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A Clinical Study of Topical Mucopolysaccharides & Polydeoxyribonucleoprotein (Foltene®) Therapy in Alopecia

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We performed clinical trials to evaluate the therapeutic effects of Foltene® in patients of the several types of hair fallings. Thirty patients with male pattern baldness, alopecia areata and seborrheic alopecia were included in this study. Foltene® was applied every other day for 40 days, and followed by maintenance therapy of twice application a week. The duration of whole therapy was 6 months.

We conclude that Foltene® is an effective and agent for male pattern baldness, alopecia areata and seborrheic alopecia from the following results.

Ten patients with male pattern baldness was treated with Foltene® for 6 months. Foltene® had therapeutic effects of 50% in hair regrowth, 70% in decreased hair falls, 30% in decreased dandruff, 50% in decreased seborrhea. Thirteen patients with alopecia areata was treated with Foltene® for 6 months. Foltene® had therapeutic effects of 61.6% in hair regrowth, 53.9% in decreased in hair falls, 53.9% in decreased dandruff, 77.0% in decreased seborrhea. Seven patients with seborrheic alopecia was treatment with Foltene® for 6 months. Foltene® had therapeutic effects of 85.8% in hair regrowth, 57.2% in decreased hair falls, 42.9% in decreased dandruff, 85.8% in decreased seborrhea. The degree of therapeutic sucess was related to the duration of therapy. The side effects were as followed: itching sensation developed in 2 patients (6.7%); tingling sensation in 3 patients (10.0%); burning sensation in 1 patient (3.3%); erythema in 3 patients (10.0%).

Key Words: *Mucopolysaccharides & Polydeoxyribonucleoprotein, Alopecia*

INTRODUCTION

Foltene® (major ingredient: Trichosaccharide), a mixed substance (Piazza et al., 1963) of mucopolysaccharides and polydeoxyribonucleoprotein extracted from connective tissue animal viscera, which is functioned to reduce viscosity of blood and increase blood circulation in local ischemic tissue, has been used as medicine for arteriosclerotic disease.

Especially, few investigators found the effect of hair growth by mucopolysaccharides which is the most important ingredient, incidentally through animal test (Rovesti, 1963; Bonadeo and Rovesti, 1963), and also, trichogenic action of mucopolysaccharides which is essential nutritive substance was recognized, and then, it was named as "Trichosaccharide" (Rovesti, 1963; Gazzani and Venier, 1963; Roversti,

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1967).

We performed clinical trials to evaluate the therapeutic effects of Foltene® in 30 patients of male pattern baldness, alopecia areata and seborrheic alopecia for 6 months, and its effects are shown below.

MATERIALS AND METHOD

1. Materials

This study was made on patients of male pattern baldness, alopecia areata and seborrheic alopecia among outpatients of non-cicatrical alopecia those who had visited to Ewha Womans University hospital for 6 months from, March to August, 1986. The number of patients totalled 30 consisting of 11 male and 19 female (Table 1).

Table 1. Age & sex distribution of alopecia patients

Age (Yr)	Male (%)	Female	Total (%)
0 - 10	1 (3.3)	3 (10.0)	4 (13.3)
11 - 20	3 (10.0)	2 (6.7)	5 (16.7)
21 - 30	7 (20.0)	2 (6.7)	8 (26.7)
31 - 40	1 (3.3)	7 (23.3)	4 (13.3)
41 - 50	0	4 (13.3)	4 (13.3)
51 - 60	0	0	0
61 - 71	0	1 (3.3)	1 (3.3)
Total	11 (36.7)	19 (63.3)	30 (100.0)

pts: patients

In classification of alopecia, 10 patients (7 males and 3 females) were found to be "male pattern baldness", 13 patients (2 males and 11 females) to be "alopecia areata" and 7 patients (2 males and 5 females) to be "seborrheic alopecia" (Table 2).

In the age distribution of patients, most of alopecia was shown in 21-30 age group in male and 31-40 age group in female case (Table 1).

In period of alopecia, many cases were shown between 2 and 5 years in case of male pattern baldness and alopecia areata and "within one year" in case of seborrheic alopecia (Table 2).

