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Polymers for Colon Targeted Drug Delivery: A Review

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ABSTRACT: The colon targeted drug delivery (CTDDS) has significant implications in the field of Pharmacotherapy. Recently the oral colon targeted drug delivery systems have gained enormous importance for delivering different kinds of therapeutic agents for both local and systemic administration. Targeting of drugs to the colon via oral administration not only protect the drug from degradation or release in the stomach and small intestine but also ensures abrupt or controlled release of the drug in the proximal colon. There are several designs of drug delivery systems which deliver the drug quantitatively to the colon and then trigger the release of drug. This review emphasizes various types of polymers used in formulation design for colon targeted drug delivery systems.

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INTRODUCTIONS:

Drug delivery is the method of administering Pharmaceutical compound to achieve a therapeutic effect in humans being [1,2]. Drug delivery technologies alter drug release, absorption, distribution and elimination profile of drug. Thus it offers several benefits to the drug like enhancement product effectiveness, safety and patient compliance. The drug targeting to specific sites offers better therapeutic action with many advantages that are prevention of side effects and reduction of doses in comparison to the non-targeted drugs. For targeting of drug to a particular site in gastrointestinal tract need special property which is mostly absent in control release drug delivery system.

The drug targeting to the colon offers local and systemic treatment of various colonic diseases. It also delivers the protein and peptides by systemic absorption [3,4]. The CTDDS has significant treatment of large intestine diseases such are Crohn's disease, irritable bowel syndrome, ulcerative colitis and colon cancer. The drug delivery by CTDDS maintain high level of drug at colon, thus significantly cure several disorders. The proteolytic activity of colon mucosa is very less. Thus colon is a suitable place in GIT for systemic absorption of proteins and peptides. The colon due to its near neutral pH and longer transit time, the CTDDS offers various therapeutic benefits.

A dosage form when passes in GIT faces several obstacles to reach colon. So dosage form to target the colon must be formulated to overcome these obstacles. A formulation design successful shall be achieved for one drug for colon delivery if the drug is protected from degradation or release in the stomach. Then only the controlled release of drug is possible in the colon [5,6]. The polymers are used either as alone or in combination form to target the drug at colon. It is now acknowledged that polymers can greatly impact the rate of release and absorption of drugs.

COLON SPECIFIC POLYMERS:

Polymers are high molecular weight macromolecules. The polymers are very large chains with several functional groups. These polymers can be blended with low and high molecular weight materials. Polymers are becoming leading role in designing several novel drug delivery systems. The surface and bulk properties are taken into consideration for designing of polymers for various drug delivery applications [7]. In designing of Novel drug formulations, several technological development includes that are drug modification by chemical means, career based drug delivery and drug entrapment in polymeric matrices that are placed in desired bodily compartments. These technical developments in drug delivery approaches improve human health [8].

Pharmaceutical application of polymers:

The polymers are used to achieve taste masking of unpleasant taste drugs. The polymers are also used as a binder in tablets, as viscosity impacting and flow controlling agent in liquids, suspension and emulsions. The polymers are used as film coating to disguise the unpleasant taste of drug and to enhance drug stability. The polymers are employed to modify drug release characteristics [9].

MECHANISM OF COLON TARGETING:

Most significantly and widely used mechanisms for delivery of drug from CTDDS at colon is to coat the formulation using natural or synthetic polymers. In this technology, the drug is present in the core (Containing active moiety with other suitable excipients) of the formulation which is coated with layers of polymer coatings. The first coating is an acid-soluble polymer and outer coating is an enteric polymer. During the transit of formulation through the GI tract, the formulation remains intact in the stomach due to enteric protection, but the enteric coating will dissolve in the small intestine, where the pH is above 6. The enteric coating starts to dissolve at the pH 5 in the small intestine. On entry of formulation into the colon, the polysaccharide coating will starts to dissolve. The bacteria will enzymatically degrade the polysaccharide into organic acid. This lowers the pH of the surrounding system and results in the dissolution of the surrounding system. This results in dissolution of acid-soluble coating and subsequent drug releases [10-12].

BIODEGRADABLE POLYMERS:

Biodegradation is a natural process in which organic chemical substances in the environment are converted to simpler compounds, mineralized and redistributed through elemental cycles such as carbon, nitrogen and sulphur cycles. The biocompatibility and biodegradability properties of biodegradable polymers make it use in the biomedical applications. Biodegradable polymers are extensively used for temporary aids such as sutures, tissue-supporting scaffolds and drug delivery devices [10]. Polymers exhibit its properties in the living body within limited time and then gradually degrade into soluble molecule which can be excreted from the body [11]. An ideal biodegradable polymer with the property of bicompatiblity, should ideally offer processability, sterilizability and storage stability during use for biomedical applications [12]. The merit of degradable polymers is that they are broken down into biologically acceptable molecules that are metabolized and removed from the body via normal metabolic pathways.

