2.1 AIM OF PRESENT WORK

Analgesics are the drugs of choice for the management of a variety of acute and chronic inflammation and chronic degenerative orthopaedies. The major drawback to analgesic drug use is the preponderance of gastrointestinal (GI) side effects encountered when administered orally. The most common GI adverse effects include GI perforations, ulcerations, and bleeding, all of which may require hospitalization. The analgesic mediated toxicity is often dose related. Thus reduction in serum concentration should also lessen the risk of potentially serious systemic adverse effects secondary to analgesic induced prostaglandin inhibition such as acute renal insufficiency, nephritic syndrome, analgesic gastropathy, prolonged bleeding time, and fluid retention. This creates a need for an alternative route of administration that bypasses the gastro-hepatic metabolism of the drug. The transdermal route is such an alternative.

Transdermal delivery systems offer several distinct advantages. They avoid factors that affect the gastrointestinal absorption of drugs, such as pH, enzymatic activity, and drug–food interactions and bypass first-pass effect. Provide multiday sustained release delivery (useful for drugs with short biological half-lives requiring frequent oral or parenteral administration), hence improve patient compliance. Allow rapid termination of drug effects when necessary.

However, SC plays the major role in regulating the barrier function of the skin because of its unique nature, which creates an interstitial lipoidal environment. Several techniques have been developed to overcome this barrier including chemical (penetration enhancers) and physical techniques (iontophoresis, electrophoresis, and sonophoresis) or combination of both.

The iontophoresis is a non-invasive technique which provides simplified therapeutic regimen (drug input kinetics can be modulated by the current profile) and leads to improved patient compliance. It is a promising delivery technique for the charged and uncharged molecules having high and low molecular weights. A variety of drugs has been delivered across the skin by this technique.

Vesicular systems are considered very promising in overcoming this permeation barrier of skin by acting as permeation enhancers or even as vehicles for bioactive materials. They can be used as vehicles for controlled percutaneous drug delivery. Proniosomes are...
semisolid liquid crystal (gel) which can be converted into niosomes upon hydration, overcome many of the problems of niosomes and liposomes like chemical instability, high costs, vesicle aggregation, fusion, leaking, or hydrolysis of entrapped drugs. Additionally, the combination of novel carrier and iontophoresis could be utilized to synergize the delivery of drugs.

In the present study, an attempt has been made to enhance transdermal delivery of analgesics by formulating it into proniosomal gel which was further facilitated by application of iontophoresis. Both proniosomes and iontophoresis enhance transdermal permeation by two different mechanisms and combination of both was thought to have synergistic effect that resulted in higher transdermal flux of analgesic.

### 2.2 OBJECTIVES OF PRESENT WORK

- To select analgesic drugs (naproxen, lornoxicam, tramadol HCl).
- Identification of drug by melting point, UV spectrum and FTIR.
- To develop calibration curve of drugs using suitable analytical method (e.g. UV).
- To carry out preformulation studies of drugs (e.g. Solubility, Partition coefficient, pKa, Permeability coefficient) and goat skin membrane (e.g. Water uptake, Lipid content).
- To prepare suitable formulation of drug (e.g. proniosomal gel).
- To carry out evaluation of prepared formulation. (encapsulation efficiency (EE), vesicle size, DSC analysis, microscopical studies like optical and TEM, *in-vitro* release study )
- To carry out *in-vitro* permeation study using Franz diffusion cell.
- To carry out *in-vivo* study for optimized formulations.
- To carry out stability study for optimized formulations.
- To study the effect of iontophoresis on the permeation of drug.
- To prepare drug cationic proniosomal gel.
- To study the combined effect of iontophoresis and proniosome on *in-vitro* permeation of drugs through goat skin.