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Review Paper

A Review of Transdermal Anti-Aging Patch

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ABSTRACT

Acetyl-hexapeptide-3 (AHP-3)is a small peptide with good anti-wrinkle efficacy and safety profile. How ever,due to its hydrophilicity and high molecular weight ,its skin permeation is generally poor. An innovative microneedle (MN)patch such as the curved, flexible or personalised MN patch is a viable avenue to deliver AHP .How ever, the well-researched geometrical relationship of MN on a flat MN patch can not be assumed for these novel MN patch due to acomplex mix of axial and shear forces. In this study,Skin wrinkles result from a myriad of multifaceted processes involving intrinsic and extrinsic aging. To combat this effect, plant stem cells offer a renewable and eco-friendly source for various industries, including cosmeceuticals. Salvia miltiorrhiza (SM), which contains the bioactive compound Rosmarinic acid (RA) and has been proposed for its anti wrinkle effect.Aging can be seen as the accumulation of changes in cells and tissues as a result of increased disorderliness of biological regulatory mechanisms. Alteration of intrinsic factors like hormone processes, genetics, and cellular metabolism in conjunction with exposure to extrinsic factors like UV radiation, pollution, and other chemicals are responsible for structural and physiological changes of the skin that result in the formation of fine lines, wrinkles, and other blemishes. Both preventive and treatment methods can be used when combating factors responsible for the degradation of skin integrity over time. Proper nutrition and protection from UV rays are important methods in remaining pro-active against excessive damage from Reactive Oxidative Species (ROS).

INTRODUCTION

Skin aging is associated with dryness and decrease of skin elasticity and flexibility. Hyaluronic acid (HA) is an endogenous linear polysaccharide that consists of repeating N-acetyl-D-glucosamine and D-glucuronic acid units Aproximately 50% of the total body HA is normally found in the extracellular matrix of the dermis of the skin; HA organizes and maintains its structure to reduce the appear once of wrinkles. This is due to the high

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water-binding capacity and swelling properties of HA1. Moreover, the safe, biocompatible, and biodegradable properties of HA make it applicable to safe cosmetic products and in the field of dermatology The first indication of ageing often presents itself as folds or creases in the skin, or commonly known as wrinkles. These wrinkles are most commonly found in the pri orbital region of the face When an individual with wrinkles becomes excessively anxious over his/her facial outlook, several psychosocial issues can result, such as reduced ability to work or their self esteem may take a plunge. As such, to improve the psychosocial aspects of these individuals, simple and efficacious therapy for treating wrinkles is vital. Acetyl-hexapeptide-3 (AHP-3) is a topically administered anti-wrinkle small peptide.

Its main mode of action involves inhibiting the release of a neurotransmitter, namely, acetylcholine. This inhibition results in a reduction of repeated contractions involving facial muscles that regulate facial expressions. This, in turn, decreases the formation of expression wrinkles. These wrinkles are creases or folds in the facial region due to repeated contractions of the same area [4–6]. Furthermore, AHP-3 is an attractive candidate for anti-wrinkle treatment due to its demonstrated efficacy, with a ~49% improvement of wrinkles after 4 weeks of a twice a day regimn

As concerns about the physical manifestation of aging grow and people continue to take an active role in either the prevention or reversion of aging skin, treatment methods have become more accessible and normalized in the modern world. While anti-aging claims are an effective marketing tool in drawing consumers to a product or procedure, these claims must be backed up with actual mechanisms that work to rejuvenate the skin - whether it is through stimulation of collagen production or the removal of damaging reactive oxidative species

Aging Process

Graying hair, shrinking stature, and cracking joints are all tell -tale signs of aging everyone hopes to escape, with the most famous indication being the appearance of fine lines and wrinkles on the skin. Wrinkles are the creases and folds that form in the skin as a by-product of the aging process as the skin loses its elasticity over time. As the separation of the body from the outside environment, the skin is impacted by aging factors that are both intrinsic and extrinsic. Intrinsic aging is determined genetically and describes the unavoidable physiological process resulting in the development of fine wrinkles in thin, dry skin. Extrinsic aging factors encompass environmental factors such as sun exposure, air pollution, and smoking that produce rough textured skin and the formation of deeper, coarse wrinkles .47

