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Final Report – Observational Study CLR-AGA

Influence of the Preparation CLR-05 on Cumulated Hair Thickness and Density in Women affected by Androgenetic Alopecia (AGA)

Aim of the observational Study

Would topically applied CLR-05 be able to maintain hair density and cumulated hair thickness in females with androgenetic alopecia?

Measuring Methods

Patients

- Women with moderate androgenetic alopecia
- At the beginning of the study: 29 women
- At the end of the study: 24 women
- 5 women stopped participating in this study without giving any reason

Application

Twice daily: 2 ml of CLR-05 tincture

Duration of observational study

3 visits:

1. Baseline visit
2. After 3 months
3. After 6 months

Parameters studied

Evaluation of the following parameters during screening (E1), after 3 months (E2) and after 6 months (E3):

1. Questionnaires for judgement of tolerance
2. Trichoscan: Hair density, cumulated hair thickness, terminal hair density.

Results:

Trichoscan:

The enclosed tables show the detailed results obtained by means of Trichoscan measurement.

Data of statistical significance are only those yielding p-values < 0.05 according to the Wilcoxon test.

From the results obtained the following conclusion can be drawn:

During treatment with CLR-05, hair density, cumulated hair thickness and terminal hair density do not suffer significant change; that means, hair density, cumulated hair thickness and terminal hair density are maintained.

Tolerance as judged by the physician:

	Mark 1	Mark 2	Mark 3	Mark 4	Mark 5	Mark 6
Tolerance	11	12	1	0	0	0

(Marks ranging from 1 "very good" to 6 "very bad")

Summarized Conclusion:

Presently, there are two types of substances designed for topical treatment of androgenetic alopecia in females: topically applied estrogens and topically applied minoxidil. Therapies of androgenetic alopecia involving topical therapeutics primarily aim to prevent alopecia from progressing. Particularly patients affected by slight to moderate androgenetic alopecia with rapidly progressing hair loss consider cessation of the latter to be the main aim of therapy, and they will experience considerable improvement in their quality of life in the long term. For this reason, the present observational study was conducted to see whether topically applied CLR-05, which was found to reduce the telogen rate in preliminary studies, would be able to stop hair loss in females with moderate alopecia.

The results obtained in the present observational study showed that topically applied CLR-05 used by female patients with moderate androgenetic alopecia over a period of 6 months prevented the androgenetic alopecia from progressing. Hair density and terminal hair density as well as cumulated hair thickness did not change. These results allow to conclude that androgenetic alopecia in females does not progress during topical treatment with CLR-05, ie. progression of this disorder is stopped. At the same time, the observational study showed that CLR-05 was well tolerated in the treatment of androgenetic alopecia.

29.11.05
(Datum)


(Unterschrift)

Hair Tonic "CLR-05"
with Follicusan™

April 2004

Phase	Trade Name	INCI Name	w/w %	Supplier
A	Citrate buffer, pH 6.4	Water (Aqua), Sodium Citrate, Citric Acid	74.10	
	Isopropanol	Isopropanol	20.00	
	Abil B 88183	PEG/PPG-20/6 Dimethicone	0.50	Goldschmidt/ Degussa
	Follicusan™	Water (and) Alcohol Denat. (and) Panthenyl Ethyl Ether (and) Milk Protein (and) Lactose (and) Inositol (and) Acetyl Cysteine (and) Acetyl Methionine (and) Sodium Citrate (and) Citric Acid	5.00	CLR
	Phenonip	Phenoxyethanol (and) Methylparaben (and) Ethylparaben (and) Butylparaben (and) Propylparaben (and) Isobutylparaben	0.40	Clariant

Manufacture:

Mix in given order.
Adjust pH to 6.4.

