



A Randomized, Double-Blind, Single Centre, Placebo-Controlled Clinical Study to Assess the Efficacy and Safety of Advanced Senolytic Skin Rejuvenation Cream in Reducing Skin Aging, Dry Skin, Melasma, Wrinkles, Crow's Feet and Fine Lines

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Abstract

Background: Skin aging is a natural process influenced by both internal and external factors. Intrinsic factors like genetics and hormonal changes, along with extrinsic factors such as environmental stressors, contribute to changes in skin appearance and function. With aging, collagen and elastin production declines, leading to wrinkles, fine lines, and sagging skin. The skin becomes drier, thinner, and vulnerable to external damage. The objective of this study is to evaluate the efficacy and safety of "Advanced Senolytic Skin Rejuvenation Cream" in reducing Skin Aging, Dry Skin, Melasma, Wrinkles, Crow's Feet, Fine Lines. **Material & Methods:** The study was conducted to assess the efficacy of the investigational product in reducing Anti-aging signs, Dryness, Melasma, Wrinkles, Crow's Feet and Fine Lines. Digital images captured by a DSLR camera were utilized for evaluation. The assessment involved the use of the Fitzpatrick Wrinkle and Elastosis Scale and the MelasQoL Questionnaire. Safety was measured through AEs/SAEs reported during the study. **Results:** It was observed that the test product shows better primary and secondary efficacy result with respect to the placebo group. There were 68.34% reduction in aging signs, 69.27% improvement in melasma and 54.11% reduction in wrinkles, crow's feet and fine lines recorded for the test product. No SAE was reported during the study conduct. **Conclusion:** Test product indicated better efficacy results with no linked AEs compared to the placebo group. The advanced skin rejuvenation cream showed a significant improvement in aging signs compared to the placebo cream at week 4 ($p < 0.05$) and week 12 ($p < 0.001$).

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INTRODUCTION

Skin aging is a natural process that is accelerated by a variety of environmental and intrinsic factors, such as ultraviolet radiation, pollution, and hormonal changes.^[1] Creams are used for skin for a variety of reasons, including moisturizing, protecting, and treating various skin conditions. The skin is the body's largest organ and serves as a barrier between the body

and the outside environment. As such, it is exposed to a wide range of environmental factors, such as sun exposure, pollution, and harsh weather conditions, which can cause it to become dry, irritated, or damaged. Creams can be used to address many of the common signs of aging and skin concerns & can be used to address intrinsic and extrinsic skin aging, dry



skin, melasma, wrinkles, crow's feet, fine lines, and age spots.

Aging cream, also known as anti-aging cream, is a skincare product designed to address the signs of aging on the skin. As we age, our skin undergoes changes that result in wrinkles, fine lines, age spots, and a loss of firmness and elasticity. These signs of aging can be caused by a variety of factors, including genetics, sun damage, and lifestyle choices such as smoking and poor diet. Aging creams typically contain ingredients that aim to reduce the appearance of these signs of aging and improve the overall health and appearance of the skin. These ingredients can include antioxidants, peptides, retinol, hyaluronic acid, and other nourishing and moisturizing agents. For example, antioxidants can help protect the skin from free radicals that can cause damage, while peptides can help stimulate collagen production, which can improve skin elasticity and firmness. Retinol, another common ingredient in aging creams, can help reduce the presence of fine lines and folds by increasing cell turnover and promoting collagen production. Aging creams can be used as part of a daily skincare routine to help maintain a youthful, healthy complexion. It is important to note that while aging creams can be effective, they cannot reverse the aging process entirely and results may vary based on individual skin types and concerns.

The cream is used to address intrinsic and extrinsic skin aging, dry skin, melasma, wrinkles, crow's feet, fine lines, and age spots. As Intrinsic aging refers to the natural aging process that occurs as we get older, while extrinsic aging is caused by external factors such as sun exposure, smoking, and pollution.^[12] Aging creams can contain

