Comparative Study of the Efficacy of Topical Corticosteroid : Five Locally Made and One Brand Name Creams†

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Abstract

The aim of this study was to evaluate the efficacy of 5 locally made clobetasol propionate creams compared with a brand name product.

The study was divided into 3 parts 1) pharmacological study, 2) vasoconstriction test, and 3) double blind clinical trial.

The results showed that the pharmacological properties of the locally made products were not different from the brand name product. Product C and D could diffuse through cellulose acetate membrane 3 fold more than the brand name product. Product D and E caused less vasoconstriction than the brand name product. This double blind study showed that all locally made products could improve psoriasis to the same extent as the brand name product, but there was more recurrence of psoriasis while using all the locally made products.

It was concluded that locally made products were as effective as the brand name product in the treatment of psoriasis evaluated over a 2 week peroid, but more recurrence was observed with locally made products.

Key word : Topical Steroid, Locally Made, Brand Name, Clobetasol Propionate

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Topical corticosteroids are used for numerous dermatologic diseases especially inflammatory diseases. There are many locally made products in Thailand, but no report has appeared in the literature about the efficacy of these locally made topical coticosteroids in comparison with a brand name product. Topical corticosteroids were classified into 7 classes according to potency. The most potent one (class 1) and most expensive one is clobetasol propionate.

The purpose of this study was to evaluate the efficacy of 5 locally made clobetasol propionate (product A, B, C, D, E) in comparison with a brand name product both *in vitro* and *in vivo*.

MATERIAL AND METHOD

The study was divided into 3 parts 1) pharmacological studies, 2) vasoconstriction test, and 3) double blind clinical trial.

1. Pharmacological studies of 5 locally made clobetasol propionate creams and a brand name product included the following;

1.1. Tests for physical properties of creams

1.1.1. Physical appearances such as color and odour were recorded the results at room temperature.

1.1.2. Viscosity measurement using Hakke rotational cone-plate viscometer with sensor PK 2/1 at 30°C

1.1.3. pH measurement using the digital pH meter with sure-flow combination pH electrode at room temperature.

1.2. Tests for chemical properties of creams

1.2.1. Measurement of the amount of active ingredient in each cream using HPLC. The details of analysis were as follows:

Assay (HPLC method) :

Internal standard solution	: Prepare a solution of beclomethasone dipropionate in methanol having a concentration of 0.4 mg/ml
Assay preparation	: Dissolve an accurately weighed quantity of the test substance in methanol standard solution to obtain a solution having a known concentration of about 0.3 mg/ml
Standard preparation	: Proceed as directed for assay preparation using clobetasol propionate reference standard.

Chromatographic conditions :

Mobile phase	: Prepare a solution filtered and degassified of acetonitrile in water containing approximately 60 per cent (v/v) of acetonitrile.
Column	: S.S. 15 cm x 0.46 cm. Novapak C-18 or equivalent
Detection	: UV 254 nm.
Procedure	: Introduce 20 μL of the assay standard preparation into the chromatograph and calculate the assay by the internal standard procedure.

1.2.2 Calculation of the amount of active ingredient in percentage of the label amount.

1.3 Study the diffusion rate of steroid creams

The details of the study were as follows :

A USP Six Spindle Dissolution Tester (Vanderkamp® 600 VanKel Industries, Chatham, NJ) was used for evaluation of Enhancer cell. The flash assembly was modified because 200 ml capacity flasks were used instead of the standard 900 ml flasks. It was essential to use smaller receptor volumes to obtain samples of detectable concentrations of steroid for the HPLC analysis. The flask centering ring assembly modification differed from the standard flask assembly in that it included an additional plate adapter to hold the smaller size 200 ml flask in the center, an evaporation plate that fitted on the evaporation cover such that together they covered the flask completely at the top, and smaller size paddles ($^1/_4$" shaft) at $^1/_4$" collected to fit the paddles.