Factors determining the biodegradation of polymers:

Several factors that are affecting the degradation biodegradable polymers such are chemical structure,

chemical composition, distribution of repeat units in multimers, presents of ionic groups, presence of unexpected units or chain defects, molecular weight, molecular-weight distribution, morphology (amorphous/ semicrystalline, microstructures, residual stresses), presence of low-molecular-weight compounds, processing conditions, annealing, sterilization process, storage history, shape, site of implantation, adsorbed and absorbed compounds (water, lipids, ions, etc.), physicochemical factors (ion exchange, ionic strength, and pH), physical factors (shape and size changes, variations of diffusion coefficients, mechanical stresses, stress- and solvent-induced cracking, etc.) and mechanism of hydrolysis (enzymes versus water) [12,13].

NATURAL POLYMERS IN COLON TARGETING:

For the development of solid oral dosage forms for colonic delivery of drugs, the natural polysaccharides are extensively used [13]. Biodegradable polymers are generally hydrophilic in nature. These polymers have limited swelling characteristic in acidic pH. Several colonic bacteria secretes many enzymes. These enzymes can cause hydrolytic cleavage of glycosidic bonds of natural polysaccharides. The enzymes are C-D-galactosidase, amylase, pectinase, C-Dglucosidase, dextranase and D-D-xylosidase. The natural biodegradable polysaccharides polymers used in designing of dosage form for delivery into colon pectin, starch, guar gum, amylose and karaya gum. The linear polysaccharides remains intact in stomach and small intestine but the bacteria of human colon degrades them and thus make them potentially useful in colon targeted drug delivery systems [14].

PECTIN:

Pectins are water soluble, non starch linear, heterogeneous polysaccharides that consist of D-1, 4 D-galacturonic acid and 1, 2 D-rhamnose with D-galactose and Darabinose side chains (Fig 1). It is refractory to host gastric and small intestinal enzymes. The pectin is almost degraded by the colonic bacterial enzymes to produce a series of soluble oligalactorunates [15,16]. The alkali metal salts of pectinic and pectic acids are soluble in water. The pectin get swell if used alone in water. But on exposing to aqueous fluids of GI tract, the drug gets release from formulation by diffusion technique. The pectin microspheres for oral colon control delivery of indomethacin could be prepared by Spray drying method followed by cross linking with calcium chloride [17,18]. Drug release from pectin microspheres was increased by the addition of pectinase. The research revealed that the release of indomethacin from pectin microsphere was less in acidic pH while it was stimulated at neutral pH (pH 7.4).

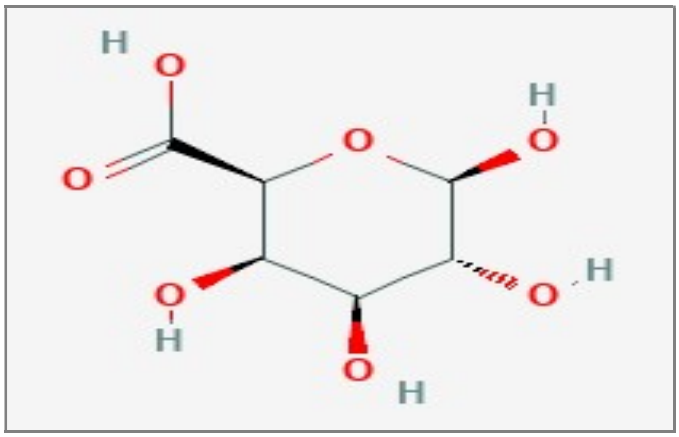

Fig 1. Chemical structure of Pectin.

CHITOSAN:

Chitosan is a high molecular weight polycationic polysaccharide derived from chitin by alkaline deacetylation. Chitosan is consisting of the repeated units of (2-amino-2-deoxy-D-gluco-pyranose) which are linked by (1-4) C-bonds (Fig 2) [19,20]. Chitosan possess various ideal properties of nontoxic, biodegradable, biocompatible and bioactive polymer. As chitosan swell in the intestinal pH, it is used for the colon targeted drug delivery. Chitosan capsules were used for colonic delivery of an antiulcerative colitis drug (5-Aminosalicylic acid). The research study demonstrated that there is a marked increase in the release of drug from chitosan capsule was observed in the presence of the rat caecal content [21]. As chitosan dispersed system is dissolves easily under acidic conditions, an additional outer enteric coating was also provided to prevent the release of drug from chitosan dispersed system in the stomach [22].

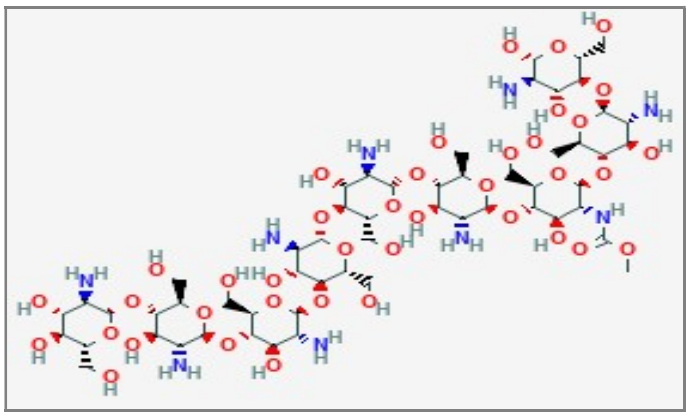

Fig 2. Chemical structure of Chitosan.

