HR9
Hair Activating System

EFFICACY

EVALUATION

REPORT

FINAL REPORT

EFFICACY EVALUATION ON PARTICIPANTS,

OF COSMETICS PRODUCTS

Report: #62A214, 07.July.2014

Products: 1. HR9 scalp activator for Men & Women

2. HR9 hair activator for Men & Women

Forms: HR9 scalp activator for Men & Women - Liquid

HR9 hair activator for Men & Women - Liquid

Aplication: Application onto the scalp.

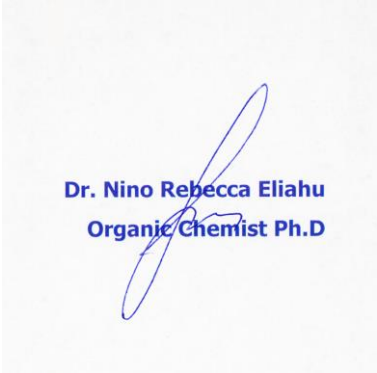
Regulation: All the Ingredients and components in these products are formulated to match the CTFA 13th Edition nomenclature, the CAS # and EINECS, The EU directive 1223/2009 for cosmetic products; and in accordance with FDA guidelines.

Study monitor: Genin Oded (Chemist)

Study investigator: Dr. Nino Eliahu **Ph.D**

Technical supervisor: Benitah Yoram (Trichologist consultant)

Location: Natura Laboratories



Efficacy Study of HR9 Hair System

(Patent Pending)

Purpose:

Objective of study is to test the efficacy, activity and safety of **HR9 Hair System** on scalp via a comparative analysis and the effects of the products on men and women with androgenetic alopecia, hair shedding and hair thinning.

Scalp's Skin types tested	Products being used
All scalp's skin types	All the products mentioned in page 1, in accordance with the instructions for use.

Study Design:

Vivo efficacy, activity and safety Study.

Study details:

This trial was a clinical/laboratory trial.
This trial was conducted in the laboratory environment.
At the laboratory: 32 participants were tested.
During the coming 120 days; the method of application was tested and conclusions were done.

Experimental plan:

Group study.

Methodology:

Before / after

Zone:

Scalp

Application frequency:

In accordance with the attached instructions for use.

The participant’s study:

Participants were selected by the condition of their hair; accelerated hair loss, hair shedding, thinning hair, partially baldness, receding hair line. They were evaluated for the process convenient; adverse reaction after the treatment; reaction and action after; 3 days; after 30 days and after 120 days.

Primary objective:

The primary efficacy endpoint was to see no reactions, none whatsoever towards the products, no irritations, and to summarize participant's convenience.

Secondary objective:

The Secondary efficacy endpoint was to see the effect on the scalp’s skin; general status of the hair; general visual of the hair, measuring the hair growth, measuring the hair modes and changes (Telogen – Anagen ratio), measuring the hair thickness changes; and the efficacy of the products and the treatment.

Participant's criteria

Eligibility:

Ages Eligible for Study: 29 Years to 60 years old.

Genders Eligible for Study: Females and males.

Participant's inclusion Criteria:

Participant must be healthy.

Participant must have a hair withdrawal.

Participant must have male androgenetic alopecia (Norwood scale 2,3,4,).

Participant must have female androgenetic alopecia.

Participant gave her/his written consent.

Participant must be aware of the necessity and duration of the study so that perfect adhesion to the protocol established by the clinical trial laboratory could have been expected.

Participant must be intellectually competent, and able to understand the purposes of the study.

Participant's exclusion Criteria:

Participant’s with the following symptoms and conditions were excluded:

Have skin problems, irritating rash, surface wounds on scalp, seborrhea and any type of skin disease.

Use of topical or systemic treatment during the previous weeks, which may be liable to interfere with the assessment of the cutaneous acceptability of the studied product.

Excessive exposure to sunlight or UV rays within the previous 30 days.

Participant enrolled in another clinical trial during the study period.

Not able to understand the purposes of the study.

Participant's questionnaire:

Answers given by the subjects to a subjective evaluation questionnaire are used to evaluate the characteristics, the efficacy and the tolerance of the studied product. These subjective criteria give, in particular, accurate information regarding product appreciation.