Prior to starting the diffusion study, the water bath was set at 37°C. Water was used as the receptor plate medium. The enhance cell including the cream was placed into the dissolution flask. The flask assembly was then completed, the receptor phase medium (200 ml) was poured into the flask, and the paddles rotated at 100 rpm. Samples were withdrawn at 0.33, 0.66, 1, 2, 3, 4, 5, 6, 7, 8, 10 and 12 hours. At each sample interval, and exact volume of the flask sample was withdrawn from each flask and replaced immediately with an identical volume of fresh medium. A correction factor was included in the calculations to account for the drug lost in the samples. Study of diffusion rate of steroid cream was conducted using cellulose acetate membrane in the Enhancer cell. A set of six diffusions was run to obtain the cumulative release profile.

2. Measurement of the efficacy of steroid creams by vasoconstriction test

Ten kinds of creams were studied by vasoconstriction test. These included 5 locally made clobetasol creams (A, B, C, D, E), one brand name clobetasol cream (class 1), betamethasone dipropionate cream (class 3), betamethasone valerate cream (class 5), hydrocortisone cream (class 7) and placebo. The study was performed on the backs of 30 normal volunteers with informed consent, age between 18-45 years old. Ten kinds of creams were blindly and randomly put into the plastic syringes, then each cream in the syringe was put in a Finn chamber in a double-blind, randomized fashion. Approximately 5 mg of cream was put in each chamber. Four sets of 10 creams in Finn chambers were prepared for each volunteer. The backs of the volunteers were cleaned with clean water, wiped dry and then four sets of 10 creams in Finn chamber on Scanpor® were placed on the back of each volunteer. Each set of Finn chamber was opened at 2, 4, 6, 8 hours, respectively. The creams on the backs of the volunteers were wiped off with a clean cloth soaked with clean water. The result of the test was read by 3 physicians half an hour after each set was removed. The score of the visual test was as follows: 0 = no blanching, +1 = slight blanching with an ill-defined border, +2 = intense blanching but not occupying the test area, +3 = intense blanching occupying the entire test area. The diameter of each vasoconstric-

tion area was also measured by these 3 physicians. The degree of redness at each vasoconstriction area was measured using a reflectant spectrophotometer by one physician.

The score of the visual test, diameter of vasoconstriction areas and the result of measurement by reflectant spectrophotometer were evaluated statistically using ANOVA, Chi-square test and Fisher exact test as appropriate. The p-value<0.05 was considered to be statistically significant.

3. Randomized, double-blind, right/left clinical trial

The clinical trial was conducted to compare the efficacy of a brand name clobetasol cream with 5 locally made products in a randomized, double-blind study. Sixty patients who had chronic plaque psoriasis were enrolled into the study with informed consent.

The inclusion criteria were 1) age more than 18 years, 2) psoriatic lesions symmetrically distributed on arms or legs, overall area involvement of skin lesions not more than 20 per cent of the body surface area, 3) previous topical therapy discontinued for at least 2 weeks; oral, parenteral treatments or phototherapy discontinued for at least 1 month before starting the clinical trial, 4) the patients must sign the informed consent.

The exclusion criteria were 1) age less than 18 years, 2) skin lesions involving more than 20 per cent of the body surface area, 3) pustular psoriasis, guttate psoriasis, erythrodermic form of psoriasis, 4) pregnancy or lactation, 5) concurrent systemic diseases or AIDS.

The brand name clobetasol cream and 5 locally made products were put into identical 10 g tubes randomly. Each patient received two kinds of creams, one is a locally made cream, the other is a brand name cream. Both the physicians and patients did not know which tube contained which kind of cream. The patients were suggested to apply one cream on one arm or leg and apply the other cream on the other arm or leg in a double blind, randomized fashion. About 12 patients would be randomly treated with each locally made cream. The creams were thinly applied twice a day for 2 weeks, after that cold cream was applied instead for another 2 weeks. The patients were followed-up at 2 and 4 weeks after starting treatment. The creams applied on each side of the arms or legs were not to exceed 10 g per week. The total amount of creams for 2 weeks for each patient were not to exceed 40 g. Other skin lesions that were not specified for evaluation were treated with cold cream.

