

EVALUATION OF TOPICAL ANTI-WRINKLE AND FIRMING (AWF) FOR WOMEN, ANTI-WRINKLE AND FIRMING (AFM) FOR MEN AND DEEP WRINKLES FOR WRINKLES ON FACE AND NECK

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ABSTRACT

Wrinkles are the clinical manifestation of 'cutaneous aging'. 'Anti-Wrinkle and Firming (AWF) for Women', 'Anti-Wrinkle and Firming (AWF) for Men' is an Integral Correction Serum specifically for woman and man for the treatment of fine wrinkles. Deep Wrinkles' is an Integral Correction Serum that significantly reduces the appearance of deep wrinkles. An open labelled, prospective, multi-centric clinical study was conducted to determine the efficacy, safety & quality of life parameters with 'AWF for Women', 'AWF for Men' and 'Deep Wrinkles' in the treatment of fine to deep wrinkles on face and neck in 30 patients (10 patients in each group) for 12 weeks. The patients were assessed for Modified Fitzpatrick Wrinkle Scale (MFWS), improvement in 'Quality of Life', 'Patient Satisfaction Questionnaire', Physician's and Patient Global Assessment Grade for improvement in wrinkles and Photographic assessment at baseline, 6 weeks and 12 weeks. The average MFWS at baseline was 1.8, 2.1, and 2.7 which was reduced to 1.1, 1.6, and 2.1 after 12 weeks of treatment with AFW, AWM and Deep Wrinkles respectively. Average grade for Physician's global assessment improved from 1, 1, and 1 at baseline to 2.1, 2.6, and 2.7 at the end of 12 weeks treatment. Patient's global assessment also showed similar grades of improved from 1, 1, and 1 at baseline to 2, 2.7, and 2.2 at the end of treatment with AFW, AWM and Deep Wrinkles respectively. There was an overall improvement in 'Quality of Life' in terms of improvement in the wrinkles at the end of 6 weeks (Grade 2.6, 2.5, 2.3) and 12 weeks (Grade 2.9, 2.9, 2.7) at the end of treatment with AFW, AWM and Deep Wrinkles respectively. The overall 'Patient Satisfaction' was found to be good at the end of 12 weeks of treatment (Grade 2.5, 2.5, 2.5) with AFW, AWM and Deep Wrinkles respectively. Of the thirty patients, 1 patient for AFW, 1 patient for AFW and 2 Patients on 'Deep Wrinkle' complained of the adverse events like burning sensation. The results of this study show that AWF for Women, AFM for Men and Deep Wrinkles (DW) have a good potential for the treatment of wrinkles.

Keywords: Topical *Mentha piperita* oil, *Cymbopogon citratus* oil, Wistar rats, Hematological and Histopathological factors, diabetes wound healing.

INTRODUCTION

Wrinkles are the clinical manifestation of 'cutaneous aging' and factors associated with wrinkles could be 'intrinsic' and 'extrinsic'. [1] Intrinsic skin aging is determined largely by genetics and occurs in spite of the individual's environment. Clinically, intrinsic skin aging manifests by signs such as increased dryness, wrinkles, and skin thinning. Photoageing is the superposition of chronoultraviolet (UV)-induced damage on intrinsic ageing and accounts for most age-associated changes in skin appearance. [2] Manifestations of photoaging include superficial and deep wrinkles, development of a leathery texture, skin roughness, atrophy and dyspigmentation.

Extrinsic skin ageing primarily arises from UV-light exposure. Approximately 80% of facial skin ageing is attributed to UV-exposure.[3] Most of the photoaging effects occur by age 20. The amount of damage to the skin caused by the sun is determined by the total amount of radiation exposure and the person's pigment protection. Changes in the epidermis caused by the sun include thinning of the epidermis and expression of epidermal lesions such as actinic keratoses, basal cell carcinomas, and squamous cell carcinomas. In the dermis, solar effects cause collagen to break down at a higher rate than seen with just chronologic aging. The dermis and hypodermis become atrophied during ageing, with a reduction of collagen,[4,5] of certain glycosaminoglycans (GAG)[6-9] and of the adipose tissue of the hypodermis.[4,10] These reductions lead to wrinkle formation. On the otherhand, elastic tissue hypertrophy produces huge amounts of elastotic material, which increases the magnitude of the wrinkles.[4,5,11-13] With the advent of solar elastosis matrix metalloproteinases are produced in large quantities.

The most critical step in the treatment of wrinkles is sun avoidance and sunscreen use. Prevention and progression of wrinkles can be achieved by usage of a broad spectrum sunscreen regularly, about

20 to 30 minutes before sun exposure in addition to maintaining the moisture balance of the skin.