2. Study method

Foltene ® was applied at the eveing on the areas of the scalp where hair has thinned, and subsequently massage lightly with the finger tips, in order to ensure effective penetration of the active principles. Foltene ® was applied every other day for 40 days, and followed by maintenance therapy of twice a week. In addition, we warned them that slight erythema and "feeling of hotness" may developed on the skin, temporarily.

The following objective criterias were adopted in every patient to evaluate the degree of hair growth.

A. Capillogramme: At the first visit and the end of the treatment, hairs were cut down to the scalp on the area to be studied and the number of hair bulbs per unit surface were evaluated.

B. Trichogramme: 40 to 50 (20) hairs were taken from the top of head and, by means of a morphological test of the roots of these hairs carried out under a microscope, and were evaluated the percentage of hairs at the anagenic, catagenic or telogenic phase.

Table 2. Distribution of the duration of alopecia according to the types of alopecia

Types	MPB		AA		SA		Total	
Duration (Yr)	No. of pts		No. of pts		No. of pts		No. of pts	
	Male	Female	Male	Female	Male	Female	Male	Female
- 1	0	0	1	3	2	2	3	5
2 - 5	4	2	1	7	0	2	5	11
6 - 10	2	1	0	1	0	1	2	3
11 - 15	0	0	0	0	0	0	0	0
16 - 20	1	0	0	0	0	0	1	0
Total	7	3	2	11	2	5	11	19

MPB : Male pattern baldness SA : Seborrheic alopecia
AA : Alopecia areata pts : patients

Trichogramme performed at the first visit at the end of the treatment.

* (Characteristics of hair in each cycle:
  Anagenic hair: dark keratogenic area
  Catagenic hair: Reduced keratogenic area with the smaller root than the stem
  Telogenic hair: clear & atrophic bulb)

C. Clinical evaluation: We evaluated the efficacy of Foltene ® according to the state of hair and patients views on the results.

In order to do, this we adopted the following objective criterias;

Worse : Aggravation
Poor : No effect
Fair : Appearance of vellus hairs
Good : Between fair & excellent degree
Excellent : Appearance of terminal hairs

In case of seborrheic alopecia, we described the expression of patient's view on reduction degree of hair-fall, dandruff, and evaluated seborrheic alopecia according to the following objective criterias;

Worse : Aggravation
Poor : No effect
Fair : Appearance of vellus hairs & Slight decreased (<½)
Good : Between fair & excellent degree
Excellent : Appearance of terminal hairs & Marked decreased (>½)

RESULTS

1. Efficacy of Topical medicine

1) Efficacy of Foltene® on male pattern baldness

The result of Capillogramme showed 23.2 in average at the first visit, after treatment, was increased to 29.3.

Anagen/Telogen (A/T) ratio of male patients showed 0.61 in average at the first visit, and then, the ratio of A/T after medical treatment was increased to 1.69. In addition, A/T ratio of female patients was increased to 1.05 from 0.30. Thus, it is indicated that Anagen was increased (Table 3).

In therapeutic effects by period of applying Foltene®, and it showed 100% excellent efficacy at 18th weeks after application. In addition, when patients applied Foltene® for more than 20 weeks, there was decrease in hair-fall, significantly.

Even in reduction of dandruff and seborrhea, generally, we observed that the longer period applied for Foltene®, the better therapeutic effect (Fig. 1).

Degree of growth of new hair and disappearance of hair, reduction of dandruff and seborrhea were classified into 5 grades. In the growth of new hair, applying Foltene® for 6 months showed clinical effect of 50.0%, and, in disappearance of hair, it showed reduction of 70.0%, and also dandruff and seborrhea showed 30.0% and 50.0% reduction, respectively (Table 4).

2). Efficacy of Foltene® on alopecia areata

The result of Capillogramme showed 22.5 in average at the first visit, after treatment, was increased to 29.8.

A/T ratio of male patients showed 0.32 in average at the first visit, and then, the ratio of A/T after medical treatment was increased to 1.13.

