Diabetes mellitus is a chronic illness in which the pancreas produces an insufficient amount of insulin or the insulin produced is unable to be used effectively by the body. Most oral antidiabetic drugs show low oral bioavailability and need to be taken more than once daily due to short half-lives, resulting in poor patient compliance. The transdermal delivery systems have appeared as a prospective hope in diabetes management due to the benefits that they offer as compared to invasive injection and oral dosage forms.

Transdermal drug delivery (TDDS) is the movement of drug molecules through the stratum corneum (outermost layer of the skin) into the systemic circulation. However, transdermal delivery of drugs is generally restricted by the barrier function of the skin for which stratum corneum is responsible.

- Only few drugs can be delivered through the transdermal route that have the suitable properties such as:
  - Low dose (dose < 10 mg/day).
  - High clearance
- Several methods have been employed to improve transdermal drug absorption such as physical techniques, chemical permeation, and biochemical methods.

### Advantages of TDDS

- Easy to use (self medication).
- Avoid GIT absorption problems for drugs.
- Avoid FP hepatic metabolism of drugs.
- Improve bioavailability.
- Improve patient compliance.
- Easy termination of drug in case of toxicity.
- Reduce frequency of dosing.

### Ideal properties of drug used for TDDS

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Properties</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dose</td>
<td>&lt; 10 mg/day</td>
</tr>
<tr>
<td>Half-life</td>
<td>10 hrs or less</td>
</tr>
<tr>
<td>Molecular weight</td>
<td>&lt; 600 Da</td>
</tr>
<tr>
<td>Partition coefficient Log P</td>
<td>Between 1-5</td>
</tr>
<tr>
<td>Skin reaction</td>
<td>Non irritating and non-sensitizing</td>
</tr>
<tr>
<td>Melting Point</td>
<td>&lt; 250 °C</td>
</tr>
<tr>
<td>Oral bioavailability</td>
<td>Low</td>
</tr>
</tbody>
</table>

### Classification of studied antidiabetic drugs

- **Sulfonylureas**
  - Glibenclamide
- **2nd generation**
  - Glipizide
  - Gliclazide
- **3rd generation**
  - Glimepiride
- **Thiazolidinedione**
  - Pioglitazone
- **Meglitinide**
  - Repaglinide
- **Biguanides**
  - Metformin
- **α-glucosidase inhibitor**
  - Voglibose

### Comparison between IV, Oral and TDDS

<table>
<thead>
<tr>
<th>Advantages</th>
<th>IV</th>
<th>Oral</th>
<th>TDDS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Avoid hepatic first-pass effects</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Constant drug levels</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Self-administration</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Termination of therapy</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
</tr>
</tbody>
</table>

### Application of TDDS

- For treatment angina pectoris (Nitroglycerine patch).
- For treatment hypertension (Clonidine).
- Hormones (testosterone gel).
- Smoking cessation (Nicotine).
- Antieptic (Promethazine Transdermal Gel).
- Anti-inflammatory (Ketoprofen and Diclofenac patch).
- Contraceptive (Evrat patch).
- Cosmetic.

### Transdermal delivery technique

- **Patch, Ethosomal gel, Nanogel and Transfersome**
- **Microemulsion, Patch, Film and Nanoemulsion**
- **Patch, Film, Ethosomes and Proniosomes**
- **Ethosomes, Liposomal film, Patch, proniosomal gel and Transfersomes**
- **Nanostructured Lipid Carriers (NLC), Patch, proniosomes and Nanotransfersomes**
- **Microemulsion gel, Solid Lipid Nanoparticles (SLN), Patch, Film and Ethosomes**
- **Hydrogel-forming microneedles, SLN, Proniosomal gel and Patch**
- **Nanoparticles scaffold film and Patch**

### Transdermal researches outcome

- Increase entrapment efficiency, enhance transdermal flux and improve bioavailability.
- TDDS can be considered as a promising route for delivering antidiabetic drugs.