

## Transdermal Route for Peptide and Protein Drugs

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### Abstract

Advances in biotechnology and pharmaceutical technology have resulted in tremendous growth in peptide and protein drugs. Despite the growth and importance of protein drugs, most of these drugs are delivered via hypodermic injections. Patient acceptance and compliance are the major disadvantage of delivering protein and peptide drugs via injections. Therefore, number of different routes such as oral, nasal, pulmonary and transdermal have been explored to deliver peptide and protein drugs. Transdermal route avoids the first pass metabolism, offers convenience and painless delivery. In this review, delivery of protein and peptide drugs via transdermal route has been discussed.

**Keywords:** Transdermal Route; Peptide Drug; Protein Drug

### Introduction

Recent advances in biotechnology have resulted in tremendous growth and approval of peptide and protein therapeutics. Peptide and proteins drugs such as Humira®, Rituxan®, Enbrel® are among the top selling drugs in the US right now [1,2]. Most of the protein therapeutics are delivered via injections and major disadvantages of this delivery method are patient acceptance and compliance. Various non-invasive routes such as transdermal, oral, nasal, pulmonary have been studied to deliver peptide and protein drugs. Among these routes, transdermal delivery possesses several advantages which include avoidance of first pass metabolism, less frequent dosing, patient compliance and convenience. Ready access of the skin to compromise and breach of the stratum corneum makes the transdermal route promising for the protein delivery. Various techniques such as iontophoresis, electroporation, microneedles and sonophoresis have been explored to deliver peptide and protein drugs [1,3].

Passive techniques utilizing chemical enhancers have also been used for the delivery of small peptides. In a study by, Magnusson, *et al.* ethanol was used to enhance the delivery of thyrotropin releasing hormone which is a small peptide with molecular weight < 400 Da [4]. This technique may not work well with large peptides. In a study by Chen, *et al.* a peptide itself has been used to increase the insulin delivery and reduced glucose levels when applied onto the rat skin. In this study, a peptide enhancer and insulin mixture was applied and enhanced plasma insulin levels were observed through the rat skin [5].

Iontophoresis, in which a few miliampere of current is applied over a small area of skin, has also been used to increase the flux of peptides. In a study by Pillai, *et al.* transdermal iontophoresis was applied to insulin and its flux enhancement was observed in different buffers and salt concentrations. It was observed that flux of insulin increased up to 0.05M sodium chloride concentration and flux enhancement was observed to be higher in phthalate buffer as compared with citrate buffer [6]. Sonophoresis is a noninvasive technique in which low frequency ultrasound are used to enhance the flux across the skin. Sonophoresis has also been used to increase the permeation of protein and peptide drugs.

Microneedles have been studied extensively to deliver protein drugs via transdermal route. In a Phase II trial by Radius Health, Inc., abaloparatide-TD a microneedle system for parathyroid hormone related protein was shown to have positive effect on bone mineral density. Corium International, Inc. has also shown positive results in osteoporosis using their MicroCoR PTH microneedle technology in delivering parathyroid hormone [7-9]. Microneedle technology has also been studied to deliver vaccines.

### Conclusion

Transdermal route for delivering peptide and protein drugs have been studied extensively in both academia and industry. A number of transdermal protein drugs are also in clinical trials but for transdermal protein drugs to get approved, one has to think about both the delivery and the regulatory pathway. Although there are many challenges associated with the transdermal route in delivery of protein drugs, there is great potential in this noninvasive route and hopefully there will be transdermal protein drug products in the market in near future.

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