Cosmetic active molecules from various sources with complementary biological properties for optimum effectiveness for effective management of wrinkles are a current trend in antiaging. With recent advances in pathophysiologic understanding of aging processes we know that hormonal profile, oxidative stress and inflammatory insults are major contributors. According to the free radical theory of ageing, reactive oxygen species (ROS), primarily arising from oxidative cell metabolism, play a major role in both chronological ageing and Photoaging.[14] Oxidative stress and inflammation in the skin can result from both normal and pathological reactions and whatever the cause, both the process has a big influence on skin ageing. There are effective ways of modulating these mechanisms with a combination of selected commercially available actives formulated in a serum. The cosmetic active molecules are derived from vegetable, marine, peptides, and biotechnological sources with complementary biological properties for optimum effectiveness.

In Photoaging process, the equilibrium between the down regulation and the up regulation of 16 certain mechanisms is lost, and that causes the physical signs of aging. This serum contains a core anti-ageing technology (Regen 16) that addresses all known major mechanisms involved in skin pigmentation. Regen-16 is a patented technology and combines major active ingredients as a base for fighting the signs of skin aging. This includes (1) Abyssine, (2) Hyaluronic Acid, (3) Bisabolol, (4) Créatine, (5) Euk-134, (6) Flavagrum, (7) Glycerin, (8) LNST, (9) Moist 24, (10) MRT EX, (11) Net DG, (12) 330 Regederme, (13) Sepilift, (14) Squalene, (15) Tyrostat, and (16) Vitamin E.[15] 'Anti-Wrinkle and Firming (AWF) for Women' is an Integral Correction Serum that contains in addition

to Regen 16 Technology, the following additional ingredients namely Neutrazen, PhytoCell Tec Alp Rose, Skin Influx, Snap 8 C, Vivendin, Willow Bark, Coenzyme Q10 and Retinol. Studies have shown that its use visibly reduces the appearance of wrinkles and fine lines, improves tone for firmer skin, lightens pores for smoother looking skin and lightens the complexion for more luminous & radiant look.

'Anti-Wrinkle and Firming (AFM) for Men' is an Integral Correction Serum that is specifically formulated for male skin addressing the anatomical and physiological differences found between male and female skin. It contains in addition to Regen 16 Technology, the following additional ingredients Juvinity, Orsirtine GL, PhytoCellTec Alp Rose, and Vivendin. Studies have shown that its use maintains and prolongs the firmness, tightness and structure of male skin.

'Deep Wrinkles' is an Integral Correction Serum that significantly reduces the appearance of deep wrinkles. In addition to Regen 16 Technology contains following additional ingredients Guanidine complex, Lupinol, PhytoCellTec Alp Rose, Tego pep-17, and Retinol cyclosystem complex.

This integrated approach to skin ageing and appearance of wrinkles was tested in Indian patients by conducting a clinical study to determine the efficacy and safety of topical 'Anti-Wrinkle and Firming (AWF) for Women', 'Anti-Wrinkle and Firming (AFM) for Men' and 'Deep Wrinkles' in the treatment of wrinkles in face and neck. The aim of the study was to assess the efficacy, safety and quality of life parameters after treatment with as Anti-Wrinkle and Firming in patients with wrinkles on face and neck.

Study Design

This was an open labelled, prospective, multi-centric study conducted in patients with wrinkles on face and neck. This was conducted in accordance to the ICH-GCP guidelines with approval from Independent Ethics Committee. Written Informed consent was obtained from these patients after a thorough explanation of the study.

Patients with wrinkles on the face and neck were included in the study. These patients agreed to restrain from prolonged exposure to the sun for the length of the study. Patients were excluded from the study if they had any history of hypersensitivity to any ingredients, were pregnant or lactating women, already applying anti-aging, skin lightening or Alpha hydroxy acids (AHA) based or retinol based cosmetics in the last 3 months, having any dermatological disorder of face or have planned for any surgical treatment of the face.

Study Drug and Treatment

Patients with Wrinkles were provided either with 'Anti-Wrinkle and Firming (AWF) for Women' or 'Anti-Wrinkle and Firming (AFM) for Men' or 'Deep Wrinkles' and were instructed to apply the formulation twice a day after the use of a cleanser for a period of 12 weeks.

All patients were instructed to apply Hydra-Seal SPF 25 (Moisturizer with Sunscreen) liberally enough to all sun-exposed areas that it forms a film when initially applied. It should be applied at least a half an hour before going out in the sun since it takes 20-30 minutes for sunscreen to be absorbed by the skin.

Study Methodology

After confirming eligibility, each of the patients was provided with Pearl Cleanser, Anti-Wrinkle And Firming (AWF) for Women or Anti-Wrinkle And Firming (AFM) for Men or Deep Wrinkles (DW) and Hydra-Seal SPF 25. The regimen of 'cleansing' with Pearl Cleanser, 'application' with Anti-Wrinkle And Firming (AWF) for Women or Anti-Wrinkle And Firming (AFM) for Men or Deep Wrinkles (DW) and 'sealing' with Hydra-Seal SPF 25 was to be followed in each of the patient for study duration of 12 weeks.

Patient assessment was done at Baseline, end of 6 weeks and 12 weeks of treatment period. At the first visit (Baseline) a detailed history was taken, examination was done and photograph of the affected facial region was taken. During the 2nd visit (end of 6

weeks) and 3rd visit (end of 12 weeks), the assessment for efficacy and safety was done.

For assessment of efficacy, Modified Fitzpatrick Wrinkle Scale (MFWS) were evaluated. In this, the Wrinkle depth is graded on a scale of 0 to 3 as follows: 0= No wrinkle. No visible wrinkle; continuous skin line; 0.5= Very shallow yet visible wrinkle; 1= Fine wrinkle. Visible wrinkle and slight indentation; 1.5= Visible wrinkle and clear indentation. <1mm wrinkle depth; 2= Moderate wrinkle. Clearly visible wrinkle, 1to2mm wrinkle depth; 2.5= Prominent and visible wrinkle. > 2mm and < 3mm wrinkle depth; 3= Deep wrinkle. Deep and furrow wrinkle; >3mm wrinkle depth. During the 2nd visit (end of 6 weeks) and 3rd visit (end of 12 weeks), the assessment for efficacy was done by comparing with the baseline photograph.

The improvement in 'Quality of Life' was assessed through a questionnaire namely, Did you notice any beneficial change in face during period of application of product?; Does your face appear more youthful now than before you started using the product?; How family, friends and people at work evaluated results? Would you like to continue the treatment?; Would you recommend the treatment to others? Was subjectively assessed by the Physician at Visit 2 and 3 and graded accordingly as Grade 1: Very Unsatisfied; Grade 2: Unsatisfied; Grade 3: Satisfied; and Grade 4: Very satisfied.

Similarly the patient rated the response through 'Patient Satisfaction Questionnaire' namely, Overall Satisfaction, Improvement in skin tone and complexion, Improvement in firmness of the skin, Moisturizing effect, Pleasant to Use and Rating as compared to previously used anti-wrinkle products (if any), as Average (Grade 1), Good (Grade 2), Very Good (Grade 3) and Excellent (Grade 4) on Visit 2 and 3.

Physician's and Patient's Global Assessment Grade for improvement in wrinkles were graded as Grade 0: Worse; Grade 1: No Change; Grade 2: Slightly Improved; Grade 3: Improved; Grade 4: Much Improved.

RESULTS

Thirty patients with fine to deep wrinkles were included in the study with 10 patients each Anti-Wrinkle And Firming (AWF) for Women or Anti-Wrinkle And Firming (AFM) for Men or Deep Wrinkles (DW), who completed 12 weeks of therapy.

Results - Anti-Wrinkle and Firming (AWF) for Women

The average MFWS (Modified Fitzpatrick Wrinkle Scale) at baseline (Visit 1) was 1.8 which was reduced to 1.4 after 6 weeks of treatment (Visit 2) and further reduced to 1.1 after 12 weeks of treatment (Visit 3), as shown in figure 1.

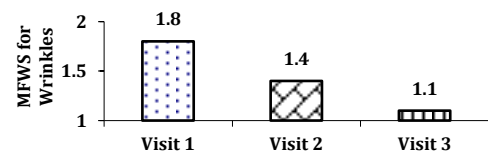


Figure 1: Average MFWS score at Visit 1 (Basal), Visit 2 and Visit 3

The Physician's and Patient's global assessment showed improvement in wrinkles at visit 2 and visit 3, as shown in figure 2. Average grade for Physician's global assessment improved from 1 at baseline to 2.1 at the end of 12 weeks treatment. Patient's global assessment also showed similar grades of improved from 1 at baseline to 2 at the end of treatment.

