



Review Article

Recent evolutions in development of Antiaging Cosmetics and Pharmaceuticals: A Review

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ABSTRACT

Background: Anti-aging formulations in the pharmaceutical industry represent a burgeoning field aimed at addressing the physiological changes associated with aging. This abstract explores the key aspects of these formulations, emphasizing their significance in promoting healthier aging. These formulations typically incorporate a myriad of compounds, including antioxidants, peptides, and retinoid, known for their potential to counteract oxidative stress and stimulate collagen production. The abstract delves into the rationale behind these choices, elucidating their mechanisms of action and synergistic effects. Moreover, the abstract highlights the innovative delivery systems employed to enhance the efficacy of anti-aging formulations, such as nanoparticle encapsulation and transdermal patches. The discussion encompasses how these advancements contribute to improved bioavailability and sustained release, optimizing therapeutic outcomes. It also touches upon the regulatory landscape governing anti-aging pharmaceuticals, underscoring the need for rigorous testing to ensure safety and efficacy. It addresses ongoing research endeavors, including the exploration of novel bioactive compounds and personalized approaches based on genetic factors. **Conclusion:** In conclusion, the abstract synthesizes the current landscape of anti-aging formulations in the pharmaceutical industry, emphasizing their multifaceted approach to mitigating the effects of aging. The integration of cutting-edge technologies and a deeper understanding of aging processes position these formulations as promising interventions in promoting longevity and maintaining overall well-being.

INTRODUCTION

The three layers of the skin namely epidermis, dermis, hypodermis; form an effective barrier to the external environment, allow the transmission of sensory information, and serve a significant role

in maintaining homeostasis. The dynamic epidermis continually produces a protective outer layer of corneocytes as cells undergo the process of keratinization and thermal differentiation. Collagen and elastic filaments of the dermal layer

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provide the underlying tensile strength of the skin, whereas the layer of subcutaneous fat provides a store of energy for the body [1]. Exogenous or extrinsic and endogenous or intrinsic elements work together to influence the complicated biological process of skin aging. Since the appearance and condition of the skin are seen to be key indicators of a person's general "well-being" and sense of their own health, several anti-aging

techniques have been developed in recent years [2]. Between 2022 and 2027, the global anti-aging market is projected to expand at a compound annual growth rate (CAGR) of about 6.7%. The market is expected to grow from its estimated 63 billion US dollars in 2021 to 93 billion US dollars by 2027 [34].

Aging:

Sr. No.	Types of Aging	Intrinsic	Extrinsic
a.	Factors involved	Collagen & elastin's production reduces resulting in collapse of dermal structure.	Cigarette smoke, pollution, UV radiations exposure.
b.	Results	Dry; flaky; saggy skin, fine lines, wrinkles.	Hyperpigmentation, leathery appearance, dry skin, deep wrinkles
c.	Synonym	Chronological aging [10]	Premature/ photoaging [11]

Classic skin aging theories:

- Free radical and oxidative stress theory
- Inflammation theory
- Photoaging theory
- Non-enzymatic glycosyl theory [3]

Free Radical and Oxidative Stress Theory:

In 1956, Denham Harman discovered that Reactive Oxygen Species (ROS) stockpile over the period of time further contributing to aging [4]. After research of 16 years, Harman himself explained mitochondria as an actual base of ROS being the basis for free radical aging concept [5].

Inflammation Theory:

Many Senescence Associated Secretory Phenotypes (SASP) are secreted by senescent fibroblasts and keratinocytes at the skin's surface, such as MMPs, IL-1, IL-6, TNF- α , and other proinflammatory cytokines. By encouraging the generation of Reactive Oxygen Species (ROS) and triggering the ATM (Ataxia Telangiectasia Mutated)/p53/p21-signaling

pathway, these pro-inflammatory cytokines cause the senescence of skin cells [6]. Simultaneously, as skin cells become inflammatory, this will trigger a greater production of MMPs, which will break down collagen and cause the skin cells to relax and wrinkle [7], [8].

Photoaging Theory:

The increase exposure to the ultraviolet radiations results in the increased production of the ROS and high MMPs levels. Henceforth, leading to pigmentation and wrinkles on skin [9].

Non-Enzymatic Glycosyl Theory:

The non-enzymatic reaction between the free reducing sugar moieties and free amino groups of proteins, DNA and lipids produces Advanced Glycation End Products (AGEs) which is irreversible Maillard reaction. Further accumulation of AGEs causes imbalanced cellular homeostasis and protein morphism resulting in darkening of skin and aging [10][11][12].

METHODOLOGY:

Table 1: Marketed antiaging formulations with brand name & ingredients.

Sr. No.	Brand name/ Type	Ingredients
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1	Garnier Wrinkle Lift Antiaging Cream (Semi-synthetic)	Water, Dimethicone, Glycerine, Octyldodecanol, Stearic Acid, Palmitic Acid, Peg-100 Stearate, Glyceryl Stearate, Palm Oil, Isohexadecane, Cetyl Alcohol, Soybean Protein, Eryngium Maritimum Extract, Shorea Robusta Seed Butter, Malus Domestica Fruit Cell Culture Extract, Shea Butter, Tin Oxide, C13-14 Isoparaffin, PEG-20 Stearate, Beeswax, Potassium Cetyl Phosphate, Sodium Cocoyl Glutamate, Sodium Hydroxide, Myristic Acid, Poloxamer 338, Disodium EDTA, Hydrogenated Polyisobutene, Hydrolyzed Rice Protein, Capryloyl Salicylic Acid, Caprylyl Glycol, Citric Acid, Laureth-7, Xanthan Gum, Pentylene Glycol, Ethylhexylglycerin, Polyacrylamide, Retinyl Palmitate, Tocopherol, Pentaerythrityl Tetra-Di-T-Butyl Hydroxyhydrocinnamate, Potassium Sorbate, Methylparaben, Sodium Benzoate, Ci 77891 / Titanium Dioxide, Mica, Linalool, Benzyl Alcohol, Fragrance[13].
2	Cosrx Retinol 0.1 Cream (Semi-synthetic)	Water, Caprylic/Capric Triglyceride, Propanediol, Glycerine, Tocopheryl Acetate, Cetearyl Alcohol, Trehalose, Panthenol, Butyrospermum Parkii (Shea) Butter, Glycine Soja (Soybean) Oil, Ammonium Acryloyldimethyltaurate/VP Copolymer, Dimethicone, Glyceryl Polymethacrylate, Helianthus Annuus (Sunflower) Seed Oil, Polyglyceryl-10 Stearate, Hydrogenated Lecithin, Hydroxyethyl Acrylate/Sodium Acryloyl dimethyl Taurate Copolymer, Carbomer, Tromethamine, Glyceryl Stearate, Polysilicone-11, Sodium Sulphite, Tocopherol, Daucus Carota Sativa (Carrot) Root Extract, Retinol(0.1%), Allantoin, Glyceryl Caprylate, Oryza Sativa (Rice) Bran Wax, Tocotrienols, Stearic Acid, Polyglyceryl-3 Methyl glucose Distearate, Palmitic Acid, Disodium EDTA, Ethylhexylglycerin, Adenosine, Sorbitan Isostearate, Elaeis Guineensis (Palm) Oil, BHT, Beta-Carotene, Myristic Acid, Lauric Acid, Ascorbic Acid, Limnanthes Alba (Meadowfoam) Seed Oil, 3-O-Ethyl Ascorbic Acid, Glutathione, Sodium Hyaluronate, 1,2-Hexanediol, Hydrolyzed Hyaluronic Acid, Sodium Hyaluronate Crosspolymer, Hyaluronic Acid, Sodium Acetylated Hyaluronate [14].
3	Age-Defining Ritual (Natural)	Kashmiri saffron, pure cow's ghee, gold Bhasma, glycerin, kokum seed butter, aloe vera [15].
4	Glopetra Vitamin-C 20% Serum (Semi-synthetic)	24k Gold Dust, Ethyl Ascorbic Acid, Hyaluronic acid, glutathione & vitamin- E acetate, Glycerin, Caprylic Capric Triglyceride, Dimethicone 350, Propylene glycol, Triethanolamine & Perfume [16].
5	The Derma's 0.3% Retinol Face Serum (Semi-synthetic)	Behenyl, C Serum, Capric, Caprylic, Cyclopentasiloxane, Dimethicone, Ethylhexyl, Polysorbate 20, Retinol, Triglyceride, Vitamin C [17].
6	Himalaya Anti-Wrinkle Cream (Natural)	Aloe Vera, Grape [18].
7	Clinique Smart Clinical Repair Wrinkle Serum (Semi-synthetic)	Acetyl Hexapeptide, Algae, Caffeine, Caprylyl Glycol, Citric Acid, Hexapeptide, Hyaluronic Acid, Isohexadecane, Mineral Oil, Neuropeptide, Palmitoyl, Polysorbate 20, Retinol, Squalane Oil, Tocopheryl Acetate, Vitamin A, Vitamin E [19].
8	Lakme Absolute Youth Infinity Serum (Semi-synthetic)	89% Pure Pro Retinol C complex, Vitamin A, Pro Collagen boosters [20].

