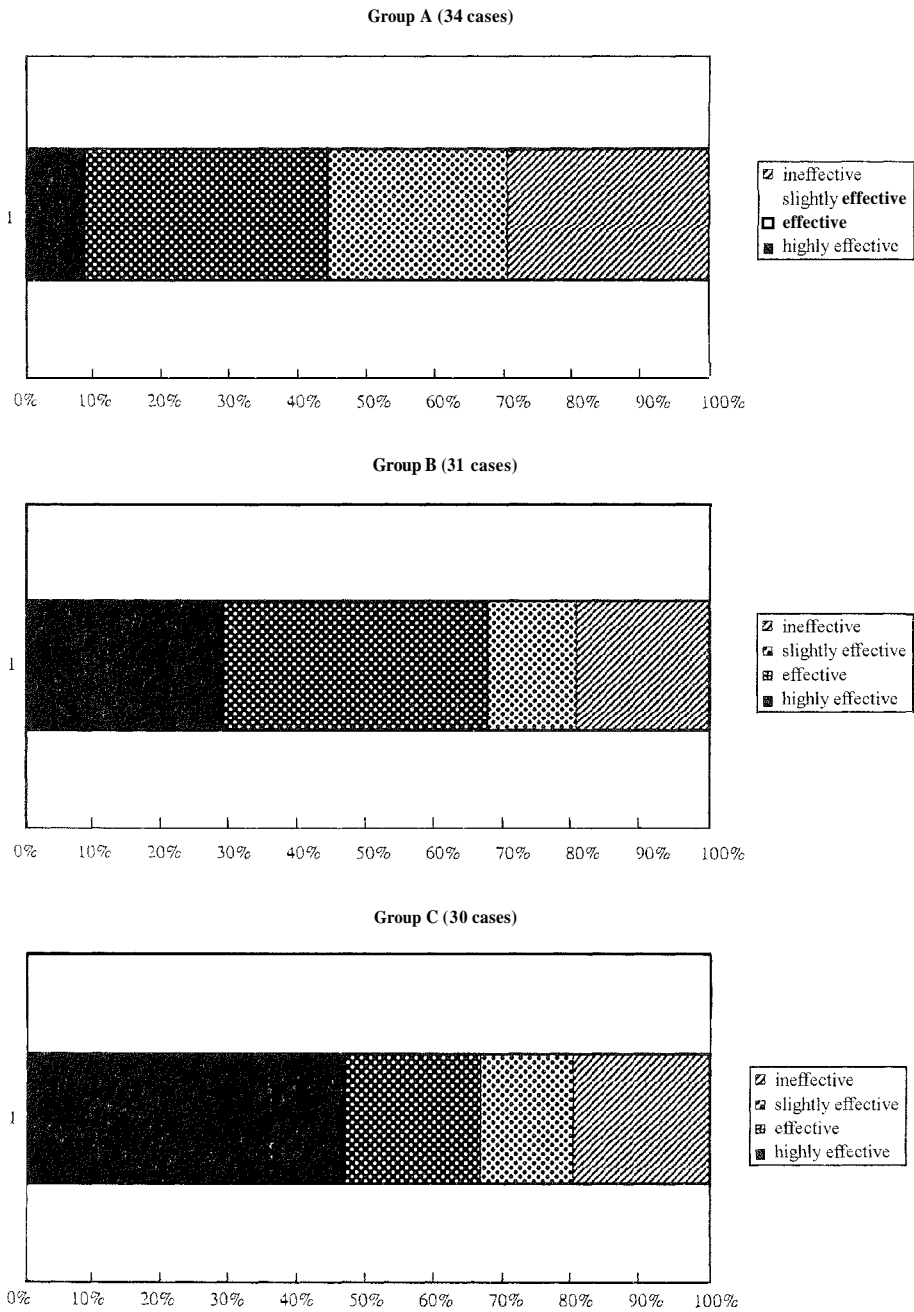


Figure 2 Effectiveness

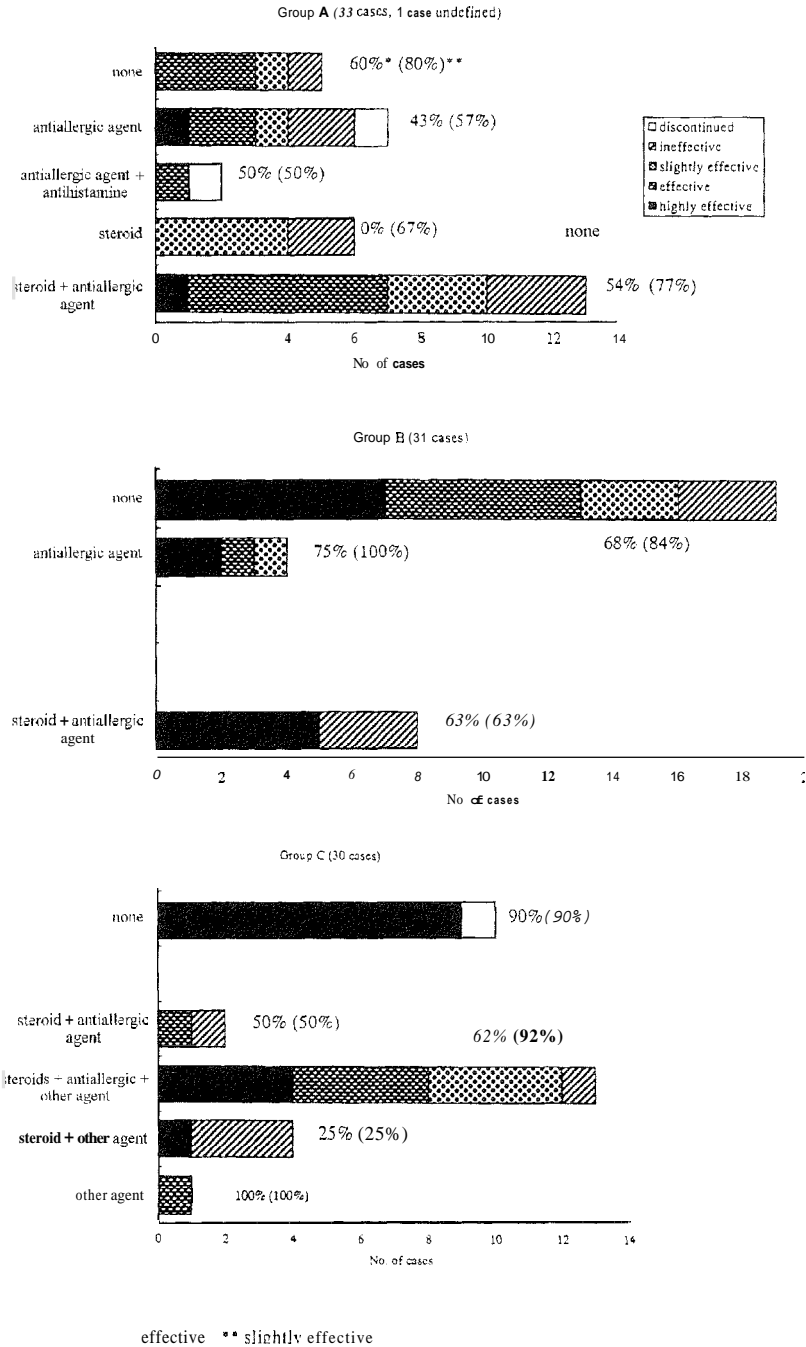


Figure 3 Effectiveness of Perilla cream when used with and without other medicines