ingredients such as retinol, antioxidants, and peptides that can help to reduce the appearance of fine lines and wrinkles, improve skin elasticity and firmness, and protect the skin from further damage. Dry skin can be treated with creams that contain emollients and humectants, which help to hydrate and moisturize the skin.^[3] These ingredients can include glycerin, hyaluronic acid, and shea butter, among others. Melasma is a condition that causes dark patches on the skin and can be treated with creams that contain ingredients such as hydroquinone, retinoids, and vitamin C, which can help to lighten and brighten the skin.^[4] Cream can also contain ingredients such as alpha-hydroxy acids (AHAs) and beta-hydroxy acids (BHAs) that can help to exfoliate the skin and reduce the appearance of age spots and discoloration. Age Spots: In this, it contains hydroquinone, kojic acid, or other skin lightening agents can help to reduce the appearance of age spots on the skin.^[5] Finally, this study product that contain peptides, antioxidants, and other nourishing ingredients can help to reduce the appearance of crow's feet, fine lines, and other signs of aging around the eyes. Here are 5 Boosters of Elastin, Collagen and ECM namely Ascorbic Acid, Glucoside – AA2G,^[6,7] Resveratrol,^[8] Dill Seed Extract,^[9,10] Coenzyme Q10,^[11] and Tetra Hydro Curcumin-THC.^[12] Elastin, collagen, and extracellular matrix (ECM) are important components of the skin that contribute to its elasticity, firmness, and overall appearance.^[13] Aging creams often contain ingredients that can boost the production of these proteins in the skin to help reduce the signs of aging. A) Retinoids: Retinoids, such as retinol, are derivatives of vitamin A that can stimulate collagen production in the skin.^[17] They can also help to



improve skin texture, reduce the appearance of fine lines and wrinkles, and increase skin thickness. B) Collagen-Peptides: Peptides are short chains of amino acids that can stimulate collagen production and improve skin properties such as elasticity, skin moisture, and transepidermal water loss. They can also help to reduce the appearance of skin aging, dryness, fine lines and wrinkles.^[14] C) Vitamin C,^[15] Vitamin C is a powerful antioxidant that can help to protect the skin from free radical damage. It can also stimulate collagen production and improve skin texture and tone. D) Hyaluronic acid,^[16] Hyaluronic acid is a natural substance found in the skin that can help to retain moisture and improve skin elasticity. It can also help to reduce the appearance of fine lines and wrinkles. E) Growth factors: Growth factors are proteins that can stimulate cell growth and division.^[18] They can help to promote the production of collagen and other ECM components in the skin, leading to improved skin texture, elasticity, and overall appearance.

MATERIAL AND METHODS

This was a randomized, double-blind, single centre, placebo-controlled study to Assess the efficacy and safety of an advanced senolytic skin rejuvenation cream for improving skin texture, hydration, and reducing the appearance of skin aging signs. The study was approved by the institutional review board and it was initiated after the written EC approval. After approving the criteria, 100 participants were selected for the study. Subjects were the aged between 30 and 60 years were recruited from a dermatology clinic. All participants provided written informed consent before participating in the study and it was conducted

in accordance with the ethical principles of the Declaration of Helsinki.

Participants were excluded if they had any skin conditions that could interfere with the study results or if they were allergic to any of the ingredients in the creams. And they were randomly assigned to either the intervention or placebo group using a computer-generated randomization schedule. While conducting the study written instructions were provided to them for applying the cream correctly and consistently. They were instructed to wash their face and hands before apply cream on specific areas on face with soft hand no extra force were applied, cream would be applied in circular motion. The intervention group received the advanced senolytic skin rejuvenation cream, while the placebo group received a cream with similar texture, color, and scent, but without the active ingredients. Both groups applied the creams twice daily for 12 weeks.

By providing clear instructions and ensuring that participants are applying the cream correctly and consistently, to obtain accurate and reliable data on the effectiveness of the test product in clinical study. The Outcome were assessed at baseline, week 2, week 4, week 8 and week 12 of the study.

As we know, skin elasticity plays a crucial role in the formation and appearance of crow's feet, wrinkles, and fine lines. The severity of crow's feet, wrinkles and fine lines was assessed through the Fitzpatrick Wrinkle and Elastosis Scale which used to assess wrinkles and elastosis (a loss of skin elasticity).

Melasma is a common skin condition characterized by hyperpigmentation or dark



spots on the skin, usually on the face. To evaluate the efficacy of test product over the Melasma reduction Participate responses were collected over Melasma Quality of Life Questionnaire. Anti-aging signs were measured via Digital camera imaging, with DSLR camera due to its high resolution, manual controls, customizable lenses, and image stabilization features to obtain accurate and reliable data on the effectiveness of anti-aging treatments on Baseline, visit-3 and visit-5 (EOS).

RESULTS

100 subjects were enrolled in this clinical study, where they lie between the age group of 30-60, males and females in good physical shape. The test product was well accepted by all participants, with no significant adverse reactions reported during the study period.

