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A REVIEW ON DETACHABLE MICRONEEDLES FOR ACTIVE DELIVERY SYSTEM

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Abstract: Microneedles are one of the microscale physical enhancement methods that greatly expand the spectrum of actives for transdermal and intradermal delivery. Some new methods are used in transdermal administration of the actives are hypodermic needles, tropical creams and transdermal patches. Now days in the active delivery system the microneedles are mostly used to enhance the delivery of the active through this route and deal with the various problems. Detachable microneedles that detach from the patches during administration. Delivering bioactive compounds into skin tissue has long been a challenge due to the stratum corneum layer of the skin, which serves as a barrier for the molecules are able to reach the site of action. Detachable microneedles are filled with actives like retinol, hyaluronic acid, ceramide and glycolic acid which are excellent antiaging agent which are used for the treatment of the deeper of skin aging.

Keywords: -Skin- Structure and function; Skin-Aging: Microneedles; Detachable Microneedles; Mechanism; Evaluation.

INTRODUCTION

SKIN

Skin is the largest organ in the body and covers the body's entire external surface. It is made up of three layers the epidermis, dermis and hypodermis, all three of which vary significantly in their anatomy and function.

Epidermis

Epidermis is the outer, protective and thinner layer of the skin. It is in contact with the outer environment. Sweet glands, hair follicles and other epidermal appendages are laying of epidermis. It is made up of approximately 15 to 20 tightly packed layers of cells. Most of the cells in this layer are keratinocytes, or squamous cells. It does not contain any blood vessels.

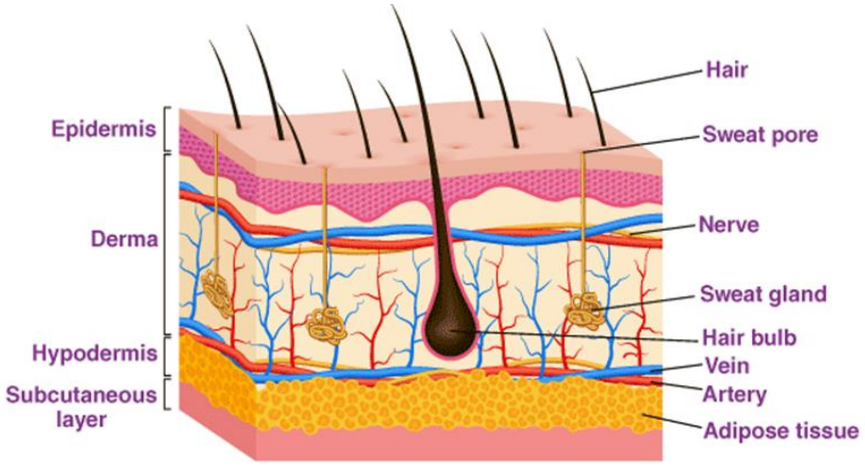

Fig no. 1; Internal structure of Skin

Layers of Epidermis

The layers of the epidermis include the Stratum Basale (the inner portion of the epidermis), stratum spinosum, stratum granulosum, stratum lucidum, and stratum corneum (the most outer portion of the epidermis).

Stratum Basale, also known as stratum germinativum, is the deepest layer, separated from the dermis by the basement membrane (basal lamina) and attached to the basement membrane by hemidesmosomes. The cells found in this layer are cuboidal to columnar multiplicatively active stem cells that are constantly producing keratinocytes. This layer also contains melanocytes.

Stratum spinosum, it is also called as Prickle cell layer. It contains 8 to 10 rows of polyhedral cells that fit closely together. They are spine like appearance. The cells appear to be covered with prickly spines because the cells shrink apart when the tissue is prepared for microscopic examination.

Stratum granulosum, it consists of 3 to 5 rows of flattened cells. The cells developed darkly staining granules of a substance called keratohyalin. The nuclei of the cells in the stratum granulosum are in various stages of degeneration.

Stratum lucidum, 2-3 cell layers, they present in thicker skin found in the palms and soles, they are clear, flat, dead cells that contains droplets of an intermediate substance that is formed from keratohyalin and is eventually transformed to keratin.