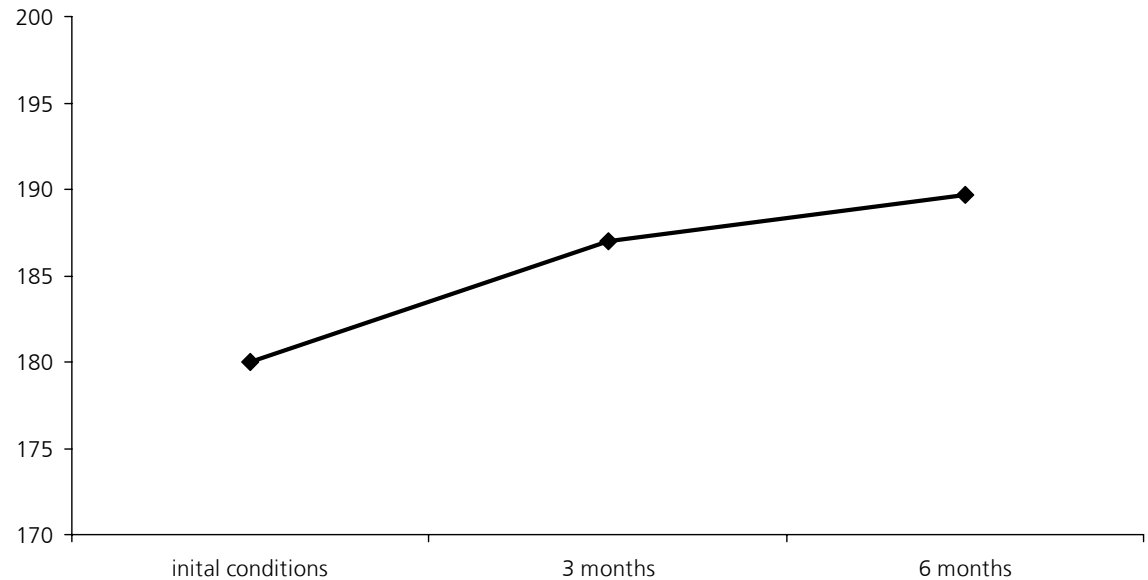
The recommendations and formulations given are based on our knowledge and experience in the field of technical application. They are, to the best of our belief, correct, but are offered without obligation. Those who use our recommendations and formulations as well as those who process CLR Active Agents are themselves responsible for the adherence to prevailing statutory regulations and the observance of patent rights as well as other protective rights for other companies.

Influence on Hair Density

Hair density [1/cm²]

Trichoscans were made from 24 female volunteers suffering from *Alopecia androgenetica*. A formulation with 5% Follicusan™ was applied on the scalp twice daily .

Standard healthy hair density ~ 200/cm²

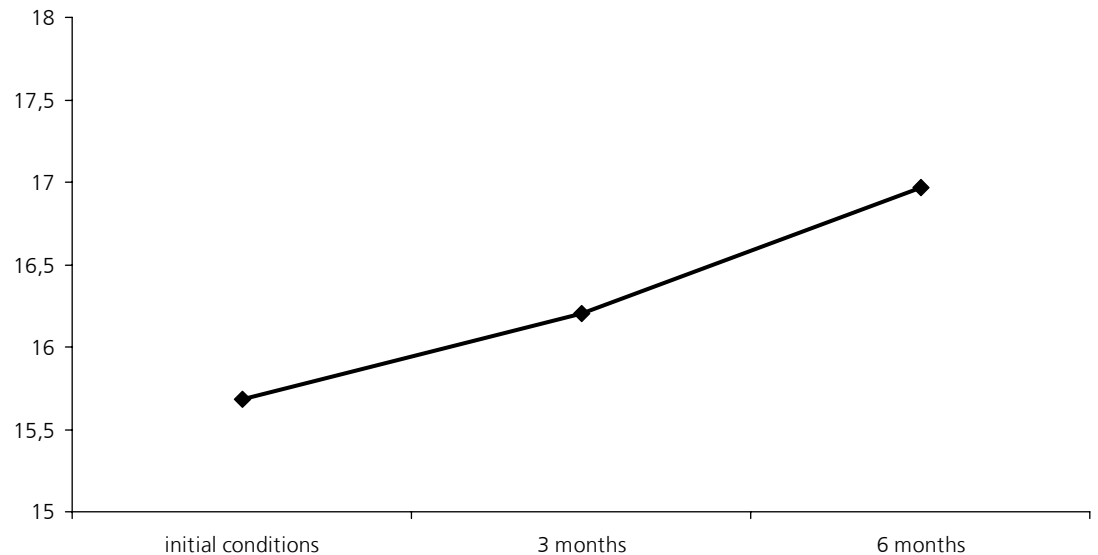


Influence on Cumulative Hair Thickness

Cumulative hair thickness [mm/cm²]

Trichoscans were made from 24 female volunteers suffering from *Alopecia androgenetica*. A formulation with 5% Follicusan™ was applied on the scalp twice daily.