9	Lotus Bakuchiol Advanced Antiaging Duo (Semi-synthetic)	Bakuchiol, Retinol [21].
10	Swiss Beauty Antiaging Elixir Serum (Semi-synthetic)	Water, butylene glycol, simmondsia, chinensis (jojoba) seed oil, trehalose, arbutin, sorbitan stearate, sucrose coclate, cetearyl alcohol, panthenol, allantoin, olea europaea (olive) fruit oil, madecassoside, water, houttuynia cordata extract, achillea millefolium flower extract, artemisia princeps leaf extract, xanthan gum, carnosine, sodium hyaluronate, methylparaben, ethylhexylglycerin, caprylyl glycol, perfume [22].

The above mentioned as some of the marketed formulations used widely for their efficient and safe results. Natural, semisynthetic as well as synthetic anti-aging products are used by the population. Water, retinol, vitamin-C, vitamin-E, vitamin-A, hyaluronic acid, glycerin, and collagen boosters are predominantly used as constituents for the preparation purpose.

Table 2: Research articles with results/conclusion.

Sr. No.	Title	Results/Conclusion
1	Anti-aging and Sunscreens: Paradigm Shift in Cosmetics	Over exposure to the sunrays leading to skin disorders. Henceforth, sunscreens are developed in different dosage forms such as oral pills, topical nanoparticle formulation. Meanwhile, use of cyanobacteria-a biological compound which has better efficacy in protecting skin from UV radiations [23].
2	Formulation and evaluation of Skin anti-aging nano cream containing Canola oil	Use of Canola oil in nano cream preparations show higher anti-aging activity when compared with the cream formulations having Canola oil [24].
3	All- natural' anti-wrinkle emulsion serum with <i>Acmella oleracea</i> extract: A design of experiments (DoE) formulation approach, rheology, and in vivo skin performance/efficacy evaluation	<i>Acmella oleracea</i> natural extract loaded emulsion serum found to be with promising potential and efficacy as antiaging formulation [25].
4	Skin anti-aging strategies	Extrinsic aging is avoidable, whereas natural aging is genetically set. In addition to trying to remove signs of aging from the skin cosmetically, aesthetic dermatology should also play a major role in preventing, regenerating, and postponing skin aging by combining knowledge of potential local and systemic therapy, instrumental devices, and invasive procedures. This will fill a research gap and become a major area of focus for aging studies [2].
5	Potential of natural products as drug leads possessing antioxidant and anti-aging properties	The significant impact of external conditions on the amounts and types of existing secondary metabolites, employing naturally occurring herbal items during research topic and storage necessitates the use of numerous safeguards. Therefore, to ensure the actions of the botanical medications under evaluation, thorough

		metabolic profiling and standardization should be carried out. In order to further solidify the presumed biological activities and their suitability for processing as pharmaceutical dosage forms, preclinical and clinical research should be conducted in conjunction with both isolated chemicals and botanical medications. Additionally, toxicity, pharmacokinetics, and pharmacodynamics [26].
6	Hyaluronan and the process of aging in skin	The biological aspect of Hyaluronic acid and its metabolic cycles are in their infancy. The enzymatic steps that constitute extracellular and intracellular Hyaluronic acid cycles are beginning to be sorted out [27].
7	Recent advances in anti-aging medicine	In places where the population is getting older, especially in wealthy nations, anti-aging medicine is a rapidly expanding profession. classifies the various anti-aging therapies that are now available based on how they work. CRM refers to substances that mimic the effects of calorie restriction; examples of these are resveratrol, which activates the sirtuin pathway, peganol, which inhibits the GH/IGF-1 axis, and metformin, which activates AMPK. In the aged, hormone replacement therapy (HRT) has been extensively utilized to ameliorate symptoms related to frailty, body composition, cardiometabolic disorders, neurodegenerative diseases, and overall quality of life. Hormone replacement therapy includes estrogen, progesterone, testosterone, and DHEA. HRT should be taken cautiously since it raises the risk of thromboembolism and several cancers. The makeup of a healthy gut microbiota using probiotics and prebiotics [28].
8	Trends in the Use of Botanicals in Anti-Aging Cosmetics	Between 2011 and 2018, the percentage of botanical preparations in anti-aging product formulation grew. <i>Vitis vinifera</i> , <i>Butyrospermum parkii</i> , and <i>Glycinesoja</i> have held the top three spots over this time. These three plant species have demonstrated efficacy as anti-aging active components, as have <i>Theobroma cacao</i> and <i>Glycyrrhiza glabra</i> . The efficacy of these botanical preparations has been demonstrated both in vitro and in vivo, and they stand out for their content in substances with interest for anti-aging cosmetics. It is remarkable that polyphenols, mostly flavonoids but also stilbenes, are included in all these formulations. The most commonly occurring flavonoid family among the top 10 botanical preparations was flavan-3-ols, which was followed by proanthocyanidins, anthocyanins, flavanols, isoflavones, and tannins. Conversely, there is insufficient or no data to support the use of certain botanical species, notably <i>Simmondsia chinensis</i> , <i>Helianthus annuus</i> , <i>Calendula officinalis</i> , <i>Limnanthes alba</i> , and <i>Acacia decurrens</i> , as anti-aging actives [29].
9	Antiaging agents: safe interventions to slow aging and healthy life span extension	Many antiaging compounds target the calorie-restriction mimetic, autophagy induction, and putative enhancement of cell regeneration, epigenetic modulation of gene activity such as inhibition of histone deacetylases and DNA methyltransferases, are under development. It appears evident that the exploration of new targets for these antiaging agents based on biogerontological research provides an incredible opportunity for the healthcare and pharmaceutical industries. The present review focus on the properties of slow aging and healthy life span extension of natural

