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Nanocarrier Mediated Cutaneous Drug Delivery System

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ABSTRACT
Nanocarrier drug delivery system new a now a days but rapidly developing science where materials use in thesmall-scale range serve as optimistic diagnostic tools to deliver drug to achieve therapeutic effect atspecific targeted sites in a controlled manner. Nanotechnology has been multiple advantages in treating chronic long-term diseases. there is a various dominant application of the nanomedicine (chemotherapeutic agents, biological agents, immunotherapeutic agents etc.) in the treatment of various diseases. This review, represents an updated summary of recent advances in the Feld of nanocarriersmediated drug delivery systemsThe opportunities and challenges of nanomedicines in drug delivery from natural and chemical origin examples are also discussed. The cutaneous drug delivery represents acorrect option for the management of skin diseases. However, the skin has a very complex and difficultframework, although the skin barrier is disturbing in some of hypodermic diseases. The nanocarrier mediated cutaneous delivery look to propose a hope to provide targetedand potent drugs into specific sites of the skin with decrease side effects. This review highlights the recent approaches, anatomy and physiology of skin, drug design and drug delivery process and also mechanism, application. Here, we review on nanocarrier mediated cutaneous drug delivery.

I. INTRODUCTION

To increase drug penetration, a variety of various forms of drug delivery methods have been created in the field of nanotechnology and nanocarriers. The skin barrier inhibits the drugs from penetrating easily, as the skin is naturally refractive to highly hydrophilic or highly lipophilic compounds. CDDS use for the treatment of dermatological disease is preferred by most patients and physicians for a local effect where it can reduce the demand for administration and their side effects. Various chemical and physical perfect have been examined in the previous decades to bypass the skin barrier, the majority of which damaged stratum corneum.The use of small nanometre-sized carriers to improve skin penetration or localization in a non-invasive manner is a new method. Nanocarriers can help with medication delivery by encapsulating pharmaceutical active ingredients and forming specialized properties including penetrating the hair follicle, interacting with the skin's lipid for transport, and forming a depot form for long-term release.Improved penetration through all routes across the skin, including intracellular and intercellular, according to nanocarriers' increased surface area to volume ratio. In this review, we will look at some of the newest research, as well as the anatomy and physiology of skin, drug formulation and delivery, and mechanism and administration. A review of nanocarrier-mediated cutaneous medication delivery is presented here.

For decades, a great deal of work into achieving successful drug delivery into skin tissue. Because it is so simple to administer, the cutaneous drug delivery system (CDDS) is a popular technique of administration. Due to the skin barrier, a large portion of medications are still administered through needles. Needle injections, in general, have two major drawbacks. The first is pain and needle anxiety, and the second is infections caused by needle re-use and accidental injury. Injections are uncomfortable and painful, which contributes to needle fear and lowers quality of life. According to certain research, 30 percent of adults suffer from needle fear.Unintentional needle damage is a more serious concern for both the patient and the clinician. Hundreds of millions of dollars have been spent on more health care, while infectious disease transmission has soared. Specifically, the stratum corneum (SC), which is the epidermis' thin outer layer, is responsible for the skin's remarkable barrier characteristics. The stratum corneum, unlike the other body tissues, is made up of corneocytes that are surrounded by an extracellular environment of lipids organised in numerous lamellar bilayers.These lipids stop the body from losing too much water and prevent hydrophobic medications with a low molecular weight from entering. Following their entrance into superficial dermal capillaries, drugs administered via the skin tissue as

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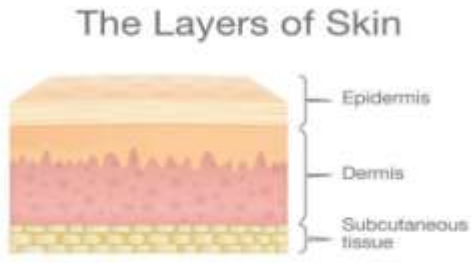
systemic treatment face a substantial challenge. As a result, several strategies of skin penetration have been investigated to improve medication delivery through the SC.