Efficacy Endpoint

Anti-aging Sign

Digital camera imaging was used to assess anti-aging signs in the study participants. High-resolution images of the face were captured using the digital single-lens reflex (DSLR) camera with consistent lighting conditions, a neutral background, and a standardized pose. Images were taken at baseline visit 03 and at the end of the study to evaluate changes in anti-aging signs over time. The camera was set up in a standardized position, with a fixed distance between the subject's face and the lens. The lighting conditions were also standardized, with the use of a soft box to ensure even illumination across the face. At each visit, three images were captured: one frontal view, and two oblique views at 45-degree angles. The images were saved in RAW format for later

analysis. Participants were instructed to avoid wearing makeup or other skincare products on the day of imaging to minimize any confounding effects.

Two experienced dermatologists were recruited to evaluate the digital images captured at each study visit to assess the anti-aging signs of the participants. The dermatologists were blinded to the treatment group of the participants and assessed the images using a standardized scoring system. To ensure consistency in scoring, the dermatologists underwent a training session prior to the start of the study in which they were shown a set of digital images with known anti-aging signs and instructed on how to score each sign. The dermatologists also met regularly throughout the study to discuss any discrepancies in scoring and to ensure consistency in their assessments and they were satisfied at 1 point.

The scoring system consisted on a 5-point likert severity scale to evaluate the severity of various anti-aging signs. The dermatologists evaluated each image for the presence and severity of these signs and provided a score ranging from 1 to 5 for each sign. A score of 1 indicated no evidence of the sign, while a score of 5 indicated severe presence of the sign.

The data collected by the dermatologists were entered into a database and analyzed using appropriate statistical methods to determine the efficacy of the treatment in reducing anti-aging signs.

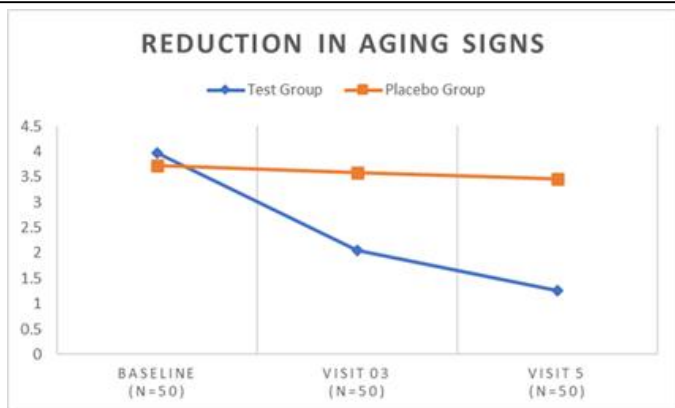


Figure 1: Reduction in aging signs over the 5-point likert scale from baseline to end of the study visit:

The subjects were divided equally in test group and placebo group. Initially at baseline, study population falls b/w the criteria of major to moderate anti-aging signs in both groups, but the difference was started shown in v-3 and v-5. Table 01 clearly shows that there were 68.34 % reduction in aging signs for the test product, which indicate the change from baseline to EOS visit while the reduction in placebo was nominal.

Skin Dryness:

Skin dryness was assessed through visual analog scale (VAS). This scale typically ranges from 0 to 10, with 0 indicating no dryness and 10 indicating severe dryness. Table 02 clearly represents that test group marked a visible improvement in skin dryness at visit 05 in compared to baseline visit.

Skin Elasticity:

Reduction in the appearance of wrinkles, crow feet and/or fine lines was evaluated by skin elasticity which was assessed by Fitzpatrick Wrinkle and Elastosis Scale, that is a validated

and widely used tool in dermatology research. The scale assessed skin change based on both the degree of wrinkle formation and the extent of elastosis, or damage to the elastic fibers in the skin over 4-point scale from 0 (No wrinkles or elastosis) to 3 (Severe wrinkles and/or elastosis).

The table 03 represented the transformation from baseline to each evaluated visit. The changes in the scores were then analyzed statistically to determine the effectiveness of the treatment. Major improvement in skin elasticity were shown in visit-5 in test group while placebo group shown the nominal improvement. There were 54.11% improvement in skin elasticity for test product. Satisfactory changes shown in below [Figure 2].

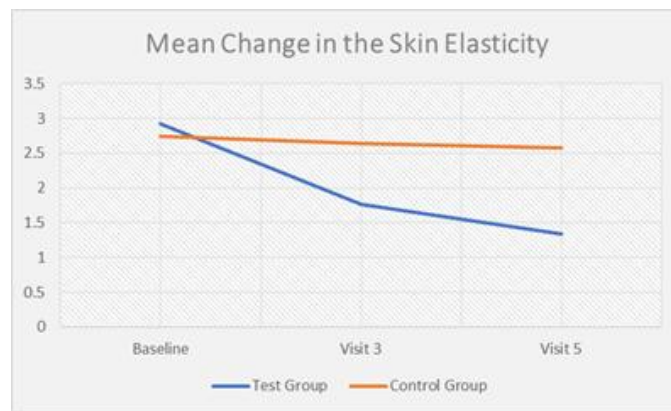


Figure 2: Mean change in the skin elasticity

Melasma:

To evaluate the reduction in severity of melasma, MelasQoL Questionnaire was used that consist 10 questions related to the emotional, social, and functional aspects of life that may be affected by melasma. Responses of the participants were collected on a scale of 1 (not bothered at all) to 7 (bothered all the time),

that represents/grade their quality of life with respect to melasma. Total MelasQoL score ranges from 7 to 70, with higher scores indicating worse quality of life. At the baseline visit, subjects scored their quality of life to ~60. Table 04 showed that at the end of the visit, placebo group rated no change while test group rated their quality of life at 18.28 with 69.27% improvement.

Safety endpoints:

There was only one incident of skin irritation with mild severity was reported in placebo group. Further, no Serious Adverse Event was noted down during conducted the study.

Table 1: Reduction in aging signs over the 5-point likert scale from baseline to end of the study visit.

	Baseline (N=50)	Visit 03 (N=50)	Visit 5 (N=50)	Change from Baseline to EOS Visit (%)	P- value
Test Group	3.98	2.06	1.26	2.72 (68.34%)	<0.001
Placebo Group	3.72	3.58	3.46	0.26 (6.99%)	<0.001

Table 2: Mean change in the skin dryness.

	Baseline	Visit 3	Visit 5	Change from Baseline to EOS Visit
Test Group	7.58	6.52	4.94	2.64 (34.83%)
Control Group	7.68	6.94	6.2	1.48 (19.27%)

Table 3: Mean change in the skin elasticity

	Baseline	Visit 3	Visit 5	Change from Baseline to EOS Visit
Test Group	2.92	1.76	1.34	1.58 (54.11%)
Control Group	2.74	2.64	2.58	0.16 (5.84%)

Table 4: Mean responses over MelasQoL Questionnaire

SN		Placebo		Test Product	
		Baseline	Visit 05	Baseline	Visit 05
1	The appearance of your skin condition	5.88	5.48	5.98	2.04
2	Frustration about your skin condition	6.02	6	6.08	1.76
3	Embarrassment about your skin condition	6	5.52	5.9	1.84
4	Feeling depressed about your skin condition	5.98	5.78	6.08	1.9
5	The effects of your skin condition on your interactions with other people (e.g. interactions with family, friends, close relationship, etc.)	6.02	5.82	6.04	1.86
6	The effects of your skin condition on your desire to be with people	5.8	5.52	5.82	1.82
7	Your skin condition making it hard to show affection	5.94	5.84	5.92	1.78

8	Skin discoloration make you feel unattractive to others	5.86	5.72	5.76	1.74
9	Skin discoloration making you feel less vital or productive	5.92	5.6	6.04	1.94
10	Skin discoloration affecting your sense of freedom	6.04	5.9	5.88	1.6
	Total Score	59.46	57.18	59.5	18.28

DISCUSSION & CONCLUSIONS

As we grow older, our skin loses its vibrant appearance and begins to wrinkle. Age-associated wrinkles arise primarily from the loss of structural proteins called collagens. Skin aging refers to the gradual changes that occur in the skin as a natural part of the aging process. It is characterized by a wide range of clinical signs, including dryness, wrinkles, hyperpigmentation, and loss of elasticity, which can have a significant impact on the quality of life of affected individuals. The development of effective and safe interventions for skin aging is therefore a major area of research in dermatology. In recent years, senolytic agents have emerged as a promising class of compounds for skin rejuvenation, based on their ability to selectively eliminate senescent cells that contribute to tissue dysfunction and inflammation. The aim of this study was to evaluate the efficacy and safety of an Advanced

Senolytic Skin Rejuvenation Cream in improving the clinical signs of skin aging, including dryness, melasma, wrinkles, crow's feet, fine lines, and age spots, in a randomized, double-blind, placebo-controlled clinical trial. This study concluded the reduction in anti-aging signs, decline in the appearance of wrinkles, crow feet and/or fine lines, reduction in severity of melisma. The advanced skin rejuvenation cream showed a significant improvement in skin texture, hydration, wrinkles, age spots, crow's feet, fine lines, and melasma as compared to the placebo cream over the visits. advanced skin rejuvenation cream resulted 68.34% reduction in aging signs and 54.11% and 69.27% improvement in skin elasticity (wrinkles, crow's feet, fine lines) and melasma respectively. No serious adverse events were reported, and a single incidence of mild adverse event was reported in placebo group.

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