		products from various biological resources, endogenous substances, drugs, and synthetic compounds, as well as the mechanisms of targets for antiaging evaluation. These bioactive compounds that could benefit healthy aging and the potential role of life span extension are discussed [30].
10	Anti-Aging Potential of Phytoextract Loaded-Pharmaceutical Creams for Human Skin Cell Longevity	Human skin is constantly exposed to UV radiation from sunshine, which causes various pathobiological changes in cells. The primary strategy for treating photoaging is photoprotection, however cosmeceuticals could be employed as a backup treatment. The type of these harmful molecular alterations determines the therapy strategies to be used. Many lotions containing botanical extracts have been created and evaluated for their ability to prevent aging. The antiaging properties of cream formulations that have been discovered may be the result of many ingredients working in concert. Of all the botanicals, phenolic acids and flavonoids seem to be the most effective at preventing damage caused by UV radiation; however, more research is required to determine whether these compounds have antiaging properties [31].
11	Anti-aging efficacy of topical formulations containing niosomes entrapped with rice bran bioactive compounds	The semi-purified rice bran extracts containing the bioactive chemicals F, O, and P entrapped in niosomes (Gel nio, Cream nio, and Cream RBO) have been investigated in this study for their potential to reduce skin aging properties. These formulations demonstrated not only the inhibition of MMP-2 activity and stimulation of human fibroblast growth in the semi-purified rice bran extracts containing F, O, and P, but also the improvement of skin properties on 30 human volunteers' skin for 28 days following the application of Gel nio and Cream nio, including hydration, pigmentation, thickness and roughness, and skin elasticity. Furthermore, the shown effectiveness of Cream RBO has validated the combined antiaging benefits on the skin of the entrapped and unentrapped bioactive components from rice bran in niosomes within [32].
12	Coriander (<i>Coriandrum sativum</i> L.) essential oil and oil-loaded nano-formulations as an anti-aging potentiality via TGFβ/SMAD pathway	Coriander oil in medicinal dosage forms has anti-wrinkle properties that may be beneficial in modifying extrinsic aging [33].
13	Kojic acid applications in cosmetic and pharmaceutical preparations	The primary therapeutic action of KA is its ability to lighten obvious sun damage, age spots, or scars, which results in anti-aging effects on the skin. In cosmetics, the Cosmetic Ingredient Review Expert Panel (CIREP) states that 1% concentrations are safe to use. Additionally, KA has demonstrated antibacterial qualities that can destroy several common bacterial strains—such as acne-causing bacteria—even at very low dilutions. Research has also indicated that KA may have antifungal effects. Additionally, there have been reports of its use in the treatment of ringworm, candidiasis, and yeast infections. A few negative effects and drawbacks are connected to the use of KA in cosmetics. The primary adverse

		effect of KA is contact dermatitis, which is characterized by irritation, rashes, itchy skin, and pain, especially in those with sensitive skin [35].
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RESULT:

It can be concluded that the extrinsic factors affect the aging of skin mostly like smoking, UV exposure for a long time, environmental changes, pollution mostly and rarely intrinsic factors affect the same except if any genetic variation is present. Extrinsic skin aging is controlled by use of pharmaceutical anti-aging formulations on a large scale. It is anticipated that between 2022 and 2027, the global anti-aging market will expand at a Compound Annual Growth Rate (CAGR) of roughly 6.7%. It is estimated that the market will grow from its 2021 size of about 63 billion US dollars to 93 billion US dollars by 2027. The several ingredients used substantially are, retinol, vitamin-C, vitamin-E, vitamin-A, hyaluronic acid, glycerin, collagen boosters and water which gives significant efficacy to reduce wrinkles, fine lines, dull & dark skin, pigmentation on the skin superficially as well helps the skin get nourished intrinsically. Shoulder-to-shoulder novel technologies have been found recently. Those are nanocream delivery system technology is innovated in Cannola oil anti-aging preparation, injectable skin rejuvenation and dermal fillers, Autologous Platelet-Rich Plasma (PRP); Hormone Replacement Therapy (HRT), ginsenosides; major active chemical constituent of ginseng of which topical application induces HAS-2 gene expression aiding to increase level of hyaluronic acid, GH/IGF-1 axis inhibition method & MMP-2 inhibition method.

CONCLUSION:

Anti-aging formulations are extensively in trend now-a-days due to the increase in skin difficulties like pigmentation, dark patches, UV radiations exposure, dry & dull skin, vitamin-C deficiency, vitamin-E deficiency. Meanwhile, herbal plants are transferred into anti-aging dosage forms as the

side effects will be least with natural benefits to the skin health with long term aids.

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