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The study of colon-specific drug delivery system

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Abstract
Conditions including Crohn's disease, ulcerative colitis, colon cancer, and other similar conditions regional illnesses may be better treated using medication delivery systems that target of the colon in particular.

Keywords: Medications, effectively, orally, benefits

Introduction

Medications are most effectively administered when taken orally. When it comes to giving people their medication, it's the most convenient option. Absorption from the gastrointestinal system (GIT) after a standard dose is taken by mouth forms is dependent on pharmaceutic parameters, patient-related factors, and the drug's physicochemical qualities, among other things. If medicines need to be kept away from the tough climate of the upper digestive system or when localized administration of the pharmaceuticals in the colon is necessary, this is a major downside. The number of benefits that come from dosage forms that go into the gut instead elevated in the upper gastrointestinal tract. Colorectal cancer, inflammatory bowel illness (Ulcerative colitis and Crohn's disease), and infections may be effectively treated with oral medication delivery to the colon because the medicine can reach high local concentrations with low adverse effects from leaking into the upper GI tract or being absorbed too rapidly.

Delivering a therapeutic dose of medication to a specific location in the body in a timely manner while keeping the concentration where it needs to be is the main goal of any method for delivering drugs. The term "targeted drug delivery" refers to the process of delivering a medicine to a specific area with the goal of achieving a therapeutic concentration while preventing the medication from reaching other, less important areas. For medications that are unstable, poorly soluble, not very specific, don't stay in the body for long, are poorly absorbed, and don't have a high treatment index. A tailored method for giving drugs is the way to go.

If the medicine is neither degraded nor rendered inactive while in route to the target location, Some drugs may work best when they are delivered to specific areas of the body. Simultaneously, it may lessen the severity of side effects caused by improper disposal and reduce the toxicity of powerful medications by lowering the dosage. Nontoxicity, biocompatibility, biodegradability, and *in vitro* and *in vivo* physicochemical stability are excellent characteristics of a targeted delivery method. A relatively straightforward, repeatable, and cost-effective distribution system preparation is required. The discovery and use of an organ-specific characteristic is crucial to targeted medication delivery.

When it comes to treating specific areas of in the gut, focused medicine delivery saves lives for people with illnesses like IBD, colon cancer, and irritable bowel syndrome. The upper parts of the GI tract don't take well medicines that have polar structures or are easily hydrolyzed in the small intestine by enzymes and chemicals, especially proteins and peptides. This makes it difficult to attain clinically meaningful bioavailability of these medications. In addition to the possibility of oral administration of macromolecular medications, More effective treatments are available for ailments including Crohn's disease, ulcerative colitis, irritable bowel syndrome, and inflammatory bowel disease with drugs that are delivered through the gut.

From the mild discomfort of regular bowel movements to the debilitating effects of inflammatory bowel disorders and, finally, the deadly third most common malignancy in both sexes, colon cancer, there is a spectrum of significant conditions associated to the colon.

Literature Review

A.L.A. Sesink, D.S.M.L. Termont, J.H. Kleibeuker, and R.V.D. Meer (2021) [1] say that researchers have been trying to figure out what variables can influence how far colon cancer might spread. Each section of the large intestine has its own set of statistics, perhaps because its etiological variables are distinct from one another. The research also looked at factors that have been shown or are thought to have contributed to the onset of this disease, and it came to the conclusion colon cancer is the second most dangerous cancer in the US.

In their study, L. Yang, J.S. Chu, and J.A. Fix (2022) [2] examined the design, practicality, and *in-vivo* site selectivity of the pressure-controlled CODESTM formulation method. It shown that a medicine delivery mechanism tailored to the colon is necessary and beneficial. When used alone, the three main approaches prodrugs, systems that rely on pH and time, and systems that are triggered by microflora do not achieve the desired level of specificity for the colon. However, when combined, these methods can provide the kind of pinpoint accuracy that is necessary for effective drug delivery.

Metanidazole (MTZ) was created by Mundargi, Mundargi, Patil, Agnihotri, and Aminabhavi (2017) [3] for use in the colon. Among the polysaccharides that have been tried are guar gum, pectin, xanthan gum, betacyclodextrin (CD), carrageenan, and methacrylic acid-g-guar (MAA-g-GG) gum. To find out if the mixtures made were suitable as CSDDS, an *in vitro* study was carried out. Some versions were covered with Eudragit-L 100 to protect them in the digestive system, which made them even easier to target in the gut. According to statistical analysis of release data, protective coatings greatly enhanced the release of MTZ.