Stratum corneum, this layer consists of 25 to 30 rows of flats, dead cells completely filled with keratin. These cells are continuously shed and replaced by cells from deeper strata. They serve as an effective barrier against light and heat waves, bacteria, and many chemicals.

Cells of the Epidermis

- Keratinocytes
- Melanocytes
- Langerhans' cells
- Merkel's cell

Keratinocytes The outermost layer of the skin is the keratinous layer, they formed by division in the stratum basale. The cells of the outer layers contain large quantities of a protein called keratin. The keratinous layer is made of tightly packed dead cells, which gives the skin protective capabilities.

Melanocytes Melanocytes are derived from neural crest cells and primarily produce melanin, which is responsible for the pigment of the skin. They are found between cells of stratum basale and produce melanin. UVB light stimulates melanin secretion which is protective against UV radiation, acting as a built-in sunscreen. Melanin transferred to neighbouring keratinocytes by "pigment donation"; involves phagocytosis of tips of melanocyte processes by keratinocytes.

Langerhans' Langerhans cells are involved in the body's immune system. These cells originate from bone marrow and migrate to the epidermis. They interact with white blood cells called helper T cells in immune responses. They are easily damaged by UV radiation.

Merkel Cell Merkel cells (MCs) constitute a very unique population of postmitotic cells scattered along the dermo-epidermal junction. These cells that have neuronal contacts with somatic sense afferents are regarded to have a vital role in sensory perception. Several concerns exist till date as to their origin, multiplication, and relevance in skin biology.

Dermis

The dermis is a connective tissue layer sandwiched between the epidermis and subcutaneous tissue. The dermis is a fibrous structure composed of collagen, elastic tissue, and other extracellular components that includes vasculature, nerve endings, hair follicles, and glands. The role of the dermis is to support and protect the skin and deeper layers, assist in thermoregulation, and aid in sensation. Fibroblasts are the primary cells within the dermis, but histiocytes, mast cells, and adipocytes also play important roles in maintaining the normal structure and function of the dermis.

Hypodermis

The hypodermis lies between the dermis and underlying organs. It is commonly referred to as subcutaneous tissue and is composed of loose areolar tissue and adipose tissue. This layer provides additional cushion and insulation through its fat storage function and connects the skin to underlying structures such as muscle. The hypodermis is deep to the dermis and is also called subcutaneous fascia. It is the deepest layer of skin and contains adipose lobules along with some skin appendages like the hair follicles, sensory neurons, and blood vessels.

Function of Skin

The skin performs a variety of functions which may affect body metabolic system. Being the outer most system, the skin is susceptible to mechanical abrasion, bacterial, temperature, etc.

Protection from the environment

At the stratum corneum, it's sort of takes after brick and mortar they made up of cells called corneocytes that acts as bricks. These bricks are tightly bound, or glued together, by mortar-like fats such as ceramides, cholesterol, and fatty acids. This layer also contains a protein called filaggrin, which helps make natural moisturizing factors (NMF) for the skin.

Your skin barrier has several functions. It protects you from:

- Pollution
- Ultraviolet rays
- Irritation, inflammation, and infection
- Dehydration
- Toxins

It regulates water loss from the inside out, retains moisture, and keeps you hydrated. The skin barrier also blocks entry to most topical actives, or those you put on your skin.

Protection in the form of a barrier

Skin protects against physical injury, wear and tear, to certain extent against ultraviolet radiation. It prevents penetration of noxious foreign materials including water and micro-organism. Skin works as a chemical, physical and biological barrier in the body. As a chemical barrier melanin, acid mantle, low pH, the natural antibiotic human defensing and catholicizing contribute.

Thermoregulation

The process of maintaining the internal body temperature constant is known as thermoregulation. Skin contributes to this by responding to changes in the external environment and changing the body heat loss or heat retention processes accordingly.