Compliance assessment:

If the protocol was not respected and if the deviation was minor, the technician or the investigator in charge of the study warned the subject of the importance of respecting the prescribed protocol. If the participant persisted or if the deviation was major, the participant was declared non-compliant. In this case; the participant was removed from the study for non-compliance.

Under normal conditions of use at home, no compliance control could be carried out during the test. However, the participant had filled in, every day, a daily log.

Associated treatment during the study:

No use of dermopharmaceutical or cosmetic product other then the studied products was authorized on the scalp and hair during the study. Only shampoo (any) was authorized. No excessive exposure to sunlight or UV rays during the study was authorized.

Trial period

Product reception:

06.Jan.2014

Beginning of the study:

14.Jan.2014

End of the study:

29.May.2014

First published result after final evaluation:

24.June.2014

Total participants:

32

Location:

Natura laboratories.

Operational aspect

Trial schedule:

- **On Day 0**
  - The participants came to the laboratory; they read, signed and dated the information sheet (instructions for use of the products and restrictions related to the study) and informed consent **forms** in duplicate. These documents were also signed and dated by the person who conducted the informed consent discussion. The participants received a copy.
  - Implementation of a high frequency Echography of the Epidermis and Dermis of the scalp zone of each participant was completed; this is to determine the scalp's skin thickness & condition before/after.
  - Acquisition of "Before" picture of the whole head top area of each participant was completed; using special chin holder facility for accurate position.
  - Implementation of temporary red dot tattoo on the scalp, ~~this is~~ to measure the hair growth and hair status (Anagen-Telogen ratio) by using Dermo Scan HD with Trichoscan software. Trichoscan photo "Before" was taken at day 0. Dermo Scan protocol attached.
  - The treatment was performed at the participant's home and the participants received HR9 activator kit to use in accordance with the instruction for use.
  - Distribution of the daily log and of the studied products to the participants who applied it in accordance with the instructions for use.
- **On Day 3**
  - The participants came for evaluation of reactions; irritations; and to summarize participant's convenience.
- **On Day 30**
  - The participants came for general evaluation; visual analysis and collecting organoleptic data in regarding the convenience of the treatment; the substances and the instructions for use.

- **On Day 120**

  - The participants came back to the laboratory for the final evaluation.
  - The participants brought back the daily log (D0-D120) and the remaining products.
  - Last implementation of a high frequency Echography of the Epidermis and Dermis of the scalp zone of each participant was completed.
  - Acquisition of “After” picture of the whole head top area of each participant was completed; using special head holder facility for accurate position.
  - Last “After” TrichoScan photo was taken at day 120.
  - The subjects answered of the subjective evaluation questionnaire.

Adverse events/serious adverse events protocols

Definitions:

An adverse event is defined as any expression or noxious and not wanted symptom suffered by participants taking part in biomedical research, whether or not it is related to the studied product(s). A serious adverse event (SAE) is defined by one of the following criteria:

- Death,
- Life threatening,
- Hospitalization,
- Persistent or significant disability or incapacity,
- Congenital anomaly,
- Overdose,
- Cancer,
- Other event considered clinically significant by the investigator.

Documentation:

All adverse events related to the studied product (adverse effect) were reported in the case report from (CRF) and the study report.

All concomitant treatments were reported in the CRF and the study report.

All serious adverse events were reported in the CRF and the study report.

Notification:

All adverse effects were transmitted by fax or e-mail to the sponsor within 48 hours after knowledge of their occurrence (according to the investigator's advice).

All serious adverse events were transmitted by fax to the sponsor within 24 hours after knowledge of their occurrence, and then confirmed by mail within 48 hours.

Follow-up:

When an adverse effect persisted at the end of the study, the investigator ensured that the subject was followed up until total resolution without taking off the application of the obligations and the responsibilities of the sponsor.

Early termination of the study

Study exit conditions:

- In compliance with the Helsinki declaration (1964) and its successive updates and with the French law 2004-806 dated August 9, 2004 concerning public health (ref: 1 to 3 in so.1), subjects had the right to exit from the study at any time and for any motive.
- The investigator could also have interrupted the subject participation in the study prematurely in the case of an inter-current disease or adverse effect.
- The sponsor could have demanded that any subject be excluded from the study for major infringements of the protocol. For administrative reasons or any other motive.