Third, the skin barrier is responsible for transporting nutrients through itself and into the skin to preserve the health of the major organ. Ultimately, these tasks in conjunction operate to maintain homeostasis among the body's many systems . If the skin barrier does not work as, it should, the epidermis will become vulnerable to damage and unable to fight off external aggressors, such as free radicals that can result in the formation of discoloration and premature wrinkles. In fact, up to 90% of visible skin aging is due to environmental factors, such as sun exposure 48

Aging and Role of Collagen

Collagen is the most abundant protein present in mammalians, serving as one of the main building blocks for a range of tissue types including bones, skin, muscles, and hair. 49 The 3 parallel polypeptide strands are found in a left-handed, polyproline II-type helical formation with a one-residue stagger forming a right-handed triple helix This stagger contains a special amino acid sequence specifying that every third amino acid must be glycine while the 2 remaining residues are

often either proline or hydroxyl proline This structure results in incredible stability and versatility of the protein, allowing it to play key roles throughout the body in various forms. In the skin, collagen fibers are found in the dermis layer to form fibroblasts where new cells can grow in addition to playing a role in replacing and restoring dead skin cells 50

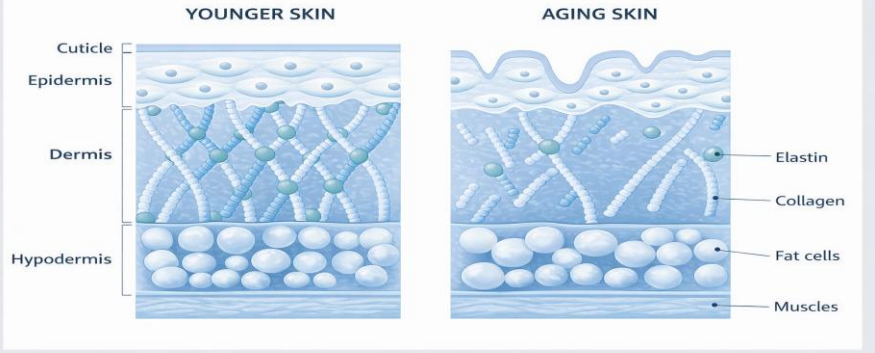


Figure 1.

Aging and Its Molecular Mechanism

Human aging, unlike sickness, is a progressive time-related process. It varies from person to person, and corresponds biologically to a loss of homeostasis, an increase in the organism's sensitivity and susceptibility to disease and death, and the progressive degeneration of cells, tissues, and organs associated with advancing age . These aspects of deterioration are called senescence, and are responsible for the weakening of an individual's health.17

They also cause physiological changes in "regular" aging, such as menopause and decreased kidney function, and age-related disorders, such as coronary heart diseases, in "ordinary" aging. Several variables contribute to the loss of homeostasis, which is ultimately the consequence

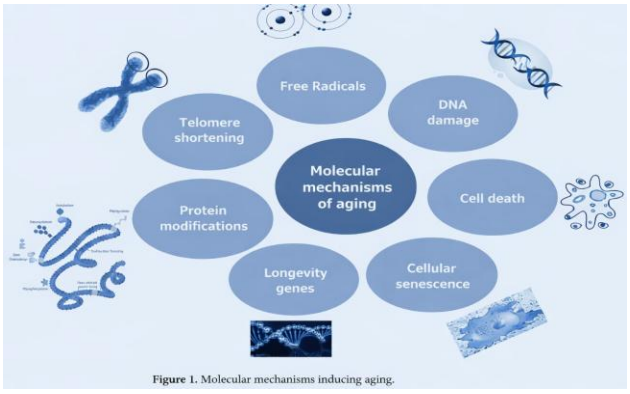


Figure 1. Molecular mechanisms inducing aging.

