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Transdermal Drug Delivery Systems

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Research Article

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ABSTRACT

Transdermal drug delivery has developed significance in the field medicine, but it has to develop its potential in order to use it as an alternative to oral route of drug delivery and intravenous injections. The First-generation transdermal delivery systems have been used for delivery of small, lipophilic, low-dose drugs. Second-generation delivery systems are used for chemical enhancers, non-cavitational ultrasound and iontophoresis. Third-generation delivery systems, thermal ablation can be used as a penetration enhancer. Micro needles and thermal ablation are widely used through clinical trials for delivery of vaccines and macromolecules. Using these novel second- and third-generation features, transdermal delivery has increased its significance in the current medical field.

INTRODUCTION

Transdermal drug delivery system (TDDS) has been in use since a very long time. The most commonly used were creams and ointments for skin disorders. The absorption of the drug through the skin from the patch can be confirmed by the presence of side effects of the drug or formulation. Many drugs have been applied to the skin for systemic treatment. The term Transdermal drug delivery system includes all the topical formulations in which the active ingredient is delivered into the circulation[1-8]. TDDS has been designed to provide controlled and continuous delivery of drugs through the skin into the systemic circulation. Moreover it also overcomes first pass metabolism unlike other drug delivery systems and painful drug delivery. Hence, the transdermal delivery systems are of great interest and important in recent time [9-14].

In TDDS, the active ingredient of the formulation or the drug is delivered directly into the blood stream through the skin. The main asset of this type of drug delivery is that, the delivery of drug is controlled as well as painless. In TDDS, the medicated patch has many components like liners, adherents, drug reservoirs, drug release membrane, etc. which play a vital role in the release of drug through skin [15-22].

Principle of Transdermal Drug Delivery

The principle involved in the working mechanism of a transdermal patch is very simple. A transdermal patch or a skin patch is a medicated adhesive patch that is adhered to the skin to transport a specific dose of medication through skin into the circulation. The drug to be delivered is applied in high dose to the inside of the patch, which is sealed on the skin for long period of time [23-29]. By the process of diffusion, the drug enters the blood stream through the skin. Until there exists high concentration of the drug in the patch and low concentration in blood, the drug diffuses continuously into the blood for a longer period of time maintaining constant concentration of the drug in the blood flow [30-37].

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Types of Transdermal Drug Delivery Systems

Various types of transdermal patches were designed as the time passed on. The types of transdermal patches varied from one another in the method of application. The four main types of transdermal Drug Delivery Systems are discussed in detail.

Membrane permeation controlled system

In this type of transdermal patch, the drug cache (drug reservoir) is encapsulated between metallic plastic laminate which is impermeable to the drug and a rate controlling polymeric membrane with defined drug permeability [38-45]. The molecules of the drug are allowed to release in to the skin only through the polymeric membrane. In the drug reservoir compartment, the drug solids are either dispersed in polymer matrix or suspended liquid medium of more viscosity to form a paste like suspension. A thin layer of adhesive polymer is placed over the polymeric membrane, which will be intimate contact with the skin **(Figure 1)** [46-57].

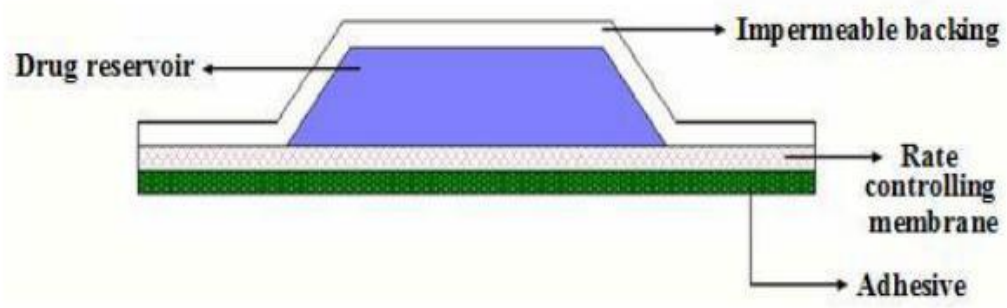

Figure 1: Membrane permeation controlled system

The intrinsic drug release from this type of drug delivery system is given as:

$dq/dt=C_r/1/P_m+1/P_a$

Where,

C_r=Concentration of the drug in reservoir compartment

P_m=Permeability coefficient of Rate controlling membrane

P_a= Permeability coefficient of adhesive layer

Matrix diffusion-controlled system

In this type of TDDS, the drug reservoir is formed by dispersing the drug solids homogenously in a hydrophilic or lipophilic polymer matrix [58-64]. This polymer matrix containing the drug is molded into a disc of predetermined surface area and thickness. This medicated polymer disc is then leashed to an occlusive base plate in a compartment made of drug impermeable metallic plastic laminate backing **(Figure 2).**

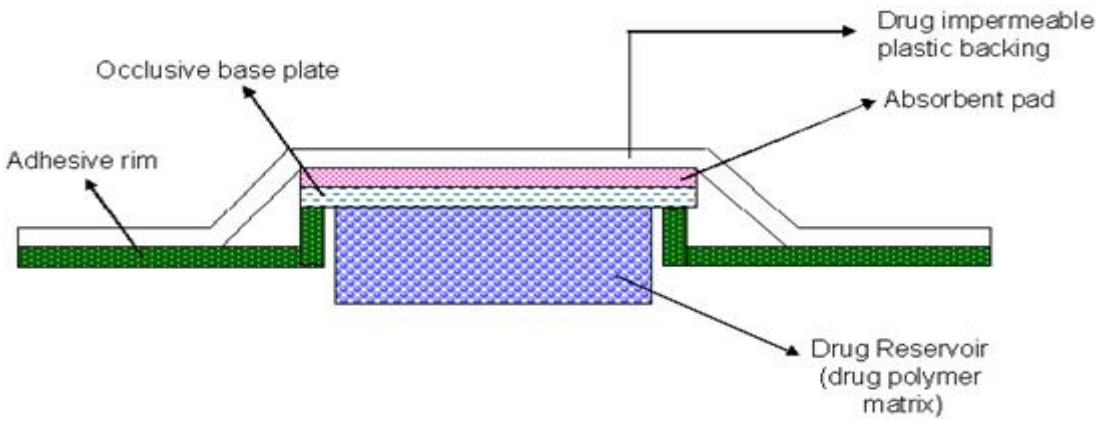

Figure 2: Matrix diffusion-controlled system

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The release rate of the drug in matrix diffusion-controlled system is given as:

$$dq/dt=\sqrt{(AC_p \times D_p)/2t}$$

Where,
A=Initial drug loading dose in polymer
C_p=Concentration of drug in polymer
D_p=Drug diffusion from polymer
t=Time taken

Adhesive dispersion-type system

This type of TDDS is a mutated form of membrane permeation controlled system. In this type, the drug cache is formed by directly dispersing the adhesive polymer [65-74]. Now this medicated adhesive is spread by solvent casting onto a flat sheet of metallic plastic laminate which is impermeable to the drug. This metallic laminate will form a backing to the thin drug reservoir layer **(Figure 3)** [75-82].

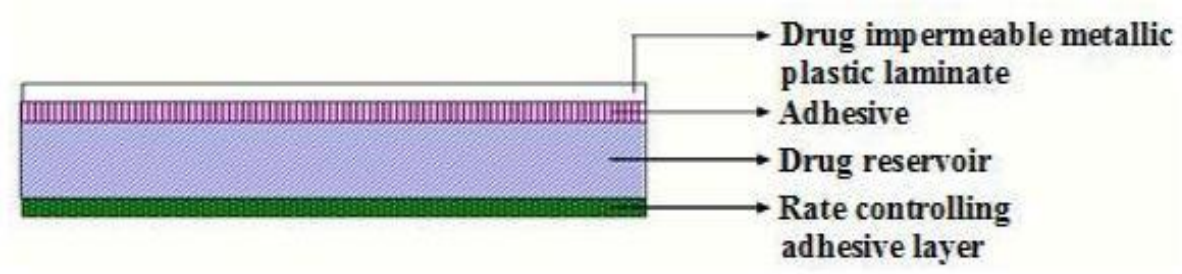

Figure 3: Adhesive dispersion-type system

The rate of drug release in adhesive dispersion-type system is given as:

$$dq/dt=(K_{a/r} \times D_a)/C_r$$

Where,
$K_{a/r}$=Partition coefficient between adhesive layer and drug reservoir layer
D_a=Drug diffused through the skin
C_r=Concentration of drug reservoir