Nevertheless, premature removal of a high percentage of subjects from the study could have made the study difficult or impossible to interpret. Consequently, any premature exit without valid motives should have been avoided as much as possible and was carefully documented in the case report form, the final report and if necessary in the Adverse Event form.

Every premature exit must have been classified under one of the following headings:

- Adverse event occurrence.
- Serious Adverse event occurrence.
- Withdrawal of consent.
- Untraceable panelist.
- Appearance of non-inclusion criteria.
- Non-adherence to the protocol.
- Other reason.

Replacement conditions:

No replacement was foreseen as additional subjects were planned to be included in the study.

Collection and validation of data:

According to the law “INFORMATIQUE ET LIBERTES” (ref: 4 in s8.1), an identification code was attributed to each participant on purpose to keep her/his identity confidential. This code consists in: the first letter of the participant’s surname and the first letter of her/his first name.

The personnel in charge of the study (technician, physician) added data to participant case report form and to a computerized data base. Data was validated by the project manager.

Audit and trial monitoring visit:

An audit and/or trial monitoring visit might be carried out at the sponsor’s request or by the appropriate regulatory authority. It allowed verification that the study was conducted according to the determined protocol as well as current regulations.

Quality assurance and quality control:

In order to ensure the conformity of the clinical trials to the study sponsor’s requirement, A quality management protocol was written.

This quality assurance system includes GMP and regulation requirements.

Each study report is subject to quality control by a QA technician. The proofreader has been chosen because he (she) is not involved in the audited study. The inspection of the study report allows for confirmation that the results reflect exactly the studies raw data.

Studied products

Confidentiality procedure:

The products supplied by the sponsor were encoded.

Storage:

Before the beginning of the study, products were kept at room temperature in a dedicated air conditioned room. This room was locked and access controlled.

Aspects:

All products are liquid.

Method of the scalp's skin measurement & evaluating:

Tests in VIVO for Epidermis and Dermis thickness changes were performed with High and low frequency echography.

Thickening of the scalp will clearly show acceleration of Collagen and Elastin activity; hence better bonding of the skin's tissues, better tightening effect and better ground for the hair roots anchoring and regrowth.

The measurement principle is that of the Echograph: an ultrasound beam is emitted by piezo-electric ceramics. This beam is partially reflected by the interfaces separating two part of different ultrasound impedance.

This method permits bi –dimensional visualization of the skin on the Epidermis and Dermis. It is also possible to measure skin thickness (Epidermis + Dermis). The accuracy of this method is estimated to be 2%.

The ultrasound used is equipped with a 20 MHz probe. The probe is applied directly to the skin. A contact gel provides homogeneous diffusion of the signal.

Image analysis software is used to calculate the average thickness of the skin (dermis+ epidermis).

An ultrasonic beam is emitted by a piezo-electric ceramic. This beam is partially reflected by the interfaces separating the two different ultrasonic impedance's media. At a frequency of 13 MHZ, the zone of exploitable echogenicity is in the hypodermis.

This method permits two dimensional visualization of subcutaneous fatty tissue. It is also possible using this method to quantify the effect of thickening of the skin by measuring the increase in the Dermis thickness.

Probe enables operation in B mode. The probe is applied directly to skin. A contact gel is used to ensure uniform signal distribution.

The device is connected to a laser printer.

The Dermis thickness is measured in mm. These measurements are taken at each kinetic, a measurement on the lateral side, one on the supero-antrior side. And the last one on the intero-anterior side, then the average of three measurements is also studied.

Calibrating and adjusting systems aligned with the measurement system ensure the precision of the technique.

The analysis software allows to calculate, for each kinetic, the volume of a defined zone.

Method of “Before” and “After: visual pictures

Digital photography:

The images were acquired using a KODAK EASY SHARE DX6490 camera. (© Eastman Kodak Company, 2003 - Kodak and Easy Share are trademark of Eastman Kodak Company).
The camera was set up to the best quality of image (2304 x 1728 pixels, 4.0 Mp).

Archives:

The report will be securely archived for 6 months from the date of dispatch of the final report. At the end of this period, the study archives will be destroyed unless otherwise stipulated in writing by the sponsor.

All the documents relating to this study are archived during the 6 months at Natura laboratories archive. After 6 months the documents will be destroyed.