Preventive Measure as Anti-Aging Efforts

A popular preventive measure for reducing or delaying the appearance of wrinkles is through nutrition to combat the effects of reactive oxygen species (ROS). Reactive oxygen species are generated as by-products when molecular oxygen is utilized by aerobic organisms to perform essential metabolic reactions within the body. ROS is a term used to define any oxygen-containing reactive including hydrogen peroxide (H2 O2), hydroxyl radicals (˙OH), peroxyl radicals (LOO˙), and more In addition to involvement in metabolic processes, ROS also play important roles in wound healing, inflammatory responses, and apoptosis. As the skin functions as a barrier to protect from external

harmful agents, when the skin becomes inflamed high levels of ROS are generated for the purpose of removing and destroying invading microorganisms and breaking down any damaged tissue. As mediators of inflammatory responses, ROS activate cell signeling to increase the production and release of pro inflammatory cytokines to instigate inflammatory responses 51

Changing the Perception

When considering anti-aging, there are two ways of looking at it: perception versus making real changes to the skin. To simply change perception, multiple methods can be used such as filters for a blurring effect or the use of makeup like foundation and concealers to lessen the appearance of any unwanted fine lines. It is important to note that many makeup brands will advertise their products as having the ability to reduce the appearance of wrinkles which is important to distinguish from will reduce wrinkles. The difference is that the former is a cosmetic claim whereas the latter is a drug claim. The FDA defines cosmetics as "articles intended to be rubbed, poured, sprinkled, or sprayed on, introduced to, or otherwise applied to the human body for Cleansing, beautifying, promoting attractiveness, or altering the appearance"52

Types of rapidly separable MN patches with slow degradation

A MN patch typically contains hundreds of MNs connecting with the patch backing, and the dimensions of each MN are generally 150 ~ 1500 μm in length, 50 ~ 250 μm in width, and 1 ~ 25 μmin tip diameter. Rapidly separable MN patches with slow degradation are mainly divided into three classifications based on their working mechanisms: 1) MN patches with fast dissolvable backing

Microneedle (MN) patches with fast-dissolvable backing are advanced transdermal delivery systems designed to deliver drugs, vaccines, or cosmetic actives quickly, painlessly, and without sharps waste. Below are the key details in a clear, study-ready format.

MN patches consist of:

Microneedles (50–900 μm) that painlessly penetrate the stratum corneum A fast-dissolving backing layer that dissolves rapidly on skin contact

3. Mechanism of action

Patch applied to skin

1. Microneedles penetrate outer skin layers
2. Backing layer absorbs moisture and dissolves rapidly
3. Microneedles dissolve or detach and release drug
4. Skin reseals naturally within hours

Advantages

> Painless and needle-free
> No biohazard sharps waste
> Rapid drug release
> Improved patient compliance
> Self-administration possible
> Enhanced bioavailability vs topical delivery

MN patches with weakened junctions between backings and MN tips

mechanically separable microneedle patches are designed so that the microneedle (mn) array detaches from the backing layer by a simple mechanical action (pressing, twisting, peeling, or sliding) after insertion into the skin. this allows the to remain embedded or to deliver their payload while the backing is removed Mechanically separable MN patches are transdermal systems Mns penetrate the skin A deliberate mechanical force causes separation of the MN layer from the backing The backing is removed, while absorb or remain temporarily in skin 53