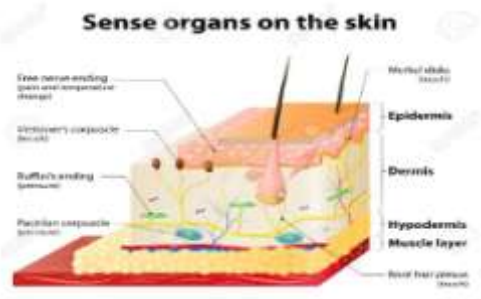
Anatomy and Physiology of Skin: -

The skin, also known as the cutaneous membrane or tegument, covers the body's exterior surface.

It is a sensory organ that is the body's largest organ in terms of surface area and weight. The biggest organ in the body, skin covers the whole exterior surface of the body. The epidermis, dermis, and hypodermis are the three layers that make up the skin, each with its own structure and function. The skin is made up of a complex network that acts as the body's first line of defence against viruses, UV rays, chemicals, and mechanical harm.It also regulates the amount of water released into the environment and the temperature. The relevant anatomical structures of the epidermal layer of the skin, as well as their structure, function, embryology, vascular supply, innervation, surgical considerations, and clinical relevance, are discussed in this article. Human skin is comparable to that of most other animals, and it is especially similar to that of pigs. Regardless of the fact that nearly all human skin has hair follicles, it can appear hairless. Hairy and glabrous skin are the two main forms of skin (hairless). The adjective cutaneous refers to the surface of the skin (from Latin cutis, skin).

Because the epidermis, dermis, and hypodermis contain specialised sensory nerve systems that sense touch, surface temperature, and pain, the skin works as a sense organ.





- Sweet gland
- Vasodilation and vasoconstriction

Cutaneous sensation

- Meissner's corpuscles
- Pacinian corpuscles
- Root hair plexuses
- Pain heat/cold receptor

Metabolic function

- Vitamin d synthesis

Blood reservoir

- Shunt more blood into the circulation when needed

Excretion

Nanocarriers For Cutaneous Drug Delivery

Colloidal structures with a mean diameter of less than 500 nanometres are classed as nanocarriers (Neubert, 2011). Liposomes, nanoparticles (NPs), nano-emulsions, and microemulsions are among the new nanocarriers being studied for TDD. Higher drug diffusion for TDD systems in the target area, enhanced physicochemical stabilisation of the drug-loaded in nanoparticles, and prolonged and regulated drug delivery are only a few of the advantages of NPs. Lipid-based NPs including liposomes, solid lipid nanoparticles (SLNs), niosomes nanostructured lipid carriers (NLCs), and nano-emulsions have also been widely used for TDD delivery (Patzelt et al., 2017).For cutaneous medication delivery, skin, the largest organ of the human body, provides a painless and compliant interface. In comparison to injections and oral drug delivery, cutaneous drug delivery improves patient compliance, avoids hepatic metabolism, provides sustained and controlled delivery over long periods of time, concentrates active agents at the site of disease, and eliminates systemic side effects. Recent biotechnology breakthroughs have paved the way for very promising, potent, and precise molecular targeting therapies. Although advances in drug delivery technologies have allowed some of these innovative medications to be used successfully in clinical trials, the number of effective cutaneous drugs remains limited. Despite over four decades of intensive research, the technology's success remains restricted.

Nanocarrier Skin Penetration

Nanoparticles have been increasingly common in consumer products during the previous