L.F. Asghar, S. Chandran (2016) [4], used xanthan gum-containing matrix bases including using pH-responsive polymers (Eudragit L100 & S100) to make a controlled-release dose form of indomethacin that is targeted to the gut. The first set of drugs to come out of the various matrix bases was much lower, resulting in regulated release lasting 14-16 hours. It follows that this formulation's matrix architecture might find use as a CSDS device, thanks to its scalability benefits.

M.L. Lorenzo-Lamosa, C. Remunan-Lopez, J.L. Vila-Jato, M.J. Alonso (2018) [5], proved the effectiveness of a hybrid system, exhibiting released in a specific way and biodegradable based on pH. Chitosan microcores embedded with diclofenac-containing acrylic microparticles make up the system. The medication was effectively microencapsulated Eudragit L-100 and Eudragit S-100 were used after being sprayed into chitosan microcores.

The Case for Colonic Drug Administration

1. Drugs that are active at the mucosal level may be used topically, which can lessen side effects in colonic illness therapy.
2. When it comes to colon diseases like inflammatory bowel disease, cancer, infections, and ulcerative colitis, it is very important.
3. It also offers a chance to understand how sulfide and other non-steroidal anti-inflammatory drugs (NSAIDs) work. Sulfide, for example, is converted to its active moiety in the colon and may inhibit the growth of colon polyps, the initial stage of colon cancer, through a localized mechanism of action.
4. The gut may be able to easily take some medicines.
5. The colon is superior to the small intestine for the absorption of drug enhancers.
6. The big gut has the ability to absorb medications that include proteins.

Benefits of Colonic Drug Administration

1. By administration of medications via the colon, patients suffering from colonic illness may get therapy at the site of infection while experiencing less systemic adverse effects and a lower dosage.
2. If a protein or peptide is hydrolyzed or even if it doesn't get absorbed well delivery of drugs via the bowel able to get into the bloodstream through the rectal drug delivery system.
3. Chronotherapy, which includes injecting drugs into certain parts of the gut, may be a successful treatment for conditions such as arthritis, angina, and asthma.

Colonic Drug Delivery Drawbacks

1. Indigestion and the small intestine's pH may be different for each person, which can cause medication release at an undesirable region. Therapy may not be successful if the pattern of medication release varies from patient to patient.
2. The site specificity of formulation is reduced since the small intestine and caecum both have the same pH level.
3. The lack of specificity in medication delivery to the colon is the main drawback of this method.
4. Drug targeting to the colon might be adversely impacted by changes in colonic microbiota caused by diet and illnesses. Different types of food in the gastrointestinal system (GIT) may change how drugs work in the body. Because people who are sick have a different pH level in their gastrointestinal system (GIT) than healthy volunteers, products that release medicine based on the pH of the target area are not working as well as they should.
5. If the rate of enzyme degradation is too slow, it might disrupt the breakdown of polymers, which changes the way medications are released.
6. If there is a time dependent colonic drug delivery system, the medication might be released at an undesirable place due to significant changes in stomach retention time.

Problems with CSDDS

1. Formulations that are taken by mouth must stop the release of medications throughout the larger intestine, particularly in the gut, which is the most distal portion of the gastrointestinal system.
2. The method may have difficulty dissolving and releasing its medication contents in the colon due to its low fluid environment and thick luminal components.
3. Additionally, the indigenous microflora of the colon might influence the stability of the medicine released via metabolic breakdown.
4. A decrease in the amount of free drug present because the medicine can link to mucus, gut fluids, or generic feces, which makes the medicine less stable.