GUAR GUM:

Guar gum is a polysaccharide composed of linear chain of C 1, 4-linked mannose residues to which galactose residues are 1, 6-linked at every second mannose, forming short side-branches (Fig 3) [23]. The gelling, drug release retarding properties and susceptibility to microbial degradation in large intestine make the guar gum to be used in colon targeted drug delivery systems. Guar gum was found to be a colon-specific drug carrier in the form of matrix, compression coated tablets and microspheres [24]. The colorectal cancer is treated by chemoprevention using Guar gum-based matrix tablets of rofecoxib [25]. The research study reported use of colons specific guar gum–based tablet of 5-Fluoro Uracil [24,25].

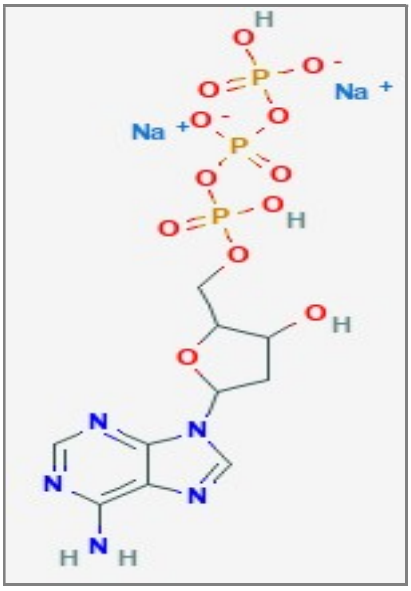

Fig 3. Chemical structure of Guar gum.

CHONDROITIN SULFATE:

Chondroitin sulfate is a soluble mucopolysaccharide polymer (Fig 4). It is used in large intestine as substrate by *Bacillus thetaiotaomicron* and *Bacillus ovatus*. The water soluble ability of Chondroitin sulfate enables it to act as a barrier in the formulation of the colon targeted drug delivery. Rubistein, *et al*. (1992) formulated an indomethacin matrix by using cross-linked Chondroitin sulfate. They found that the varying concentration of cross linked Chondroitin sulfate in formulations causes variation in drug targeting to colon [25]. Amrutkar, *et al*. (2009) prepared indomethacin matrix tablet using Chondroitin sulfate and chitosan as carrier and binder for colon specific delivery [26].

DEXTRAN:

Dextran is a polysaccharide water soluble polymer consisting of D-1, 6 D-glucose and side chain of D-1, 3 D-glucose units (Fig 5) and it is degraded by colonic microbial enzyme dextranases [3,19]. The dextran possess characteristics that are water solubility, biocompatibility and biodegradability. The recent research study shows that the dextran is a potential polysaccharide polymer which can sustain the delivery of proteins, vaccines and drugs. Injectable and degradable dextran-based systems for drug delivery were generated by a crosslinking reaction with photo-polymerization or free radical polymerization. McLeod, *et al*. (2006) synthesized glucocorticoid-dextran conjugates containing dexamethasone and methylprednisolone were attached to dextran using dicarboxylic acid linkers (succinate and glutarate) for treatment of colotis. Dextran conjugates resisted hydrolysis in upper GI tract contents but was rapidly degraded in cecal and colonic contents where the bacterial count is high [27]. The research study showed that the therapy and reported that recombinant DNA (chloramphenicol acetyl transferase) was effectively encapsulated in cationic liposomes. The liposome was integrated within dextran and this system could stop *in vivo* transfection efficiency within the colon epithelium wall [28].

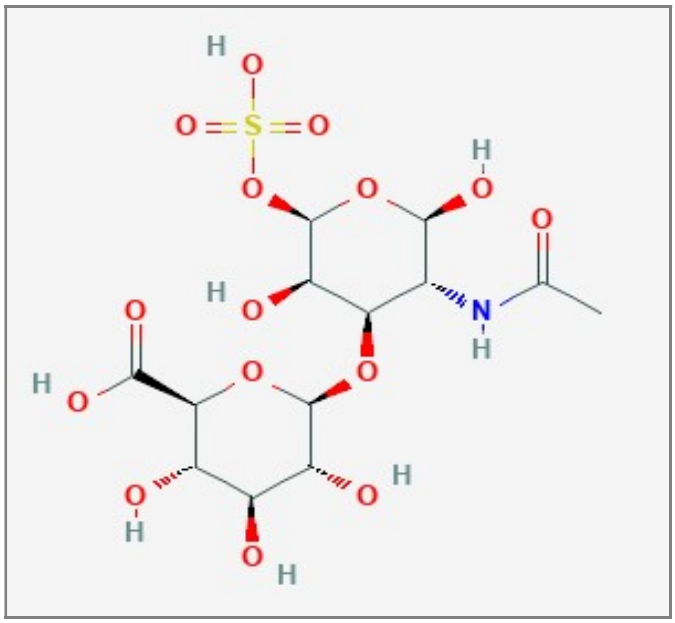

Fig 4. Chemical structure of Chondriotin sulphate.