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few decades. Since the 1990s, sunscreens and cosmetics actually contains nano-sized titanium dioxide and zinc oxide have been used to protect skin from harmful ultraviolet radiation, and more recently, silica nanoparticles and fullerenes have been added to some cosmetic formulations to act as desiccants and free radical scavengers, respectively. While the nanoparticles in these formulations aren't meant to penetrate skin, their existence indicates a change in biomedical science and consumer product development toward nano-enabled items. Many studies addressing the impact of nanoparticles on skin toxicity have been spurred by the rise in consumer items containing nanoparticles and research on nanoparticles as TDD systems.Many of these early studies focus at nanoparticle skin penetration in ex vivo or in vivo skin models, as well as nanoparticle cytotoxicity in in vitro skin cell models. For years, the belief has been that unbroken skin creates an impenetrable barrier to nanoparticles; nevertheless, there is enough proof to show that nanoparticles can penetrate skin depending on size, charge, and material. Beyond the size and charge dependence of skin penetration, which is the focus of this section, other factors such as nanoparticle doses, structure, biological adhesiveness, and in vivo dissociation can influence skin permeation and biologic activity.Because delivery through the skin is less painful than injection, skips first-pass metabolism in the liver, and may be designed for delayed and consistent drug release into systemic circulation, nanocarriers are being studied for a variety of uses in TDD. Nanocarriers have been studied for use in the transdermal delivery of vaccines, antihypertensive medicines, antiparkinsonian medicines, and chemotherapeutics for these reasons. Healthy skin, on the other hand, acts as a physical barrier to xenobiotic chemicals and particulates, and nanoparticles can permeate intact skin in different ways depending on their size, charge, and composition. Because skin barrier disruption enhances nanoparticle penetration, nanocarriers are well suited to treating skin diseases including psoriasis and atopic dermatitis, which have skin barrier deficiencies.

Advantages and disadvantages

Advantages

Provides stable plasma levels, which is beneficial for medications that require stable plasma levels.
Longer duration of action Less frequent dosing
Allow the Food and Drug Administration some flexibility Patches on the Human Skin are being removed. Patients who are not eligible for dose administration might use this alternative route to receive drugs that are both hydrophilic and lipophilic.
Efficacy has improved.
Toxicity is reduced.
Distribution Improvement
Customer Satisfaction Increased

Disadvantages

The skin's minimal permeability limits the number of medications that can be used.
Drug-induced local oedema, itching, and erythema produced by the adhesive or other excipients in the patches
Irritation at the administrative location.
Large-scale production difficulties
Lipids disrupt the stratum corneum's integrity.
Polymorphic transition is a possibility.
This drug delivery system's manufacturing costs are extremely high.
It's possible that this product will induce allergic responses.

Various Types of Nanocarrier-Based Drug Delivery Systems

types
1. Polymeric Nanoparticle
2. Solid Lipid Nanoparticle
3. Nanosuspension
4. Polymeric Micelles
5. Ceramic Nanoparticles
6. Liposomes
7. Dendrimers
8. Magnetic Nanoparticles
9. Nano shells Coated with Gold
10. Nanowires
11. Nanopores
12. Quantum Dots
13. Ferrofluids

Several new nanocarrier-mediated drug delivery methods are currently in use to deliver chemotherapeutic drugs to specific areas. Figure 3 shows the structural representation of several nanocarrier-based delivery systems. Polymeric nanoparticles, liposomes, polymeric micelles, carbon nanotubes, dendrimers, and solid lipid nanoparticles are examples of essential nanocarriers. Quantum dots and magnetic nanoparticles the next sections go over all these nanocarriers.Nanocarriers Developed from Polymer

Nanoparticles are made from natural polymers such as albumin, heparin, and chitosan, as well as cellulose and xanthan gum, for the targeted delivery of nucleotide-based medicines, oligonucleotide pharmaceuticals, and proteins. In recent years, clinics have begun testing

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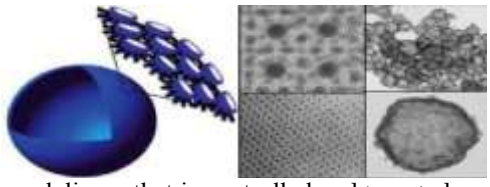
nanometrepaclitaxel-loaded nanoparticles for the treatment of metastatic mammary gland tumours.

1. POLYMERIC NANOPARTICLE

Size is small. Capillaries are easily penetrated. Drug build-up at the target site. Preparation is done with biodegradable materials. Drug release that lasts a long time.