Mechanism of Separation

1. Patch is pressed onto skin

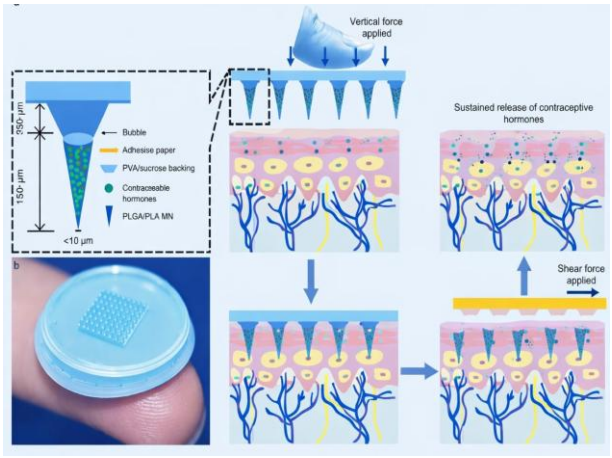
2. Mns fully insert into epidermis/dermis
3. Mechanical action applied (peel, bend, twist, or press)
4. Weak interface fractures
5. Backing layer detaches

Separable arrowhead MN patches

Separable arrowhead microneedle patches are an advanced class of mechanically separable MN systems in which only the arrowhead-shaped needle tips detach from the backing and remain embedded in the skin, while the shaft/backing is removed after application. 54

Mechanism of Action

1. Patch pressed onto skin
2. Arrowhead tips penetrate epidermis/upper dermis
3. Mechanical force (press/peel/twist) applied
4. Weak junction fractures
5. Arrowhead tips remain embedded
6. Tips dissolve slowly and release drug



Hydrogel-based mn patches

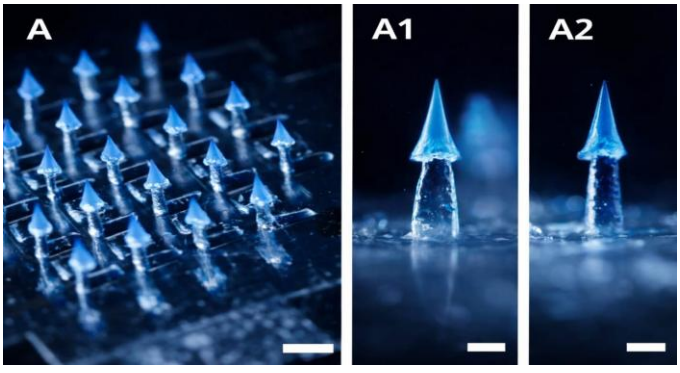
hydrogel-based microneedle patches are minimally invasive transdermal delivery systems composed of cross-linked, water-swellable polymer microneedles. upon insertion into the skin, the microneedles absorb interstitial fluid, swell, and create microchannels for controlled drug diffusion

Working Mechanism

Patch is applied with gentle pressure
Microneedles penetrate the stratum corneum
Hydrogel mns swell by absorbing skin fluid
Drug diffuses through swollen mn matrix
Controlled and sustained drug release occurs

Advantages

1.Painless and patient-friendly
2.No sharp waste (non-dissolving but removable)
3. Controlled and sustained release
4. High drug stability
5. Reduced infection risk
6. Suitable for self-administration



Biomedical applications of rapidly separable long-acting MN patches

MN patches have been extensively applied in biomedical drug research because of their unique properties, such as enablingse lf administration ,achieving high drug delivery efficiency, and possessing excellent biocompatibility] . Rapidly separable long acting MN patches that can quickly implant drug-loaded MN in to skin and keep sustained release of drug over a long period 31

Microneedle Patch, an Ideal Transdermal Delivery System

Microneedle patch technology, as an innovative drug delivery system, has demonstrated immense potential and diverse applications in the field of medical health. In recent years, researchers have propelled the rapid development of microneedle patch technology across various therapeutic domains through innovative design and material selection.27 In terms of transdermal drug delivery, microneedle patches leverage their minimally invasive nature to effectively penetrate the skin's surface layer, facilitating rapid drug absorption and release. For instance, the integration of flexible surface acoustic wave technology with microneedle patches has enhanced the transdermal delivery capability of macro molecular drugs.28 Additionally, a lipid nanocapsule-microneedle array patch loaded with Fenretinide has provided a novel administration method for the chemoprevention of breast cancer, enhancing drug bioavailability by improving local drug distribution. A proof-of-concept study has also successfully fabricated a three-layer dissolving microneedle (TDMN) to enhance the bioavailability and brain delivery of Rivastigmine, a drug for the treatment of Alzheimer's disease. In the treatment of specific diseases, microneedle patch technology has made significant progress. 56It has been combined with microneedle patches to improve the therapeutic effects of drugs for common diseases such as cancer,Alzheimer's disease, and skin wounds. Beyond these conditions, for the issue of insomnia, researchers have developed a traditional Chinese medicine microneedle patch that optimizes microneedle design through finite element analysis, achieving effective drug delivery and improved sleep effects. In the field of obesity treatment, researchers have reported a rapidly adhering, water-soluble nanoparticle microneedle patch composed of a soluble hyaluronic acid microneedle matrix and weakly acidic, degradable Rosiglitazone nanoparticles.

This patch has shown significant weight loss effects in a mouse model without affecting skin integrity, offering a suitable weight loss method for working populations. In the treatment of gout, a milestone study has developed a new dissolvable micro needle system encapsulating ethosomal formulations of Colchicine and Iguratimod for the treatment of recurrent gout.In diabetes management, a bilayer hydrogel microneedle patch based on polyvinyl alcohol and carboxy methyl chitosan has enabled rapid detection of blood glucose levels through in situ colorimetric analysis. Additionally, a painless, soft microneedle sensing patch has been developed to achieve on-site, accurate, and continuous glucose monitoring through a high mechanical strength microneedle base and thin-layer fluorescent hydrogel sensor.55

Microneedle Patch for Skin Photoaging

Treatment People have applied substances to the skin for therapeutic effects for thousands of years. Transdermal drug delivery plays an important role in medical practice, but its potential as an alternative to oral and subcutaneous administration has not been fully realized. In the clinical application of low-dose, lipophilic, and low-concentration drugs, the surface applica tion

of transdermal drug delivery systems has steadily increased.25

However, in delivering biological macromolecules and vaccines such as insulin, parathyroid hormone, and influenza vaccine, there is yet to be an effective transdermal delivery method due to the large molecular size. One of the biggest challenges for transdermal delivery is the limited number of drugs that can be administered through this route. Under current delivery methods,23

successful transdermal drugs typically have a molecular weight of only a few hundred Daltons, with an octanol-water partition coefficient favoring lipids, and require daily doses of milligrams or less. Transdermal delivery of hydrophilic drugs, peptides and large molecules (such as DNA or small interfering RNA) presents special challenges. As a result, microneedle technology has begun to attract the attention of researchers, who are trying to use this technology to achieve high- efficiency transdermal delivery of these difficult-to-deliver drugs.24

Extracellular vesicles (evs), including exosomes (30–150 nm) and microvesicles (100–1000 nm), are lipid bilayer–enclosed nanoparticles secreted by cells. Evs carry proteins, lipids, mrna, mirna, and signaling molecules, making them promising therapeutics for regenerative medicine, immunomodulation, wound healing, and skin rejuvenation.

However, conventional ev delivery (topical or injection) faces limitations such as poor skin penetration, rapid degradation, and low local retention. Microneedle patches overcome these barriers by enabling minimally invasive, localized, and controlled ev delivery.