Evaluation procedure

One of the authors would select a lesion on each side of the arms or legs for evaluation. The lesions were of equal severity and almost equal size. Before starting therapy, the sizes of lesions on each side of the extremities were measured and recorded. The induration, erythema and scale were determined by 5-point scale as follows :

Induration : 0 = no thickness, 1 = feels firm, 2 = raised, 3 = thick, 4 = very thick
Erythema : 0 = no redness, 1 = slightly pink, 2 = pink, 3 = red, 4 = dark red
Scale : 0 = no scale, 1 = slight scale, 2 = scaly, 3 = flaky, 4 = very flaky

Table 1. Physical appearances, viscosity and pH of 5 locally made clobetasol creams and a brand name cream.

Product	Physical appearances	Viscosity (cps.)	pH
A	thick white cream, natural odour	22,700	5.0
B	yellowish-white cream, natural odour	21,000	5.5
C	milky–white cream, natural odour	18,500	6.0
D	milky-white cream, natural odour	22,500	5.4
E	thick white cream, natural odour	20,500	5.5
Brand name	white cream, natural odour	19,500	5.0

The patients were followed-up at 2 and 4 weeks after starting therapy. At each visit, the skin lesions on the treated areas were evaluated as mentioned above. Global assessment by both the physicians and patients were also recorded using a 5-point scale as follows:- 1 = worse, 0 = no change, 1 = slightly improved, 2 = much improved, 3 = cleared.

The side effects of topical clobetasol, which included hypo or hyperpigmentation, burning sensation, skin irritation, folliculitis, acneiform eruption, skin atrophy, hair change, etc., were also recorded at each visit.

Statistical analysis

The data before and after treatment with each locally made cream were compared with the brand name cream as a percentage. Then the statistical difference between each locally made cream and brand name cream was calculated using the Wilcoxon match pair signed rank test which is a non-parametric method because of the small number of patients in each group (about 10-12 patients were treated with each cream).

RESULTS

1. Pharmacological studies

1.1. Tests for physical properties of creams

Physical appearance, viscosity and pH of 5 locally made clobetasol creams were not different from those of the brand name cream (Table 1).

1.2. Tests for chemical properties of creams

The active ingredient of clobetasol in 5 locally made creams was not different from the brand name cream (Table 2).

1.3. Study the diffusion rate of steroid creams

Cream C and D showed about 2-3 fold higher diffusion rate than the brand name cream, while creams A, B and E had an equal rate of diffusion compared with the brand name cream (Table 3).

2. Vasoconstriction test

Five locally made clobetasol creams, cream based, corticosteroid creams of classes 7, 5, 3 were compared with a brand name clobetasol cream in causing vasoconstriction on the backs of 30 normal

Table 2. Active ingredients of clobatasol in 5 locally made creams and a brand name cream (calculated as % label amount).

Product	Measured 1	Measured 2	Average
A	107.12	106.11	106.62
B	109.21	107.88	108.55
C	95.14	95.62	95.38
D	108.01	106.78	107.40
E	99.50	98.70	99.10
Brand name	96.11	94.21	95.16

Table 3. Diffusion through cellulose acetate membrane of 5 locally made creams compared with a brand name cream at various times.

Product	Amount of clobetasol creams diffused at various times (mcg)					
	15 min	30 min	45 min	60 min	90 min	120 min
A	263.24	297.96	329.80	364.88	393.28	434.72
B	308.04	341.64	372.72	401.00	440.20	460.68
C	631.96	767.96	888.20	998.89	1,143.16	1,279.04*
D	544.20	766.64	886.40	1,002.64	1,163.00	1,325.80*
E	262.32	286.68	309.92	339.40	359.96	386.44
Brand name	266.04	318.76	362.00	383.28	421.36	444.40

* increased diffusion 3 fold that of the brand name cream

volunteers. The measurement of diameter of vasoconstriction areas showed that the peak time which showed significant difference was at 8 hours after applying the patch test. Cream base, corticosteroid creams of classes 7, 5, 3, and locally made creams D and E caused significantly less vasoconstriction than the brand name cream ($p<0.05$, ANOVA test). Locally made creams A, B, C caused similar vasoconstriction to the brand name cream (Table 4).

