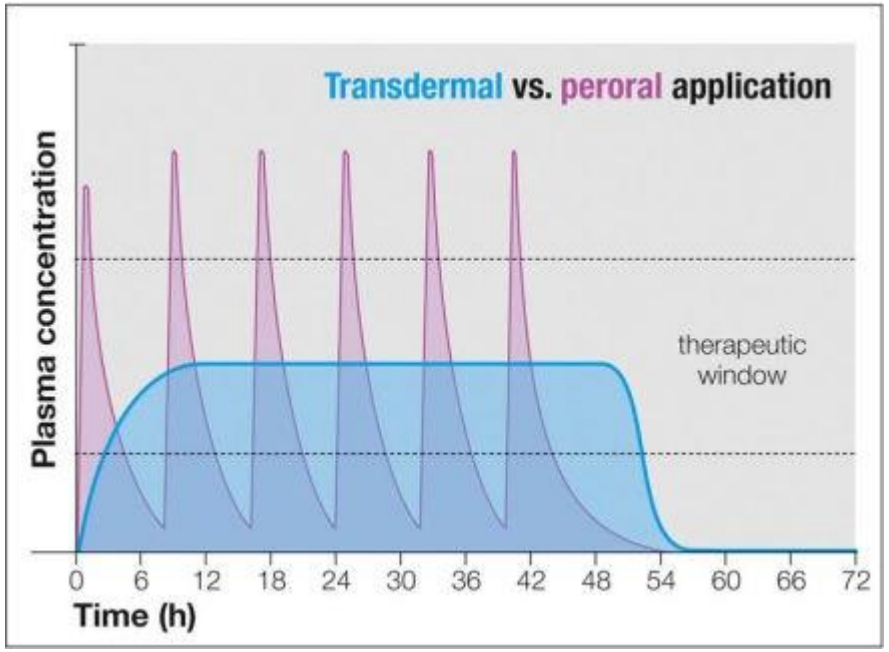
SYSTEMS FOR CONTROLLED DRUG DELIVERY AND DELIVERY MECHANISMS

9. WEEK

TRANSDERMAL THERAPEUTIC DRUG DELIVERY SYSTEMS

Transdermal therapeutic systems (TTS) are defined as ‘self-contained’ discrete dosage forms which, when applied to the intact skin, deliver the drugs, through the skin, at a controlled rate to the systemic circulation.



BENEFITS OF TTS

The advantages of Transdermal delivery over other delivery modalities are as follows:

- Avoidance of ‘first-pass’ metabolism of drugs.
- Peak plasma levels of drugs are reduced, leading to decreased side effects.
- Reduction of fluctuations in plasma level of drugs.
- Utilization of drug candidates with short half-life and low therapeutic index.

- Easy termination of drug delivery in case of toxicity.
- Reduction of dosing frequency and enhancement of patient compliance. For transdermal drug delivery system to be effective, the drug must obviously be able to penetrate the skin barrier and reach the target site.

LIMITATIONS OF TTS

- Drug requiring higher blood level can not be administered.
- Transdermal Patches may not add to all types of Skin.
- Unsuitable for drugs that irritate or sensitize the skin.
- Useful for only low doses of drugs.
- Higher molecular weight candidates (>500 Da) fail to penetrate the stratum corneum.
- Drugs with very low or high partition coefficient fail to reach systemic circulation. Such candidates can not be delivered across the skin without effectively making suitable modifications in the conventional Transdermal delivery systems.