Types of Microneedles Used for EV Delivery

a) dissolving microneedles

Fabricated from hyaluronic acid, PVA, PVP, gelatin, or chitosane

EVs are encapsulated within the needle matrix

MNs dissolve after insertion, releasing EVs directly into skin layers

b) Hydrogel-Forming Microneedles

Made from crosslinked PEG, HA, or PVA-based hydrogels

MNs swell upon absorbing interstitial fluid

EVs diffuse from a reservoir or backing layer into skin

Recent Clinical Study of Microneedle Patch for Skin Aging Treatment

the concept of microneedles was proposed in the 1970s, but it was not until the 1990s that the microelectronics industry provided the microfabrication tools necessary to create these small structures, allowing for experimental validation. since the first study on microneedle transdermal drug delivery in 1998,70 most research has focused on metal needle manufacturing techniques for developing microneedle heads for drug applications.21 clinically, metal microneedle injectors or microneedle rollers are more commonly used, while the application of microneedle patches remains limited. however, there was a clinical trial about microneedle patch for anti-aging recently, the study evaluated a novel dissolving microneedle patch (da-mnp), which has been verified for its skin puncture ability, safety, and efficacy through clinical research.23 the da-mnp contains a hyaluronic acid polymer backbone, acetyl octapeptide-3, l-ascorbic acid 2-glucoside, and sodium cyclic lysophosphatidic acid, and is manufactured using den® technology. compared to the placebo mnp, the da-mnp treatment group demonstrated more effective anti-aging effects in improving eye wrinkles, reducing trans-epidermal water loss (tewl), enhancing skin elasticity and lifting, and exhibited no adverse reactions.22

Microneedle-Mediated Anti−Wrinkle Therapy

Microneedle-Mediated Anti−Wrinkle Therapy MNs are widely used in transdermal drug delivery because of their safe, painless, and non-invasive drug administration. Their construction mimics the needles with a very MNs are widely used in transdermal drug delivery because of their safe, painless, and non-invasive drug administration. Their construction mimics the needles with a very narrow diameter and length, which penetrate through the stratum corneum and move into the layers of the dermis without affecting blood vessels or the sensory neurons of pain [16].

MNs also help the drug get absorbed in the ISF and ease the ISF to diffuse through the skin painlessly Thus, it is one of the painless dosage forms that can be narrow diameter and length, which penetrate through the stratum corneum and move into the layers of the dermis without affecting blood vessels or the sensory neurons of pain [19].

MNs also help the drug get absorbed in the ISF and ease the ISF to through the skin painlessly [18]. Thus, it is one of the painless dosage forms that can be administered by patients without supervision [50]. The greatest barrier in transdermal drug delivery is the route of administration, which is stratum corneum (SC). SC is the initial protective layer of the skin, which hinders the absorption of drugs into the skin. The microneedle technique can surpass the SC due to its micron-sized needle with a solid base size ranging from 25–2000 μm that can easily be inserted into the stratum corneum of the skin [17], Moreover, it has become a technique of interest for transdermal immunotherapy and can ensure the delivery of active molecules such as antibodies, aller gens, and other agents of therapeutic advantage directly to the skin [14]. In a recent case study, coated MN has been used to mitigate the symptoms of allergic rhinitis by regulating administered by patients without supervision . The greatest barrier in transdermal drug delivery is the route of administration, which is stratum corneum (SC). SC is the initial protective layer of the skin, which hinders the absorption of drugs into the skin. The microneedle technique can surpass the SC due to its micron-sized needle with a solid base size ranging from 25–2000 μm that can easily be inserted into the stratum corneum of the skin [13], and thus this trait is considered to be one of the major advantages of the microneedle technique

Moreover, it has become a technique of interest for transder mal immunotherapy and can ensure the delivery of active molecules such as antibodies, allergens, and other agents of therapeutic advantage directly to the skin [50]. In a recent case study, coated MN has been used to mitigate the symptoms of allergic rhinitis by reg ulating IgE in mice model through the skin. Two Phase I trials are currently being con ducted to assess the safety and immunological response to allergy immunotherapy com pared to the subcutaneous immunotherapy



Table 1. Microneedle-mediated treatment studies related to skin wrinkles in the last few decades.