Visual test by scoring the areas of vasoconstriction (score 0-3) by 3 physicians showed that at 4, 6, 8 hours after applying the patch test, cream based and corticosteroid cream class 7 significantly caused less vasoconstriction than the brand name cream ($p<0.05$, Chi-square test) (Table 5).

Measurement by Mexameter showed that at 8 hours cream B and E caused significantly less vasoconstriction than the brand name cream ($p<0.05$, ANOVA test) (Table 6).

3. Clinical trial

Six patients were lost to follow-up, fifty-four patients completed the study while 10-12 patients were randomly treated with each locally made cream on one side of the arms or legs (Table 7) and the brand name cream on the other side of the extremities. When evaluated at day 1 (before the start of treatment), the scores of erythema, induration, scale, and global assessment by the physicians and the patients were not significantly different between the sides

Table 4. Vasoconstriction test: measurement of diameter of vasoconstriction areas. Comparing cream based, corticosteroid cream of classes 7, 5, 3, locally made clobetasol creams (A, B, C, D, E) with a brand name clobetasol cream at various times.

Product	P-value (ANOVA test)			
	2 hours	4 hours	6 hours	8 hours
Cream base	1.000	0.000*	0.000*	0.000*
Class 7	1.000	0.000*	0.000*	0.000*
Class 5	1.000	1.000	0.327	0.009*
Class 3	1.000	1.000	1.000	0.000*
A	1.000	1.000	1.000	1.000
B	1.000	1.000	1.000	0.129
C	0.000*	1.000	1.000	0.653
D	1.000	0.128	0.257	0.004*
E	1.000	1.000	0.615	0.000*

* p-value<0.05

Table 5. Vasoconstriction test: visual score. Comparing cream based, corticosteroid creams of classes 7, 5, 3, locally made clobetasol creams (A, B, C, D, E) with brand name clobetasol cream at various times.

Product	P-value (ANOVA test)			
	2 hours	4 hours	6 hours	8 hours
Cream base	↑	0.020*	0.0001*	0.0001*
Class 7	↑	0.020*	0.0001*	0.0001*
Class 5	no difference	0.451	0.501	0.273
Class 3	p=0.433	1.000	1.000	0.451
A	↓	1.000	0.731	1.000
B	↓	0.451	0.501	0.451
C	↓	0.741	1.000	1.000
D	↓	0.091	0.320	0.451
E	↓	0.451	0.105	0.273

* p-value<0.05

Table 6. Vasoconstriction test: measurement with mexameter. Comparing cream based, corticosteroid creams of classes 7, 5, 3, locally made clobetasol creams (A, B, C, D, E) with a brand name clobetasol cream at various times.

Product	P-value (ANOVA test)			
	2 hours	4 hours	6 hours	8 hours
Cream based	↑	0.000*	0.000*	0.774
Class 7	↑	0.000*	0.000*	0.103
Class 5	no difference	0.104	0.272	0.329
Class 3	p=0.602	0.911	0.721	0.140
A	↓	0.958	0.560	0.307
B	↓	0.783	0.621	0.001*
C	↓	0.579	0.552	0.807
D	↓	0.063	0.290	0.994
E	↓	0.440	0.454	0.000*

* p-value<0.05

Table 7. Number of patients randomly allocated for treatment with 5 locally made creams compared with brand name clobetasol cream who completed the 4 week study.

Creams	Number of patients in each group
A	11
B	10
C	11
D	12
E	10
Total	54

treated with 5 locally made creams and those treated with the brand name cream (Table 8).