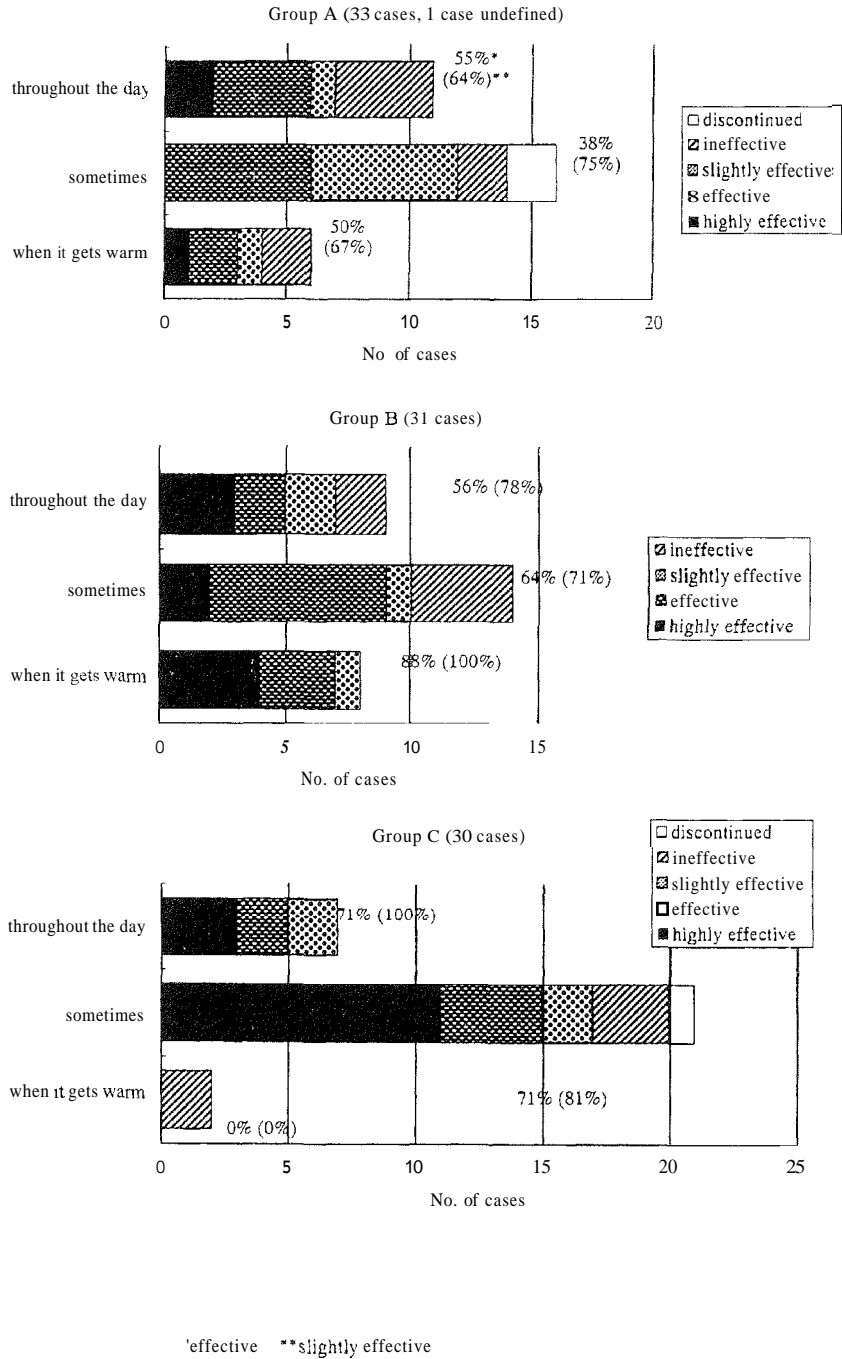
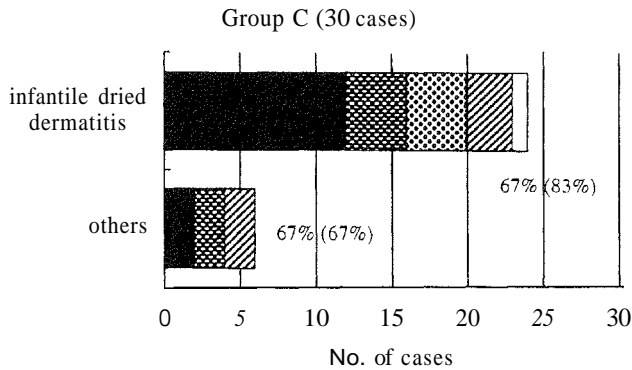
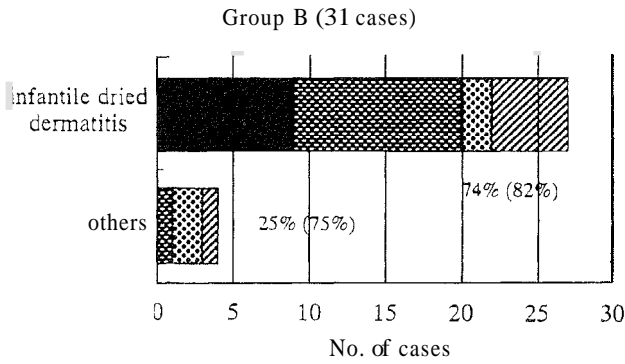
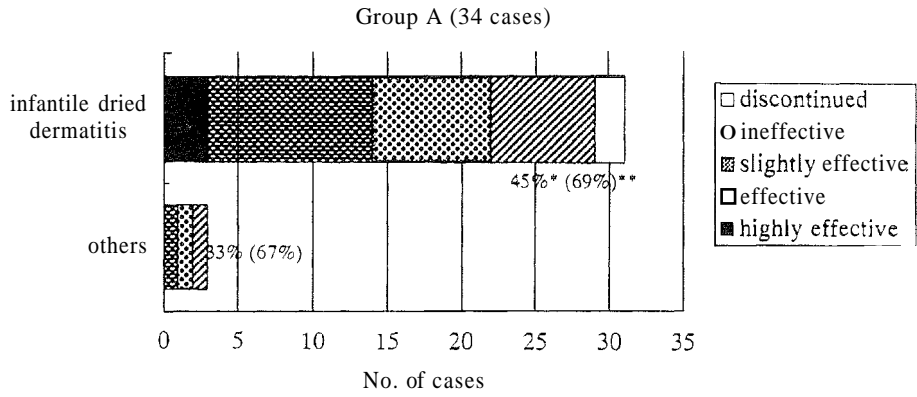