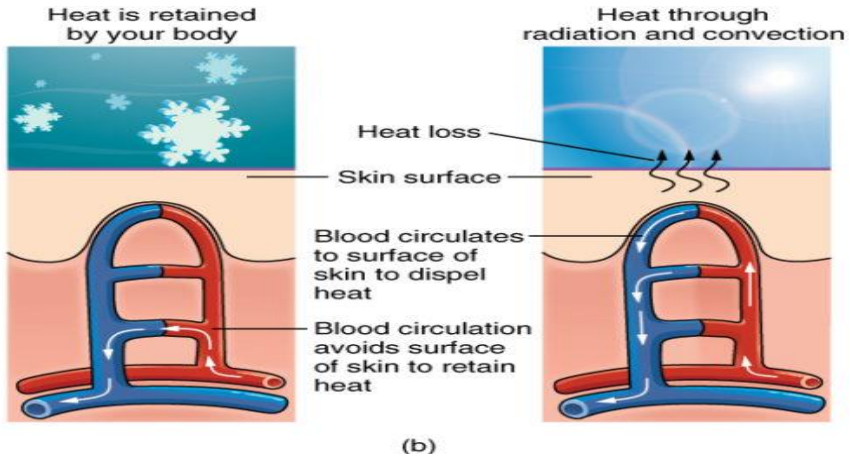

Fig no. 2 Thermoregulation of the skin

Hydration Skin maintains the moisture level of the skin by discharging perspiration and the oily sebaceous materials that is the skins best lubricant.

Synthesis It has important endocrine functions such as the synthesis of Vitamin D3, sex hormones and pheromones.

Sensation The nerve endings under the skin make us aware of heat, cold, pain and pleasurable sensations. It transmits incoming stimuli and plays an important role in social behavior.

Absorption The skin permits certain substances to pass through its tissues. These include fat soluble vitamins (A, D, E and K), certain actives and the gases oxygen and carbon dioxide.

Elimination of waste Skin is an excretion organ via its sebaceous and sweat glands. It helps in eliminating the toxic waste products and water from the body.

Skin aging

Skin ageing is a process in which skin quality deteriorates with age due to the synergistic effects of chronological ageing, photo-ageing, hormonal deficiency and environmental factors. In skin ageing, there is a reduction in the number of fibroblasts that synthesize collagen and vessels that supply the skin which leads to an increase in laxity and hence forms wrinkles. During aging, facial appearance changes dramatically. The age-dependent shrinking of sweat glands which causes them to move upward toward the skin surface, concomitantly inducing an upward movement of the subcutaneous adipose layer just beneath the sweat gland and thereby causing dermal cavitation. These large and frequent defects at the bottom of the dermal layer result in the deterioration of dermal elasticity, which in turn promotes sagging.

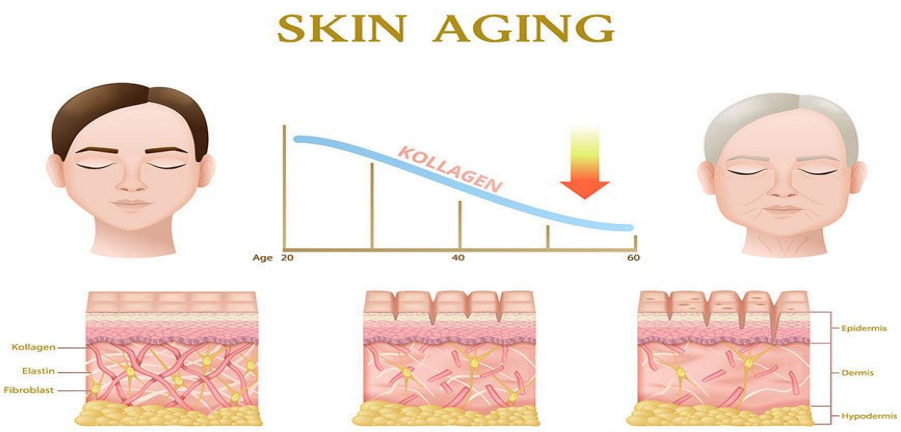

Fig no. 3: Skin aging

Treatment

Skin aging is treated with various procedure and numerous topical agents. They are removing the damaged of epidermis and some of how the dermis. Several antioxidants incorporated into the topical skin care products including vitamin C and E, hyaluronic acid, retinoid. Although there are several treatments are now popular in market, detachable microneedles are one of the treatments now in progress in skin care for skin ageing treatment.