At day 14 after starting treatment, there was no significant difference between the sides treated with 5 locally made creams and those treated with the brand name cream in all parameters. When the total score of erythema, induration and scale were calculated, there was also no significant difference between the sides treated with 5 locally made creams and the sides treated with the brand name cream (Table 8). After clobetasol cream was discontinued for 2 weeks (day 28), there was more recurrence at the sites treated with the 5 locally made creams in terms of erythema, scale, and global assessment of the physicians and patients. No difference was detected after evaluation of the induration of skin lesions (Table 8). When the total score of erythema, induration and scale were evaluated at day 28, there was significant difference between the sites treated with 5 locally made creams compared with those treated with the brand name cream (Table 8).

When assessment was done for each group of patients, cream A showed no significant difference from the brand name in all parameters at days 1, 14 and 28 except the global assessment by the patients at day 28 that showed significant difference from the brand name cream (Table 9). Cream B showed more recurrence at day 28 when assessed by all parameters (Table 10). Cream C, D and E showed no significant difference from the brand name at days 1, 14 and 28 when evaluated by all parameters (Table 11, 12, 13).

No side effects from the 5 locally made creams and the brand name were detected during the 2 weeks of treatment.

DISCUSSION

From the pharmacological studies no difference was found in the physical and chemical properties of 5 locally made clobetasol creams compared with the brand name cream except the amount of clobetasol released through the cellulose acetate membrane; creams C and D could diffuse through artificial membrane 2-3 fold more than the brand name cream when measured at 15, 30, 45, 60, 90 and 120 minutes (Table 3). It is possible that creams C and D cannot remain within the membrane for a long time; the cream may have to be applied more frequently than the brand name cream and there may be more systemic side effects when using creams C and D, because a larger amount of these two creams

Table 8. Comparison among the sides treated with 5 locally made creams (54 patients) with the sides treated with a brand name cream at day 1 (before treatment), day 14 after treatment, day 28 (2 weeks after discontinuation of treatment).

Day	P-value (Wilcoxon match pair signed rank test)					
	Erythema	Induration	Scale	Global assessment by physicians	Global assessment by patients	Erythema + induration + scale
1	0.0833	1	1	1	1	0.2568
14	0.1167	0.2526	0.7815	0.2055	0.3111	0.3572
28	0.0277*	0.6964	0.0003*	0.0209*	0.0043*	0.0020*

* $p<0.05$

Table 9. Comparison of the sides treated with creams A (11 patients) with the sides treated with a brand name cream at day 1 (before treatment), day 14 after treatment, day 28 (2 weeks after discontinuation of treatment).

Day	P-value (Wilcoxon match pair signed rank test)					
	Erythema	Induration	Scale	Global assessment by physicians	Global assessment by patients	Erythema + induration + scale
1	0.3173	0.3173	1	1	1	0.3173
14	0.2568	1	1	0.6547	0.3173	0.4537
28	0.1025	0.5637	1	0.7389	0.0143*	0.1875

* $p<0.05$

Table 10. Comparison of the sides treated with creams B (10 patients) with the sides treated with a brand name cream at day 1 (before treatment), day 14 after treatment, day 28 (2 weeks after discontinuation of treatment).

Day	P-value (Wilcoxon match pair signed rank test)					
	Erythema	Induration	Scale	Global assessment by physicians	Global assessment by patients	Erythema + induration + scale
1	1	1	1	1	1	1
14	0.4142	0.2059	0.5637	0.1975	1	0.4606
28	0.0196*	0.0339*	0.0339*	0.0235*	0.0461*	0.0111*

* $p<0.05$

Table 11. Comparison of the sides treated with cream C (11 patients) with the sides treated with a brand name cream at day 1 (before treatment), day 14 after treatment, day 28 (2 weeks after discontinuation of treatment).

Day	P-value (Wilcoxon match pair signed rank test)					
	Erythema	Induration	Scale	Global assessment by physicians	Global assessment by patients	Erythema + induration + scale
1	0.1573	0.3173	1	1	1	0.5637
14	0.6547	0.4142	0.3173	0.3173	1	0.3991
28	1	0.1797	0.3173	0.4142	0.8907	0.7055

Table 12. Comparison of the sides treated with cream D (12 patients) with the sides treated with a brand name cream at day 1 (before treatment), day 14 after treatment, day 28 (2 weeks after discontinuation of treatment).

