**2: LITERATURE REVIEW: COLONIC DRUG DELIVERY**

1. **Y.S.R Krishnaiah et al (1998)** developed a colonic drug delivery system with guar gum for indomethacin and done in vitro and in vivo evaluation. In vitro drug release studies revealed that showed that compression coated indomethacin core tablets able to protect the drug release under conditions simulating to GI tract. In vivo study showed tablet disintegration in ascending colon and drug distribution in colonic region. 78.

2. **M. Zahirul I. et al (1999)** coated placebo tablets and mesalazine tablets Eudragit L100-55 and Eudragit S100 by spraying aqueous systems. In vitro study revealed that this system is suitable for colon targeting. 79.

3. **Claudia S. Leopold (1999)** reviewed coated dosage forms to achieve colon specificity, presented coating materials counting pH dependent polymer, time controlled polymer and microbially triggered polymer for colon targeting drug delivery. 80.

4. **W.A. Chan et al (2001)** described the use of methylacrylic acid–methylmethacrylate copolymers, (Eudragit) for coating to achieve colon targeting based on pH approach. Calcium pectinate beads of theophylline were prepared and then coated with Eudragit S100 in an aqueous phase with a fluidized-bed spray coater. In vitro drug release was measured in simulated colonic condition and demonstrated practicability of the Eudragit S coated capsules to deliver the drug to the colon. 81.
5. **M.E. Sangalli et al (2001)** demonstrated a system based on time dependent approach containing antipyrine as model drug, evaluated in vitro and in vivo by determining salivary concentration of drug by HPLC as well as by gamascintography. The results showed potential of the system invivo and invitro for colon targeting\(^{60}\).

6. **T. Hideyuki et al (2002)** studied the colonic drug delivery of 5-Aminosalicylic acid (5-ASA) using chitosan capsules for ulcerative colitis. In vivo study revealed that chitosan capsules reached the colon at 3.5hr after oral administration in rats. \(^{82}\).

7. **V.R. Sinha et al (2002)** developed a tablet core containing polysaccharides xanthan gum, guar gum, chitosan or synthetic polymers like Eudragit E as a binder with Indomethacin, the core tablets were enteric coated with Eudragit-L 100. The study showed potential of chitosan as a binder as compare to guar gum for colon targeting\(^{83}\).

8. **C.W. Leong et al (2002)** studied the film forming properties of a commercial aqueous ethylcellulose dispersion (Surelease) mixed with a range of ratios of an amylose/butanol complex in the presence of a range of concentrations of a plasticizer. They concluded that the degree of degradation of film was directly related to the amylose content of the films and demonstrated amylose ability of colon targeting\(^{84}\).

9. **L. G. Maria et al (2003)** prepared a matrix tablet of diclofenac sodium containing sodium chloride and Eudragit in different ratio for time-
controlled system. They concluded that by varying the ratio, colon targeting can be achieved with zero order release profile\textsuperscript{5}.

10. **V.R. Sinha et al (2003)** review article presented a detail account of bacterial approach for colon targeting with emphasis on microbial count in colon and their role. They also elaborated the list of bacterial sensitive polymer for colon drug release including amylose along with ethyl cellulose\textsuperscript{86}.

11. **C. I. Valentine et al (2004)** in their review explained that Eudragit FS 30D is more superior than Eudragit S100 for colon specific drug delivery since it dissolves at controlled rate than Eudragit S100. In vivo scintiography in human with Eudragit FS 30 D coated formulation also showed superior results for colon specific drug release than Eudragit S100\textsuperscript{87}.

12. **F. S. Lee et al (2004)** presented a comparison of two fermentation model for in vitro evaluation of microbially triggered system. One system consisted of an enzyme-based fermentation and other with conventional fermentation model inoculated with human faecal bacteria. The results of the both system are equivalent suggesting use of enzyme system for in vitro screening of amylose formulations for colonic drug delivery\textsuperscript{88}.

13. **D. R. Friend (2005)** reviewed a detail account oral drug delivery system for inflammatory bowel disease (IBD) The review presented the impact of disease condition on oral targeted delivery in treatment of IBD also presented approaches for colon targeting which include pH, time,
bacterial triggered mechanism as well as currently used in marketed products\textsuperscript{11}.

14. **A. Akhgari et al (2005)** prepared the Eudragit S100 and Eudragit L100 coated pellets using FB coater and level of coating for colon specific drug delivery optimized by factorial design. The variables included the ratio of two polymer and the coating level. Lag time and percent drug release were selected as response variables The results demonstrated application of factorial design as suitable tool for coating optimization to achieve colon delivery\textsuperscript{89}.