Table 3. Trichogramme (Anagen/Telogen ratio) on Male pattern baldness

Sex	Male		Sex	Female	
No.	Before	After	No.	Before	After
1	0.14	0.17	1	0.30	0.36
2	0.50	0.39	2	0.11	2.00
3	1.50	3.00	3	0.50	0.80
4	0.86	3.00			
5	0.50	1.00			
6	0.67	3.00			
7	0.13	1.25			
Average	0.61	1.69		0.30	1.05

Table 4. Clinical response in Male pattern baldness (%)

	Worse	Poor	Fair	Good	Excellent	Availability
Hair regrowth	20.0	30.0	20.0	20.0	10.0	50.0
Decreased hair falls	20.0	10.0	30.0	20.0	20.0	70.0
Decreased dandruff	10.0	60.0	20.0	10.0	0	30.0
Decreased seborrhea	20.0	30.0	20.0	20.0	10.0	50.0

A/T ratio of female patients also was increased from 1.94 to 3.16, thus showing much more increase of A/T ratio in female case than that in male case (Table 5).

Table 5. Trichogramme (Anagen/Telogen ratio) on Alopecia areata

Sex	Male		Sex	Female	
No.	Before	After	No.	Before	After
1	0.50	0.25	1	0.67	1.88
2	0.13	2.00	2	1.00	5.25
			3	0.07	1.50
			4	1.00	8.00
			5	0.05	1.33
			6	0.30	1.75
			7	1.00	2.17
			8	6.00	8.00
			9	1.00	2.00
			10	0.25	2.67
			11	0.13	0.25
Average	0.32	1.13		1.04	3.16

In the therapeutic effect by period of application of Foltene®, from 2 weeks after application of Foltene® new hair appeared, and reduction of disappearance of hair, dandruff and seborrhea were shown. Thus, we observed that the longer period of application is, the better effect of medical treatment obtained.

However, considering that such therapeutic effects as appearance and growth of hair, reduction of disappearance of hair, reduction of dandruff and seborrhea were at lower level comparatively, it was found that therapeutic value does not improved continuously on steady basis (Fig. 2).

In the clinical effect, new hairs appeared at 61.6%, and disappearance of hairs showed 53.9% reduction. In addition, dandruff and seborrhea showed 53.9% and 77.0% reduction ratio respectively (Table 6).

3) Efficacy of Foltene® on seborrheic alopecia

The result of Capillogramme was increased from 22.3 to 26.9.

A/T ratio of male patients were reduced from 2.57 to 2.1, thus showing reducing tendency, and A/T ratio of female patients were increased from 0.62 to 1.68, thus showing a tendency of increase (Table 7).

Even in therapeutic value by period of application, we could observe that the longer period of application is, the more its effects become increased (Fig. 3).

In the clinical effects, new hairs appeared at 85.8%, and disappearance of hairs at 57.2%, and reduction ratio of dandruff and seborrhea were shown 42.9% and 85.8% respectively (Table 8).

2. Family history

We could find each family history from 7 persons (or 70.0%) out of 10 patients of male pattern baldness, and 1 person (or 7.6%) out of 13 male patients of alopecia areats.

Table 7. Trichogramme (Anagen/Telogen ratio) on Seborrheic alopecia

Sex	Male		Sex	Female	
No.	Before	After	No.	Before	After
1	5.00	4.00	1	0.67	0.67
2	0.14	0.25	2	0.25	0.75
			3	1.50	5.00
			4	0.50	0.30
			5	0.18	1.67
Average	2.57	2.13		0.62	1.68

Table 6. Clinical response in Alopecia Areata (%)

	Worse	Poor	Fair	Good	Excellent	Availability
Hair regrowth	0	38.5	30.8	23.1	7.7	61.6
Decreased hair falls	15.4	30.8	7.7	23.1	23.1	53.9
Decreased dandruff	0	46.2	15.4	23.1	15.4	53.9
Decreased seborrhea	15.4	7.7	15.4	23.1	38.5	77.0

