International Journal of Advanced Technology in Engineering and Science
Vol. No.4, Issue No. 08, August 2016
www.ijates.com
ijates
ISSN 2348 - 7550

NANO DRUG DELIVERY THROUGH VARIOUS DRUG DELIVERY SYSTEMS FOR BIOMEDICAL APPLICATIONS

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ABSTRACT

Transdermal drug delivery system is the system in which the delivery of drug occurs through the skin in a controlled and predeterminedmanner, hence it improves the therapeutic efficacy of the drug. Skin is the largest organ of human body. It is an effective medium for the absorption of drugs particularly for small molecular size. An advantage of transdermal drug delivery system is that the patch delivers the drug safely without any pain because the drug is delivered through the skin at a controlled rate. The disadvantage of transdermal drug delivery is that there is a difficulty in absorption of drug because of large molecular size, resulting in lower levels of blood/plasma. There are many types of transdermal patches which are available in the market (nicotine patch, fentanyl patch, estrogen-progestin contraceptive patch, scopolamine patch, nitroglycerinpatch, lidocaine patches etc.) when we introduce nanotechnology in transdermal patches then these patches can be used for the drugs which has large molecular size.Nano patches are small sized which has about 20,000 micro-projection per square centimeter on its surface.Nanoparticle can increase drug efficiency and reduce side effects. Nanomaterials have large functional surface and higher loading capacity.Nanoparticles of gold are non-toxic and as a base metal it is inert under physiological conditions without any ion release. This article covers the introduction of Transdermal Nano drug delivery system, advantages and disadvantages of these system, factors that affect percutaneous absorption in the transdermal Nano drug delivery, the components of transdermal Nano patches and types of Nano patches.

Keywords: Nano Drug Delivery, Transdermal Nano Patches, Nanomaterials, Therapeutic Efficacy

I. INTRODUCTION

Transdermal drug delivery system can be defined as the administered medications in the form of patches. When these patches are applied to the skin, it delivers the drug through the skin at a controlled rate. We all know that, common form of drug delivery is oral route. But this route has some significant drawbacks like first pass metabolism, drug degradation in gastrointestinal tract. Especially it is very convenient way for the patients who forget to take their medicines. In recent years, it has been shown that skin is the most useful route for drug delivery. Transdermal drug delivery system provides the controlled and continuous delivery of drugs through

the skin to the systemic circulation. It is a type of adhesive patch that is placed on the skin to deliver any type of drug. Through a diffusion process, drug enters into the blood stream. There is a high concentration in the patch and low concentration in the blood, drug is diffused by the diffusion process. Drug will keep diffusing into the blood for a long span and it maintains the constant concentration of drug into the blood flow[18]. Transdermal patches were developed in the 1970s and in 1979 it was approved by FDA for the treatment of motion sickness. There are so many types of transdermal products in the market like patches of scopolamine for motion sickness, nicotine for quitting smoking, estrogen for menopause and for the prevention of osteoporosis after menopause, nitroglycerin for angina, and lidocaine for the pain relief of shingles [13]. To increase the range of drugs available for transdermal delivery, the use of nanocarriers has emerged as an interesting and valuable alternative for delivering lipophilic and hydrophilic drugs throughout the stratum corneum with the possibility of having a local or systemic effect for the treatment of many different diseases. There are many types of nanocarrierslike nanoparticles, ethosomes, dendrimers, liposomes, etc. They are very different in structure and chemical nature. They are very small to be detected by the immune system, and they can deliver the drug in the target organ using lower drug doses in order to reduce the side effects [9,10].

II. ADVANTAGES OF TRANSDERMAL NANO DRUG DELIVERY SYSTEMS: [8,9,20,21]

- Delivery of drug is totally painless so, there is no need of injections.
- It eliminates the gastrointestinal side effect.
- It also improves the patient compliance because of simpler, pain free delivery.
- Drug is delivered in controlled and predetermined manner in order to increase the therapeutic efficacy of drug and reduced the side effect of drug.
- It avoids the first pass metabolism of drugs.
- Oral route of administration is inadvisable for the patient experiencing nausea or vomiting. So, in this case transdermal patches are best.
- It also achieves consistent plasma levels like in intravenous infusion but it is noninvasive in nature.
- Self-medication is possible.
- It reduces the frequency of dosing.
- It is a controlled delivery so that it results in more reliable and predictable blood levels.
- In case of toxicity rapid termination is possible. It can be administered by simply removing the transdermal drug delivery system (patch).