CYCLODEXTRIN:

Cyclodextrin is a cyclic oligosaccharide consisting of six to eight glucopyranose units joined by D-(14) glucosidic linkage (Fig 6). Cyclodextrins consist an internal lipophilic cavity, which can make complex with hydrocarbon materials. Cyclodextrins remains intact with the core materials during their passage throughout the stomach and small intestine of the GI tract. In the

colon, they undergo fermentation in the presence of vast colonic microfloras into small monosaccharide and thus absorbed from these regions [28]. The results of *in vivo* research study in rat reveal that these conjugates were stable in stomach and small intestine. The study suggested that Cyclodextrin can be used for colon specific delivery of drug [29].

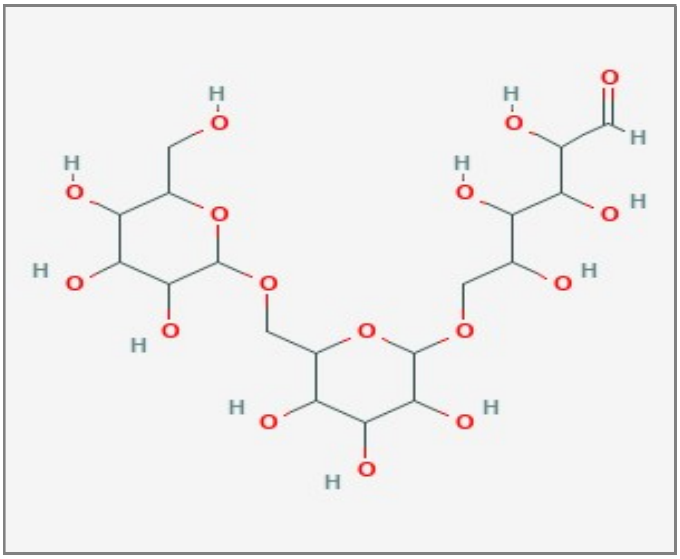

Fig 5. Chemical structure of Dextran.

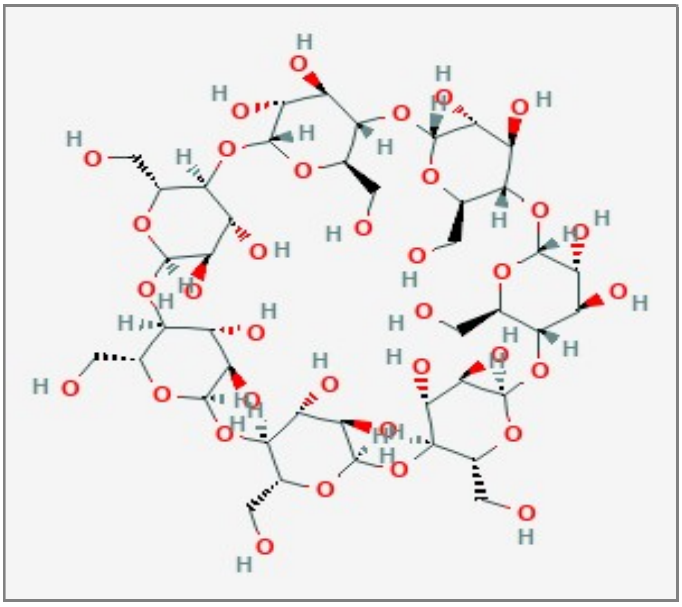

Fig 6. Chemical structure of Cyclodextrine.

INULIN:

Inulin is a naturally occurring glucofructan polymer. It consists of C 2-1 linked D-fructose molecule having a glycosul unit at the reducing end (Fig 7). It can resistant to the hydrolysis and digestion in the upper gastrointestinal tract. The endogenous secretions of human digestive tract cannot hydrolyze the Inulin [30]. The colon harbouring bacteria that Bifidobacteria can ferment the inulin. Vervoort, *et al*, developed inulin hydrogels for colonic delivery of drugs and investigated the swelling property of hydrogel [31]. The scientists, Vervoort and Rombaut, investigated the *in-vitro* enzymatic digestibility of the inulin hydrogels using an inulinase preparation derived from *Aspergillus niger*, which could diffuse into the hydrogels resulting in the degradation of the hydrogels [32].

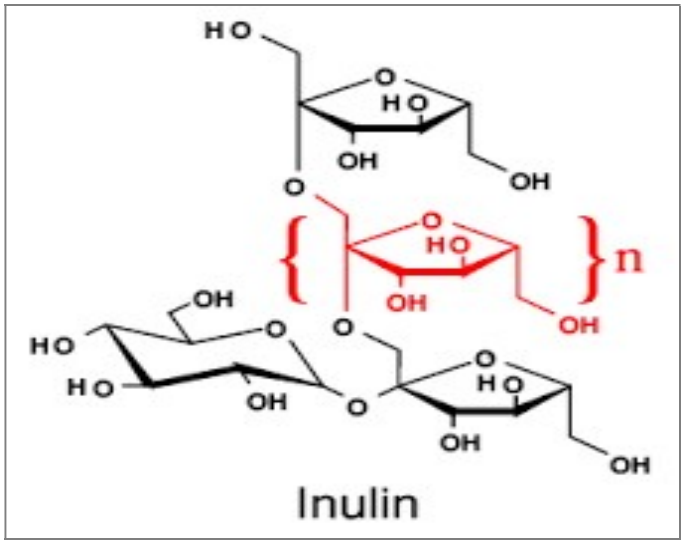

Fig 7. Chemical structure of Inulin.