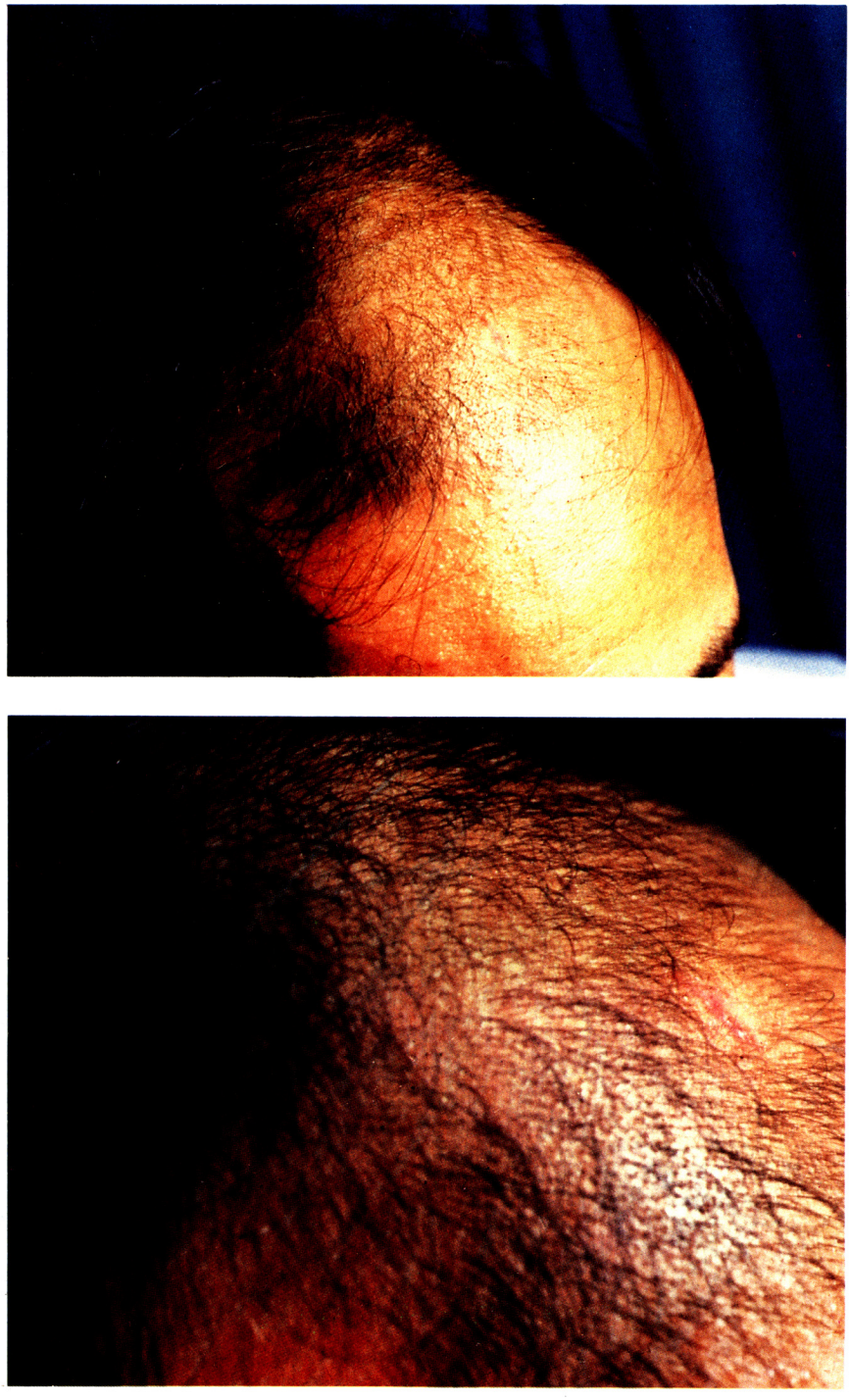

Fig. 1. Upper, pretreatment appearance of patient with male pattern baldness. Lower, appearance after 8 weeks of topical Folten® use.

Fig. 2. Left, pretreatment appearance of patient with alopecia areata. Right, appearance after 14 weeks of Foltene® use.