BASIC COMPONENTS OF TTS

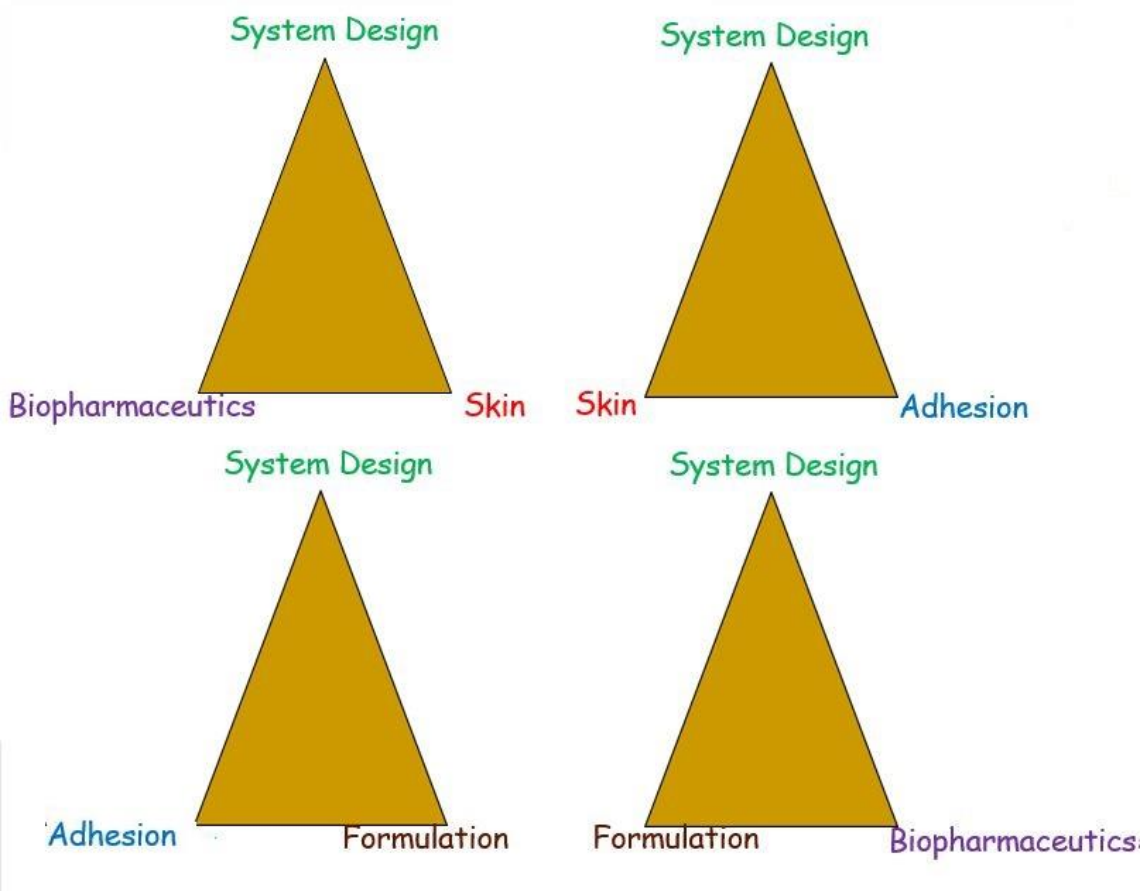
The components of transdermal devices include:

1) Polymer matrix and permeation enhancers

2) Physico-chemical properties of drug

3) Skin characteristics

4) System components



1) Polymer matrix and permeation enhancers

- The polymer controls the release of drug from the device. The polymer used should be stable, non-reactive with the drug, inexpensive, should allow the drug to diffuse properly and release through it.
- Permeation enhancers are compounds, which promote skin permeability by altering skin as a barrier to the flux of a desired penetrant.

2) Physico-chemical properties of drug

For successfully developing a Transdermal drug delivery system, the drug should be osen with great care. The following are some of the desirable properties of a drug for transdermal delivery.

- The drug should have molecular weight less then 1000 Daltons.
- The drug should have affinity for both lipophilic and hydrophilic phases.
- The drug should have a low melting point.

- The half-life of drug should be short.
- The drug should be potent with a daily dose of the order of a few mg/day.
- The drug must not induce a cutaneous or allergic response.
- Drugs, which degrade in the GI tract or inactivated by hepatic first-pass effect, are suitable candidates for transdermal delivery.
- Tolerance to the drug must not develop under the near zero-order release profile of transdermal delivery.

- Drugs which have to be administered for a long period of time or which cause adverse effects to non-target tissues can also, be formulated for transdermal delivery.

3) Skin characteristics

- Skin temperature, pH value, skin hydration, physiological and pathological condition of skin are the important factors that affected the permeation of the drugs to the systemic circulation.

4) System components

a) Adhesives: The fastening of all transdermal devices to the skin is done by using a pressure sensitive adhesive, which can be positioned on the face of the device or to the back of the device and extending peripherally.

b) Backing Membrane: They are flexible and they provide a good bond to the drug reservoir, prevent drug from leaving the dosage form through the top, and accept printing. It is an impermeable substance that protects the product during use on skin.