Colon anatoms and meteorology: The colon, or lower digestive system, is made up of the colon, rectum, and anal

canal and extends from the ileocecal junction to the anus. The colon is divided into several portions, such as the splenic flexure, ascending colon, sigmoid colon, hepatic flexure, and transverse colon, and the downstream colon. About 1.5 meters is its length. Located at the colon's base, the transverse colon offers the greatest range of motion. On average, its breadth is about 65 centimeters. Regardless, its breadth varies from 9.0 cm in the caecum to 2 cm in the sigmoid colon. Crescentic folds called plicae semilunaris provide the colon 1300 cm^2 of increased surface area, even though it lacks villi like the small intestine. The four components are the serosa, the submucosa, the muscularis externa, and the mucosa. One layer that lines the outside of the large intestine is called the serosa. One layer of squamous mesothelial cells makes up arioler tissue. One of the major protective layers of the large intestine is the muscularis externa. There are two layers to it: one that runs the length of the colon and one that covers it. Directly underneath the mucosa is a layer of elastic tissue called the submucosa. The elements that comprise the mucosa are the epithelium, lamina propria, and muscularis mucosae. A layer of smooth muscle is called the muscularis mucosae that lies between the mucosa and the lamina propria.

Segmenting and propulsive motions are the two main types of colonic action. The sac-like haustra develops during segmenting motions performed by circular muscles. Less often, on average, three or four times a day, does the body undergo the substantial propelling action linked with feces and the action of longitudinal muscles. The proximal colon is characterized by retrograde motions, which enhance retention in the ascending colon and caecum. Segmental movement causes feces to flow slowly towards the rectum in the colon's middle region, whereas propulsive action is predominant in the colon's distal section.

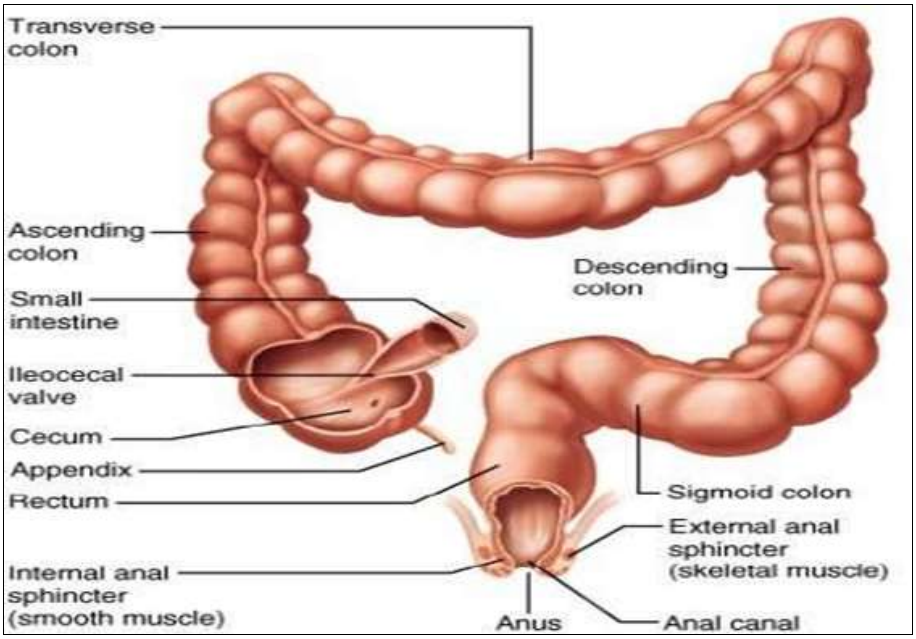

Fig 1: Anatomy of colon

Functions of colon

What the stomach performs for four main things, such as

1. Making an environment that is good for microbial development inside the colon, like Bacteriods, Eubacterium, and Enterobacteriaceae.
2. A place where feces are stored.
3. Getting rid of the stomach's contents at the correct moment.
4. Taking in minerals and bicarbonate and potassium ions are released when water from the lumen is removed, and concentrates the excrement.

Table 1: Small-scale anatomical and physiological characteristics intestine and colon

S. No.	GIT segment	Length (m)	Surface area (m^2)	pH	Microorganism	Transit time
1.	Stomach	0.2	0.1	1.5	$\leq 10^2$	Variable
2.	Small intestine					
	Duodenum	0.3	0.1	6.9	≤ 10	2hr
	Jejunum	3	6.0	6.9	$\leq 10^5$	1.5hr
	Ileum	4	6.0	7.6	$\leq 10^7$	1.5hr
3	Large intestine	1.5	0.3	8	$\leq 10^{11}$	$\leq$48hr

pH of the colon

Known changes have happened in the digestive system pH across and among individuals. The pH of the GI fluid is affected by dietary factors, illness status, and food consumption.6, 7, 8. Various regions of the human gastrointestinal system have average pH values, which may be found in Table 2.

