CHAPTER 3: REVIEW OF LITERATURE

Jelvehgari M., et.al. (2006) have prepared Benzoyl peroxide microsponges by quasi emulsion solvent diffusion method and evaluated for antibacterial activity and skin irritancy. Their study concludes that controlled release of BPO from a delivery system to the skin could reduce the side effects while reducing percutaneous absorption. Topical delivery system with reduced irritancy was successfully developed.

Mine Orlu M., et.al. (2006) have designed colon specific drug delivery system containing Flurbiprofen microsponges by quasi emulsion solvent diffusion. They have also entrapped FLB into a commercial Microsponge® 5640 system using entrapment method. Mechanically strong tablets prepared for colon specific drug delivery were obtained owing to the plastic deformation of sponge-like structure of microsponges. In-vitro studies exhibited that compression coated colon specific tablet formulations started releasing the drug at the 8th hr. corresponding to the proximal colon arrival time due to the addition of enzyme, following a modified release pattern while the drug release from the colon specific formulations prepared by pore plugging the microsponges showed an increase at the 8th hr. which was the time point that the enzyme addition made.

John I D'souza., et.al. (2008) have developed Fluocinolone Acetonide microsponges by quasi emulsion solvent diffusion and suspension polymerization methods. They have incorporated microsponges in gel base and evaluated for anti-inflammatory activity. The results concluded that controlled release of drug to the skin could reduce the side effect while reducing percutaneous absorption showing comparative anti-inflammatory activity with the gels containing free drug.
Vikas Jain., et.al. (2010) have prepared Eudragit based microsponges with potential for colonic delivery. They have chosen Dicyclomine as a model drug. *In-vitro* dissolution study showed that increase in drug : polymer ratio resulted in a reduction in the release rate of the drug from the microsponges. Drug release was bi-phasic with an initial burst effect with 16-30 % of the drug was released in the first hr. Cumulative release for the microsponges over 8 hrs. ranged from 59-86 %.

Vikas Jain., et.al. (2010) have developed Paracetamol loaded microsponges. The colon specific formulations were prepared by compression coating of microsponges with Pectin: hydroxypropylmethylcellulose (HPMC) mixture followed by tabletting. *In-vitro* studies exhibited that compression coated colon specific tablet formulations started releasing the drug at the 6th hr. corresponding to the arrival time to proximal colon.

Grimes Pearl E., (2004) has developed a new formulation of (Hydroxyquinone) HQ 4% with retinol 0.15% entrapped in microsponge reservoirs to release HQ gradually to prolong exposure to treatment and to minimize skin irritation.

Kawashima Y., et.al. (1992) have prepared prolonged release microsponges of Ibuprofen by novel emulsion solvent diffusion method. The obtained results concluded that internal porosity of microsponges could be controlled by changing the concentration of drug and polymer in emulsion droplets. With lower concentration of Ibuprofen in ethanol, the resultant microsponges had higher porosity, about 50%. Microsponge compressibility was much improved over physical mixture of drug and polymer owing to plastic deformation of their sponge like structure. The more porous microsponges produced stronger tablets.
Bhise S. B., et.al. (2010) have prepared Rifampicin loaded porous microspheres by emulsion solvent diffusion method. They have used Eudragit RLPO and glyceryl monostearate. The results obtained concluded that the microsponge formulation provide oral controlled release that can prevent acid decomposition and provide better biopharmaceutical properties. Furthermore, the microspheres can be evaluated for preventing the interaction with isoniazid, other drugs and foodstuffs. Stability studies in simulated gastric fluid (SGF) indicated that low relative decomposition of 18.5% was achieved with high drug to low polymer ratio of 1:4.