APPROACHES USED IN THE DEVELOPMENT OF TTS

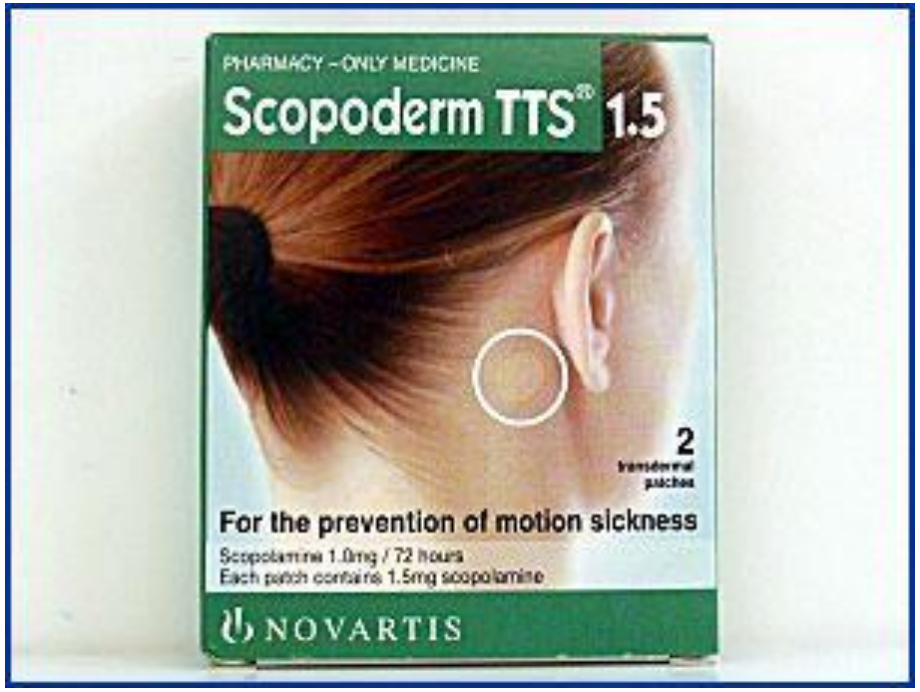
Four different approaches have been utilized to obtain transdermal therapeutic systems:

1) **Membrane Permeation – Controlled Systems**

In this type of system, the drug reservoir is totally encapsulated in a shallow compartment moulded from a drug-impermeable metallic laminate and a rate controlling membrane which may be micro-porous or non-porous. The drug molecules are permitted to release only through the rate-controlling membrane. In the drug reservoir compartment, the drug solids are either dispersed in a solid polymer matrix or suspended in an unreachable, viscous liquid medium such as silicone fluid to from a paste like suspension.

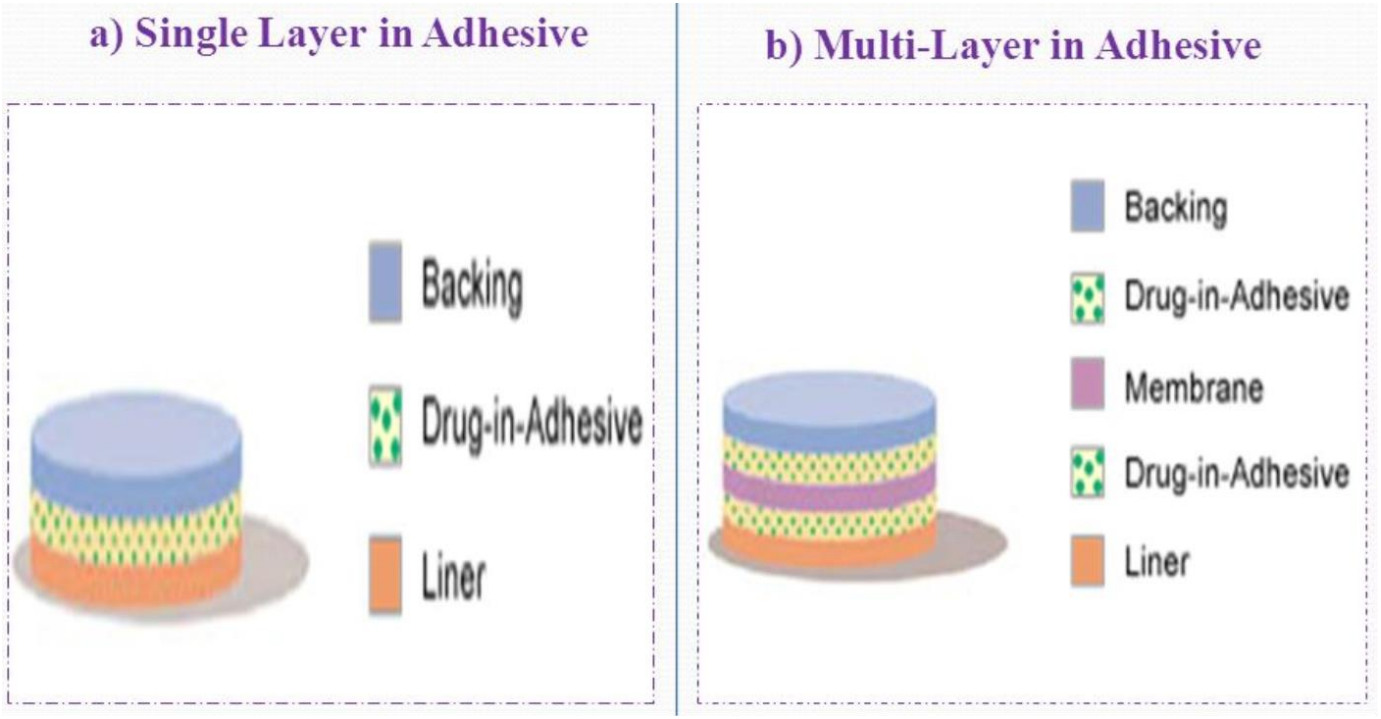
- **Transdermal-Nitro®** Nitroglycerin-releasing transdermal system for once a day medication in angina pectoris.

- **Scopoderm® TTS (Transderm-Scop)** Scopolamine-releasing transdermal system for 72 hrs prophylaxis of motion sickness.



2) Adhesive Dispersion-Type Systems

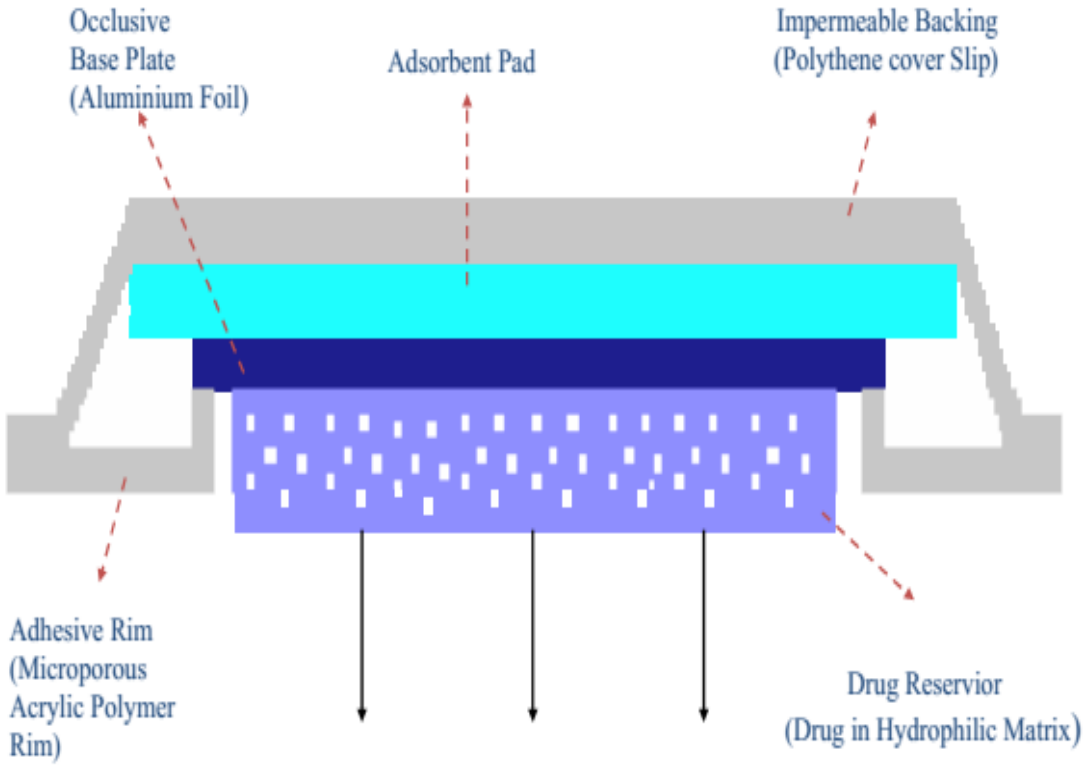
This system is a simplified form of the membrane permeation-controlled system. Here the drug reservior is formulated by directly dispersing the drug in an adhesive polymer.