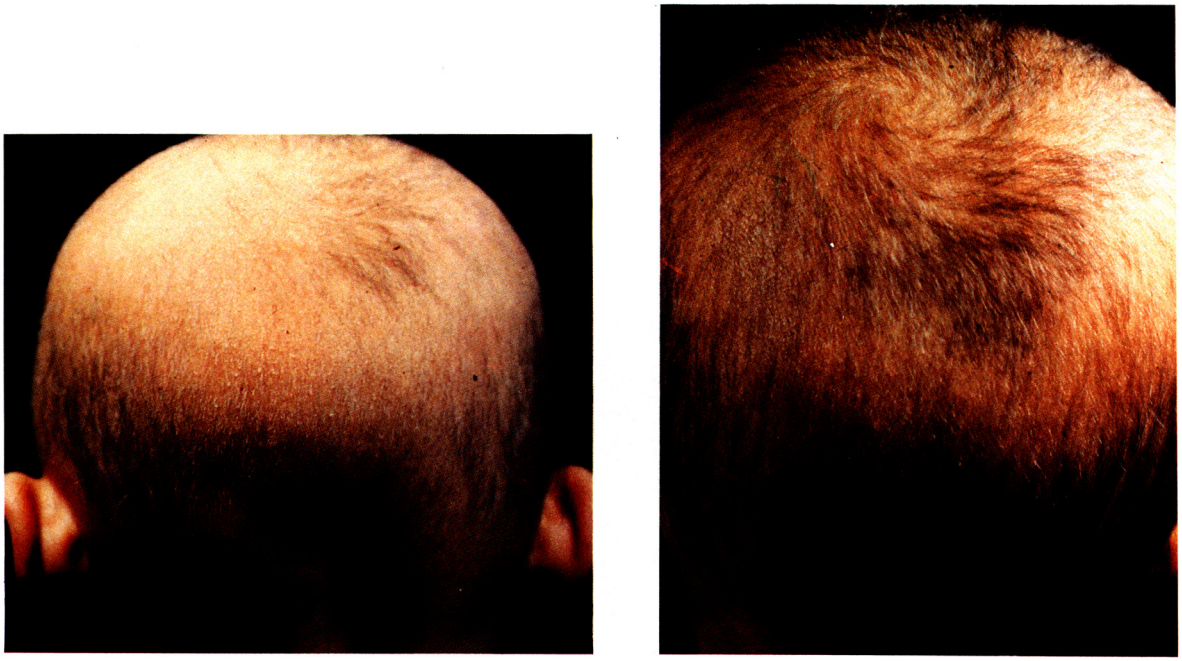

Fig. 3. Left, pretreatment appearance of patient with seborrheic alopecia, Right, appearance after 5 weeks of Folten® use.

Table 8. Clinical response in Seborrheic alopecia (%)

	Worse	Poor	Fair	Good	Excellent	Availability
Hair regrowth	0	14.3	28.6	42.9	14.3	85.8
Decreased hair falls	14.3	28.6	14.3	28.6	14.3	57.2
Decreased dandruff	0	57.1	28.6	14.3	0	42.9
Decreased seborrhea	0	14.3	28.6	14.3	42.9	85.8

3. Adverse effects

The cases in which erythema and "feeling of hotness" (or burning) were made on skin of head for a while were excluded, and only cases in which such degree were so severe or had been continued for a long time.

Of total 30 patients, tingling sensation and erythema made by 3 patients (or 10.0%), itching sensation by 2 patients (or 6.7%), and burning sensation was felt by a patient (or 3.3%).

DISCUSSION

Alopecia means a situation that few hairs are placed or no hairs are placed at the place where normal number of hair be placed and is made on head mainly. Alopecia is classified into non-cicatrical alopecia and cicatrical alopecia according to "whether or not hair follicle is damaged", and also, for typical examples of non-cicatrical alopecia, male pattern baldness and alopecia areata can be mentioned (Riecky, 1980).

The cause of alopecia has been unknown so far. However, it is considered that, generally, factors or causes of alopecia include senility, disturbance of blood circulation, unbalance of nutrition, and hormone, hereditary disease, excessive dandruff and seborrhea (Meyer et al., 1961).