III. DISADVANTAGES OF TRANSDERMAL DRUG DELIVERY SYSTEMS

- It is uncomfortable to wear because sometimes local irritation is a major problem and erythema, itching and local edema can be caused by drug, the adhesive or other excipients in the patch formulation.
- Heat, cold, sweating and showering prevent the patch from sticking to the surface of skin for more than one day. A new patch has to be applied daily.
- Patches should be carefully discarded after use because they could cause serious side effects if ingested by young children or pets.

- Because of skin's low permeability, it limits the number of drugs.

IV. STRUCTURE OF SKIN

Skin is the largest organ of the human body. It has sensory nerve endings of pain, temperature and touch. Skin is composed of two distinct layers:

4.1. Epidermis is the upper layer of skin. It is composed of stratified squamous epithelium. Its thickness is different on different parts of body. It has several layers like Stratum germinativum ,spinosum , granulosum , andlucidum.

4.2. Dermis is the inner layer of skin and it is composed of a strong connective tissue containing collagen and elastic fibers. On the basis of tissue structure, the dermis can be divided into a superficial papillary region and a deeper reticular region. The Structure in Dermis are:Blood vessels, Sensory nerve endings, Lymph vessels, Hairs , sebaceous glands and Arrectorpilli muscle [23,24].

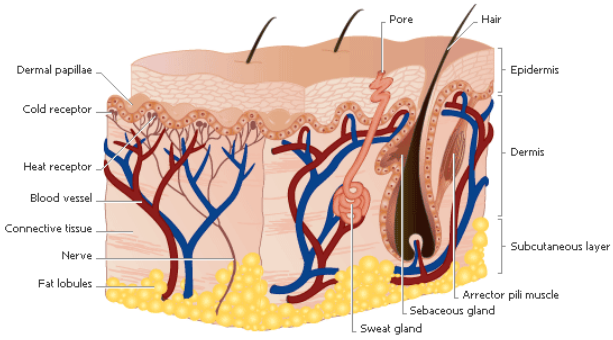

Figure1. Structure of Skin

V. FACTORS IMPORTANT FOR TRANSDERMAL DRUG DELIVERY:[18]

A. Condition of the skin in cases the skin is abraded or cut will permit drugs to gain direct access to subcutaneous tissues and the capillary network obviating the designed function of the TDDS.
B. B Physical and chemical properties of drugs.
C. C Molecular weight of a drug is an important factor.
D. D Drug concentration is an important factor. The amount of drug percutaneously absorbed per unit of surface area per time interval increases as the concentration of the drug substance in the TDDS is increased
E. E More drug is absorbed through percutaneous absorption when the drug is applied to a larger surface area.
F. F The skin hydration favors percutaneous absorption because TDDS act as occlusive moisture barriers through which the sweat from the skin cannot pass. So, it increases the skin hydration.
G. G Drug absorption will be more when the medicated application is permitted to remain in contact with the skin for long time.

VI. COMPONENTS OF TRANSDERMAL PATCHES:[14,17,18,20]

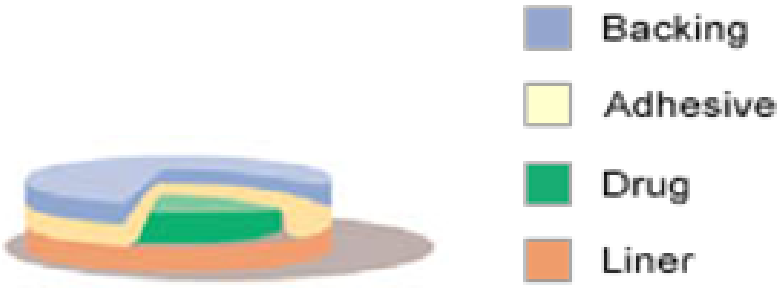

Figure2: Components of Transdermal Patches.

- Liner - It protect the patch when we stored the patch for a long period of time. Before use liner is removed.
- Drug - Drug solution is in direct contact with release liner eg. Nicotine.
- Adhesive - It adhere the components of the patch and the patch to the skin eg. acrylates, silicones.
- Membrane–It Controls the release of drug from the reservoir and multilayer patches.
- Backing -It is a process by which we can save the patch from outer environment.
- Permeation enhancers - Controlled amount of drug isreleased by the use of permeation enhancerseg. terpenes, pyrrolidones, alcohol, ethanol, surfactants like sodium lauryl sulfate, pluronic F127 etc.

