3,729,560 TREATMENT OF HAIR AND SCALP WITH COMPOSITIONS CONTAINING ESTROL
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9 Claims
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ABSTRACT OF THE DISCLOSURE

Improvement or alleviation of certain undesirable conditions of the scalp, including certain types of non-irreversible hairfall using estrol, and compositions thereof particularly useful in such treatment.

BACKGROUND OF THE INVENTION

In the past, many claims have been made concerning the successful treatment of "baldness" by means of various different topical preparations but, as far as is known to the present applicant, none of these has proved effective.

Such lack of success is to be expected, inasmuch as the common baldness in men, also designated "male pattern baldness" or "premature baldness," may be considered primarily a physiological reaction in persons having a constitutional, often inherited, tendency toward this type of baldness. The presence of a normal amount of the male sex hormone, testosterone, is the main eliciting factor in individual prone to the development of such premature baldness, which may also be designated "andro-genetic" (meaning that it depends upon or is elicited by male factors). It has long been known, that castration may stop the further progress of this type of baldness, and that systemic treatment with the male sex hormone testosterone will again cause further hair loss in such cases.

It is not claimed that this type of male pattern baldness or androgenetic baldness, in which cases the hair follicles of the affected areas have already adapted themselves to the production only of an unpigmented, almost invisible down of no cosmetic value, can be cured or even improved or ameliorated by the treatment or compositions of the present invention, or that any hair growth whatever can be produced in an already bald area. In contrast, however, in male pattern or androgenetic alopecia (thinning out of the hair), the process of successive degeneration of the hair follicles has only begun and should therefore be reversible or at least delayable, if an adequate treatment can be found.

In addition, it is not presently possible to suggest that the treatment or compositions of the invention be used in alopecia areata (reversible hair loss leading to temporary baldness in rounded patches) and definitely no recommendations is made for use in alopecia totalis (total baldness of the scalp, sometimes also including eyebrows, eye lashes, and body hairs). In such form, the background of the baldness is uncertain and topical treatment of the type discussed here is not of any proved value. However, as stated, the present invention is not concerned with treatment of such conditions.

In addition, in those cases where hairfall is elicited by toxic or metabolic influences, such as febrile infections or anemia, or by some sort of mechanical traction, such circumstances must obviously be elucidated and removed, if hairfall from such causes is to be eliminated. Such treatment is accordingly no part of the present invention.

In addition, baldness in patches due to various conditions leading to atrophy of the hair follicles is beyond the scope of any treatment or compositions contemplated by the present invention.

HAVING now disclaimed any association with the quackery of the past relating to anti-baldness preparations, and having established certain areas in which the treatment and compositions of the present invention are not applicable, the present applicant will now proceed to describe the areas in which his novel treatment and compositions are effective.

SUMMARY OF THE INVENTION

The present invention relates to the employment of the stated compound for the treatment of certain particular conditions of the scalp for the improvement or alleviation thereof. The conditions which may be treated and thus improved or alleviated are in principle reversible types and accordingly subject to improvement. These include hairfall (effluvium or defluvium), hair thinning (alopecia) and specifically the male and female pattern types of hairfall or hair thinning (also designated alopecia androgenetica). In such conditions, the treatment and compositions of the invention have been shown to produce a marked diminution in the rate of hairfall.

Employment of the particular compound constituting the active principle of the present invention, such substance having a demonstrable hormonal effect (sexual and/or non-specific) which is directed to the permanent target organ (the scalp and its appendages), but at the same time producing a negligible effect on the internal or primary sex organs, is of the essence of the invention. Because of the fact that the compound of the invention has such unique properties, it is possible to treat the target organ in question, namely, the scalp, topically with sufficient and extremely high concentrations of the hormone, actually relatively great quantities thereof, without the risk of unwanted systemic side effects upon resorption of the active material from the sites of topical application.

The primary application of the active material is in the form of solutions or suspensions in a volatile solvent, usually in an alcoholic fluid vehicle, preferably in an aqueous alcoholic fluid vehicle, but other non-toxic pharmaceutically and topically acceptable organic solvents may also be employed. Solvents comprising at least mainly volatile components are definitely preferred, said volatile components representatively being a lower alcohol, e.g., ethyl or propyl alcohol, mixtures thereof, preferably together with some water, which is less volatile but still a slowly evaporating component, and the solvent may also contain minor amounts of other non-harmful solvents of lesser or no volatility. The active principle may, however, also be applied alone or in combination with other substances or in vehicles of other types, e.g., salves, ointments, or the like, for production of the desired effect, although other vehicles do not appear desirable for optimum results and are cosmetically less acceptable.

As far as can be ascertained by the present applicant, the material employed as active ingredient in the method and compositions of the present invention has hitherto not been used or even suggested for the purposes of the present invention. In brief, the findings upon which the present application is based are as follows:

After some months of topical treatment of the scalp with the active ingredient of the present invention, namely, estrol, in the form of lotions and solutions, preferably of a volatile, e.g., alcoholic, nature, the following effects can be obtained in a large percentage of patients treated, particularly females:

A) A pathologically-increased hair shedding can be decreased even down to normal values, according to the impression of the patient, and according to hair samples collected over a lengthy time span.

B) The status of the hair roots by microscopic evaluation in some cases can be shown to have improved as to
the percentage of actively growing ("anagen") roots in relation to dormant ("telogen") roots in an extracted hair tuft.

In female patients especially, reports of their hair dressing and family of a general impression of an improved general condition of the hair, sometimes to a considerable degree, is not uncommon.

FURTHER BACKGROUND OF THE INVENTION

Estriol is a normally occurring estrogenic hormone in human beings, but it is not very active estrogenically as shown by the most commonly used animal tests. Estradiol, the most studied human estrogen, has about three hundred to five hundred times greater estrogenic effect than its metabolite and product, estriol, when studied by the commonly employed Allen-Doisy test which measures vaginal cornification in spayed mice or rats. Estriol also has a very weak effect on the endometrium (inner layer of the uterus). Therefore, until recently, this hormone has been considered mainly as an unimportant by-product of estradiol metabolism. Neither has estriol been suggested for treatment of the scalp or hair and certainly not as an agent for topical application to the scalp for its effect upon hair follicles which exerts no disturbing systemic effects after resorption from these application sites. A search of the literature has failed to reveal any attempt to employ the active ingredient of the invention for treatment of hairfall, alopecia, or other conditions of the scalp or hair.

The finding of the present applicant that the active ingredient of the invention exerts local action upon the scalp and hair but no measurable systemic effect was unpredictably and contra-indicated by the results of earlier workers. For example, topically applied ethyl estradiol, an active estrogen, was tested with negative results on the productivity of the androgen-sensitive sebaceous glands of the forehead, at which site the estrogen was directly applied. The authors point out that their own studies rule out the possibility that estrogens antagonize androgens when applied at the level (or site) of the target organ and that many studies indicate that hormones with opposing actions on a specific target organ ordinarily do not exhibit competitive inhibition when applied at the site of the target organ (Strauss, Kilgman and Pochi, J. Investig. Dermatology 39, 139-155 1962). Thus, such locally-directed activity of the particular estrogen which is the active ingredient of the present invention and competitive inhibition of androgen at the target organ where applied is contraindicated by the results and statements of these workers as late as 1962. In their opinion, the results (as desired in this case) would have to depend on estrogens depressing mitumary output of gonadotropin, which in turn would depress the production of androgens from testicles and adrenals. Also, the estrogens might possibly depress androgen production by a direct effect on the adrenals.

However, the present results contradict the conclusions of Strauss et al. as being much too generalized. Topical application of the active ingredient of this invention has definitely produced observable, even measurable, effects on the hair, particularly in different types of female pattern alopecia (hair thinning) and usually also a decrease in the concomitant oiliness of the hair, and without undesirable side effects, as already noted.

Although not wishing in any way to be limited by theory, one possible explanation for the present results and their contradiction of prior art workers may be that, although with men having a very strong trend to at least partial baldness, estrogenic treatment by any route would have small chance of success, in men with a weaker trend to baldness, that is, a less pronounced sensitivity to androgens in certain scalp areas, a local alteration of the androgen-estrogen balance by topical application of the active ingredient of this invention might produce a delaying effect in this particular target organ, namely, the hair follicles in certain sexually dependent scalp areas, even if the same active ingredient might not affect the sebaceous glands outside the scalp.

In women with different types of female pattern alopecia (alopecia androgenetica), this sensitivity of hair follicles in certain scalp areas to androgen and the trend to a high degree of hair thinning is obviously much weaker, because of their inherent androgen-estrogen balance, and in such cases topical treatment could conceivably produce still better chances of success.

These theoretical considerations, particularly the latter one, seem to agree well with the experience of the present applicant as to topical treatment with the active ingredient of the present invention, especially when administered in a volatile, e.g., dilute alcoholic, solvent.

Another factor and mechanism which, however, must also be considered in this respect is the age-dependency of male pattern alopecia, which frequently increases with the age of the subject. Obviously, the earlier in their way to "premature aging" the hair follicles are when estriol treatment is started, the greater chance of a successful delay in the aging (and alopecia-prone) process.

Whatever the reason or scientific explanation may be, topical application of the active ingredient and compositions of the present invention has produced remarkably good effects in female patients with diffuse hairfall or thinning of the "female pattern alopecia" type (alopecia androgenetica), including one or more of the following: Decrease in hair shedding, even down to normal values; obvious decrease in weight of hair samples collected regularly over a long period; improvement of hair roots by microscopic evaluation showing decrease in inactive telogen count to active anagen count in tufts of hair extracted during successive visits; an improved general condition, texture, life, lustre, laying possibility and so on.

In men with male pattern alopecia, results have been much less spectacular, but still sufficiently successful to warrant continuation of the treatment over a period of several years.

As already noted, the various side effects which commonly appear in patients treated with estrogens did not appear when using the active ingredient and compositions of the invention in the manner of the present invention. It thus appears that one can actually speak of a separated hormonal activity in the sense that the active ingredient is active at the site of topical application for purposes of the present invention, but produces, as far as has been observed to date, no systemic effects on the internal sexual organs upon resorption.

Obviously, the treatment and compositions of the invention are more effective in the more diffuse type of alopecia in women known as "female pattern alopecia," also known as "androgenetic alopecia," several variants of which pattern are common. At any rate, the type of hairfall in both male and female patients which responds to and which can be expected to show some response to a treatment can generally be called the "androgenetic" type, as distinguished from other types previously mentioned. It is of course only a non-irreversible type of hairfall that can be treated successfully according to the present invention, since obviously no useful purpose is or can be served, except perhaps reduction of oily seborrhea, by treating a man having a very strong hereditary trend to hairfall and consecutive patterned alopecia, and particularly when this process has already progressed to actual baldness. For this reason, the typical male pattern baldness, which can really be considered as a secondary male sexual characteristic developing in persons with a strong hereditary trend to abnormally high productivity of the hair follicles in certain areas of the scalp to androgen, particularly to testosterone, must be expected to respond much more slightly if at all to any treatment, and such is the observed fact when employing the treatment and compositions of the present invention. Thus, only in men with a weaker trend to baldness can
any observable reduction in hairfall and/or the resulting thinning out of the hair be expected. In women, where the trend toward baldness because of the female hormone balance is much less, the observable effect is much greater and occurs more frequently.

Just what mechanism is involved is still not free from doubt. The activity of estrogen in evoking a marked increase in the activity of several amino acid-activating enzymes involved in the biosynthesis of protein, and thus also with hair growth phenomenon, may be a factor. Considering the very high rate of mitotic (cell division) activity in the hair follicle (which delivers scalp hair at a rate of 0.3+ mm. per day), a mechanism of this type may by itself be a possible explanation for the favorable clinical findings reported in the present application. The exact mechanism or reason for the favorable effects observed is, however, not completely understood.