XANTHAN GUM:

The gram-negative bacterium *Xanthomonas campestris* form a high molecular weight extra cellular polysaccharide produced by the fermentation that is xantham gum (Fig 8). Xanthan is a free flowing powder and at low concentrations soluble in both hot and cold water to give viscous solutions. It is used as thickening and stabilizing agent. Xanthan gum solutions offer very good stability to the formulation as they are least affected by changes in pH both in both alkaline and acidic conditions [33]. Xanthan gum and hydroxypropyl methylcellulose were found as the suitable hydrophilic matrixing agents for preparing modified release tablets.

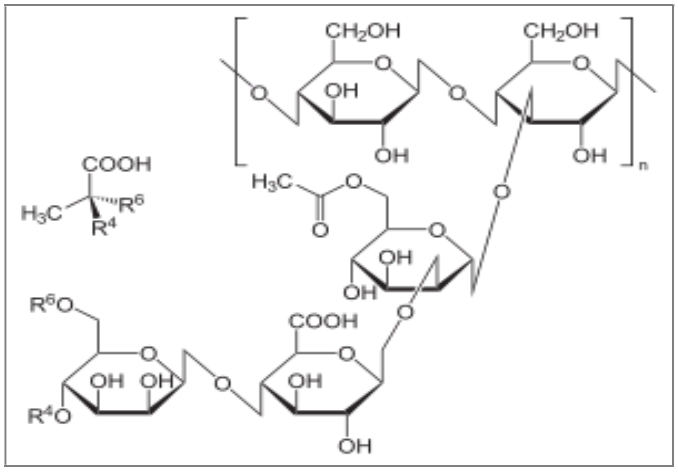

Fig 8. Chemical structure of Xantham Gum.

AMYLOSE:

Amylose is unbranched linear polymer of glucopyranose units (D-1, 4-D-glucose) linked through D–D-(1-4) linkage (Fig 9). Amylose is resistant to pancreatic amylases but it gets degraded by the bacteroids, bifido bacterium [33]. Amylose is used in tablet coating as it can form film by gelation. Addition of ethyl cellulose to amylose gives a suitable polymer mixture for colon targeting. Cumming, *et al*. used a mixture of amylase and ethocel (1:4) to prepare microspheres of [13C] glucose which was used as a surrogate for drug delivery [34].

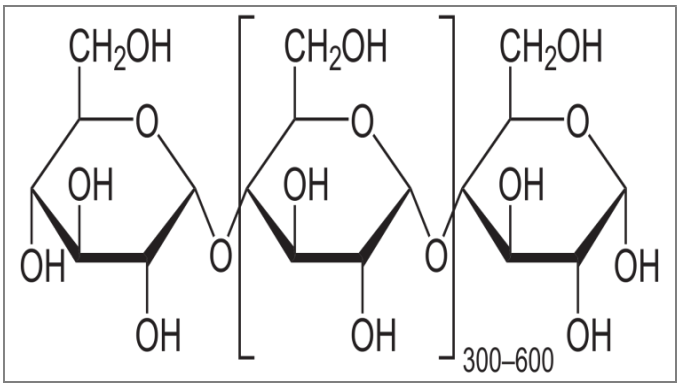

Fig 9. Chemical structure of Amylose.

LOCUST BEAN GUM:

Locust bean gum (Carob gum) contains natural polysaccharides (Molecular weight of 310000). It is derived from the endosperm of the seed of the 'Carob' (*Ceratonia siliqua* Linn, Family: *Leguminosae*). It is irregular shaped molecule with branched C-1, 4- D-galactomannan units (Fig 10). Locust bean gum is slightly soluble in cold water. It requires heat to achieve full hydration and maximum viscosity [35]. Raghavan, *et al*. (2002) proved that the combination of locust bean gum and chitosan (4:1) is a potential coating material for the core mesalazine and this complex possess better dissolution profile, higher bioavailability and hence a potential carrier for drug targeting to colon [36].

ALGINATES:

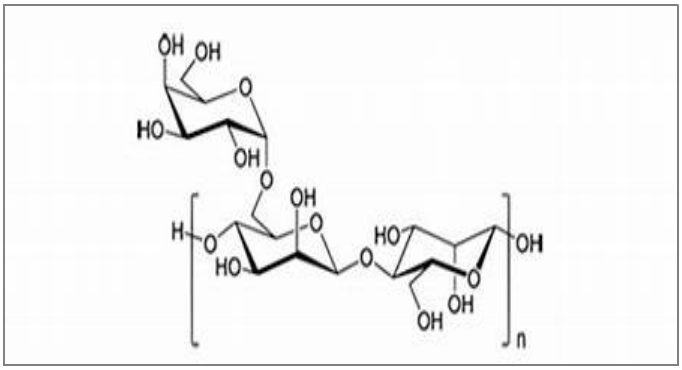

Fig 10. Chemical structure of Locust Bean gum.

