LITERATURE REVIEW

8. **Tokumoto S. et al. (2006)** have studied the combined effect of electroporation and iontophoresis on a high molecular weight peptide insulin through transdermal delivery and observed an enhanced insulin permeation.

9. **Ammar H.O. et al. (2006)** facilitated aspirin transdermal permeation from different topical bases viz. carboxy methyl cellulose gel, vaseline, hydrocarbon gel, hydrophilic base and polyethylene glycol ointment base. After 24 hours diffusion study result showed that hydrocarbon gel and CMC gel base were giving more drug permeation in vitro. Chemical enhancer combination like propylene glycol and alcohol showed maximum aspirin enhancement.

10. **Sebastiani P. et al. (2005)** studied the efficiency of lactic acid as permeation enhancer for three different charged drug molecules across the skin. They also studied combination of lactic acid and iontophoresis as a means of drug delivery. The results showed that lactic acid had some effects on model drug permeation across the skin.

11. **Nair V.B. et al. (2004)** investigated the effects of terpenes and iontophoresis on the *in vitro* permeation of arginin vasopressin through rat skin and the biophysical changes induced by the chemical enhancers in the stratum corneum. Among different terpenes studied maximum enhancement ratio was observed with cineole.

12. **Meidan V.M. et al. (2003)** have examined the influence of co-formulations of chemical enhancers (azone, oleic acid, menthol, cineole and terpineol) on buspiron hydrochloride permeation, both without iontophoresis and with iontophoresis to look for possible synergistic effects. The results showed that at low current iontophoresis (0.5 mA/cm²), a higher steady state flux of approximately 350 µg/cm²h was observed.

13. **Aqil M. et al. (2006)** prepared the transdermal drug delivery system of pinacidil monohydrate and monitored the antihypertensive effect of drug on hypertension induced rats *in vivo*. They found a significant fall in blood pressure in rats for 48 hours upon single patch application of pinacidil TDDS.
14. **Ozguney I.S. et al. (2006)** delivered diclofenac sodium through rat skin by preparing different formulations like microemulsion and gel containing carbopol as gelling agent and dimethyl sulfoxide as penetration enhancer and compared with commercial topical formulation. They found significant flux of drug from microemulsion formulation than gel that due to penetration enhancer.

15. **Coceani N. et al. (2003)** characterized the rat skin permeation properties by mathematically modeling. By *in vitro* experiments they found that permeability of acyclovir drug was by diffusion.

16. **Afouna M.I. et al. (2003)** upon *in vivo* experiment on hairless mice investigated the effect of azone on antiviral efficacy of cidofovir and acyclovir topical formulation in treatment of HSV-1 infections. Cidofovir with azone formulation was effective in treating HSV-1 infection. Whereas acyclovir with azone formulation did not show much efficacy.

17. **Liu H. et al. (2006)** studied effects of various vehicles and permeation enhancers on topical delivery of cyclosporine A across rat skin. Ethanol 40% showed highest flux of drug across skin among other vehicles like ethyl oleate, isopropyl myristate, propylene glycol. Skin pretreatment with methanol 10% or sodium lauryl sulphate 0.05% shorten lag time of drug penetration into skin compare to azone 5% and n-methyl pyrrolidon.

18. **Prasad R. et al. (2007)** observed effect of different wave forms viz. square, sine, exponentially decaying pulses and DC iontophoresis alone or in combination with terpenes or ethanol on transdermal methotrexate hydrogel patch on mice skin. Square wave in combination with alcoholic menthol solution showed maximum drug enhancement and flux.

19. **Shishu et al. (2006)** formulated griseofulvin in carbopol hydrogel containing propylene glycol and n-methyl-2-pyrrolidone as permeation enhancers. Propylene glycol enhanced drug release rate by increasing its solubility and partitioning. NMP enhanced drug flux by 6 fold.

20. **Al-khalili et al. (2003)** evaluated transdermal buspirone hydrochloride delivery using iontophoresis and terpenes in hydroxy propyl methyl cellulose and carboxy methyl...
cellulose gel base. Menthol with iontophoresis showed highest drug permeation from HPMC gel.

21. Morel E.M. et al. (2006) used wireless, portable, handheld, computer controlled iontophoretic device that allowed self administration of 5% acyclovir cream for herpes labialis treatment. For patients with lesions in erythema group, healing time was 3 days shorter for active group than placebo group.