A healthy hair is 0.12 mm thick, with a density of ~200/cm², the cumulative hair thickness is ~24 mm/cm².

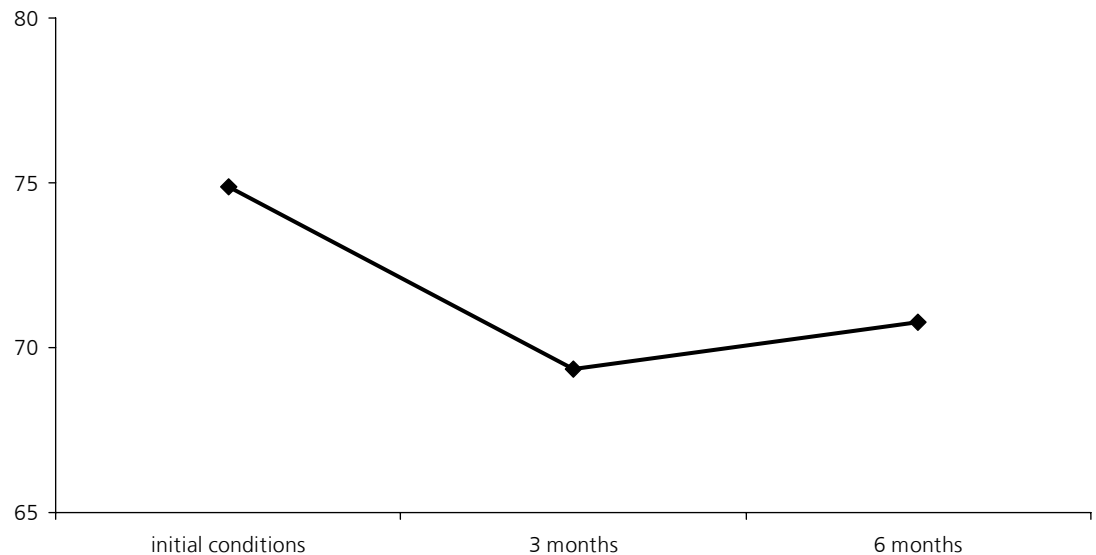


Influence on Anagen Ratio

Anagen ratio [%]

Trichoscans were made from 24 female volunteers suffering from *Alopecia androgenetica*. A formulation with 5% Follicusan™ was applied on the scalp twice daily.

Standard healthy percentage of hair in anagen phase ~ 85%.



Stud04 Marburg CLR (Result02a.txt)

Frauen

Visit 2 - Visit1

Haardichte

Student's t-test - Wilcoxon test

Variable	N	Mean	SD	Min	Q1	Median	Q3	Max	IQR	Nall	NAs
Visit 1	24	180.01	34.1	120.9	153.6	185.91	206.1	240.6	52.5	27	3
Visit 2	25	186.98	43.1	125.4	153.9	175.24	212.1	278.1	58.2	27	2
Diff (2-1)	22	-2.35	29.7	-74.4	-14.9	1.29	15.2	49.8	30.1	27	5

Paired t-test

```

data:  Visit 2 and Visit 1
t = -0.3709, df = 21, p-value = 0.7144
alternative hypothesis: true difference in means is not equal to 0
95 percent confidence interval:
 -15.53542  10.83252
sample estimates:
mean of the differences
      -2.351448

```


Visit 2 - Visit1

16.09.2005

Wilcoxon signed rank test with continuity correction

data: Visit 2 and Visit 1

V = 116.5, p-value = 0.9861

alternative hypothesis: true mu is not equal to 0

Kum. Dickendichte**Student's t-test - Wilcoxon test**

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Variable      N      Mean      SD      Min      Q1      Median      Q3      Max      IQR      Nall      NAs
Visit 1       24     15.685     4.09     9.03     11.94     15.925     18.29     23.13     6.35     27       3
Visit 2       25     16.207     5.29     8.99     12.58     15.037     17.55     28.23     4.96     27       2
Diff (2-1)    22     -0.507     2.45    -5.57     -1.84     -0.283      1.46      3.57     3.31     27       5
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Paired t-test
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```
data: Visit 2 and Visit 1
t = -0.9698, df = 21, p-value = 0.3432
alternative hypothesis: true difference in means is not equal to 0
95 percent confidence interval:
 -1.5951733  0.5805207
sample estimates:
mean of the differences
      -0.5073263
```

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Wilcoxon signed rank test
```

```
data: Visit 2 and Visit 1
V = 106, p-value = 0.5235
alternative hypothesis: true mu is not equal to 0

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Vellushaardichte**Student's t-test - Wilcoxon test**

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Variable      N    Mean    SD      Min      Q1    Median    Q3     Max     IQR    Nall    NAs
Visit 1       24    3.37    2.36    0.000    2.263    2.587    4.53    9.70    2.26    27     3
Visit 2       25    4.37    2.54    0.647    1.940    4.527    6.47    9.70    4.53    27     2
Diff (2-1)    22    1.06    2.71   -3.233   -0.647    0.323    3.23    7.11    3.88    27     5
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Paired t-test
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```
data: Visit 2 and Visit 1
t = 1.8308, df = 21, p-value = 0.08136
alternative hypothesis: true difference in means is not equal to 0
95 percent confidence interval:
 -0.1438262  2.2601291
sample estimates:
mean of the differences
      1.058151
```

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Wilcoxon signed rank test with continuity correction
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```
data: Visit 2 and Visit 1
V = 127.5, p-value = 0.07061
alternative hypothesis: true mu is not equal to 0
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Terminalhaardichte**Student's t-test - Wilcoxon test**

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Variable      N      Mean      SD      Min      Q1      Median      Q3      Max      IQR      Nall      NAs
Visit 1       24     176.64     32.9     120.9     152.4     183.00     202     230.9     50.0      27       3
Visit 2       25     182.61     43.9     115.8     152.0     169.42     208     276.1     56.3      27       2
Diff (2-1)    22      -3.41     29.5     -71.1     -20.0       1.62      16      46.6     36.1      27       5
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Paired t-test

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```

data: Visit 2 and Visit 1
t = -0.5428, df = 21, p-value = 0.593
alternative hypothesis: true difference in means is not equal to 0
95 percent confidence interval:
 -16.47266   9.65346
sample estimates:
mean of the differences
      -3.409599

```

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Wilcoxon signed rank test with continuity correction

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```

data: Visit 2 and Visit 1
V = 119, p-value = 0.8202
alternative hypothesis: true mu is not equal to 0

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Anagenrate**Student's t-test - Wilcoxon test**

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Variable      N      Mean      SD      Min      Q1      Median      Q3      Max      IQR      Nall      NAs
Visit 1       24      74.87     12.5     42.6     69.4     76.29     84.05     90.5     14.6     27       3
Visit 2       25      69.35     13.4     37.7     63.5     72.93     78.39     88.8     14.9     27       2
Diff (2-1)    22      -5.63     12.6     -39.3    -11.9     -2.92      2.18     11.0     14.1     27       5
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Paired t-test
```

```
data: Visit 2 and Visit 1
t = -2.0927, df = 21, p-value = 0.0487
alternative hypothesis: true difference in means is not equal to 0
95 percent confidence interval:
 -11.23087405 -0.03535649
sample estimates:
mean of the differences
      -5.633115
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Wilcoxon signed rank test
```

```
data: Visit 2 and Visit 1
V = 73, p-value = 0.08541
alternative hypothesis: true mu is not equal to 0

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Visit 3 - Visit1

Haardichte

Student's t-test - Wilcoxon test

Variable	N	Mean	SD	Min	Q1	Median	Q3	Max	IQR	Nall	NAs
Visit 1	24	180.01	34.1	120.9	153.6	185.91	206.1	240.6	52.5	27	3
Visit 3	22	189.67	48.2	108.0	152.3	192.05	230.4	266.4	78.1	27	5
Diff (2-1)	19	1.26	40.8	-87.3	-19.4	5.82	28.1	56.3	47.5	27	8

Paired t-test

```
data: Visit 3 and Visit 1
t = 0.1345, df = 18, p-value = 0.8945
alternative hypothesis: true difference in means is not equal to 0
95 percent confidence interval:
 -18.41590  20.93442
sample estimates:
mean of the differences
      1.259262
```

Wilcoxon signed rank test