A big part of how chemicals are absorbed from the gut is where the mixture is placed. The small intestine's passage time is more stable than those of the stomach and colon, according to reports10. As dose forms enter the colon, particle size affects colon transit. The transit time through the colonic area is slower for smaller particles compared to bigger ones, But the travel time isn't really affected by the

number and size of bigger groups. Evidence suggests that compared to tablets, pellets go through the ascending colon more rapidly. Therefore, pellets are preferable than pills. The passage Table shows the duration of the solid mixture in various sections of the digestive tract.

Table 2: The GI tract's average Ph

Location	pH
Oral cavity	6.2 - 7.4
Oesophagus	5.0 - 6.0
Stomach	Fasted condition: 1.5 - 2.0 Fed condition: 3.0 - 5.0
Small intestine	Jejunum: 5.0 - 6.5 Ileum: 6.0 - 7.5
Large intestine	Right colon: 6.4 Mild colon and left colon: 6-7.6

The stomach's pH can change from person to person and within a topic.

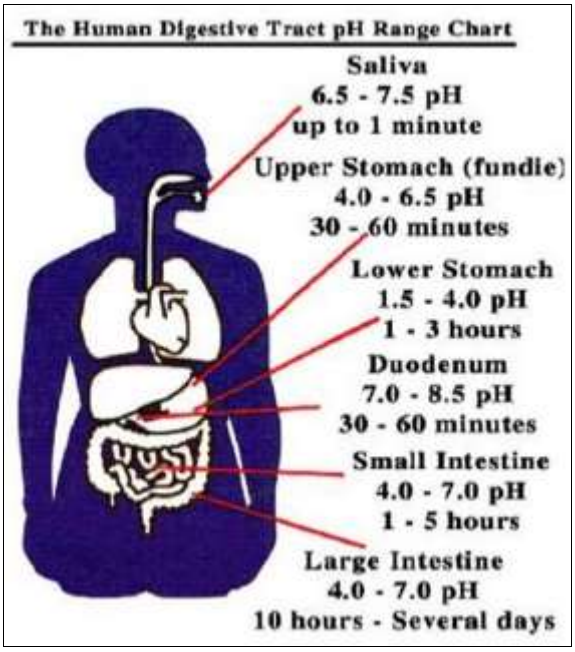

Fig 2: The human digestive tract pH range chart

Gastrointestinal transit

How quickly a dosage form is emptied from the gut can vary a lot based on things like how much the person is eating, whether they are hungry, and the dosage form itself, such as its size and mass. It takes around 53.3 hours for the tube to get from the mouth to the anus. Males have a shorter overall mean colonic transit time (25.0 hours) compared to females. In table 3, we can see how long it takes for modest doses to undergo intestinal transit.

Table 3: The dosage form's transit time in the GIT

Organ	Transit time of dosage in GIT (hrs)
Stomach	<1 (Fasting), > 3 (Fed)
Small intestine	3-4
Large intestine	20-30

Colonic Diseases

1. Inflammatory bowel disease (IBD)

Fig. 3. Inflammatory bowel disease (IBD) includes conditions such as ulcerative colitis (UC) and Crohn's disease (CD), which is a group of unknown intestine illnesses. Colorectal cancer can happen to people IBD, a chronic inflammatory bowel illness condition that comes and goes and is marked by excessive inflammation in the digestive system.

An immunological response that is dysregulated in genetically sensitive individuals towards the host microflora may explain why it is said that one million people in North America have inflammatory bowel disease (IBD). When it comes to their reasons, inflammation profiles, symptoms, and ways of treating, UC and CD are often very different from one another.

Crohn's disease

An inflammatory bowel condition called Crohn's disease often results in fistulas that lasts for years and produces granulomatous inflammation anywhere in the digestive system. In 1932, the first written accounts of Crohn's illness were penned by Crohn, Ginzburg, and Oppenheimer.

