3.1 Aim of Work

The aim of the present work was to develop stable ethosomal suspension based gels of hydrophilic drug Ropinirole HCl to provide its sustained release, that of lipophilic drug Felodipine to improve its bioavailability and to compare relative efficacy of the formulations. Drugs chosen possess entirely different set of physicochemical properties and shall demonstrate the effect of these differences on the formulations prepared using similar methodology.

3.1.1 Rationale of Work

For many drugs the most common form of delivery of drugs i.e. the oral route has significant drawbacks- namely poor bioavailability due to hepatic first pass metabolism and the tendency to produce rapid blood level spikes (both high and low), leading to a need for high and/or frequent dosing, which can be both cost prohibitive and inconvenient. These drawbacks can be overcome by transdermal drug delivery system (TDDS). Transdermal route is ideal due to following advantages

- It is a non-invasive route
- It gives sustained and controlled release thus reduces dosing frequency and improves patient compliance
- It reduces fluctuations in plasma drug concentration thus ensures maximum utilization of drug
- It avoids hepatic first pass effect
- It is ideal for drugs which are potent (dose <10 mg), have short half life and poor oral bioavailability

3.1.1.1 Ropinirole HCl qualifications

Ropinirole HCl is non-ergoline dopamine agonist used for the treatment of Parkinson’s disease. For incorporation of drug through transdermal route, the drug must have adequate lipophilicity and low melting point. While Ropinirole HCl is hydrophilic in nature and has high melting point (243-250°C) rendering it difficult to penetrate the skin on its own. Hence the drug is encapsulated within the aqueous compartment of ethosome. The properties of Ropinirole HCl which make it a candidate for the delivery through skin in the form of ethosome are as follows
• It has high solubility and low permeability
• It has high melting point (243-250°C) not allowing it to permeate through skin directly
• It is a potent drug having dose of 0.25-10 mg
• It has moderate oral bioavailability (45-50%) owing to its hepatic first pass metabolism
• It has short half life (5-6 hr). So, controlled release is desired.

3.1.1.2 Felodipine qualifications 69,72
Felodipine is a long-acting 1,4-dihydropyridine calcium channel blocker (CCB). It acts primarily on vascular smooth muscle cells by stabilizing voltage-gated L-type calcium channels in their inactive conformation. Felodipine is used to treat mild to moderate essential hypertension. It is quickly and almost absorbed orally but owing to extensive first pass metabolism oral bioavailability is very poor (13-18%). The drug has a low melting point and is highly lipophilic hence has good transdermal permeability. Thus Felodipine fulfils most of the criteria required of a drug candidate for transdermal formulation like
• It is a potent drug having 5-20 mg
• Its melting point is < 200°C (142-146°C)
• It has low bioavailability (< 20%)
• Though it has a longer half life (11-14 hours) but has fluctuating plasma levels so is not a naturally sustained acting drug
• Its log P value is 3.8, a bit too high for transdermal patch formulation
The last factor renders its formulation as a patch difficult therefore it is worthwhile to attempt its ethosomal formulation which may act as a counterpoint to Ropinirole HCl formulation.

3.2 Plan of work

The aim of the work is expected to be met by dividing it into certain objectives which are to be taken up in following order
1. Developing or evaluating assay procedures of drugs which would be of frequent use for planned formulations.
2. Fixing amount of the drugs in their formulation.
3. Preparing primary formulations using different concentration of excipients.
4. Optimizing formulation based on certain evaluation parameters.
5. Preparing final formulations and evaluating them on more parameters.
6. Comparing them to conventional formulations on similar evaluation parameters.
7. Fixing dose for in-vivo study on rat based on in-vitro studies performed during evaluation of final formulation.