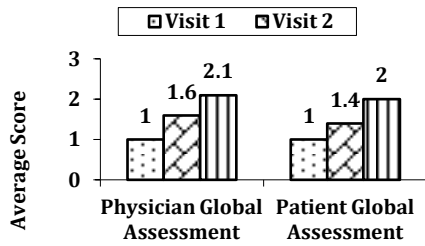


Figure 2: Physician and Patient global assessment at each visit

There was an overall improvement in 'Quality of Life' in terms of improvement in the wrinkles at the end of 6 weeks (Grade 2.6) and 12 weeks (Grade 2.9), as shown in figure 3. All the patients responded that they would like to continue the treatment and would recommend the treatment to others. The overall 'Patient Satisfaction' was found to be good at the end of 6 weeks (Grade 2) and 12 weeks of treatment (Grade 2.5), as shown in figure 3

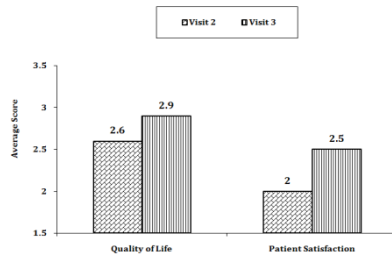


Figure 3: Quality of Life & Patient Satisfaction Questionnaire at Visit 2 and Visit 3



Figure 4: photographic assessment for Anti-Wrinkle and irming (AWF) for Women at Visit 1, Visit 2 and Visit 3

Results - Anti-Wrinkle and Firming (AFM) for Men

The average MFWS (Modified Fitzpatrick Wrinkle Scale) at baseline (Visit 1) was 2.1 which was reduced to 2 after 6 weeks of treatment (Visit 2) and further reduced to 1.6 after 12 weeks of treatment (Visit 3), as shown in figure 4.

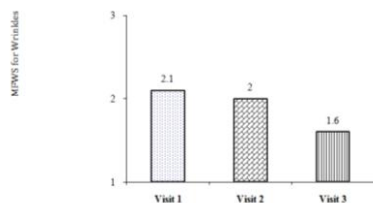


Figure4: Average MFWS score at Visit1(Basal),Visit 2 and Visit 3

The Physician's and Patient's global assessment showed improvement in wrinkles at visit 2 and visit 3, as shown in figure 5. Average grade for Physician's global assessment improved from 1 at baseline to 2.6 at the end of 12 weeks treatment. Patient's global assessment also showed similar grades of improved from 1 at baseline to 2.7 at the end of treatment.

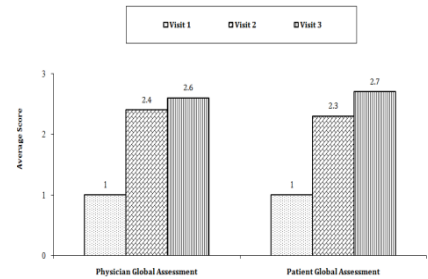


Figure 5: Physician and Patient global assessment at each visit

There was an overall improvement in 'Quality of Life' in terms of improvement in the wrinkles at the end of 6 weeks (Grade 2.5) and 12 weeks (Grade 2.9), as shown in figure 6. All the patients responded that they would like to continue the treatment and would recommend the treatment to others. The overall 'Patient Satisfaction' was found to be good at the end of 6 weeks (Grade 2) and 12 weeks of treatment (Grade 2.5), as shown in figure 6.

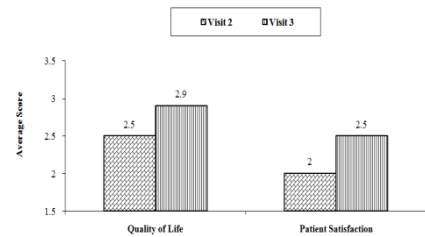


Figure 6: Quality of Life & Patient Satisfaction Questionnaire at Visit 2 and Visit 3



Figure 7: photographic assessment for Anti-Wrinkle and Firming (AFM) for Men at Visit 1, Visit 2 and Visit 3

One patient for Anti-Wrinkle and Firming (AFM) for Men dropped out of study due to adverse event.

Results - Deep Wrinkles

The average MFWS (Modified Fitzpatrick Wrinkle Scale) at baseline (Visit 1) was 2.7 which was reduced to 2.6 after 6 weeks of treatment (Visit 2) and further reduced to 2.1 after 12 weeks of treatment (Visit 3), as shown in figure 8.

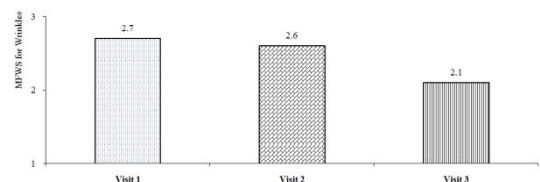


Figure8: Average MFWS score at Visit 1(Basal),Visit 2and Visit 3

The Physician's and Patient's global assessment showed improvement in wrinkles at visit 2 and visit 3, as shown in figure 9. Average grade for Physician's global assessment improved from 1 at baseline to 2.7 at the end of 12 weeks treatment. While Patient's

global assessment also showed grades of improved from 1 at baseline to 2.2 at the end of treatment.

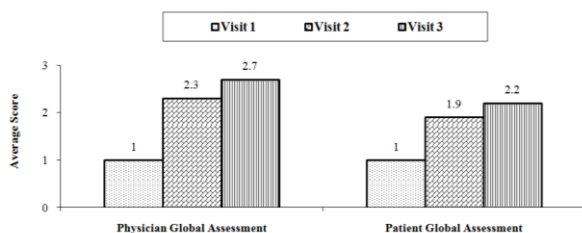


Figure 9: Physician and Patient global assessment at each visit

There was an overall improvement in 'Quality of Life' in terms of improvement in the wrinkles at the end of 6 weeks (Grade 2.3) and 12 weeks (Grade 2.7), as shown in figure 10. All the patients responded that they would like to continue the treatment and would recommend the treatment to others. The overall 'Patient Satisfaction' was found to be good at the end of 6 weeks (Grade 2.1) and 12 weeks of treatment (Grade 2.5), as shown in figure 10.

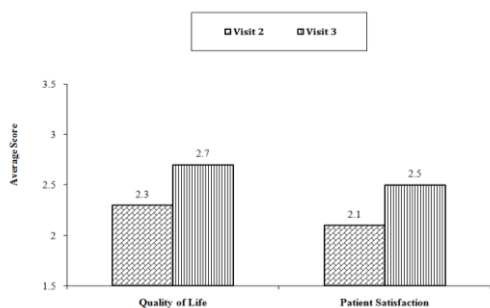


Figure 10: Quality of Life & Patient Satisfaction Questionnaire at Visit 2 and Visit 3



Figure 11: photographic assessment for Anti-Wrinkle and Firming (AFM) for Men at Visit 1, Visit 2 and Visit 3

Two patients in Deep Wrinkles (DW) group were lost in follow-up.

Assessment of Adverse Events

Of the thirty patients, one patient for Anti-Wrinkle and Firming (AFW) for Women complained of acne form eruptions and the one patient complained of burning sensation. One patient of Anti-Wrinkle and Firming (AFM) for Men showed papules on hair line and other patient was dropped out of study due to extreme irritation and dryness. Two patients on Deep Wrinkle therapy showed burning and tingling sensation.

DISCUSSION

The recent introductions of Anti-Wrinkle and Firming (AWF) for Women, Anti-Wrinkle and Firming (AFM) for Men and Deep Wrinkles (DW) are a new therapeutic approach in the management of photoaging. All these three formulation contains active ingredient base with Regen-16 produced through patented technology. Regen 16 is a combination of 16 different ingredients along with other active agents targeting various probable causes of photoaging.¹⁵

A preliminary study was conducted by independent testing laboratory to evaluate anti wrinkle potential of the serum. The results demonstrated that the integral approach improved the appearance of fine lines and wrinkle as well as the tone, texture, consistency and general appearance of the skin of 20 women aged 35-62 years.¹⁵

In our study it was noted that, Anti-Wrinkle and Firming (AWF) for Women or Anti-Wrinkle and Firming (AFM) for Men or Deep Wrinkles (DW) appears to be effective and safer alternative with 3 months of therapy. In terms of efficacy, there was a mild to moderate reduction in the MFWS score for the treatment groups, brought about with 12 weeks of treatment.

One of the reason for Anti-Wrinkle And Firming (AWF) for Women or Anti-Wrinkle And Firming (AFM) for Men or Deep Wrinkles (DW) showing better results could be due to use of various combination of ingredients for an extended spectrum of activity interfering with the different steps of photoaging. The association of various ingredients with different mechanisms of action appears to be a useful strategy to improve clinical efficacy, and the risk of adverse effects as in the present study.

CONCLUSION

Great advances have been made to understand photoaging and the processes underlying photoaging in the last decade. The trend toward integration of multiple actives covering all mechanistic aspects of skin ageing process. This research has led to development of safer and more effective anti-aging products. The results of this study show that Anti-Wrinkle and Firming (AWF) for Women, Anti-Wrinkle and Firming (AFM) for Men and Deep Wrinkles (DW) have a good potential for treatment of wrinkles. The better results could be because of targeting different steps of photoaging which improves clinical efficacy with better safety profile.

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