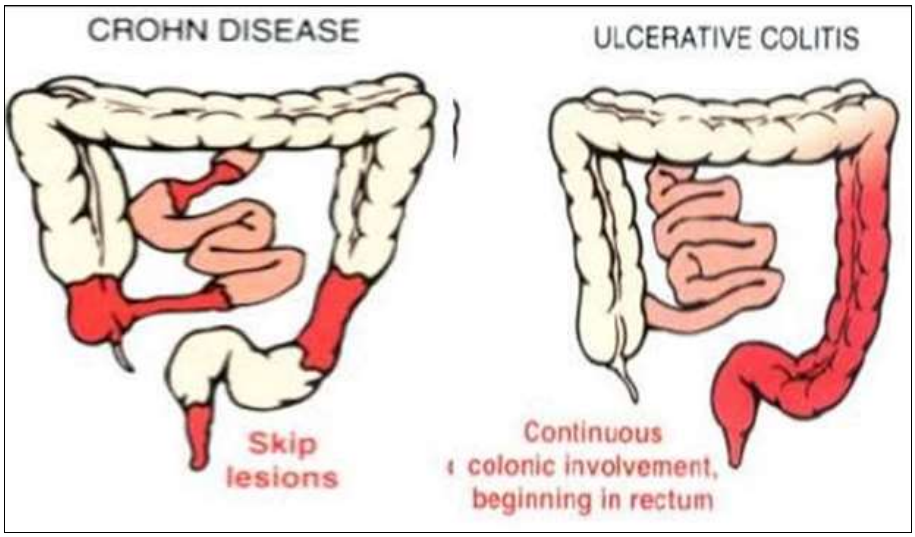

Fig 3: Locations of IBD in colon

Etiology

There is a strong interaction between environmental and genetic variables in IBD, but the exact cause is still unknown. Part of the second group is intestinal lumen factors and smoking. The link between smoking among which is Crohn's disease opposite of what was seen for ulcerative colitis. Smokers have a 4–6 times higher chance of getting Crohn's disease than nonsmokers. There is proof

that luminal factors are important because a basic diet can help people who are sick and people with Crohn's disease can get better even when their stomach is blocked with an ileostomy. Food, ischemia, immune systems, and infectious bacteria can all play a part in the process.

Pathology
Crohn's disease might be manifest as ileocolits more often than any other pattern in the gastrointestinal system. Skip lesions are the result of the disease's discontinuity. It is known that the mouth, esophagus, stomach, and anus may be affected independently, although instances like this are quite unusual.

Medications used to treat CD
Mezalizine, Azatioprine, Budesonide, Infliximab, Sulfasalazine, Budesonide, and Metronidazole.

2. Ulcerative colitis
Instead of Crohn's Disease, while this chronic inflammation disease of the colon can affect any part of the digestive system, it only affects the large intestine. Irritation of the rectum that spreads to the colon is a common symptom of the illness. Inflammation might only affect the colon on the left side or it could spread across the whole organ.

Etiology
It's not clear what caused the sickness. Among the theories being put forward are those about allergies, infections, immune reactions, and problems with the health of epithelium cells. It is also thought about the psychic idea.

Pathology
Although the rectum is involved in around 40% of ulcerative colitis cases, it is usually visible in macroscopic pathology. Though it increases to over 50% in children, only 20% of adults will have a full colon involvement. Under a microscope, the mucosa is where the majority of ulcerative colitis inflammation occurs. Red blood cells leak out of the enlarged and clogged capillaries.

Medication used to treat this illness
Balsalazine sodium, Azathioprine, Olsalazine sodium, Budesonide, Mesalazine

Colonic Cancer
A colon tumor is a growth that starts on the inside of the big intestine. Both benign polyps and malignant malignancies may develop in the large intestine. Because they cannot metastasize and are readily removed during colonoscopies, polyps pose no danger to a person's life. However, it has the potential to become cancer if left untreated. When cancer from the gut spreads to other parts of the body, a full recovery is quite improbable due to metastasis. For men, colon and rectum cancer is third, whereas for women, it ranks fourth. Colorectal cancer has become more common as a result of people's shift to Western diets.

Affective factors on colon drug absorption
The pH level and the passage time are the two physiological most influential aspects on medication release in the gut. These are the other things that need to be thought about.

- Physical characteristics of the medicine (pKa, ionisation degree).
- How long it stays in the colon as measured by the movement of the digestive tract.
- How it breaks down by bacterial enzymes and byproducts.
- How it binds to mucus selectively or not.
- How it works locally in the body.
- The disease state.
- The use of chemical enhancers that help the body absorb drugs.