**COMPOSITIONS**

The active ingredient of the invention, as previously stated, is estriol. The compositions of the invention involve the active ingredient in a pharmaceutically and cosmetically acceptable solvent, which comprises at least mainly if not entirely volatile components, such as lower alcohol preferably ethyl or isoamyl alcohol or a mixture thereof, preferably diluted with water. In such composition, the water is less volatile, but still slowly evaporating component. Minor amounts of still less volatile or non-volatile solvents of an acceptable nature may be included.

Other solvents which may also be used, and combinations thereof, include other lower alcohols, combinations thereof, acetone, combinations of other solvents with lower alcohols such as acetone plus ethanol, other combinations with methanol, ethanol, propanol or butanol; n-benzyl, dioxyne, propylene glycol, polyethylene glycol, vegetable oils, and solutions or emulsions of the foregoing with water. The presence of some water in the compositions of the invention is definitely preferred. A volatile solvent such as an alcohol, e.g., ethyl or isopropyl alcohol, or acetone is also greatly preferred. Non-volatile or only slightly volatile components are always preferably present in only minor proportions.

The concentration of the active ingredient in the solution or suspension should be at least 0.02 percent, and preferably at least 0.05 percent, and has a maximum useful upper limit of approximately 0.2 percent. Higher percentages up to about 1 percent may be used if desired but are not economically attractive. Striking results have been obtained at about 0.1 percent or slightly above, but treatment effects can sometimes be increased by increasing the concentration of the active ingredient in the compositions of the invention.

**METHOD OF TREATING**

The treatment of the invention is carried out by applying the active ingredient in any acceptable form, advantageously in a pharmaceutically and cosmetically acceptable topical solvent, and preferably in the form of a composition according to the present invention, to the scalp subject to the undesirable condition, preferably once a day. The recommended period of treatment is at least six months before a preliminary assessment of the results can be made. If no obvious hairfall is present, most male patients will require from eight to twelve months of treatment or even more before satisfactory observable results are obtained. The minimum period of treatment before favorable results have been positively effected has been approximately twelve weeks.

In any event, the recommended treatment is application to the parts of the hair and/or scalp having the undesirable condition, preferably at least once daily, and the recommended period of treatment before definite assessment of positive effect is at least six months. For maximum efficacy a year or more is usually recommended, particularly for men.

**SPECIFIC DESCRIPTION OF THE INVENTION**

The following examples of compositions and procedure which may be employed according to the present invention, are given by way of illustration only and are not to be construed as limiting.

**Example 1**

The composition most commonly used in the clinical experiments reported herein is designated Composition "OL" and has the following formula:

- Estriol 0.1 gram
- Benzalkonium chloride 0.05 gram
- Ethyl alcohol 39.9 grams
- Corrigentia odor As desired
- Distilled water To make 100 ml of solution

Use of such a composition has been found entirely satisfactory. In many cases, application of approximately 50 ml of the composition per week has been the prescribed regimen, the treatment period extending from a minimum of twelve to fifteen weeks to four years or even more. In some cases about 20 ml of the composition is administered for at least about 12 weeks or at least about 6 months.

**Example 2**

The following illustrates the preparation of a larger quantity of a composition according to the invention:

<table>
<thead>
<tr>
<th>Ingredients</th>
<th>Grams</th>
</tr>
</thead>
<tbody>
<tr>
<td>Estriol</td>
<td>500</td>
</tr>
<tr>
<td>Benzalkonium chloride 50%</td>
<td>500</td>
</tr>
<tr>
<td>Desirable odor</td>
<td>500</td>
</tr>
<tr>
<td>Ethyl alcohol, 95% by volume</td>
<td>213,000</td>
</tr>
<tr>
<td>Water to 465,000 liters</td>
<td></td>
</tr>
</tbody>
</table>

For a total of 500 liters.