22. Stagni G. et al. (2004) compared pharmacokinetic of acyclovir in skin and plasma after iontophoresis, iv-bolus and ointment administration in rabbit skin by microdialysis. Three current densities were applied viz. 1, 2 and 3 mA. Skin exposure to acyclovir after iontophoresis for 1 hr was greater than ointment and iv-bolus.

23. Kikwai L. et al. (2005) formulated spantide II lotion and gel using ethanol, PF 127, HPMC and HPC with and without n-methyl-2-pyrrolidone as permeation enhancer. Spantide II retained in epidermis than dermis in rat skin due to n-methyl-2-pyrrolidone.

24. Font F.A. et al. (2006) checked effect of chemical enhancers like polyethylene glycol 600, azone and limonene with iontophoresis on in vitro sumatriptan transdermal absorption through porcin and human skin. Azone with 0.5 mA/cm\(^2\) current showed highest flux of 901 nmol/cm\(^2\)/h compared to other enhancers. Drug flux was double in porcine skin than that of human skin.

25. Tiwari S.B. et al. (2003) facilitated transdermal delivery of ketorolac across rat skin and studied the effect of electrical factors, physicochemical factors and device related factors. Platinum and Ag/AgCl electrodes showed almost same drug flux. 0.5 mA/cm\(^2\) showed highest drug flux. Continuous current was more effective than pulsed current. Skin pretreatment with d-limonine in ethanol enhanced iontophoretic flux of drug.

27. **Huang J.F. et al. (2005)** studied effect of iontophoresis and electroporation on transdermal delivery of nalbuphine and its prodrugs from solutions and hydrogels of HPC and CMC. Iontophoresis enhanced drug permeation from citrate buffer pH 4.0 than electroporation technique. Higher concentration of HPC and CMC reduced the flux of nalbuphine.

28. **Suwanpidokkul N. et al. (2004)** checked the effects of different vehicles, chemical permeation enhancers and polymer membranes on transdermal delivery of zidovudine across pig skin. They found that out of four binary vehicles, ethanol/IPM showed enhanced flux. N-methyl-2-pyrrolidone 10% among three permeation enhancers resulted in increased drug solubility and flux. Pig skin covered with microporous polyethylene membrane reduced drug flux by 50% than that of skin alone.

29. **Sandeep H.N. et al. (2010)** prepared ophthalmic gel containing latanoprost drug for the treatment of glaucoma. They prepared different gels containing carbopol, HPMC and HPC polymers. They observed that controlled release of drug was achieved for 6 hours and at end of that time >99% of drug was released. The developed products were alternative for conventional eye drops.


31. **Bodhankar M.M. et al. (2011)** prepared topical formulations viz. ointment, cream and gel, containing volatile oils that are therapeutically active. They observed active constituents release behavior from the prepared formulations and concluded from 7 hours drug release study that prolonged release was observed with gel formulation compared to ointment and cream.

32. **Patel N.B. et al. (2010)** developed diltiazem hydrochloride patch from polymers like HPMC, SCMC and PVA. Prepared patches were characterized by different physicochemical parameters. Rat skin drug permeation study was performed *in vitro* by
iontophoretic technique. Different current density did not much affect drug release behavior from patch.

33. **Preveen M. et al. (2011)** prepared transdermal patch system of tizanidine hydrochloride by using HPMC and EC polymers. The patch system was successfully formulated and checked for various physicochemical parameters. The patch system was able to release 87% tizanidine at the end of 12 hours *in vitro* drug diffusion study.

34. **Moghimi H. et al. (2005)** permeated nicotine by iontophoresis technique through rat skin considering many parameters. Anodic type iontophoresis was better than cathodic type. 0.5 mA/cm² current density enhanced nicotine permeation by 3 fold.

35. **Vijaya C. et al. (2011)** observed effect of different permeation enhancers on transdermal delivery of venlafaxine hydrochloride across pig skin. Chemical penetration enhancers like glycerin, urea, propylene glycol and mixture of propylene glycol and ethanol were under investigation. The result showed that mixture of permeation enhancers enhanced venlafaxime hydrochloride delivery by 85% among others.

36. **Das S. et al. (2011)** formulated and evaluated herbal gel containing extracts of clerodendron infortunatum. The polymers used were SCMC and carbopol 934. The gel prepared by SCMC polymer was not smooth and stable whereas carbopol gel was good in consistency. Skin irritation study on rabbit revealed that the herbal gel was non-irritant on skin.