VII. TYPES OF NANOCARRIERS USED IN TDDS

Most important carriers for transdermal drug delivery are: Liposomes, Ethosomes, Transfersomes, Niosomes, Dendrimers, Nanoemulsions and Nanoparticles. They are too small to be detected by the immune system. Nanocarriers uses very less amount of drug so, automatically they reduce side effects[9]. Because of small sizes , nanocarriers can deliver drugs. Nanocarriers are suitable for both hydrophobic and hydrophilic drugs.

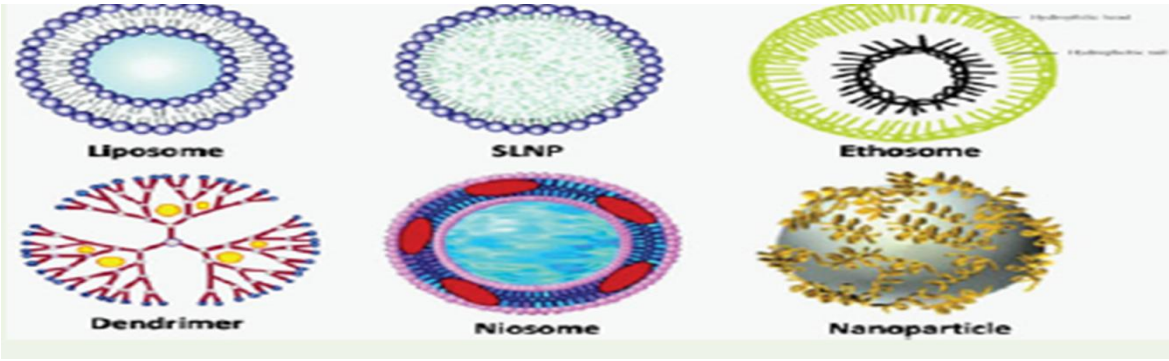

Figure3. Types of Nanocarriers

7.1. Microemulsions

Microemulsions are dispersions with droplet size from 10 to 100 nm. They do not have thetendency to coalesce. They have several physicochemical properties such as transparency,optical isotropy, low viscosity and thermodynamic stability.Most of the microemulsions have very low viscosity, which may restrict their application tothe transdermal delivery field due to inconvenient use .Microemulsions have highsolubility potential for hydrophilic drugs[2].

7.2. Nanoemulsions

Nanoemulsions are isotropic dispersed systems of two nonmiscible liquids, normally consisting of an oily system dispersed in an aqueous system, or an aqueous system dispersed in anoily system but forming droplets or other oily phases of nanometric sizes. Nanoemulsions can be prepared by three methods mainly: high-pressure homogenization, microfluidization and phase inversion temperature. They are thermo-dynamically unstable systems, as compare tomicroemulsions .They can be formulated as foams, liquids, creams and sprays . They are susceptible to Oswald ripening, and as a consequence susceptible to creaming, flocculation, and other physical instability problems associated with emulsions. Despite this, they can be stable (metastable) for long periods due to theirextremely small size and the use of adequate surfactants. Nanoemulsions are suitable for hydrophobic and hydrophilic drugs They are nontoxic and nonirritant systems,so they canbe used for skin Transdermal delivery using nanoemulsions has been reduced due to the stability problems inherent to this dosage form[2,9].

7.3. Liposomes

Liposomes are colloidal ,vesicular structures composed of one or more lipid bilayers surrounding an equal numbers of aqueous compartments. Liposomes are biocompatible, completely biodegradable, non-toxic and non-immunogenic. They are suitable for delivery of hydrophobic and hydrophilic drugs[12]. In this, membranes are usually made of phospholipids, which are molecules that have a hydrophilic head group and a hydrophobic tail group [11].Due to their inherent structural properties liposomes are capable of encapsulating hydrophilic drugs inside their aqueous phase and hydrophobic drugs inside their phospholipids bilayers[16]. Currently, many liposome-based drugs and biomedical products have been approvedfor use in clinic.Liposomes were also proposed as drug carriers that reduce toxicity and increase efficacy. Thenature of liposomes makes them one of the best alternatives for drug delivery because theyare nontoxic and remain inside the bloodstream for a long time [2]. Liposomes have become one of the pharmaceutical nanocarriers of choice for many purposes. Many liposome-based drugs and biomedical products have been approved for use as medicines. In transdermal delivery, liposomes have been used widely [9].