ACTIVE DELIVERY SYSTEM

Active delivery is the method or process of administering active compound to achieve a therapeutic effect in human's skin. For the treatment of different types of problems, the active delivery is gaining increasing importance. These routes provide promising alternatives to parenteral active delivery particularly for peptide and protein therapeutics. For this purpose, several active delivery systems have been formulated and microneedles are one of the treatments which is use now for treatment of skin aging.

MICRONEEDLES

Microneedles are a transdermal active delivery system that uses small needles with micron dimensions to penetrate the skin and deliver actives to the target area. Nowadays, there are different types of microneedles available for active delivery, including solid, coated, dissolving, hollow, and hydrogel microneedles. Detachable microneedles—microneedles that can separate from their base and be inserted into the skin in the little amount of time required for application have also been introduced recently. They can be loaded to deliver actives into the target area of the skin.

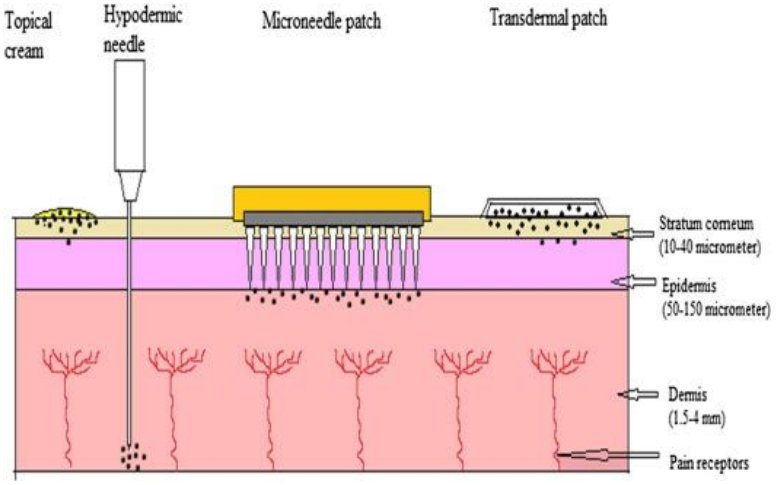

Fig no. 4: Types of Microneedles

Types of microneedles

Microneedles are divided into four structural categories: solid microneedles, coated microneedles, dissolving microneedles, and hollow microneedles. The active delivery principle of these microneedles (respectively) are the “poke and patch” approach, the “coat and poke” approach, the “poke and release” approach, and the “poke and flow” approach.

Solid microneedles

Microneedles can create pores in the skin, allowing actives to flow directly through the epidermis and into the dermis. In contradiction to conventional hypodermic needles, the microneedle enhances tolerating consistency because it does not irritate nerves.

Coated microneedles

Coated microneedles, which are coated with active substances at their tips via dipping, gas-jet drying, ink-jet printing, or spraying, have solved the complex problem of solid microneedles. The mechanism of coated microneedles for active delivery is the "coat and poke" method. The microneedle patch is put into the skin, and the active-coated microneedle tips release their contents into the skin.

Dissolving microneedles

Dissolving microneedles have several advantages over their solid and coated fellows, including their ease of production, their usefulness, and their high active loading. Dissolving microneedles often work on the "coat and poke" principle, wherein the medication is contained in the microneedle tips and is released as the microneedle firmly penetrates the skin.

Hollow microneedles

Hollow microneedles, which offer the maximum degree of accuracy, are uncommon compared to other microneedle structures. Microneedles like these are typically produced using MEMS processes such as laser micromachining, lithographic patterning, microfabrication, and X-beam photolithography, on a metal or silicon substrate. Additionally, since the "poke and flow" delivery method of empty microneedles makes them ideal for blood extraction, they have been widely used for this purpose.