37. **Darwhekar G. et al. (2011)** prepared transdermal patch of clopidogrel bisulphate using polymers HPMC, PVP and EC in their varied amounts. *In vitro* drug diffusion study was performed on prepared formulations and formulation F2 showed highest amount of drug permeation 90.06% in 24 hours diffusion study. PVP was not present in F2 and hence the drug was showing sustained release behavior.

38. **Narendra C.T. et al. (2011)** prepared nanoemulsion containing aceclofenac for transdermal drug delivery. Nanoemulsion was prepared by using oils and surfactants labrafil, triacetin, tween 80 and transcuol. Nanoemulsion gel was prepared by using carbopol polymer and other additives for comparison study of aceclofenac diffusion
study through rat skin. The result showed that aceclofenac containing nanoemulsion was more efficacious in relieving inflammation in rat by in vivo study.

39. **Merclin N. et al. (2004)** evaluated iontophoretic delivery of 5-aminolevulinic acid and its methyl eater in vitro through porcine skin by developing carbopol gel. In stratum corneum the amount of 5-aminolevulinic acid and methyl-aminolevulinic acid were significantly higher viz. 82 nmol and 751 nmol following 15 hours iontophoresis.

40. **Degim T. et al. (1998)** investigated effect of ion complex on iontophoretically delivered salbutamol sulphate drug. Result showed that presence of high concentration of NaCl solution increased amount of salbutamol through skin due to presence of Na\(^+\) ion.

41. **Ishikawa O. et al. (2002)** worked on enhancing effect of switching iontophoresis on transdermal absorption of phthalic acid (PA), benzoic acid (BA), salicylic acid (SA), p-phenylenediamine (PD), aniline (AN) and verapamil (VR) across abdominal Wistar rat’s skin and mechanisms of permeation. They found the cumulative amount of PA permeated at 6 hours was 2.7 fold higher after switching iontophoresis at an interval of 10min compared to control. Permeation of PA, BA and VR was increased after iontophoresis, whereas that of SA, PD and AN was not affected much. Skin resistant at 2 hours when 5 min interval of polarity iontophoresis was 40 and 60% as compared with controls and non-switching iontophoresis. This suggested that skin hydration played an important role in enhancement of skin permeation by iontophoresis.

42. **Chaturvedula A. et al. (2005)** evaluated the in vitro iontophoretic delivery of salmon calcitonin using self contained iontophoretic patch with build-in electrodes and compared calcium lowering effect of iontophoretically delivered with subcutaneous and intravenous injection of salmon calcitonin. Result showed that intravenously administered salmon calcitonin reduced calcaemia around 45% which was almost same by subcutaneous and iontophoretically administered (40%).

43. **Panchagnula R. et al. (2005)** evaluated ex vivo-in vivo performance, stability and irritancy potential of transdermal reservoir patch of naloxone. The transdermal gel formulation and patch were shown to be efficacious, safe, stable and non-irritant to skin. Steady state levels in vivo for 48 hours showed advantage of patch over current modes of
administration. The formulation was stable for 3 months with respect to drug content and penetration enhancer efficacy.

44. **Lim P.F.C. et al. (2006)** formulated an organogel containing appropriate enhancer for controlled delivery of haloperidol. Limonene showed enhanced drug permeation and hence incorporated into organogel comprised of GP1 and propylene glycol. Organogel as a drug vehicle decreased drug permeation and also acted as reservoir.

45. **Kotwal V. et al. (2007)** performed iontophoretic transdermal delivery of diphenhydramine hydrochloride through pig skin. They prepared gel formulation using Lutrol F-127 as gelling agent at pH 4.2 for ionization of diphenhydramine hydrochloride. Anodal pulsed iontophoresis with disc Ag/AgCl electrodes significantly increased drug permeation.

46. **Patel S.R. et al. (2007)** investigated transdermal delivery of sumatriptan succinate patch by iontophoresis *in vitro*. Increase in drug amount did not significantly increase flux. Whereas increase in pH of formulation from pH 4.7 to pH 6.8 significantly increased drug flux. *In vivo* study showed that iontophoretic patch system could resulted in drug blood level similar to observed after oral, nasal and rectal delivery.

47. **Panigrahi L. et al. (2005)** investigated effects of pH and penetration enhancers on terbutaline sulphate from pseudolatex type transdermal drug delivery system through mouse and human cadaver skin. The drug flux was maximum with phosphate buffer pH 8.0 mixed with formulation among other pH buffer solution. Further isopropyl myristate as permeation enhancer showed more permeability of drug among other organic esters.