Netal Amrutiya., et.al. (2009) have developed microsponges for topical delivery of mupirocin for sustained release enhanced drug deposition in the skin. The optimized microsponges were incorporated into an emulgel base. *In-vitro* drug release, *ex-vivo* drug deposition, and *in-vivo* antibacterial activity of mupirocin-loaded formulations were studied. Emulgels containing microsponges showed desired physical properties. Drug release through cellulose dialysis membrane showed diffusion-controlled release pattern and drug deposition studies using rat abdominal skin exhibited significant retention of active in skin from microsponge-based formulations by 24 hrs.

Ming-shi Yang., et.al. (2003) have prepared sustained release microspheres with Eudragit RS and aerosil using quasi-emulsion solvent diffusion method. Aerosil was employed as an inert dispersing carrier to improve the dissolution rate of Nitrendipine and Eudragit RS as a retarding agent to control the release rate. The drug loading of microspheres was enhanced with increasing the ratio of drug to excipients. The dissolution profiles could be modulated with adjusting the amount of retarding agent and dispersing carrier formulated.
Purushotham Rao K., et.al. (2010) have prepared and evaluated O/W cream for skin psoriasis. Salicylic acid is chosen as a model drug, which is the most effective keratolytic agent. In this work o/w emulsion based cream formulation contains suitable combination of oil phase and aqueous phase along with preservatives, prepared and subjected to various physiochemical parameters like drug content, pH, spreadability, tube extrudeability, viscosity and IR studies. It was revealed that salicylic acid o/w cream formulation should be useful for treatment of skin psoriasis.

Purushotham Rao K., et.al. (2010) have developed vanishing cream based drug formulation for the treatment of scalp psoriasis. Salicylic acid chosen as a model drug is the most effective keratolytic agent. These vanishing creams are o/w emulsion based formulation containing suitable combination of oil phase and aqueous phase along with preservatives, prepared and subjected to various physiochemical parameters such as spreadability, tube extrudability, pH, drug content, viscosity, IR studies and *in-vitro* drug release study. The study concluded that the vanishing cream based Salicylic acid formulations will be useful for the treatment of skin psoriasis when compared with ointments which are greasy and messy in nature and may cause staining of clothes. The prepared vanishing cream was pleasant; easily washable thereby increasing the patient compliance.

Schwarb F.P., et.al. (1999) have studied percutaneous absorption of Salicylic acid in man after topical administration of three different formulations. In this study, risk assessment for topical Salicylic acid as a keratolytic agent is made and compared with clinical information on Salicylic acid toxicity following topical administration. The current investigation provided new information on the percutaneous absorption of Salicylic acid from two magisterial formulations and one brand formulation used in keratolytic treatments.
Patel Rakesh P., et.al. (2009) have prepared Ketoconazole liposomes by thin film hydration technique using soya lecithin, cholesterol and drug in different weight ratios. The prepared liposomes were characterized for size, shape, entrapment efficiency, *in-vitro* drug release (by Franz diffusion cell) and physical stability. The studies demonstrated successful preparation of Ketoconazole liposomes and effect of soya lecithin: cholesterol weight ratio on entrapment efficiency and on drug release.

Najmuddin M., et.al. (2010) have designed and evaluated gels for topical delivery of water insoluble antifungal agent Ketoconazole with an aim to increase its penetration through skin and thereby its flux. Ketoconazole gel formulations were made with different polymers like carbopol 940, hydroxyl propyl methyl cellulose, methyl cellulose, and sodium carboxymethylcellulose, containing various permeation enhancers namely sodium lauryl sulphate (0.5-1.0%) and dimethyl sulfoxide (5-20%) in different proportions. The study revealed that an optimum of carbopol 940 with 0.75% SLS and carbopol 940 with 15% DMSO were found to be more suitable to give a better formulation with good drug release characteristics and consistency. Carbopol 940 with 15% DMSO (KCD3) showed better release of Ketoconazole from gel.