Figure 4 Effectiveness of Perilla cream on pruritus



*effective **slightly effective

Figure 5 Effectiveness of Perilla cream on different types of eruption

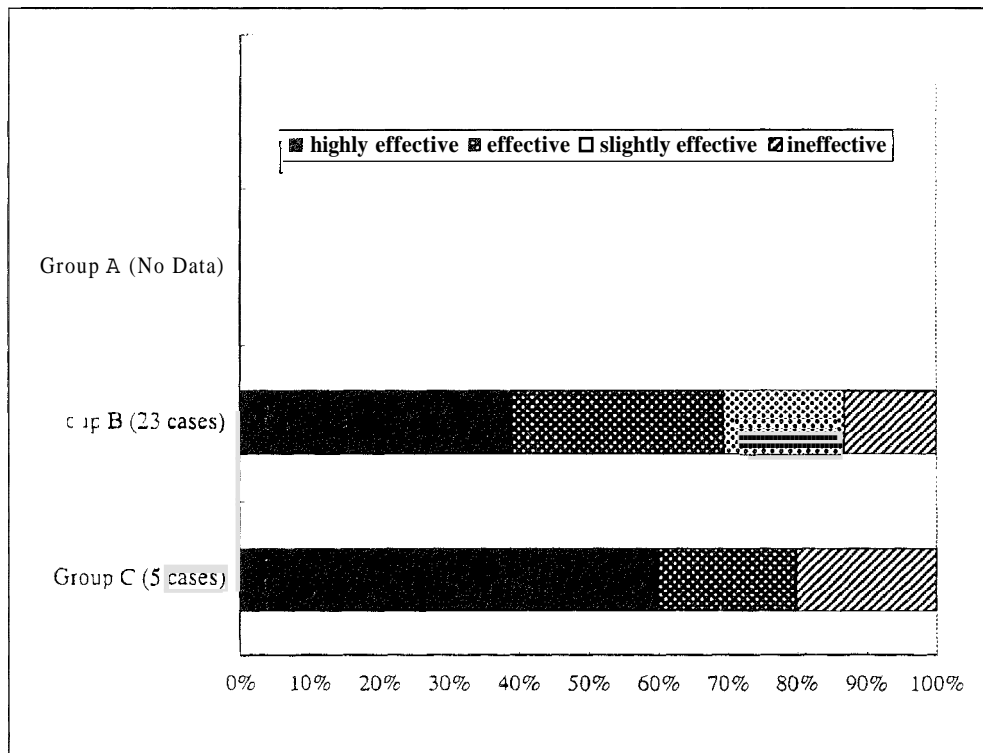


Figure 6 Effectiveness of Perilla cream (after steroid had been discontinued)

Steroid is most effective as an ointment for application, however, it has side effects. A separate preliminary study was conducted with 5% and 3% Perilla extract cream in the absence of steroids (Figure 6). In a comparison of the patients who stopped using steroids, the patients using anti-allergic medicine for external and also internal use were included in this examination. Because of the difference in the number of cases, it is difficult to compare the two groups. However, Group B has a very high effectiveness and a decrease in the amount of steroids used is to be expected based on the results of this preliminary study.

OBSERVATION SUMMARY

The percentage of the improvement in patients in Group A was 73.5% and in Group B, 80.6%. Group C showed improvement equivalent to that of Group B with the test which was given later under the same conditions. From these results, even a small amount of Perilla extract helps to improve patients with atopic dermatitis.

In the case of unchanged and aggravated results, the reason was not specified as there was no common case. In most improved cases, symptoms became aggravated after 4 to 5 days, whereafter continued application improved them within two weeks. It is presumed to be a kind of rebound phenomenon. More than 70% of the patients requested to continue the application even after the study ended and their comments on using the cream were quite favourable.

Concerning the efficacy of Perilla cream, of the 90 patients, 70–80% experienced some kind of improvement. On the whole, among the extracted natural substances, Perilla extract was recognised to be highly beneficial for atopic dermatitis. Considering there was no side effect in any of the cases, perillaldehyde free Perilla extract is expected to be used as anti-allergy medicine for a therapy in the future, and more extended trials are justified.

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