```
data: Visit 3 and Visit 1
V = 110, p-value = 0.5678
alternative hypothesis: true mu is not equal to 0
```

Visit 3 - Visit1

16.09.2005

Kum. Dickendichte**Student's t-test - Wilcoxon test**

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Variable      N      Mean      SD      Min      Q1      Median      Q3      Max      IQR      Nall      NAs
Visit 1       24     15.6850     4.09      9.03     11.94     15.93     18.29     23.13     6.35      27       3
Visit 3       22     16.9665     5.57      9.19     12.75     15.47     21.67     26.08     8.92      27       5
Diff (2-1)    19       0.0755     3.22     -6.56     -2.17      1.04      1.71      4.83     3.88      27       8
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```

Paired t-test

```

data: Visit 3 and Visit 1
t = 0.1023, df = 18, p-value = 0.9197
alternative hypothesis: true difference in means is not equal to 0
95 percent confidence interval:
 -1.474905  1.625882
sample estimates:
mean of the differences
      0.07548821

```

Wilcoxon signed rank test

```

data: Visit 3 and Visit 1
V = 103, p-value = 0.768
alternative hypothesis: true mu is not equal to 0

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Vellushaardichte**Student's t-test - Wilcoxon test**

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Variable      N    Mean    SD      Min      Q1    Median     Q3      Max     IQR     Nall    NAs
Visit 1       24    3.37    2.36     0.00     2.26    2.59     4.53     9.70    2.26     27      3
Visit 3       22    4.94    3.40     0.00     2.59    5.17     7.11    12.29    4.53     27      5
Diff (2-1)    19    1.16    4.49    -7.11    -2.59    1.94     4.85     9.05    7.44     27      8
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```

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Paired t-test
```

```
data: Visit 3 and Visit 1
t = 1.1238, df = 18, p-value = 0.2759
alternative hypothesis: true difference in means is not equal to 0
95 percent confidence interval:
 -1.006126  3.320446
sample estimates:
mean of the differences
      1.15716
```

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Wilcoxon signed rank test with continuity correction
```

```
data: Visit 3 and Visit 1
V = 121, p-value = 0.3046
alternative hypothesis: true mu is not equal to 0
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Terminalhaardichte**Student's t-test - Wilcoxon test**

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Variable      N      Mean      SD      Min      Q1      Median      Q3      Max      IQR      Nall      NAs
Visit 1       24     176.643    32.9    120.9    152.4    183.0    202.4    230.9    50.0     27       3
Visit 3       22     184.736    47.8    108.0    150.7    184.0    224.2    256.1    73.6     27       5
Diff (2-1)    19       0.102     39.1    -80.2    -24.9      8.4     28.5     51.7    53.3     27       8
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Paired t-test

```

```

data: Visit 3 and Visit 1
t = 0.0114, df = 18, p-value = 0.991
alternative hypothesis: true difference in means is not equal to 0
95 percent confidence interval:
 -18.75621  18.96041
sample estimates:
mean of the differences
      0.1021023

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Wilcoxon signed rank test

```

```

data: Visit 3 and Visit 1
V = 105, p-value = 0.7086
alternative hypothesis: true mu is not equal to 0

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Anagenrate**Student's t-test - Wilcoxon test**

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Variable      N      Mean      SD      Min      Q1      Median      Q3      Max      IQR      Nall      NAs
Visit 1       24      74.87     12.5     42.6     69.4     76.29     84.05     90.5     14.6     27       3
Visit 3       22      70.78     14.0     38.7     64.9     74.03     81.82     87.5     17.0     27       5
Diff (2-1)    19      -6.49     15.9     -43.5    -14.9     -2.22      3.75     25.0     18.7     27       8
-----

```

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-----
Paired t-test

```

```

data: Visit 3 and Visit 1
t = -1.7796, df = 18, p-value = 0.09203
alternative hypothesis: true difference in means is not equal to 0
95 percent confidence interval:
 -14.156075  1.172133
sample estimates:
mean of the differences
      -6.491971

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Wilcoxon signed rank test

```

```

data: Visit 3 and Visit 1
V = 58, p-value = 0.1447
alternative hypothesis: true mu is not equal to 0

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