Shireesh Kiran R., et.al. (2010) have formulated and evaluated the Ketoconazole nail lacquer as ungual drug delivery system for the treatment of onychomycosis. This study also examined the physical properties of membranes with the means of well-known ungual penetrate enhancers, i.e. urea, H$_2$O$_2$ and thioglycolic acid. It was concluded that urea hydrogen peroxide enhances hydration state; thioglycolate cleaves the disulphide bonds between keratin molecules, thus enhancing nail penetration of the drug.
Skiba M., et.al. (2000) have assessed the effect of formulation factors such as pH and antioxidant levels on the stability of ketoconazole in aqueous media. The effect of pH on the viscosity of the formulation has been studied. In this performation phase, ketoconazole was found to undergo less hydrolysis at alkaline pH. The viscosity of the formulation was found to be more stable at high pH values. The amount of ketoconazole (ranging from 0.25 to 2%) in the formulation has little influence on the degradation mechanism. In conclusion, the final formulation developed (pH 7, 0.1% butylated hydroxytoluene) is stable with a shelf life of around 15 months.

Jain Ankur., et.al. (2010) have investigated the potential of emulgel in enhancing the topical delivery of Ketoconazole. Emulgel formulations of Ketoconazole were prepared using 2 types of gelling agents: Carbopol 934 and Carbopol 940. The study suggested that the emulgel formulation succeed the drug release for sustained drug delivery in a controlled manner in comparison with cream.

Katarzyna Winnicka., et.al. (2012) investigated the influence of PAMAM-NH$_2$ and PAMAM-OH dendrimers generation 2 and generation 3 on the solubility and antifungal activity of Ketoconazole and to design and evaluate Ketoconazole hydrogel with PAMAM dendrimers. It was shown that the surface charge of PAMAM dendrimers strongly affects their influence on the improvement of solubility and antifungal activity of ketoconazole. The MIC and MFC values obtained by broth dilution method indicate that PAMAM-NH$_2$ dendrimers significantly (up to 16 fold) increased the antifungal activity of ketoconazole against Candida strains. The antifungal activity of the designed ketoconazole hydrogel with PAMAM-NH$_2$ dendrimers measured by the plate diffusion method was definitely higher than the pure ketoconazole hydrogel and also as compared to commercially available product.
Markand Mehta., et. al. (2012) have shown that encapsulation of Cotrimazole into microsponge would modify the release rate and also reduce side effects. In this study Clotrimazole microsponge was prepared by emulsion solvent diffusion technique by using Ethyl cellulose, HPMC K4M, Carbopol 934, Eudragit RS 100, Eudragit RL 100. Optimized batch of microsponge was further formulated as gel formulation for topical delivery. The In vitro drug release data of optimized batch were fitted into different kinetic models which showed that the drug release from gel formulations followed zero order release. Optimized gel formulation was compared with the marketed formulation and pure drug for antifungal activity, which showed that the prepared formulation was having comparative antifungal activity with marketed formulation.

Julie M., et.al. (2005) have described a spectrophotometric method for determination of Oxiconazole in raw material and in topical lotion. This method was based on the reaction of the Oxiconazole with methyl orange in buffered aqueous solution of citric acid at pH 2.3. A prospective validation of the method showed that the method was linear (r = 0.9995), precise (intra-day: CV= 1.57% and inter-day: CV= 1.50%) and accurate (mean recoveries: 99.69%). The results compared favourably with those of the HPLC method.

E. J. Van Hoogdalem., et.al. (1997) have evaluated the in-vivo nail penetration of the antimycotic Oxiconazole from a 1% w/v lotion, and to evaluate the potential penetration enhancing properties of co-delivered acetylcysteine. Six healthy volunteers were treated with 1% w/v Oxiconazole lotions with or without acetylcysteine (15% w/v), according to a left–right study design. The results suggested a variably enhancing effect of acetylcysteine on the extent of Oxiconazole nail penetration in the upper nail layers. The effect of acetylcysteine was speculated to be related to increase binding of Oxiconazole to nail constituents.