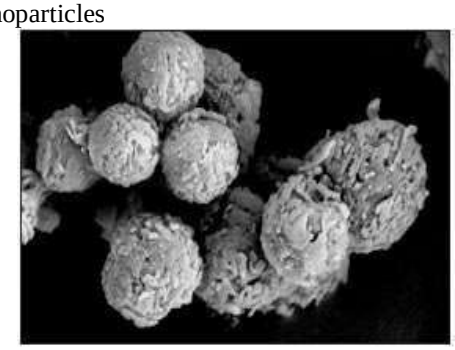
• Drug delivery that is controlled and targeted

2. SOLID LIPID NANOPARTICLE

It's a colloidal carrier system that acts as a delivery port.

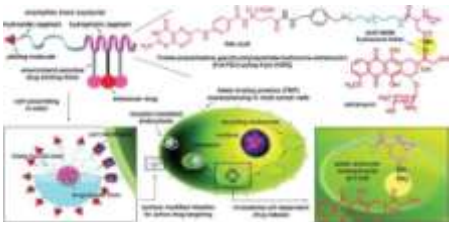
3. NANOSUSPENSION

Good for poorly soluble drugs Drug powder and surfactant in high pressure homogenisation Nanoparticles



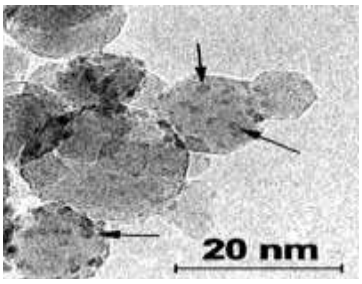
4. POLYMERIC MICELLES

Water-insoluble medicines are delivered systemically via micellar methods. In water, amphiphilic copolymers self-associate to create micelles. Renal excretion and RES are avoided when the size is less than 100 nm in diameter. Endothelial cell permeability is also caused by small size. In tumour cells, they accumulate far more than in normal cells.



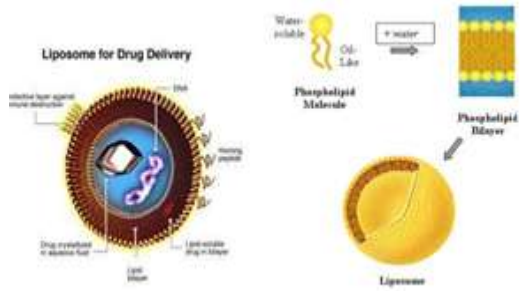
5. CERAMIC NANOPARTICLES

Easy to prepare, similar to the sol-gel method. pH has no effect on swelling or porosity. Doped molecules (enzymes, medicines) are protected from denaturation induced by pH and temperature. Biological systems are compatible. Conjugation of a wide range of monoclonal antibodies to target specific regions in vivo is simple.



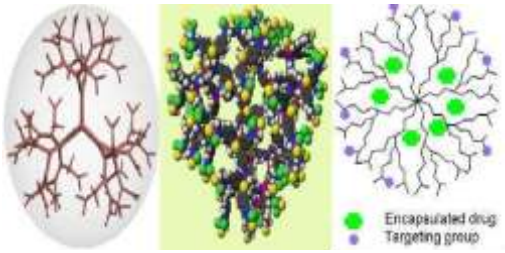
6. LIPOSOMES

Small artificial spherical shape vesicles
Prepared from natural nontoxic phospholipids and cholesterol



7. DENDRIMERS

Tree like molecules with defined cavities



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8. MAGNETIC NANOPARTICLES

Powerful versatile diagnostic tool in medicine

Use:

By attaching to an appropriate Ab, a sp molecule, a cell population, or microbes can be labelled.

As MRI contrast agents

As a means of medication delivery Magnetic immunoassay is a type of immunoassay that uses magnets to

A sensitive magnetometer detects the magnetic field generated by magnetically labelled targets.

Iron oxide [magnetite Fe203 or maghemite] is covered with a polymer like dextran.

