Chapter-3

RESEARCH ENVISAGED AND PLAN OF WORK

3.1 Research Envisaged

In the clinical management of acne, topical formulations are the preferred route of drug administration. In addition, combination therapy often proves more efficacious and better tolerated than mono therapy with a single drug so combination of Tazarotene and Hydroquinone has been attempted via delivery by liposomal gel formulation. Tazarotene is a widely used drug in the topical treatment of Acne, and other skin disorders. Tazarotene synthetically produced is retinoid commonly used in the treatment of acne. Tazarotene is a pro-drug of Tazarotenic acid, which is a receptor-selective retinoid, which has shown efficacy in the treatment of acne and other skin disorders.

In the treatment of acne vulgaris, it has greater comedogenic activity than the marketedly available topical retinoid. Hydroquinone is used for treatment of hyper-pigmentation for many years. Hydroquinone is a hydroxyphenolic chemical which inhibits conversion of dopa to melanin by inhibiting the tyrosinase enzyme. Liposomal drug delivery strategies can play an important role in improving the topical delivery by enhancing their dermal localization with a concomitant reduction in their side effects. Liposomes composed of Soya lecithin and cholesterol, with Tazarotene entrapped in the inner water compartment, prepared by the simple mechanical method vortexing the phospholipids dispersion in water. Topical liposome gels will be prepared by incorporating liposomes into a structured vehicle and drug release properties of these liposomes were investigated.

The aim of this study was to statistically optimize the vesicular formulations (Liposomes) for enhanced skin delivery of a model drug Tazarotene in combination with gel containing hydroquinone. Tazarotene was potent candidate for liposomal preparation. The active form of the drug, tazarotenic acid, is highly bound to plasma proteins (>99%) and it is excreted in the urine, these factors promote the interest of researchers to choose this drug for the formulation of controlled release formulation which maintain adequate concentration inside body to treat acne. Hydroquinone exploits the antioxidant properties when it is given in combination with liposome of Tazarotene which maintains adequate quantity of drug in skin and helps in the effective management of acne (raised, silvery flaking of the skin). But, stratum corneum forms the most formidable barrier for the penetration of drug through skin. To overcome this
barrier, the use of lipid vesicles like Liposomes in delivery systems has attracted increasing attention of researchers in recent years.

The gel formulation of Liposomes contain tazarotene in combination with hydroquinone effectively maintain concentrations of active agents to the layers of the skin. It is thought that ethanol fluidizes bilayers of the stratum corneum intercellular lipid; the soft, malleable vesicles then penetrate the disorganized lipid bilayers. The lipid vesicles provide a controlled transdermal delivery system and also serve for the solubilization of poorly soluble drugs. Combination of phospholipids and high concentration of ethanol in vesicular formulations have been suggested to be responsible for penetration and distribution in the skin lipid bilayers. The transdermal delivery offers many advantages over oral systems that include improving the systemic bioavailability of drug by avoiding first pass metabolism and thus providing a sustained, controlled drug delivery.

3.2 Plan of work

1. Literature Review
2. Selection of dosage form
3. Selection of drug candidate
4. Procurement of drug & excipients
5. Identification & characterization of tazarotene and Hydroquinone
   - UV spectrophotometry
   - IR Study
6. Preformulation studies
   - Physical Appearance
   - Melting Point
   - Determination of $\lambda_{\text{max}}$
   - Solubility study
   - Partition coefficient
   - Drug – excipients compatibility study
   - Calibration curve of drugs
7. Preparation, optimization and characterization of Liposomes
   - Optimization of Soya lecithin: Cholesterol ratio
   - Optimization of SL: Cholesterol ratio
   - Optimization of SL: Cholesterol: Carbopol ratio
   - Vesicles Shape and Transmission electron microscopy
8. Drug entrapment, formulation and optimization of liposomal gel
   - Measurement of pH
   - Determination of Viscosity
   - Spreadability
   - Encapsulation Efficiency
   - Drug Content
   - In vitro drug release of drug
   - In vivo study

9. Stability studies

10. Compilation of data and its statistical treatment

11. Result and discussion

12. Summary and Conclusion