The specific gravity of the solution is 0.93.

The first three ingredients are dissolved in the ethyl alcohol by mixing and stirring. When all is dissolved, water is added to make 465 kilograms (500 liters).

The estriol is relatively difficult to dissolve in dilute ethanol. Therefore, it is preferred to add the water only after complete solution of the estriol in the concentrated ethanol.

Variations: Estriol is practically insoluble in toluene and chloroform. In vegetable oils other than peanut oil and with additives, for instance, a few percent of benzyl alcohol, it is possible to obtain much higher amounts in solution. Other solvent possibilities are mentioned in the foregoing.

At 10° C. the solubility of estriol in 100 ml of solvent is as follows: In 95% ethanol 1.2%, acetone 0.27%, methanol 1.66%, butanol 0.57%, and dioxane 0.63%.

At 20° C. 0.006% in peanut oil, 0.8% in propylene glycol.

At 30° C. 1.65% in 95% ethanol, 0.41% in acetone, 2.02% in methanol, 0.74% in butanol, and 0.97% in dioxane.

Other pharmaceutically and cosmetically acceptable disinfectants or preservatives may be added as required and these are of course not critical to the method or compositions of the invention. The exact perfume or aroma is of course a matter of choice.

All the foregoing compositions and combinations may be employed according to the invention, but the compositions having the aforementioned percentages of active ingredients, and those containing alcohol, especially together with some water, are by far preferred.

Background information on hair growth and hair root dynamics: The root of a normal, growing scalp hair develops from the bottom of the cylindrical hair follicle,
which is molded on a vascular papilla ("dermal papilla") originating in the corium (deeper layer of skin) and capped by the hair bulb which is a rounded downward extension of the hair root. This bulb represents the matrix of the hair where the hair grows by means of a very intensive cell division ("mitosis"). The mass of new cells moves upwards along the follicular channel towards the scalp, and during this movement the cells undergo alterations in form and composition, particularly the keratinization process (transformation into horny substance), which is of the emerging hair shaft. The growing, healthy hair matrix, producing approximately 0.35 mm. of hair daily, is a tissue of very high metabolic and mitotic (cell division) activity, and therefore particularly sensitive to different toxic and other interferences.

After a certain period of active growth, the hair root will begin to regress and loses it supply of nutrition from the papillary vessels. It then transforms into a resting hair, which during a period of 3-4 months slides slowly along the follicular channel towards the scalp surface until it is shed spontaneously or after slight pulling. The dead (resting) hair is in itself not sensitive to toxic or other interferences, but is easier to epilate (i.e., pull out) than the growing hair.

Each hair follicle thus undergoes recurring cycles of active growth, regression and rest. In man, follicular activity and neighboring and neighboring follicles are normally at different stages of the cycle.

The main stages of the hair cycle are known as "anagen," the phase of active growth; "catagen," the phase of regression; and "telogen," the resting period. This sequence is invariable and irreversible; once catagen is induced, spontaneously or pathologically, telogen inevitably follows and is succeeded by a new anagen hair growing up from a reformed papilla and matrix. In the young adult human scalp the average duration of anagen is about three years (one to six years); catagen occupies two weeks or less, and telogen three to four months. At any given moment, 85-95% of scalp follicles are in anagen, 4-14% in telogen (i.e., the "telogen count" or "percentage" is 4-14), and 1% or less in catagen. If one accepts 100,000 as a rough estimate of the follicle population of the scalp, the daily molt will be in the region of 20-75 hairs.

Connection between hairfall ("effluvium") and "telogen count": (See Kligman, Archives of Dermatology 83, 175-198, 1961.) Very strong, toxic influences, particularly treatment with high doses of a cancer chemotherapy drug (e.g., of inhibiting cell division or mitosis), will damage the multiplications cells of the matrix so heavily, that the hair will break off in the follicle and fall out in the anagen phase. This "anagen effluvium" already begins one or two weeks after the administration of the drug.