Sl no	Type of mn used	Active ingredient	Method	Result	Limitation of the study	reference
1	Soluble microneedle patch	HA 16.7%(w/w)	Double-blind clinical trial done for 10 to 12 weeks on 84 Korean females with Crow's feet and evaluation of other parameters e.g., dermal density, elasticity, and hydration	Effective reduction of epidermal wrinkle after 8 weeks. Other parameters like dermal density, elasticity, and hydration had increased Efficiently penetrated skin very fast	The clinical test has been done only for Korean skin types; Discontinuation effects were not properly mentioned, giving rise to durability concerns	57. Hong,J.Y.; Ko, E.J.; Choi, S.Y.; Li, K.; Kim, A.R.; O Park, J.; Kim, B.J. Efficacy and safety of a novel, soluble microneedle patch for the improvement of facial wrinkle. J. Cosmet. Dermatol. 2018, 17, 235–241.

1. Requirements of polymers for anti-ageing patches

An ideal polymer should be:

✓ Biocompatible & non-toxic

✓ Skin-friendly (non-irritant)

✓ Good film-forming ability

✓ Controlled drug release

✓ Mechanical strength (for microneedles)

✓ Biodegradable or dissolvable

2. Common polymers used in anti-ageing skin patches

A. Natural polymers (most preferred for skin)
These are safe, biodegradable, and well-accepted by skin.

1. Hyaluronic Acid (HA)
Naturally present in skin
Strong hydrating & anti-wrinkle effect
Used in dissolving microneedle patches
Improves skin elasticity and volume

2. Collagen
Structural protein of skin
Improves firmness and reduces fine lines
Often combined with HA or PVP

3. Chitosan
Derived from chitin
Antimicrobial + wound healing
Enhances skin penetration
Used in film-forming patches

4.Gelatin

Biodegradable protein
Good mechanical strength for microneedles
Promotes skin regeneration
B. Synthetic polymers (high stability & strength)

5. Polyvinyl Alcohol (PVA)
Water-soluble & biocompatible
Used in microneedle matrix
Controls drug release

5. Polyvinylpyrrolidone (PVP)
Excellent film former
Improves skin adhesion
Common in cosmetic patches

6. Polylactic Acid (PLA)
Biodegradable polymer
Used in solid microneedles
Provides mechanical strength

7. PLGA (Poly-lactic-co-glycolic acid)

Controlled & sustained release

Used for long-term anti-ageing effects

FDA-approved polymer

Scope of Treatment for Skin Wrinkles

The challenges that researchers face while designing the required anti-wrinkle treat ment therapy largely involve finding the right antioxidants like vitamin C and E or a combination of antioxidative enzymes such as catalases and peroxidase. Apart from that, it is essential to identify if beta-carotene and vitamin A and E are provided in the right amount for the treatment as it can bring about some unwanted side effects [8,9]. In the case of stem cell therapy, the transplantation of adipose-derived stem cells in the appropri ate skin layer has to be ensured. Mistreatment of the transplantation must be avoided to ensure skin rejuvenation and produce necessary growth factors to reduce aging. In the case of hormone replacement therapy for treating skin wrinkles, it works significantly well to slow aging and improve elasticity, but the concentration and extent of the use of artificially produced hormones need to be verified as it can increase the risk of developing breast cancer [10].

With more research in the cosmetic field and the advent of technology, a variety of techniques have become available for treating wrinkles, ranging from topical creams and serums to numerous surgical procedures to smoothen out wrinkles and fine lines. One of the first vitamins approved by the FDA to treat wrinkles is vitamin A. Retinol, retinal, and retinoic acid, which have the same biological features as vitamin A, slow down the aging process and are now frequently used in anti-wrinkle treatment [11]The formulation used for their anti-wrinkle effects include alpha hydroxy acids (AHAs), poly-AHAs, complex poly-AHAs, retinoids, fish polysaccharides, anti-enzymatic agents, antioxidants, such as ascorbic acid, pycnogenol, ursolic acid, vegetable isoflavones, vitamin E, coenzyme Q10, lipoic acid, resveratrol, l-carnosine, and taurine, as well as agaricic acid and various plant extracts [80]. Even though vitamin A and retinoids are commonly used in anti-wrinkle therapy, the use of vitamin A and its derivatives in pharmaceutical and cosmetic products has been limited due to their instability and irritant properties [12].