Day	P-value (Wilcoxon match pair signed rank test)					
	Erythema	Induration	Scale	Global assessment by physicians	Global assessment by patients	Erythema + induration + scale
1	1	1	1	1	1	1
14	0.6547	1	0.5637	0.7389	1	0.7325
28	1	0.5637	0.0833	0.1573	0.1573	0.3363

Table 13. Comparison of the sides treated with cream E (10 patients) with the sides treated with a brand name cream at day 1 (before treatment), day 14 after treatment, day 28 (2 weeks after discontinuation of treatment).

Day	P-value (Wilcoxon match pair signed rank test)					
	Erythema	Induration	Scale	Global assessment by physicians	Global assessment by patients	Erythema + induration + scale
1	1	1	1	1	1	1
14	0.0833	1	0.3173	0.5637	0.1573	0.4795
28	0.3173	0.2568	0.3173	0.5775	0.1573	0.2785

can pass through the membrane. However, artificial membrane may not represent human skin. Further studies may need to be performed using human skin explants. However, creams C and D showed no difference in the treatment of psoriasis compared with the brand name cream even when the patients applied these creams the same way as the brand name cream (Table 11, 12). The hypothesis that creams C and D should be applied more frequently than the brand name cream is not true. The systemic side effects from creams C and D could not be evaluated in this study because the creams were applied to only one extremity and not longer than 2 weeks, so further observation should be done in patients who use a larger amount of these two creams for a long time.

From the vasoconstriction test, the measurement of degree of redness with the Mexameter was not as accurate as the visual test (Table 4, 5, 6). This is different from the study done by Pershing et al[1] which reported that measurement with chromameter was as accurate as visual test. This could be explained by the difference in the devices employed. By visual test, the measurement of diameter of vasoconstriction areas was more accurate than visual scores (Table 4, 5). This observation has not been mentioned before. The most appropriate time to assess the degree of vasoconstriction was at 8 hours after applying the patch test (Table 4). At this time, the authors could see the significant difference between corticosteroid creams of various classes, including some locally made clobetasol creams compared with the brand name clobetasol cream in causing vasoconstriction. Cornell et al[2] used an open test and the results were read at 16 hours instead of 8 hours. In the occlusion test, the active ingredients were absorbed more rapidly, so the vasoconstriction occurred earlier.

Creams D and E caused less vasoconstriction than the brand name cream, while creams A, B and C caused vasoconstriction at the same degree as the brand name cream (Table 4). But when the clinical trial was performed, creams D and E could improve psoriatic lesions to the same degree as the brand name cream when assessed at 2 weeks. This means that the vasoconstriction test may not accurately predict the efficacy of corticosteroid cream for treatment of psoriasis. Although Cornell et al demonstrated that vasoconstriction test correlated well with the efficacy of treatment of most corticosteroid creams, they mentioned that some corticosteroid creams did not show good correlation between vasoconstriction test and the efficacy of treatment[2].

The results of the clinical trial showed that, when all 5 locally made clobetasol creams were evaluated together, the results of treatment after 2 weeks were not different from the brand name cream. However, more recurrence was noted following the use of the 5 locally made creams after the medications had been discontinued for 2 weeks (Table 8). When each group was evaluated separately it was found that creams A, B, C, D, E could improve psoriatic lesions at 2 weeks at a similar rate to the brand name cream (Table 9, 10, 11, 12, 13). After discontinuation of clobetasol creams for 2 weeks, only cream B showed more recurrence compared with the brand name cream (Tables 9, 10, 11, 12, 13).