The pH of the digestive system may be different in people who are the same or different from each other. The pH of the GI fluid is affected by dietary factors, dietary diseases, and the food that is eaten. The normal pH levels in different parts of the adult digestive system are shown in Table.
Living in a certain part of the gut changes how chemicals from the colon are absorbed. The small intestine has a more stable passage time inside the digestive tract. Particle size determines the transit time of dose forms through the colon. Because of their superior transit time in the ascending colon, pellets are preferred over tablets. Table displays the dose form transit times in various GI tract regions.

Characteristics of drug that favors colonic drug delivery
When contrasted with the smaller intestine and stomach, the colon is a friendlier place to live. For medications that aren't well-absorbed, it has a longer retention duration and responds better to absorption enhancers. Medications used to treat colonic diseases are among those that may benefit from colon targeting. Colon medication delivery systems are also being considered for drugs that undergo metabolism in the esophagus and small intestines. It has been shown that the colonic area is an effective route of drug absorption for medicines like ibuprofen, theophylline, as well as peptides and compounds with low molecular weight. It is possible that the transfer rate needed for therapeutic activity cannot be achieved by means of the permeability of colonic epithelium. Applying a few popular colonic medication absorption enhancers could solve this issue.

Conclusion
The created formulations provide the benefit of both decreased systemic adverse effects and longer, localized medication release. Finally, these findings indicate that research show according to which the that were produced have a lot of promise for the easy treatment of colon disorders and might help find a solution to the problems with current drug delivery methods. This leads to a thicker cohesive layer, which in turn prevents the mucosal retention from being broken down by colon enzymes.

References
1. Sesink ALA, Termont DSML, Kleibeuker JH, Meer RVD. Red meat and colon cancer: Dietary haem-induced colonic cytotoxicity and epithelial hyperproliferation are inhibited by calcium. Carcinogenesis. 2021;22:1653-1659.
2. Yang L, Chu JS, Fix JA. Colon-specific drug delivery: new approaches and *in-vitro* / *in-vivo* evaluation. Int. J Pharm. 2022;235:1-15.
3. Mundargi RC, Patil SA, Agnihotri SA, Aminabhavi TM. Development of polysaccharide-based colon

targeted drug delivery systems for the treatment of amoebiasis. Drug Deve. Ind. Pharm. 2017;33:255-264.
4. Asghar LF, Chandran S. Multiparticulate formulation approach to colon specific drug delivery: current perspectives. J Pharm. Pharm. Sci. 2016;9:327-338.
5. Lorenzo-Lamosa ML, Remunan-Lopez C, Vila-Jato JL, Alonso MJ. Design of microencapsulated chitosan microspheres for colonic drug delivery. J Contro Rel. 2018;52:109-118.
6. Krishnaiah YS, Bhaskar Reddy PR, Satyanarayana V, Karthikeyan RS. Studies on the development of oral colon targeted drug delivery systems for metronidazole in the treatment of amoebiasis. Int. J Pharm. 2002 Apr 2;236(1-2):43-55.
7. Becket HA, Stenlake BJ. Practical Pharmaceutical Chemistry. 4th ed. 17. 85.
8. Indian Pharmacopoeia. Govt. of India, Ministry of Health & Family Welfare, the Controller of Publications, New Delhi. 2016;2:554-555.
9. Sethi PD. Quantitative analysis of drugs in pharmaceutical formulations. 3rd ed. New Delhi: CBS Publishers and Distributors; 548.
10. Kim KB, Hwang JS, Park BJ, Park JH. Preparation and characterization of drug-loaded polymethacrylate microspheres by an emulsion solvent evaporation method. J Microencapsulation. 2022;19(6):811-822.
11. Kshirsagar SJ. Taste masking of Tinidazole and optimization of microencapsulation. Int. J Pharm. 2016;245:1-6.
12. Prizont R, Konigsberg N. Identification of bacterial glycosidases in rat caecal contents. Dig Dis Sci. 2021;26:773-777.
13. Mason VC. Some observations on the distribution and origin of nitrogen in sheep feces. J Agric. Sci. 2019;73:99-111.
14. Salyers AA, Palmer JK, Wilkins TD. Degradation of polysaccharides by intestinal bacterial enzymes. Am J Clin. Nutr. 2018;31:S128-S130.