Especially, the cause of alopecia which has come to the front recently is that blood circulation in the haed skin becomes to be disturbed by changes of mucopolysaccharides, thus bringing up abnormal metabolism and sclerosis of tissue, and then, alopecia caused by atrophy of hair follicles (Piazza et al., 1963).

Especially in case of seborrheic alopecia, some one insist that excessive seborrhez is functioned to cover pores of skin to disturbe oxygen inhalation and then to being up atrophy of hair follicle, thus causing alopecia.

Trichosaccharides, the major ingredient of Foltene®, is polyanionic glycopetidic complex extracted from connective tissue of animal viscera, and its effect of growing hairs in process of animal study was discovered, incidentally (Agache, 1984; Riecky, 1980).

Trichosaccharides is functioned to adjust distribution of water and salts and facilitate exchange of cellule and tissue and stimulate resyntheis of protein by acting on cytodifferentiation sometimes (Sylven, 1950).

The relation between mucopolysaccharides and growth of hair has been unknown yet. However, quantitative changes of mucopolysacchrides in hair growth cycle were found, through animal study (Gazzani and Venier, 1983; Juon, 1966; Hunger-Ricci, 1967).

Namely, it was found that the density of all fractions of mucopolysaccharides in it Anagen phase was at highest level, and also, it was decreased at Catagen phase and Telogen phase. Especially, it showed the highest density at the first week of Anagen phase. In addition, heparin and other acid mucopolysaccharides are fuctioned to not only have effect on normal multiplication and differentiation of cellule of hair follicle, but also, start new hair cycle, as labile sulfur donor to help keratin synthesis in the Anagen phase.

Considering such results, it is infered that mucopolysaccharides is an essential, physiological substance for growth of hair.

Examinating Foltene® applied, it was found that if hypodermic connection tissue of head is contracted with mucopolysaccharides, sulfur content of hair follicle was increased, keratin synthesis was promoted and damaged blood circulation was improved, and then, trichogenication of hair bulb was shown (Moretti et al., 1967; Sylven, 1950; Hunger-Ricci, 1967).

In 1983, Redaelli and others reported that reduction of dandruff and seborrhea was made by applying Foltene® for 2 months. In addition, in 1984, Agache also reported that number of hair bulb and weight of

hair were increased and average length of hair became longer by applying Foltene® on head of patient for 34 days. Furthermore, Piazza and others (1963) reported that increase of growth of hair, reduction of disappearance of hair, and reduction of excessive dandruff and seborrhea were made by applying Foltene® on 30 patients of alopecia.

Various methods for medical treatment of alopecia have been know so far, and also, even effect of such method has been probed to some degree. However, our team could observe through this our study that hair was grown again, reduction of disappearance of hair was made, and also, could observe through this our study that Foltene® had not only effect of regrowing hair, reducing disappearance of hair, but also reduction of dandruff and seborrhea, in case of male pattern baldness, alopecia areata and seborrheic alopecia.

Thereafter, it is considered that topical medicine will be used as a new medicine for alopecia through days to come.

CONCLUSION

Our study by applying Foltene® on 30 patients of male pattern baldness, alopecia areata and seborrheic alopecia was resulted in obtaining the following results.

1. In case we applied Foltene® on 10 patients of male pattern baldness (7 males & 3 females) for 20 weeks or more ratio of regrowth of hair was found to be 50%, reduction ratio of disappearance of hair to be 70%, reduction ratio of dandruff and seborrhea to be 30% and 50% respectively.
2. In case we applied Foltene® on 13 patients (2 males & 11 females) of alopecia areata for 20 weeks or more, regrowth ratio of hair was found to be 61.6%, reduction ratio of disappearance of hair to be 53.9%, reduction ratio of dandruff and seborrhea to be 53.9% and 77.0% respectively.
3. In case we applied Foltene® On 7 patients (2 males & 5 females) of seborrheic alopecia for 16 weeks, growth ratio of hair was found to be 85.8%, reduction ratio of disappearance of hair to be 57.2%, reduction ratio of dandruff and seborrhea to be 42.9% and 85.8% respectively.
4. It was observed that the longer period of application is, the better efficacy of medical treatment achieved.
5. "Feelig of hotness" and erythema occured in 3 patients (or 10.0%) of total 30 patients, itching in 2 patients (or 6.7%), and irritation in 1 patient (or 3.3%), thus showing slight second effects.