The authors concluded that cream B really showed more recurrence than the brand name cream, despite the small number of patients enrolled in this group. For creams A, C, D, E when evaluated together with cream B, there was more recurrence compared with that of the brand name cream. However, when each group was evaluated separately, there was no significant difference. It is possible that the number of patients in each group (10-12 patients per group) might be too small to detect the significant difference. The appropriate number for each group should be approximately 60 patients. Further study should be done to evaluate the recurrence of lesions when using creams A, C, D, E compared with the brand name cream. However, from this study, the authors recommend that creams A, C, D, E could improve skin lesions as effectively as the brand name cream after 2 weeks of treatment. These four locally made creams which are cheaper could be used to treat skin diseases that do not recur frequently. For skin diseases that recur frequently such as psoriasis, the cost-benefit should be considered before choosing which cream to use. Further long-term follow-up should be performed to evaluate the systemic side effects after long-term use of large amounts of creams C and D due to the high diffusion rate through cellulose acetate membrane of these two creams.

In conclusion, the authors found that the physical and chemical properties of 5 locally made clobetasol creams were not different from the brand name cream. Creams C and D could diffuse through artificial membrane more than the brand name cream. Creams D and E caused less vasoconstriction than the brand name cream. Five locally made creams could improve psoriatic lesions in a similar fashion as the brand name cream. There was more recurrence of skin lesions when using the 5 locally made creams, especially cream B.

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REFERENCES

1. Pershing LK, Lambert L, Wright ED, Shah VP, Williams RL. Topical 0.050 per cent betamethasone dipropionate. Pharmacokinetics and pharmacodynamic dose-response studies in human. Arch Dermatol 1994; 130: 740-7.
2. Cornell RC, Stoughton RB. Correlation of the vasoconstriction assay and clinical activity in psoriasis. Arch Dermatol 1985; 121: 63-7.

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วัตถุประสงค์ของการวิจัยนี้เพื่อศึกษาประสิทธิภาพของยาทา clobetasol propionate ที่ผลิตในประเทศไทย 5 ชนิด เปรียบเทียบกับยาที่ผลิตจากต่างประเทศ

การวิจัยแบ่งเป็น 3 ส่วน คือ 1) ศึกษาฤทธิ์ทางเภสัชวิทยาของยา 2) ศึกษาประสิทธิภาพของยาในการทำให้หลอดเลือดหดตัว 3) เปรียบเทียบประสิทธิภาพของยาในการรักษาโรคสะเก็ดเงิน

ผลการศึกษาพบว่าคุณสมบัติทางเภสัชวิทยาของยาที่ทำในประเทศไม่ต่างกับยาที่ทำจากต่างประเทศ ยา C และ D สามารถซึมผ่านแผ่นใยสังเคราะห์ได้ 3 เท่าของยาที่ทำจากต่างประเทศ ยา D และ E ทำให้หลอดเลือดหดตัวน้อยกว่ายาที่ทำจากต่างประเทศ ยาที่ทำในประเทศทั้ง 5 ชนิดรวมกันสามารถรักษาโรคสะเก็ดเงินได้มีประสิทธิภาพเท่ากับยาที่ทำจากต่างประเทศ แต่เมื่อหยุดทายารอยโรคบริเวณที่ยาทาที่ผลิตในประเทศจะกลับเป็นใหม่ได้มากกว่าบริเวณที่ทายาจากต่างประเทศ

โดยสรุป ยาที่ผลิตในประเทศใช้ได้ผลดีเท่ากับยาจากต่างประเทศในการรักษาโรคสะเก็ดเงินเป็นเวลา 2 สัปดาห์ แต่เมื่อหยุดทายารอยโรคบริเวณที่ทายาที่ผลิตในประเทศจะกลับเป็นใหม่ได้มากกว่าบริเวณที่ทายาจากต่างประเทศ

คำสำคัญ : ยาทาคอร์ติโคสตีรอยด์, ยาที่ผลิตในประเทศ, ยาที่ผลิตจากต่างประเทศ, คลอเบตาโซล โปรปิโอเนต

ศิริเพ็ญ พัววิไล, นภดล นพคุณ, พรรณวิภา กฤษฎาพงษ์, และคณะ
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