Participants

Number of participants			Reason(s)
Included participants	Participants who completed the study	Analyzed participants	
32	30	30	Participant # 14 was untraceable
			Participant # 24 was declared non-compliant

SAFETY REPORT – ADVERSE EVENTS & IRRITATIONS

CRF #	Initials	Gender	Year of birth	Day - 3	Day - 30	Day - 120
01	BAT-L	Female	1961	0	0	0
02	SHA-N	Female	1966	0	0	0
04	SLO-M	Female	1957	0	0	0
05	YOS-S	Female	1979	0	0	0
06	AMI-F	Male	1955	0	0	0
07	SAR-B	Female	1955	0	0	0
08	OSI-Y	Male	1981	0	0	0
10	MOS-M	Male	1969	0	0	0
11	NAO-E	Male	1977	0	0	0
12	CLE-C	Female	1961	0	0	0
13	MEN-N	Female	1980	0	0	0
14	TAL-A	Male	1971			
15	BEN-C	Female	1976	0	0	0
16	DAN-L	Female	1976	0	0	0
18	MIL-Y	Female	1959	0	0	0
19	MOS-C	Male	1966	0	0	0
20	SHO-D	Male	1959	0	0	0
21	ROY-A	Female	1985	0	0	0
22	YOS-C	Male	1971	0	0	0
23	DIN-L	Female	1982	0	0	0
24	ALL-N	Female	1954			
25	IZI-Z	Female	1970	0	0	0
26	RAC-L	Female	1980	0	0	0
27	OLG-L	Female	1959	0	0	0
28	SAR-G	Male	1968	0	0	0
29	ANG-N	Female	1972	0	0	0
30	GEN-N	Male	1967	0	0	0
31	NAT-G	Male	1974	0	0	0
32	ALO-O	Male	1973	0	0	0

HR9

TEST RESULTS

TOTAL APPRECIATION AND ORGANOLEPTIC CHARACTERISTICS		
Aspect		
	Very pleasant	93%
	Pleasant	7%
Texture		
	Very pleasant	95%
	Pleasant	5%
Easy to apply		
	Very pleasant	98%
	Pleasant	2%
Easily absorbed		
	Very pleasant	96%
	Pleasant	4%
Easy to spread		
	Very pleasant	95%
	Pleasant	5%
Suitable to your scalp		
	Very pleasant	93%
	Pleasant	7%

Scalp's skin thickness and elasticity

A significant thickness increase was shown in the Dermis and Epidermis layers after 120 days of use, this shows acceleration of Collagen IIV, Collagen III and Elastin production, skin tissues bonding along with increased density of the skin layers.
The average of two sides/dimensional/volumetric increased: 21.9% which provides firm anchoring of the roots and strong effect on the follicle size which also support better anchoring. The deterioration of the scalp's skin condition was completely stopped.

The increase was observed on 100% of the participants.

CONCLUSION:

The present study has proven the effectiveness of "HR9 scalp activator" as scalp's skin repair and restorative product (patent pending as part of the HR9 hair system).

Automated Photo Trichogtam (PTG): TrichoScan

Introduction

TrichoScan is, compared to conventional and Contrast-Enhanced (CE) PTGCEPTG, an investigator-independent, automated software program, validated by Good Clinical Practice (GCP), for the analysis of hair growth, which was developed as there was need for a sensitive tool to automatically monitor hair loss and the response to treatment.

TrichoScan operates with defined values for intra- and interclass correlation between the same and different investigators. TrichoScan software analysis relies on images taken from a small analyzed area of the scalp, which is barely visible after the measurement procedures completed.

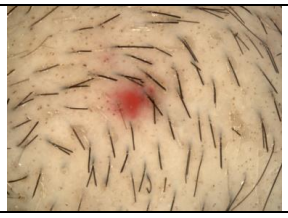
Technology

Indication

TrichoScan software has been described and validated to monitor and measure hair growth in pattern alopecia .TrichoScan is not suitable for body hair or for following other hair diseases such as alopecia areata; neither is it a diagnostic tool. For the TrichoScan software analysis to be accurate, the program must be supplied with images taken from clean skin with good contrast between the hair fiber and the skin itself. Any remnants of hair dye, dark melanocytic moles, or dark scalp skin will diminish the contrast between the skin and the hairs and the analysis will not be