15. **G. Chunsheng et al (2006)** developed meloxicam loaded colon targeted pellets coated with Eudragit FS 30 D and evaluated in vitro release and in vivo absorption in beagle dog model. Drug loaded pellets were prepared by layering drug binder (HPMC), solubilizer (cyclodextrin) solution onto pellets followed by coating with Eudragit FS 30 D. The results recommended that drug could be delivered to the colon with 15\% (w/w) coating level of Eudragit FS 30 D and this polymer coating had no significant influence on the relative bioavailability of drug\textsuperscript{90}.

16. **Y. Meissner et al (2006)**: suggested tacrolimus loaded nanoparticles prepared by simple oil/water emulsification method with biodegradable poly (lactide-co-glycolide) (PLGA) and pH-sensitive Eudragit P-4135F Nanoparticles demonstrated significant clinical activity. These nanoparticles increase drug concentration specifically inside the
inflamed tissue with a lower total amount of drug and selective accumulation in inflamed area\textsuperscript{66}.

**17. D. Pertuit et al (2007)** developed nanoparticles of 5-amino salicylic acid by nanoprecipitation methods for the treatment of inflammatory bowel disease and shown colon specific drug release after lag time\textsuperscript{65}.

**18. T. D. Fatmanur et al (2007)** developed the mesalazine tablets with alginate matrix having pH-sensitive gel-forming ability for intestinal delivery. Tablets were visualized by X-ray imaging to monitor the tablets disintegration location in the gastrointestinal system. Result demonstrated that mesalazine-alginate matrix tablet formulations delivered the drug to the small and large intestine\textsuperscript{91}.

**19. T. Marvola et al (2007)** presented the paracetamol tablet with excipient coated with Eudragit S polymer. The in vivo study was done by gammascintigraphy and evaluation proved that the products remained intact in the upper gastrointestinal tract and drug release start at the ileo-caecal junction or at the beginning of the ascending colon leading to spread the drug dose to a larger surface area for effective treatment\textsuperscript{92}.

**20. B. N. Singh (2007)** reviewed the recent patents related to various modified-release formulation technologies of colonic delivery for different drug\textsuperscript{3}.

**21. T. Oosegi et al (2008):** developed a system with EudragitS100 and L100 coated Chitosan-succinyl-prednisolone conjugate (Ch-SP)
microsphere was, by novel preparative conditions. Release of prednisolone was concealed at stomach pH but gradually increase at alkaline pH demonstrating potential of Eudragit-coated Ch-SP microspheres colon targeting delivery system of Prednisolone.

22. L. Emma M et al (2008) compared the two approach of colonic drug delivery in vivo of a Eudragit S, pH-responsive polymer and Polysaccharide/polymeric mixture of amylose/ethyl cellulose, bacterial triggered system. They concluded that the bacterially-triggered delivery concept provide better colonic delivery over the pH approach.

23. Libo Yang (2008) in his review article summarized the dissolution testing currently used in evaluating colon targeting delivery systems activated by microflora (polysaccharide) with degrading enzymes, rat ceecal contents, slurries of human fecal, and multi-stage culture systems.

24. V. C. Ibekwe (2008) demonstrated a novel colonic delivery coating based on dual mechanism of pH and bacteria triggered comprise a mixture of Eudragit S, pH-responsive enteric polymer and resistant starch a biodegradable polysaccharide in a single layer matrix film. Each trigger mechanism has the capacity to act ensuring appropriate targeting in the gastrointestinal tract irrespective of change pH or variable bacterial count. They concluded that this technology has potential for colon targeting.
25. **A. Makhlof et al (2009)** invented a novel pH-sensitive nanospheres designed of budesonide with polymeric mixtures of poly (lactic-co-glycolic) acid and methacrylate copolymer, a pH-sensitive polymer. The delivery system combined the dual mechanism of targeting (pH and bacterial approach). In vivo study in the trinitrobenzene sulfonic acid induced colitis rat model showed significant anti-inflammatory effects of dug\textsuperscript{96}.

26. **K. Gurpreet et al (2010)** presented a tablet of budesonide coated with mixtures containing chitosan and Chondroitin sulfate susceptible to microbial enzyme degradation for releasing in the colon. The system provided an unsophisticated method for delivery budesonide to the colon\textsuperscript{97}. 