Most other types of hairfall, partially those in which the damaging factor does not set in very suddenly and at the same time is not too strong, are of the "telogen effluvium" type. This entails a shortening of the anagen period by prematurely inducing a transformation to catagen, followed in a few weeks by further transformation to the telogen phase. The telogen count will therefore be much increased. The time, from the actual damage in the matrix until most of the resulting premature telogen hairs are shed, will be about 2-4 months. This long latent period between the insult and the visible shedding is obtained summary of long latent period (telogen thinning of the hair). As patients are not aware of this long latent period, the primary condition if any will not be disclosed spontaneously and only if a correct history is taken.

If the cause of telogen effluvium is a brief period of disease, toxic or dysfunctional influences, etc., the follicles will usually revert to their normal, long anagen phase, the telogen count decreases, the hairfall stops and the new-growing hairs will be restored to their earlier state and life span.

If the damaging influence is of a more continuous type, e.g., a long-lasting general disease or hormonal imbalance, the shortened anagen phase may occur also in the following batches of hair in the pertinent area, which will therefore retain an increased telogen count. Little by little, the follicles will grow narrower and shorter, delivering successively finer, less pigmented hairs with decreasing life span. These will transform into telogen and then fall out already when having attained a length of only a few centimeters. The affected region will now usually, have a very high telogen count and a decreased average hair shaft diameter. In many cases, particularly in the so-called male pattern alopecia, a partial or total transformation to thin, short, unsegmented "vellus hairs" (downy hairs) will result, making the affected areas appear more or less bald.

If an effective treatment can be given, it will, obviously, have to continue for several months, before the poorly functioning follicles will be restored to a degree, where thicker hairs with a close-to-normal life span can again be produced, and the telogen count (if increased) can reverse towards normal values. Therefore, when the possible efficacy of a new treatment is studied, no definite evaluation can be undertaken until the lapse of a considerable time span.

This theoretical consideration tallies well with the experience of the present applicant. Even patients who ultimately obtained an obvious improvement could sometimes see little effect in the first three or four months. Actually the telogen count may show a reverse towards normality before the patient has observed an evident improvement. Obviously, results after trial periods of say two or three months should not be counted when patient material is totally evaluated.

As the telogen count may vary between about 4 to 15 or even 20 percent between normal individuals (and also considerably between different areas of the same scalp), one single telogen count is often not sufficient to indicate either diagnosis or condition of the scalp. If, on the other hand, a relatively high telogen count decreases successively during a long course of treatment, this will be one indication of treatment efficacy. It should be pointed out here, that a high pretreatment count might well decrease markedly after the first period of successful treatment, to increase somewhat during further treatment, owing to the scalp having adapted its hair change dynamics to the new altered hair balance ultimately produced by the continuous treatment.

Preparation used and treatment routine: A solution of composition "OL" containing estradiol, 0.1% in 35% (weight) ethyl alcohol, also containing 0.05% of benzalkonium chloride and a small amount of perfume, was used in the investigation. The preparation is distributed in 200 ml. sprinkler-topped bottles, intended for use over a four-week period and carrying on one side a graduation for four "weekly rations."

The patients are instructed to apply the preparation to the thinning parts of the scalp once daily, using each week's ration in the intended time. Some of these bottles are given to the patient at consultation, but during continued treatment they are usually sent to the patient directly. The number of bottles delivered to each patient is recorded to control the pursuit of the treatment and the actual consumption of the preparation.

Results: Upon a recent survey of the clinical material, 122 patients had been treated and observed for a sufficiently long period (6 months or more) to allow estimation of the results.

Before and during the treatment, the patients were questioned with respect to decrease of hairfall, decrease of oiliness and dandruff (if present before treatment), improvement in the general condition of the hair, i.e., "lustre," "life," "manageability" and other subjective

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qualities, which had been impaired during the time period before treatment and regression of the thinning out often observed before treatment and in many cases being the most important reason for seeking medical advice.