Considering the above results, we could observe that Foltene® shows a remarkable therapeutic values for male pattern baldness, alopecia areata and seborrheic alopecia. We could observe only local and slight adverse effects in applying this medicine, and it is considered that Foltene® is safe agent comparatively.

REFERENCES

Agache P.: *Evaluation of the action of Foltene amples on hair growth. Communatute Economique Europeene Besancon, 20 March 1984. In; Clinical reports on Foltene, Dong-A Pharmaceutical, Seoul, 1986.*

Bonadeo I.G.: *A new product for the care of bladness and Cosm Sav-Vol. 6,9-Sep. 1963. In; Foltene, Dong-A Pharmaceutical, Seoul, 1986.*

Bonadeo I. G.: *A new product for the care of bladness and antiesthetic alteration to the scalp. Bstr from La Revista Italiana Essenze Profumi Piante Officinale, Olii Vegetali-April 1983. In; Foltene, Dong-A Pharmaceutical, Seoul, 1986*

Gazzani G. Venier A: *Experience of trichogene factors. Ivo Congreso International Di Meicina Estetica E Io Colloquio Rome, 24 March 1983. In; Foltene, Dong-A Pharmaceutical, Seoul, 1986.*

Hunger-Ricci G.: *New results on the trichogene action of Trichosaccharide. Clinica Europa-Attualita' Di Medicina-Expr from Vol. No. 6 Novermber/December 1967. In; Foltene, Dong-A Pharmaceutical, Seoul, 1986.*

Juon M: *Trichosaccharides and their action in the field of hygiene and pathology of hair follicles. Extr from the revue Parf Cosm Savons Vol. 9 No. 8-August 1966. In; Foltene Dong-A Pharmaceutical, Seoul, 1986.*

Meyer F, Kaplan D, Steigleder G.K.: *Effect of acid mucopolysaccharides on hair growth in the rabbit. Proc Soc Exp Biol Med 108: 59-63, 1961.*

Moretii G, Cipriani C, Rebora A, Rampini E, Crovato F: *Correlation of tissue mucopolysaccharides with the hair cycle. J Invest Dermatol 48: 499-503, 1967.*

Moschella, Samuel L, Hurley I: *Dermatology. 2nd ed. WB Saunders, Philadelphia, pp 1371-1386, 1985.*

Piazza P, De pita O, Rufelli M, Donati G: *Clinical evaluation of the efficacy of a product based on mucopolysaccharide in the treatment of androgenic alopecia. Instituto Dermopatico dell' Immacolata 38: 322-325, 1963. In; Clinical reports on Foltene Dong-A Pharmaceutical, Seoul, 1986.*

Rodaelli A, Ravelli M, Cavenago E, Negri M: *Clinical evaluation of an hair paroduct containing natural muco-*

polysaccharides. Universita' degli studi Di Milano, Instituto Di Clinica Dermatologica IIa, Milan, June 1983. In; Clinical reports on Folterne, Dong-A Pharmaceutical, Seoul, 1986.

Rieky M: *A Clincal trial of trichosaccharide. Ivo Congreso Internationale Di Medicina Estetico Elo Colloquio Rome, 10 June 1980. In; Foltene, Dong-A Pharmaceutical, Seoul, 1986.*

Rovesti P: *The TS complex new product for trichogene reconstitution. Extr from "Il Farmacista' No. 3 May-June 1963. In; Foltene. Dong-A Pharmaceutical, Seoul, 1986.*

Rovesti P: *New experience in tichogene bioactivation with the use of trichosaccharide. Clinical Europa-Attualita' Di Medicina-Extra from Vol. VI No. 8 November/December 1967. In; Foltene, Dong-A Phramaceutical, Seoul, 1986.*

Sylven B: *The qualitative distribution of metachromatic polysaccharide material during hair growth. Exp Cell Res 1:582-589, 1950.*