Physical enhancement.
Super saturation enhancement.
Bio-convertible prodrugs.

3.1. Ideal Properties of Permeation Enhancers

The ideal considerations of permeation enhancers:
It is needed to be pharmacologically inactive.
It is required to be non-toxic, non-irritating, and non-allergenic when placed on the skin.
For the drug concerned, the enhancer should provide proper drug release for immediate therapeutic response, predictable and sufficiently long duration of action.
After removing the enhancer, the horny layer of stratum corneum should be able to regain its traditional barrier property and should be fully recovered.
There should be a decrease in barrier function in one direction only, which implies that the permeation enhancers permit therapeutic agents into the body and do not allow efflux of endogenous materials.
It should have chemical and physical compatibility with the drug delivery system.
It should be non-damaging to viable cells.
Inexpensive and cosmetically appropriate.
Penetration enhancer used should be economical.

4. COMPONENTS OF TRANSDERMAL DRUG DELIVERY SYSTEMS

Transdermal therapeutic systems (Patches) are the most available marketed product for transdermal absorption (Fig. 3) [2]. Some of the essential components are:

- Polymer matrix/Drug reservoir
- Drug
- Pressure-sensitive adhesive (PSA)
- Permeation enhancer
- Release liner
- Backing laminates
- Other excipients including plasticizers and solvents

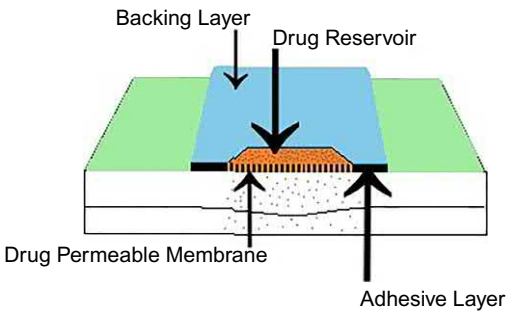

FIG. 3 Transdermal drug delivery system.

4.1. Polymer Matrix/Drug Reservoir

The polymer matrix aids in the release of the drug from the patch.

The polymers used for transdermal devices include:
(a) Natural polymers: derivatives of cellulose, gelatin, methyl cellulose
(b) Synthetic elastomers: poly-butadiene, rubber, silicone rubber, nitrile
(c) Synthetic polymers: polyvinyl alcohol, polyvinyl chloride, polyethylene.

4.2. Drug

- Drugs undergoing the first-pass metabolism
- Constricted therapeutic window
- Reduced half-life, therefore, needs frequent dosing
- A low dose of drug 25 (mg/day)
- Molecular weight should be low(<500 Da)
- Sufficient solubility in oil and water (log *P* value; 1–3)
- The melting point should be low (<200°C)

4.3. Pressure Sensitive Adhesives (PSA)

A pressure-sensitive adhesive is a substance that adheres to a substrate when gentle pressure is applied and when withdrawn, leaves no trace. PSAs play a significant role, acting as the framework that holds all the active ingredients and the means to make the patch conform to the skin. The right choice of PSA has a vital impact on system stability, the release of the active substance; possible dermatotoxicity and the effective administration of the drugs. Three major families of PSAs are: rubber-based PSAs, acrylic PSAs in the form of acrylic solutions and silicon PSAs [12].

4.4. Penetration Enhancer

They are substances which increase skin permeability by varying the barrier property of the skin. They modify the barrier in the skin to improve drug penetration either by interacting with the formulation that is applied or with the skin itself [13].

are classified as:

- Solvents: By swelling the polar pathway and by fluidizing lipids, these compounds increase the penetration. E.g., alcohols
- Surfactants: They are proposed to improve polar pathway transport, especially of hydrophilic drugs. E.g., anionic surfactants: sodium lauryl sulphate, non-ionic surfactant: pluronic F68, bile salts: sodium deoxycholate.
- Binary system: They superficially open up the unrelated *multi-laminate pathway* as well as the continuous pathways.
- Propylene glycol-oleic acid and 1, 4-butane diol-linoleic acid.
- Miscellaneous; chemicals: anticholinergic agents, etc.