In some cases, the total assessment was made only on the basis of such subjective estimation by the patient, his or her family and the hairdresser. In most cases, to this information was added a direct observation of the amount of hair in samples taken at regular intervals in connection with shampooing procedures, comparisons of photographs taken before and after the treatment, and different...

men, an improvement of the oily seborrhoea is not uncommon.

The result of a graded, total assessment of the therapeutic results, according to the above-mentioned criteria, is given in the table.

Graded assessment of therapeutic results (summary of clinical results): All together 122 patients have been treated and followed for a sufficiently long time, 6 months or more for women, preferably one year for men, to allow an evaluation of the results. On a basis of the evaluation criteria mentioned above, these patients were grouped as follows:

<table>
<thead>
<tr>
<th>Females</th>
<th>Males</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>++</td>
<td>16</td>
<td>2</td>
</tr>
<tr>
<td>+</td>
<td>24</td>
<td>24</td>
</tr>
<tr>
<td>Clearly positive</td>
<td>37</td>
<td>24</td>
</tr>
<tr>
<td>++</td>
<td>12</td>
<td>7</td>
</tr>
<tr>
<td>Improvement observed, but not sufficiently clear or well documented to be classed as ++, may get improved grade after longer observation</td>
<td>5</td>
<td>9</td>
</tr>
<tr>
<td>-</td>
<td>15</td>
<td>18</td>
</tr>
<tr>
<td>Doubtful or negative</td>
<td>35</td>
<td>35</td>
</tr>
</tbody>
</table>

On this basis, the percentage improved was 50%.

— (?) Stopped treatment too early to bring about a possible improvement. These may be classed as negative, but some might have been positive after an adequate treatment period.

Total | 35 | 35 | 70

On the basis, the percentage improved was 61/132 = 46.21%.

Except the — (?) cases, 122 patients have been studied. Including these cases, 132 patients have been treated.

In addition to these patients, two female and 12 male patients have begun treatment, but too late to have had time for a new visit which would allow sufficient observation for classification and grading purposes.

Treatment period: Some female patients, after having improved, can stop treatment after about one year, and sometimes even less, probably because the hairfall-eliciting hormonal imbalance was only temporary. Most female patients, however, have continued their treatment for longer periods. Several female patients have observed deterioration after having tried to discontinue the treatment.

Male patients usually have to employ the treatment for a longer time to attain a clear improvement, and most of these will have to continue for extended periods.

It is to be understood that the invention is not to be limited to the exact details of operation or exact compounds or compositions shown and described, as obvious modifications and equivalents will be apparent to one skilled in the art, and the invention is therefore to be limited only by the scope of the appended claims.

I claim:
1. A method of treating the scalp and hair of a human being suffering from a non-reversible condition involving hair fallout or thinning, which comprises administering topically to the area of the scalp subject to the said condition an effective amount of estriol, in a topical solvent having a concentration of estriol of 0.02% to about 1% by weight, said solvent comprising water and a further solvent component selected from the group consisting of a lower alcohol and acetone.
2. The method of claim 1, wherein ethyl alcohol is present as a further solvent component.
3. The method of claim 1, wherein isopropyl alcohol is present as a further solvent component.
4. The method of claim 1, wherein both ethyl and isopropyl alcohol are present as further solvent components.
5. The method of claim 1, wherein the concentration of estriol is at least 0.1% by weight.
6. The method of claim 1, wherein estriol is present in the said composition in a concentration of approximately 0.1% by weight in aqueous ethyl alcohol solvent.
7. The method of claim 1, wherein the composition is administered in an amount of about 20 ml. per week for a period of at least about twelve weeks.

8. The method of claim 1, wherein the composition is administered in an amount of about 20 ml. per week for a period of at least about six months.

9. The method of claim 1 wherein the composition is administered in an amount of about 50 ml. per week for a period of at least about twelve weeks.

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