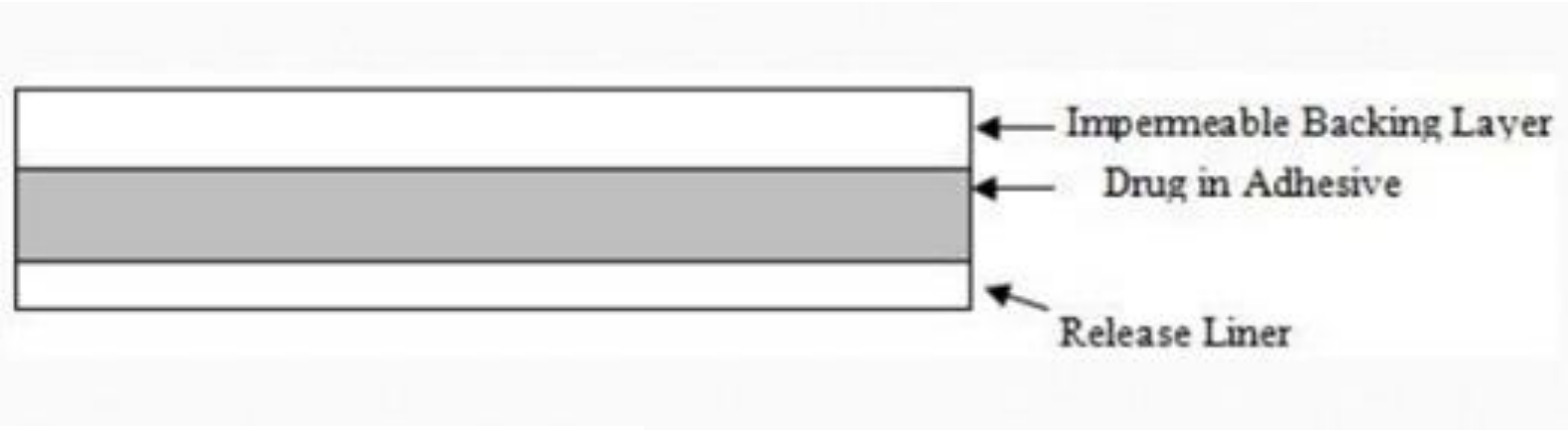
- **Deponit® TTS** Nitroglycerin-releasing transdermal system for once a day medication in angina pectoris.

3) Matrix Diffusion-Controlled Systems

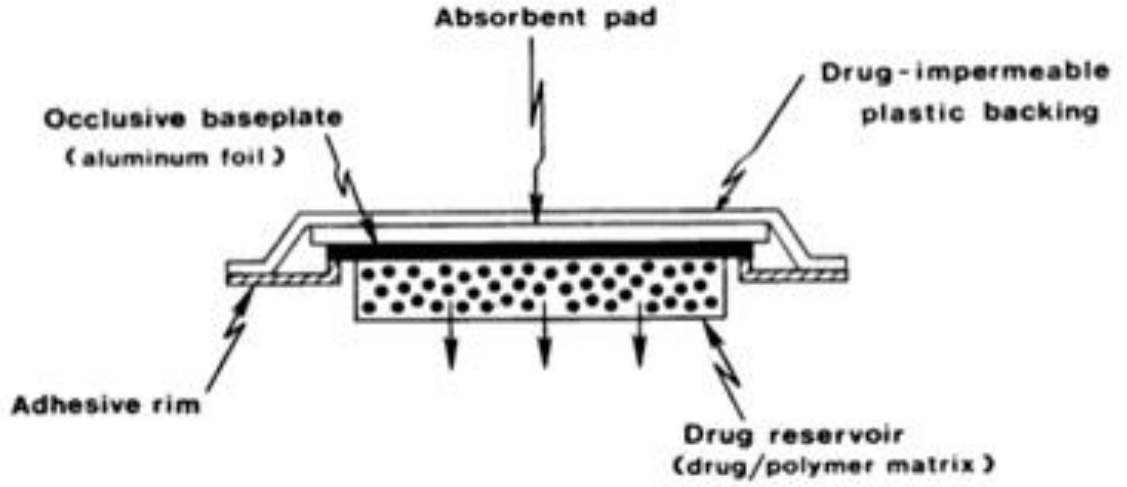
In this approach, the drug reservoir is prepared by homogenously dispersing drug particles in a hydrophilic or lipophilic polymer matrix.



- **Nitro-Dur® and Nitro-Dur® II TTS** Nitroglycerin-releasing transdermal systems for once a day medication in angina pectoris.



Nitro-Dur® II TTS



Nitro-Dur® TTS

4) Micro Reservoir Type or Micro Sealed Dissolution Controlled Systems

This system is a combination of the reservoir and matrix diffusion type drug delivery systems. The drug reservoir is formed by first suspending the drug solids in an aqueous solution of water-soluble liquid polymer viz. silicone Elastomers by high-energy dispersion technique to form several discrete, unleachable microscopic spheres of drug reservoirs.

- **Nitro Disc® TTS** Nitroglycerin releasing transdermal therapeutic system for once a day therapy of angina pectoris.