Commercial items include:

Lumiren (silicon coated iron oxide) has a 300 nm diameter.

Endorem (magnetite with a dextran coating) has 150 nm diameter.

9. NANOSHELLS COATED WITH GOLD

Infrared optical activity combines with properties of gold colloidConsist of Dielectric core (gold sulphide) or Metal shell (gold)

Surface properties of gold nano shells gold colloid.

Use:

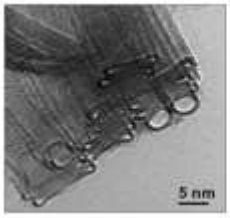
- Destroy breast cancer cells
- Antibodies to breast cancer can be directly attached to gold nano shells
- Nano shells strongly absorb infrared light while normal tissue is transparent to it
- Nano shell-antibody complex binds only to cancer cells
- Infrared laser heats up the nano shells and thus cancer cells are destroyed.

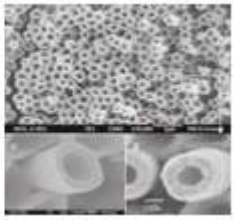
10. NANOWIRES

Linear nanostructures made from metals, semiconductors or carbon.

Modifications: Singleor multi-walled,Filled or surface modified

Use: Fillers for nanocomposites for material with sp properties





11. NANOPORES

E.g.: Aerogel produced by sol-gel chemistry

Applications:

1. Catalysis.
2. Thermal insulation.
3. Electrode material.
4. Environment filters.
5. Controlled release drug carriers.

12. QUANTUM DOTS

Luminescent semiconductor nanoparticles that absorb a lot of light Size ranges from 2 to 8 nanometers in diameter. Local and nanocrystal surface treatment affects the luminescence characteristics of semiconductors. Shell of CdSe-CdSInP&InAs: 550nm to 630nm InP&InAs: 550nm to 630nm Range: Ultraviolet near-infrared.

13. FERROFLUIDS

Colloidal solutions of iron oxide magnetic nanoparticle covered by polymer layer coated with affinity molecules s/a AbSize: 25-100 nm radius

Hence, they behave as a solution rather than suspension

Application:

- Oral Drug Delivery: Because to the increased surface area, nanosizing drugs results in a considerable improvement in oral absorption and bioavailability. Boost the solubility of saturated water.
- Entire word has been discovered to be effective in the treatment of a variety of malignancies when administered intravenously. Due to the intractable nature of taxanes in water, a TAXOL Nano-emulsion combining Paclitaxel and polyethoxylated castor oil in ethanol was developed.
- Eye Drug Delivery: To maintain drug release, biodegradable and water-soluble polymers with ocular tolerability can be utilised.
- Drug adherence to the mucosal surface improves, resulting in a longer drug residence duration at the absorption site. It allows for immediate activity to commence, followed by control. Drug distribution in the lungs: Increased drug adhesion to the mucosal surface extends drug residence time at the absorption

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site. It has a fast commencement of action and then a controlled release of active moiety, which is necessary for most pulmonary illnesses. Budesonide, a poorly water-soluble corticosteroid, has been successfully synthesised as a Nanosuspension for the administration of pulmonary drugs.

- Drug delivery that is precise. This technology has shown enormous promise in the delivery of targeted drugs, particularly to the brain. The biggest milestone in target drug delivery has been the successful targeting of the peptide Dalargin to the brain using surface modified poly (isobutyl cyanoacrylate) Nanoparticles.

II. CONCLUSION:

We also discussed about how these few significant categories of nanocarriers can be used for cutaneous medication delivery and therapeutic targeting. So, based on the findings of this study, it's possible to conclude that nanocarriers made from healthy cells-friendly biomaterials coupled with epidermal receptor cell markers for targeted and enhanced drug delivery at the site of action are superior to the standard nanocarriers system.

Finally, nanocarriers improve the transport of a variety of medications into the skin. Because of the disturbance of the skin's barrier and the proximity of the target cells, they're an ideal choice for improving skin disease treatment.

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