Alginates are linear polymers consisting of 1-4' linked C- D-mannuronic acid and D-L-guluronic acid residue arranged as blocks (Fig 11). Alginate and their derivates possess several properties such as biocompatibility, biodegradability, low toxicity, non-immunogenicity, water solubility, relatively low cost, gelling ability, stabilizing properties, and high viscosity in aqueous solutions [37]. A Eudragit L-30D–coated calcium alginates bead for colonic delivery of 5-aminosalicylic acid has been reported.

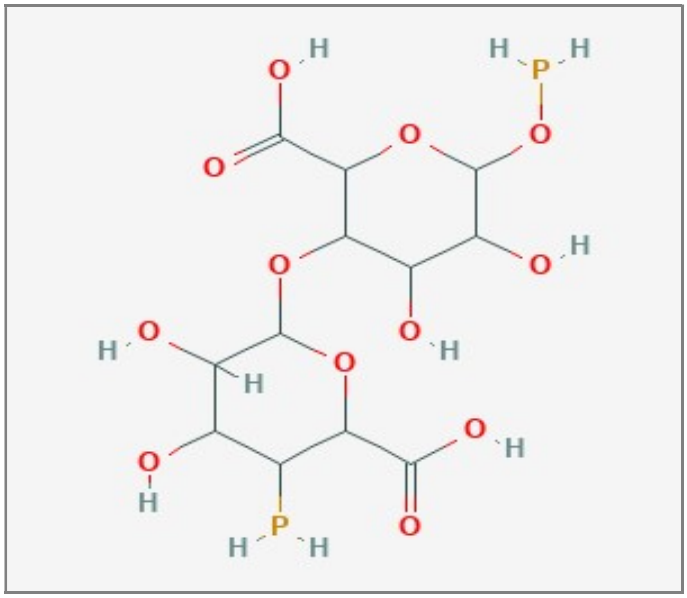

Fig 11. Chemical structure of Alginates.

SYNTHETIC POLYMERS IN COLON TARGETING:

The polymers to be used for colon targeting, must have properties like should be able to withstand the lower pH values of the stomach and small intestine (Proximal part) and should disintegrate at the neutral of slightly alkaline pH of the terminal ileum and preferably at the ileocecal junction. There are several synthetic pH dependent polymers that are acrylic acid and cellulose, used for colon targeted drug delivery. For colonic drug delivery, drug core is coated with pH sensitive polymers. The drug are delivered as tablets, capsules, pellets, granules, micro-particles and nanoparticles [38]. The pH dependent in colon specific drug delivery are insoluble at low pH levels but become increasingly soluble as pH rises.

EUDRAGIT:

Eudragit (Fig 12) products are pH-dependent methacrylic acid polymers containing carboxyl groups. The number of esterified carboxyl groups affects the pH level at which dissolution takes place. Eudragit are of three types such are Eudragit L, Eudragit S, and

Eudragit RS. Eudragit S and L are soluble above pH 7 and 6 respectively. Eudragit S coatings protect well against drug liberation in the upper parts of the gastrointestinal tract and have been used in preparing colon-specific formulations. The anti-inflammatory drug 5-aminosalicylic acid (5-ASA) can be targeted to large intestine using Eudragit S as coatings. The single unit tablets of 5-ASA by using Eudragit L as coatings is targeted on the colon in patients with ulcerative colitis or Crohn's disease [38]. The polypeptide hormone vasopressin and insulin have been administered to rats orally in Eudragit S coated single-unit capsule. Eudragit S has been used in combination with another methacrylic acid co-polymer, Eudragit L100-55, in colon-targeted systems to regulate drug delivery [39].

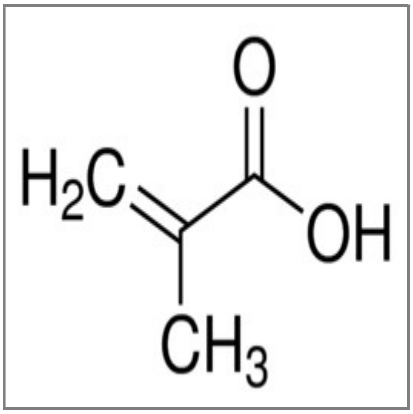

Fig 12. Chemical structure of Eudragit.

SHELLAC:

Shellac is the purified product of the natural resin lac (Fig 13). The natural resin lac is the hardened secretion of the small, parasitic insect KerriaLacca (lac insect). Shellac is the only known commercial resin of animal origin. Shellac is a hard, brittle and resinous solid. It is practically odorless in the cold but evolves a characteristic smell on heating and melting. Shellac is water insoluble. Shellac ethanolic solution is used as coatings for food applications [40]. The shellac coating layer remains intact with the dosage form during the passage in the stomach and small intestine until it reaches the colon with its higher pH, weher the dosage form is used for topical treatment of colonic diseases. The oral delivery of peptides and insulin is favoured in colon as the peptidase activity in the colon is lower than in the upper GI [41].