Table 2. Current anti-wrinkle agents in use

Reagent used in formulation	Nature	Function	Reference

Retinyl retinoate	Lipophilic	Photostable; have lower toxicity and greater skin rejuvenation than retinol; effective in treating periorbital wrinkles	[37]
Ascorbic acid	Hydrophilic	Acts as an antioxidant; effective in treating photo-aging	[38]
Hyaluronic acid	Hydrophilic polysaccharide	Increases skin moisture and reduces the appearance of f ine lines and wrinkles by improving collagen and elastin stimulation	[39-40]
Adenosine	Amino acid	Effective in treating crow's feet and frown lines by skin density, elasticity and hydration	[41-42]
Horse oil	Lipophilic	Restores stratum corneum and imparts skin-moisturizing effects	[43]
Acetyl-hexapeptide 3 (AHP-3)	Small peptide	Decreases the anisotropy of skin to help in treating skin wrinkles	[44]
Epidermal growth factor	Small water-soluble Polypeptide	Effective in treating periorbital wrinkles	[46]
Niacinamide	Vitamin B3	Improves skin elasticity, reduces skin wrinkles and fine lines, decreases hyperpigmentation and skin sallowness, minimizes pore size, and eases skin inflammation	[45]

The Potential of HMNs to Treat Skin Wrinkles

HMNs can permeate the skin more effectively than other techniques including MN patches and electroporation patches [96]. There are void spaces in HMNs filled with solution and holes at the tip that deliver the drug after skin penetration. By increasing MNs bore, it increases the flow rate, but the mechanical strength and sharpness of HMNs Their needles are micrometric in size and that makes the manufacturing process difficult and expensive Rox hed et al. published an article in 2008, where they discussed a good number of techniques in HMN preparation, with a view to finding a feasible decrease way of fabrication However, given its micrometric size, the patient's acceptance is higher than with a conventional injection Due to its high penetration and permeability, when the void is incorporated with anti-wrinkle medications, it will release the therapeutic agents readily and easily into the epidermis directly facilitating skin rejuvenation In October 2008, the HMN array got patented in the USA by a group of researchers as a transdermal drug delivery device [6].

Other drug molecules that have a high molecular weight can be effectively delivered by HMNsdirectly to the skin. The high molecular weight compound includes proteins, vaccines, and oligonucleotides is an FDA-approved MN patch manufactured by Valeritas and is used to deliver

insulin [107]. HMNs can be useful in the delivery of im munological products as well because they can deliver many dendritic cells, macrophages, lymphocytes, and mast cells into the layer of the skin [7].

CONCLUSION

As the largest organ and a physical barrier between the internal human body and harmful microbes and chemicals, the skin plays an essential role as the body's first line of defense and in maintaining homeostasis among the many systems and biological mechanisms that keep us alive.Not only is it impacted by intrinsic factors that change as the aging process advances, but it must also bear the damage inflicted by years of exposure to unavoidable damaging external factors producing visible blemishes like wrinkles, age spots, and rough patches of skin. Furthermore, as people age the slowing of cell turnover rates and reduction in collagen production result in thinner skin with irregular depressions as the elastin-collagen network of fibers breaks down and loses its structural integrity.

To combat these effects, both preventive and treatment measures can be undertaken to minimize the appearance of wrinkles. As vital metabolic reactions proceed within the body and UV radiation infiltrates from outside the body, reactive oxygen species are generated that have the ability to degrade biomolecules like DNA when produced in excess leading to oxidative stress. Preventive methods like consuming a healthy diet rich in antioxidants and minimizing sun exposure by covering up and the application of daily sunscreen can reduce the negative effects 5

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