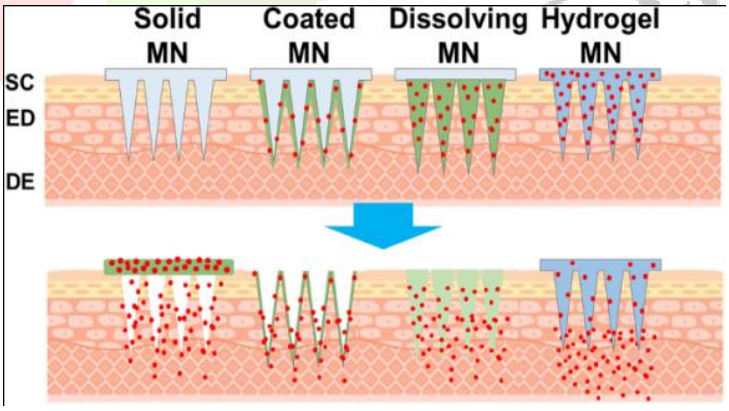

fig no. 5 Types of Microneedles

Detachable microneedle

Detachable microneedles are the type of dissolving detachable microneedles. Dissolvable microneedles (DMNs), first proving in 2005, offer an alternative delivery approach. They are made up of biocompatible materials, they dissolve in the skin tissue and are metabolized by the body. Different types of bioactive compounds can be encapsulated into DMNs and directly delivered into skin tissue. There are different fabrication materials to development of detachable microneedles are silicon, ceramic, metal, silica glass, carbohydrate, polymer.

Mechanism of Active Delivery of Detachable Microneedles

The delivery of the active through the topical route follows the diffusion mechanism. In the microneedle active delivery system, the skin is temporarily disrupted. A microneedle product is made by arranging hundreds of microneedles loaded with active in arrays on a tiny patch in order to delivery sufficient amount of active to give a required therapeutic response. It enters the stratum corneum thus bypassing the barrier layer. The active is directly placed in the epidermis or upper dermis layer which then goes into the systemic circulation and shows a therapeutic response on reaching the site of action. The microneedles are tiny, micron-sized. During insertion and removal, the pointed extremities of the microneedle tips create pores on the skin's surface. The mixture can be applied to the skin to allow the medication to gradually seep into the skin's pores.

EVALUATION OF DETACHABLE MICRONEEDLES

There are some methods to evaluate the detachable microneedles, they are following:

Characterization methods: - Particle size, polydispersity index, viscosity, zeta potential, drug release, pH, and drug content are among the characteristics.

Dimensional evaluation: - A variety of procedures are used to evaluate needle geometry and quantify the tip radius, length, and height of microneedles. The most prevalent approaches are optical and electrical microscopy.

Mechanical properties or insertion forces: - A microneedle must be sharp and narrow in order to easily enter the skin, as well as sturdy enough not to shatter while inside. The mechanical tests that are done on microneedles include insertion force, insertion depth, and failure force.

In-vitro skin permeation studies: - The diffusion cell equipment is used to determine the penetration of the medication through the skin.

In-vivo animal model studies: - For the study, hairless rats may be employed. The animal must be anesthetized using a competent procedure. Trans-epidermal water loss (TEWL) is one of the criteria taken into account. which monitored both prior to and following microneedling. This parameter is measured with a Delfin Vapometer.

CONCLUSION

The cosmetics sector benefits greatly from the detachable microneedles. Numerous small and large enterprises are presently conducting trials to bring their corresponding microneedle-based products to market. Future studies will address any legal concerns about the use of detachable microneedles and plan and create strategies to guarantee an affordable, dependable method of producing detachable microneedles in large quantities. Overall, the market for detachable microneedles appears to have a bright future due to the rapid expansion of basic contemporary industrial expertise. Microneedles have the potential to revolutionize drug delivery, but they also have other benefits, like better patient compliance, less pain and discomfort than traditional needles, and the ability to target specific areas for treatment. Researchers are currently investigating the use of microneedles for applications other than drug delivery, like diagnostics, biomarker monitoring, and even vaccination. As this technology advances, we can expect even more exciting developments and applications that could change healthcare practices in the future. Numerous innovative microneedle product concepts are now being developed, which will be very beneficial to the cosmetics sector going forward.

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