7.4 Transfersomes

Transfersomes are more flexible than liposomes. Drug delivery through transdermal route needs more flexibility and its flexibility allows the possibility of using them as transdermal vaccine vector [9]. They are sufficiently deformable to penetrate pores muchsmaller than their own size.They are metastable, which makes the vesicle membrane ultraflexible, and, thus, the vesiclesare highly deformable [2]. The difference between transfersomes

and liposomes is the higherhydrophilicity of the former, which allows transfersome membrane to swell more thanconventional lipid vesicle bilayers.

7.5 Niosomes

Niosomes are made of lipids and nonionic surfactants. They are biodegradable and minimally toxic. The niosomes were originally used in the cosmetics industry[9]. They are unilamellar or multilamellar vesicles capable ofentrapping hydrophilic and hydrophobic solutes.Niosomes possess greater stability, but it has high cost. They are versatile nanocarriers because they can be administered through various routes,including transdermal delivery. Niosomesare considered an interesting drug-delivery system in the treatment of dermatologicaldisorders. Niosomes enhance the residence time of drugs in the stratumcorneumand epidermis[2].

7.6 Ethosomes

Ethosomes contain alcohol in the lipid bilayer to make them more flexible and be able to be deformed when pressure is applied. Ethosomes allows drugs to reach deeper skin layers and systemic circulation. They are easy to prepare and considered as safe and efficient. They are soft and malleable. Ethosomes can transport highly lipophilic drugs [9]. The size ofan ethosome vesicle lies within the nanometer range. Because of small size of ethosomes penetration is higher. Ethosomes were able to improve skin delivery of drugsboth under occlusive and non-occlusive conditions [2].Ethosomes have higher quantity of ethanol. Ethanol penetration of drug into the stratum corneum by increases the fluidity of cell membrane lipids. The size range of ethosomes may vary from tens of nano meters to microns (μ). Ethosomes are the modified forms of liposomes [5]. Delivery of large molecules (peptides, protein molecules) is possible and it contains non-toxic raw material in. Ethosomes have become an area of research interest, because of its enhanced skin permeation, improved drug delivery, increased drug entrapment efficiency etc[4].

7.7 Dendrimers

Dendrimers are used in transdermal drug delivery due to its nanometer size range. They are complex molecules having very well defined chemical structures. They improved the drug solubilization and drug bioavailability by controlled and targeted delivery. Dendrimers have control over their architecture, shape and density[15]. The mainproblems with dendrimers are their poor biodegradation and inherentcytotoxicity . Dendrimers act like solubility enhancers, increasing the permeation oflipophilic drugs but, they are not good carriers for hydrophilic drug [1, 2].

7.8 Gold Nanoparticles

Nanoparticles of gold are non-toxic and as a base metal it is inert under physiological conditions without any ion release. They can be synthesized with different sizes and it has high surface area and tunable stability which is best suited for the delivery of drug. Toxicity of gold nanoparticles depends upon the physical parameters (shape, size), dose, route of delivery and exposure time [25, 27]. It can be used in numerous biomedical applications by varying its size and functionalization. In case of drug delivery generally we prefer metal nanoparticles in

diagnosis and therapeutics because of their high reactivity to the cells and its stability over high temperatures make them appropriate for drug delivery applications. Its cytotoxicity is also negligible because of physiochemical properties [26].

Gold nanoparticles have versatile surface chemistry; it allows to be coated with polymers and biological recognition molecules. These coatings make them stable, biocompatible and avoids toxicity also [25, 26].

VIII. CONCLUSION

Transdermal patches delivers the drug safely without any pain because the drug is delivered through the skin at a controlled rate. But, the disadvantage of transdermal drug delivery is that there is a difficulty in absorption of drug because of large molecular size, resulting in lower levels of blood/plasma. When we introduce nanotechnology in transdermal patches then these patches can be used for the drugs which has large molecular size. Nanocarriers have shown many advantages for topical and transdermal delivery of drugs. Most important carriers for transdermal drug delivery are: Liposomes, Ethosomes, Transfersomes, Niosomes, Dendrimers, Nanoemulsions and Nanoparticles. They are too small to be detected by the immune system. Nanocarriers uses very less amount of drug so, automatically they reduce side effects. Nanocarriers are suitable for both hydrophobic and hydrophilic drugs.

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