CONCLUSION:

As the Pharmaceutical Research progresses, the utilization of biodegradable polymers is significantly increased in the development of NDDS. This is because the biodegradable polymers are safe, non-toxic, economic and are chemically compatible with the other excipients in the formulation. This study literally demonstrated that several types of biodegradable and non-biodegradable polysaccharides are successfully used for drug delivery through colon targeted drug delivery system. Over non-biodegradable polysaccharides, the biodegradable Polysaccharides possess suitable properties for designing of colonic delivery system. This suitability is due to presence of dense microbial flora in colon. The present review study can be assessed that the polysaccharides biodegradable polymers are most promising agents for designing of colon targeted drug delivery systems.

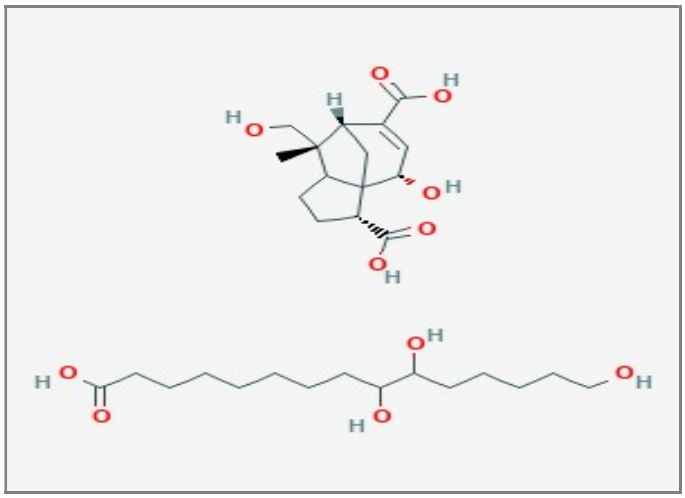

Fig 13. Chemical structure of Shellac.

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REFERENCES:

1. Wilson CG, Mukherji G, Sha HK. Biopolymers and Colonic Delivery. Vol. 2. New York: Informa Healthcare; 2008. 295-309.
2. Jose S, Dhanya K, Cinu TA, Litty J, Chacko AJ. Colon Targeted drug delivery: Different approaches. J Young Pharm, 2009; 1: 13-9.
3. Kumar RS, Kumar M, Ganesh GN, Jawahar N, Nagasamyvenkatesh D, Senthil V. Formulation and evaluation of pectin hydroxypropyl methylcellulose coated curcumin pellets for colon delivery. Asian J Pharm, 2009; 3: 138-142.
4. Vyas SP, Khar RK. Systems for colon specific delivery. New Delhi: Vallabh Prakashan; 2002. pp. 218-256.

5. Omanathanu PR. Polymers in drug delivery. Curr Opin Chem Biol, 2001: 5(4): 447-451.
6. Clochard M, Dinand E, Rankin S, Simic S, Brocchini S. New strategies for polymer development in Pharmaceutical Science - A short review. J Pharm Pharmacol, 2001; 53(9): 1175-1184.
7. Kathryn E. Uhrich, Scott M. Cannizzaro, Robert S. Polymeric System for Controlled Drug Release. Chem Rev, 1999; 99: 3181-3198.
8. Kronenthal RL. Biodegradable polymers in medicine and surgery. New York: Plenum Press; 1975. pp. 119-128.
9. Jain S, Jain NK. Pharmaceutical Product Development. New Delhi: CBS Publisher and Distributor; 2006. pp. 218-226.
10. Shirwaikar A, Shirwaikar AN, Prabu SL, Kumar GA. Herbal Excipients in Novel Drug Delivery Systems. Indian J Pharm Sci, 2008; 70: 415-422.
11. Englyst HN. Digestion of the polysaccharides of potato in the small intestine of man. Am J Clin Nutr, 2005; 45: 423-431.
12. Towle GA, Christensen O, Whistler RL, BeMiller JN. Pectin in Industrial Gums and Their Derivatives. New York: Academic Press; 1973. pp. 429-461.
13. Lee CM, Kim DW, Lee HC, Lee KY. Pectin microspheres for oral colon delivery: Preparation using spray drying method and in vitro release of indomethacin. Biotech Bioproc Eng, 2004; 9: 191-195.
14. Madziva H, Kailasapathy K, Phillips M. Alginate-pectin microcapsules as a potential for folic acid delivery in foods. J Microencap, 2005; 22: 343-351.
15. Wilson CG, Mukherji G, Sha HK. Biopolymers and Colonic Delivery. New York: Informa Healthcare; 2008; 1(2): 295-309.
16. Jain A, Gupta Y, Jain SK. Perspectives of biodegradable natural polysaccharides for site specific delivery to the colon. J Pharm Sci, 2007; 10: 86-128.
17. Tozakia H, Odoribaa T, Okadaa N, Fujitaa T, Terabeb A, Suzuki T, *et al*. Chitosan capsules for colon-specific drug delivery: Enhanced localization of 5-aminosalicylic acid in the large intestine accelerates healing of TNBS-induced colitis in rats. J Control Rel, 2002; 82: 51-61.
18. Shimono N, Takatori T, Ueda M, Mori M, Higashi Y, Nakamura Y. Chitosan dispersed system for colon-specific drug delivery. Int J Pharm, 2002; 245: 45-54.
19. Al-Saidan SM, Krishnaiah YS, Satyanarayana V, Rao GS. *In vitro* and *in vivo* evaluation of guar gum-based matrix tablets of rofecoxib for colonic drug delivery. Curr Drug Deliv, 2005; 2: 155-163.
20. Krishnaiah YSR, Satyanarayana V, Kumar DB, Karthikeyan RS, Bhaskar P. *In Vivo* pharmacokinetics in human volunteers: oral administered guar gum-based colon-targeted 5-fluorouracil tablets. Eur J Pharm Sci, 2003; 19: 355-362.
21. Al-Saidan SM, Krishnaiah YS, Patro SS, Satyanaryana V. *In vitro* and *in vivo* evaluation of guar gum matrix tablets for oral controlled release of water-soluble diltiazem hydrochloride. AAPS PharmSciTech, 2005; 6: 14-21.
22. Bauer KH, Kesselhut JF. Novel pharmaceutical excipients for colon targeting. STP Pharm Sci, 1995; 5: 54-59.
23. Hirsch S, Binder V, Kolter K, Kesselhut JF, Bauer KH. Lauroyldextran and cross- Linked galactomannan as coating materials for site specific drug delivery to the colon. Eur J Pharm Biopharm, 1999; 47: 61-71.
24. Krishnaiah YS, Rajua PV, Kumarb BD, Satyanarayanaa V, Karthikeyana RS. Pharmacokinetic evaluation of guar gum based colon-targeted drug delivery systems of mebendazole in healthy volunteers. J Control Rel, 2003; 88: 95-103.
25. Rubinstein A, Nakar D, Sintov A. Colonic drug delivery: Enhanced release of indomethacin from cross linked chondroitin matrix in rat caecal content. Pharm Res, 1992; 9: 276-278.
26. Amrutkar JR, Gattani SG. Chitosan– Chondroitin Sulfate Based Matrix Tablets for Colon Specific Delivery of Indomethacin. AAPS PharmSciTech, 2009; 10: 670-677.
27. McLeod AD, Friend DR, Tozer TN. Glucocorticoid-dextran conjugates as potential prodrugs for colon-specific delivery: Hydrolysis in rat gastrointestinal tract contents. J Pharm Sci, 2006; 83: 1284-1288.
28. Flourie B, Molis C, Achour L, Dupas H, Hatat C, Rambaud JC. Fate of A-cyclodextrin in the human intestine. J Nutr, 1993; 123: 676-680.
29. Minami K, Hirayama F, Uekama K. Colon specific drug delivery based on a cyclodextrin prodrug:

Release behavior of biphenylyl acetic acid from its cyclodextrin conjugates in rat intestinal tracts after oral administration. J Pharm Sci, 1998; 87: 715-720.
30. Dysseler BS, Hoffen MJ. Inulin. An alternative dietary fiber: Properties and quantitative analysis. Eur J Clin Nutr, 1995; 49: S145-S152.
31. Vervoort L, Kinget R. *In vitro* degradation by colonic bacteria of inulin HP incorporated in Eudragit films. Int J Pharm, 1996; 129: 185-190.
32. Vervoort L, Rombaut P, Mooter GV, Augustijns P, Kinget R. Inulin hydrogels II *In vitro* degradation study. Int J Pharm, 1998; 172: 137-145.
33. Englyst HN, MacFarlane GT. Breakdown of resistant and readily digestible starch of human gut bacteria. J Sci Food Agric, 1986; 37: 699-706.
34. Cummings JH, Milojevic S, Harding M, Coward WA, Gibson GR, Botham RL. *In vivo* studies of amylose and ethylcellulose coated [13C] glucose microspheres as a model for drug delivery to the colon. J Control Rel, 1996; 40: 123-131
35. Amnuaikit C, Ikeuchi I, Ogawara K, Higaki K, Kimura T. Skin permeation of propranolol from polymeric film containing terpene enhancers for transdermal use. Int J Pharm, 2005; 289: 167-178.
36. Raghavan CV, Muthulingam C, Amaladoss J, Jenita JL, Ravi TK. An *in vitro* and *in vivo* investigation into the suitability of bacterially triggered delivery system for colon targeting. Chem Pharm Bull, 2002; 50: 892-895.
37. Keller C, Modler RC. Metabolism of fructooligosaccharides by Biffidobacterium spp. Appl Microbiol Biotechnol, 1989; 31: 537-541.
38. Semde R, Amighi K, Devleeschouwe MJ, Moes AJ. Studies of pectin HM/ Eudragit RL/ Eudragit NE film coating formulations intended for colonic drug delivery. Int J Pharm, 2000; 197: 181-192.
39. Vishal VR, Preeti DG, Sunil PP. An overview on colonic drug delivery system. Int J Pharm Sci Rev Res, 2011; 6(2), 197-204.
40. Roda A, Simoni P, Magliulo M, Nanni P, Baraldini M, *et al*. A new oral formulation for the release of sodium butyrate in the Ileo-cecal region and Colon. World J Gastroenterol, 2007; 13: 1079-1084.
41. Trenktrog T, Müller BW, Specht FM, Seifert J. Enteric coated Insulin pellets: Development, drug release and *in vivo* evaluation. Eur J Pharm Sci, 1996; 4: 323-329.

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