Microreservoir dissolution controlled system

In this type of TDDS, combination of reservoir and matrix dispersion type is used. The drug reservoir is formed by suspending the solid drug particles in aqueous solution of water soluble polymer [83-89]. The drug suspension thus formed is homogenously dispersed in a lipophilic polymer by high shear mechanical force. As a result of this high shear mechanical force thousands of unleachable, microscopic spheres of the drug reservoir are formed [90-94]. The dispersion thus formed is thermodynamically unstable. Hence in order to stabilize the dispersion, cross linking polymers like Gluteraldehyde are immediately added into the unstable dispersion, which results in a medicated polymer disc with a constant surface area and thickness. A transdermal therapeutic system is produced by positioning the medicated disc at the centre with an adhesive rim around it and then it is spread on to the occlusive base plate with adhesive foam pad **(Figure 4)**[96-100].

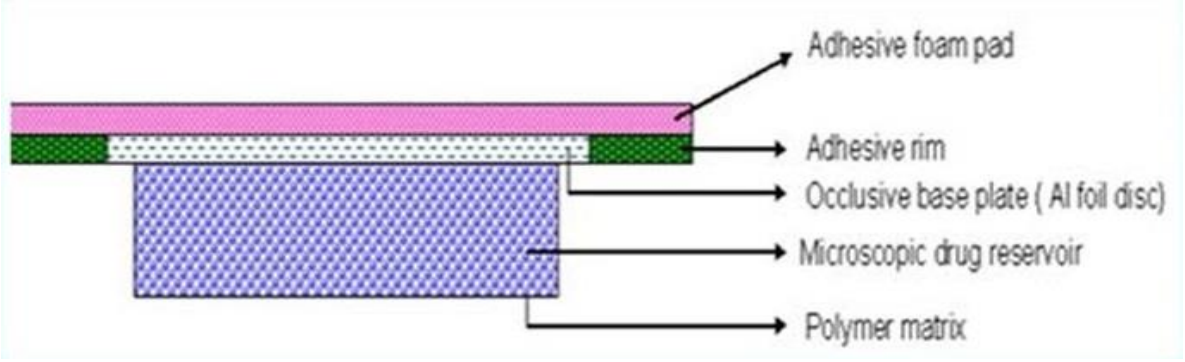

Figure 4: Microreservoir dissolution controlled system

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The rate of drug release in adhesive dispersion-type system is given as:

$$dq/dt=[(K_{m/r}K_{a/m}D_aD_m)C_r]/[(K_{m/r}D_m\delta_d)+ (K_{a/m}D_a\delta_m)]$$

Where,

$K_{m/r}$=Partition coefficient of the drug molecules from reservoir to membrane

$K_{a/m}$=Partition coefficient of drug molecules from membrane to aqueous layer

D_a=Diffusion coefficients in aqueous layer

D_m= Diffusion coefficient in membrane

C_r=Concentration of the drug in the reservoir

δ_d=Thickness of aqueous diffusion layer

δ_m=Thickness of membrane

Advantages of Transdermal Drug Delivery Systems

- TDDS avoids first pass metabolism.
- TDDS is non-invasive.
- TDDS provide therapy for longer period of time with single application.
- The Drug therapy may be terminated by removal of the transdermal patch from the skin.
- TDDS is used for drugs with narrow therapeutic window.
- Painless administration of the system.

Limitations of Transdermal Drug Delivery Systems

- Therapy is limited to potent drug molecules only.
- TDDS may cause skin irritation or contact dermatitis due to drug, excipients and enhancers.

CONCLUSION

In order to achieve successful transdermal drug delivery, the properties of the drug, the characteristics of the transdermal device, status of patient's skin are the important factors to be considered for safe and effective drug delivery. Transdermal drug delivery system is one of the best novel drug delivery system.

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