Dermo Scan results

Technical procedure

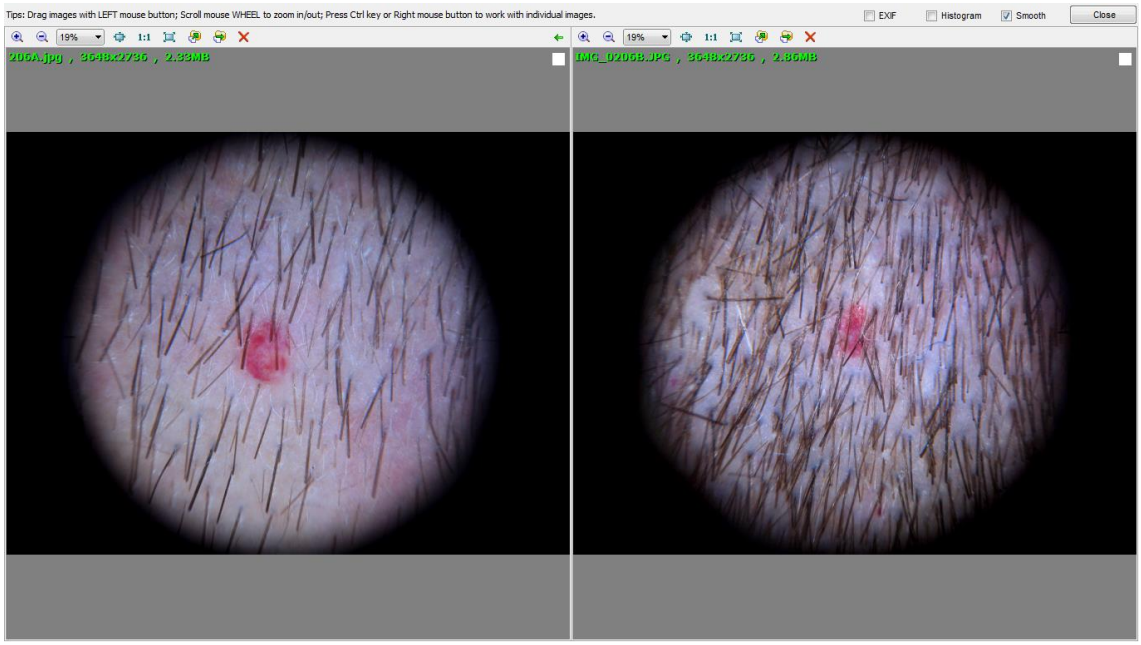
The correct clipping site is chosen. .	
The hair is shaved to about 5-7 mm length. 	
Temporary tattoo dot is performed for repeating scans on the exact same area.	
Hair dye (Goldwell Topchic) and developer (6% cream oxide) is applied for better visual.	
The camera is pressed onto the scalp; and pictures are taken for the TrichoScan analyzer.	

Suitable images for TrichoScan

As an automated image analysis tool, accurate Tricho-Scan results strongly depend on the image quality. During clinical trials all clipped areas are landmarked with a central, single red tattoo, which serves as a visible reference point throughout the study. As a digital tool, TrichoScan will always analyze the same image consistently and calculate the same results time and time again. It is also considerably quicker than manual counting and allows relatively inexperienced technicians to obtain consistent and accurate results. After taking the image the software then analyzes the scalp hair images by following a certain sequence of steps outlined below.

Method:

An area of 1 cm in diameter was chosen for the test and marked with a reference spot of temporary red tattoo. The hair was cut to 0.5-0.7 mm length and colored in black to increase contrast. The size of the area in the picture below is 0.659 cm2



The table shown above is representing the average of the results

Trichoscan measures	Results after: 120 days
Average results Hair Density per 1 cm2	Increased : 23%
Average results Density Terminal Hair per 1 cm2	Increased: 28%
Average results Hairs in Telogen mode (falling mode)	Decreased :21%

SAFETY ASSESSMENT:

Safety assessments for all the products in this trial were performed in accordance with the EU directive 1223/2009.

All the products in this trial were approved by the EU directive 1223/2009 and are registered in the CPNP system in EU territory.

Yoram Benitah
Trichologist consultant

Dr. Nino Rebecca Eliahu
Organic Chemist Ph.D

Computer edited certificate, electronically protected, valid without signature.