CHAPTER - II

LITERATURE REVIEW OF TRANSDERMAL ANTI-DIABETICS
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Despite many advances in the development of oral hypoglycemic agents, an ideal drug for treating Type II diabetes is still a distant reality. At present many therapeutic agents are available to control diabetes mellitus, which includes Insulin, Sulfonylureas, Biguanides etc.

The Sulfonylureas and biguanides have well-established experimental, clinical documentation proving their safety, better tolerability and superior pharmacodynamic effects. Therefore, it is very interesting for pharmaceutical companies to modify the pharmacokinetics of these molecules in order to make them more convenient for patient. Administration of oral hypoglycemic by conventional route is having many limitations like short duration of action, hepatic first pass metabolism, hypoglycemic episodes, gastrointestinal disturbances etc.

For treatment of type-I diabetes Insulin is administered by subcutaneous injection, which in turn associated with poor patient compliance, because of the discomforts of frequent injections and the risk of infection and inflammation at the site of injection.

Literature survey reveals that, transdermal route can serves as a better alternative for the treatment of Diabetes mellitus with better patient compliance. During recent years various experimental methodologies have been developed for facilitating transdermal delivery of many anti-diabetic drugs.

Haga et al (1997) studied transdermal iontophoretic delivery of insulin using a photoetched microdevice through the excised abdominal skin of a nude mouse. Omathanu et al (2003) studied the Transdermal iontophoresis of insulin, with respect to its physicochemical properties. Panchagnula and Pillai (2003) studied the synergistic effect of terpenes (menthone) and ethanol on transdermal iontophoretic permeation of insulin. They also investigated transdermal delivery of insulin from

Treatment of non insulin dependent diabetes (type-II) with hypoglycemic agents, especially sulfonylurea derivatives by oral route is having the major disadvantage of severe and some time fetal hypoglycemia. To overcome this limitation of therapy, many oral hypoglycemic agents are under study to develop transdermal delivery system.

Takahshi et al (1997) had investigated some sulfonylureas (Glibenclamide and chlorpropamide) for transdermal administration from an ointment base and reported promising results. Sridevi S. et al (2000) developed an acrylate based transdermal drug delivery system for Glibenclamide and evaluated it for pharmacodynamic performance in male Wister rats. TDDS significantly sustained the hypoglycemic activity for 24 h in normal rats when compared to oral administration where the effect declined after 8 h. The reduction was slow and sustained in case of TDDS when
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compared to oral administration. Sridevi et al. (2000) investigated the effect of pH and Cyclodextrin complexation on transdermal permeation of Gliquidone, it was concluded that the flux the Gliquidone can be enhanced by adjusting the pH and concentration of β-cyclodextrine.

Takahashi et al. (2001) reported the enhancing effect of iontophoresis on transdermal absorption of Glibenclamide; the results demonstrated the possibility of iontophoretic transdermal administration of Glibenclamide. Mutalik and Udupa (2002) carried out in-vitro permeation studies of Glipizide and Glibenclamide through mouse skin, found that both drug could be good candidate for development of transdermal drug delivery system. They further studied effect of some penetration enhancers on the in-vitro permeation of glibenclamide and Glipizide through mouse skin and concluded that the required flux of both the drug could be achieved with the help of chemical penetration enhancer (Mutalik and Udupa 2003).

The matrix type transdermal patch of Glibenclamide was developed by Mutalik and Udupa (2004) with combination of various polymers and evaluated for physiochemical, pharmacodynamic and pharmacokinetic properties. The results revealed that the patches successfully prevented the severe hypoglycemia in the initial hours, which is the major side effect associated with the oral route. The transdermal patches produced better improvement in all tested biochemical parameters compared to oral administration. The pharmacokinetic evaluation showed that the patches could maintain almost steady state concentration of drug within pharmacologically effective range for prolonged period time as compared to oral administration. Bennett et al. (2005) evaluated of transdermal Glipizide in a pluronic lecithin gel in healthy cats and suggested that transdermal route for Glipizide has the potential to provide a safe and effective means of controlling diabetes mellitus.
Mutarlik and Udupa (2005) developed the membrane controlled transdermal drug delivery system of Glibenclamide and evaluated for its in-vitro and in-vivo performance. The carbopol gel was used as reservoir and EC, ERL and ERS as rate controlling membrane. They reported that transdermal system with area of application of 18 cm² would be sufficient to provide required plasma concentration.

Ammar et al (2006) carried out the in-vitro permeation studies of Glipizide-β-Cyclodextrin complex through rat abdominal skin and also studied the effect of various penetration enhancers on permeation of the complexes.

Mutarlik and Udupa (2006), prepared Membrane-moderated transdermal systems of Glipizide by using drug-containing carbopol gel as drug reservoir and ethyl cellulose, ERS-100, ERL-100 and EVA as rate-controlling membranes. The developed patches were subsequently evaluated in-vitro for drug content and drug permeation studies and in-vivo for pharmacodynamic and pharmacokinetic studies in mice. Transdermal system successfully prevented severe hypoglycemia in the initial hours and it was also effective for chronic application. Jain et al (2008) investigated the iontophoretic permeation of Glipizide across the pigskin and compared with corresponding passive permeation. The target flux of Glipizide was calculated to be 0.4147 μmol/h and the highest flux obtained was 0.2727 μmol/cm²/h, which suggests that Glipizide is a promising candidate for iontophoretic delivery.

In view of the above literature survey it can be concluded that transdermal route for delivery of drugs can serve as a better alternative for the treatment of diabetes. So the study was designed with the objective to develop and evaluate the transdermal drug delivery system for an anti-diabetic drug.
2.1 References:


