AIM AND OBJECTIVE

Aim:

- To formulate Carvedilol Ethosomes.
- To formulate Sonicated and unsonicated ethosomes.
- To formulate ethosomal gel.
- To formulate liposomes.
- Induction of hypertension and measurement of hypertension.

The most used and prescribed route of drug administration in the present market is oral route (dosage form) as it is easy to produce, administer, dispense, manufacture, store, transport, and also accurate in dose etc. Even though it is having many advantages over other routes of administration, it also has the adverse effects and complications like drug is subjected to first phase metabolism can be metabolised by gastric, intestinal, hepatic enzymes due to which high dose and frequent dosing is required to reach therapeutic concentration. These demerits can be overcome by using the novel drug delivery systems, which are more effective at low dose and in comparison to oral they are more expensive which is the demerit of the this system. But they reduce the dose of drug and frequency of dosing which in turn reduce the adverse effect of the drugs.

One of the emerging routes of drug administration is trans-dermal patches that transport the active ingredient into the body through layers of skin; this system is closely similar to the cutaneous and percutaneous routes of drug administration. They avoid the systemic adverse effects of the drugs when applied on the site of action.

On consideration with the problems associated with the drug Carvedilol which is an antihypertensive agent, adrenergic agent, adrenergic beta antagonist, vasodilator agent, adrenergic alpha- antagonist that is prescribed for the Congestive Heart Failure (CHF) management along with diuretics (ACE inhibitors and others) contemplated on the entitled research work.
The management of severe CHF with Carvedilol has decreased morbidity and mortality.

1. It is a highly potent drug with short half life.

2. It has very poor bioavailability (20-40%) with oral route.

The present research work has been undertaken starting with the designing of Carvedilol Ethosomal gel containing various concentrations of ethanol, phospholipids and polymers by the cold method (Sonication) for suitable size reduction of vesicles.

The designed Carvedilol Ethosomes will be characterized for

1. Visualization

2. Vesicle size and Zeta potential

3. Transmission electron microscope

4. Entrapment efficiency

5. Assay

6. Vesicle stability

7. Solubility measurement

8. Penetration and permeation studies

9. Drug stability studies
SOURCE OF DATA

1) Review of literature from:

a. Journals – such as

- International Journal of Pharmaceutics.
- Saudi Pharmaceutical Journal.

2) www.sciencedirect.co.


4) Reference books:


5) College library.

METHODS OF COLLECTION OF DATA:

- Selection of the drug and other excipients.
- Authentication of the drug and polymer by, FTIR.
- Characterization of drug and excipients for intended formulations and to carry out the compatibility studies for selected drugs and polymers by FTIR, DSC etc.
- Formulation of ethosomes by Cold or Hot method\textsuperscript{13}.  


PLAN OF WORK

Selection of title through exhaustive literature survey was performed. Before selecting the research work the primary step was to select the drug based on various parameters namely

- Whether drug is of recent introduction.
- Utility value of the drug in terms of treatment of disease and significance for health care of patients.
- Design and development of an optimum formulation for better use of the drug.
- Whether presently available formulations are providing enhanced bioavailability and therapeutic efficacy
- Ease of availability of drugs
- Cost of drug should be optimum.
- Design and development of controlled / targeted release formulation.
- Design and development new drug with greatly improved therapeutic effectiveness and fewer or no toxic effects.
- Select the appropriate route for administration.
- Select the right drug for a particular illness.

Formulation of Ethosomes:

After doing the thorough literature survey on considering the various factors namely

1. Ease of availability of materials.
2. Simplicity of method.
3. Ethosomes are recently developed trans-dermal drug delivery system.
4. Carvedilol the drug selected for research has very poor bioavailability 25-35% by the oral route due to the first pass hepatic metabolism. However this is the method
of administration in vogue. Hence the formulation of Carvedilol as Ethosomal gel has been selected.

For preparation of Ethosomal gel the following techniques are available namely:

- Classic method

- Classic mechanical dispersion method

- Hot method

- Cold method

The cold method was selected. Seven trials of the Carvedilol Ethosomes have been contemplated to prepare by the cold method. The drug content was being fixed and the trials using these inactive ingredients namely Soya Lecithin, Ethanol, Propylene Glycol, Cholesterol, Carbopol, Tri ethanolamine in various proportions was carried out.

**Ethosomes Composition:**

They consist of combination of phospholipids and hydro-alcoholic glycolic in which the alcohol concentration is high. They are the vesicular carriers which contain different chemical structures of phospholipids such as Phosphatidyl choline (PC) Phosphaticacid, Phosphatidyl serine, Phosphatidylethanolamine, Phosphatidyl Glycerine (Ppg) Phosphatidyl Inositol (Pi), Alcohol Water hydrogenated PC, and Propylene Glycol. The Carvedilol Ethosomes contain aqueous phase to100%w/w, 0.005g of Cholesterol, 20-50% Ethanol, 10% of Propylene glycol and 2-5% Phospholipids.

**In Vitro Evaluation:**

Physicochemical characterization of Carvedilol Ethosomes

This will be done by the utilisation of following instrumental technique.

1. Visualization

2. Vesicle size and zeta potential

3. Transmission electron microscope

4. Entrapment efficiency
Out of the best formulation based on the above in vitro tests will be selected for the in vivo evaluation studies.

**In Vivo Estimation:**

- Hypertension is induced by sodium salt and Methyl Prednisolone acetate methods.
- For the assessment of hypertension, Tail-Cuff method is employed for systolic blood pressure measurement.

**NEED FOR THE STUDY:**

The increasing demand of the efficient delivery of medication with minimum side effects, improved patient compliance has resulted in inventing novel type of dosage form. This new technology involves trans-dermal route apart from the oral route. When the oral route administration of drug faces problems then trans-dermal route can be of much value. In the case of Carvedilol in which oral route is preferred to treat herpetic infections possesses limitations like poor absorption from the intestine (15-30%), dose of administration (3.125-25mg), elimination half life of 6-10hrs and side effects like hypotension and brady-cardia. Weight gain, diarrhoea, dizziness, asthenia and hyperglycemias’. Hence modification of the route of administration is a necessity for better absorption of the drug. The suitable route of administration in such cases is trans-dermal route of administration.

Due to the size and rigid character of lipid layer the penetration of Carvedilol via trans-dermal route cannot be enhanced by Liposomes or Niosomes. To enhance the permeation recently advancements have been done by reduction of the carrier size and
making more malleable lipid layer to give a novel medicament carrier "Ethosomes" whose effectiveness to enhance the penetration of drugs via skin to several times has been shown when compared to the simple cream, hydro-alcoholic solutions and Liposomal carrier. Hence there is a necessity to prepare the Ethosomes for Carvedilol to increase the penetration of the drug via skin thus reducing the frequency of administration, dose and adverse effects and thus resulting in better patient compliance.