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Is Rheology a Concern in GI Physiology?

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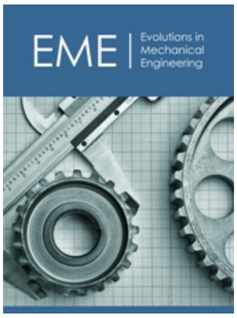

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Introduction

The small intestine is part of the gastrointestinal tract that interconnects the stomach at one end to the large intestine at the other end. As the bolus containing meal traverses the intestinal segments it undergoes rheological transformation as a consequence of digestive processes such as alkaline buffering, micelle formation, absorption of nutrients and water [1]. As the chyme (mixture of meal and gastric juice) enters the stomach through the pylorus (a valve interconnecting the stomach and the small intestine), the duodenum (first segment of the small intestine) responds to the acidic content of the chyme by buffering them with alkaline secretion of pancreas. Buffering action results in lowering the pH value of the contents, so the meal can be processed for further breakdown. Mucus secretion (a thick protective fluid) by the duodenal mucosa helps protect the mucosal layer from ulceration (acidic damage). Bile secretion of the gall bladder helps in dissolving the fat contents through micelle formation, a mechanism necessary to increase the surface area for lipases (an enzyme) to digest the fat. While the small intestine facilitates the mechanical and chemical digestion of food to its simpler form so they can be absorbed by the intestine, it also helps propel the digesta for excretion.

The small intestine is a dynamic and muscular tissue that facilitates the digestion through mixing, grinding and transferring the contents to the lower segments by eliciting contractions (popularly known as peristalsis). Inability to elicit contraction (aperistalsis) or dysfunction leads to indigestion and digestive diseases. There are two kinds of muscular contractions that drives the process-circular (CC) and longitudinal contractions (LLS or local Longitudinal Shortening). Contraction of the circular muscle layer develops radial constriction and contraction of the longitudinal muscle layer leads to shortening. Both the muscles coordinate with each other to establish flows in the lumen that are needed to process a meal of certain rheology. Onset of smooth muscle contraction is initiated by ingestion of meal. With ingestion, the digestive system switches from inter-digestive phase (characterized by irregular peristalsis referred to as Migratory Motor Complex or MMC) to digestive phase (characterized by regular peristalsis). Switching of the digestive phases of the stomach and intestine is initiated via sensing of meal in the gut. The small intestine harbors a plurality of sensors to assess the properties of food to help elicit the contractions to perform the digestion. Gut sensing allows the intestinal segments to exercise the flexibility to alter their motility patterns (i.e. contractions) depending on the nature of meal via feedback mechanisms. Let us consider an example of the distension induced responses of the stomach. During ingestion, the digestive system enters into a phase of gastric accommodation, where the food is being received as a receptacle and stored in the proximal part of the stomach; where both the sphincters (valves of the stomach at its either end) are actively closed. It is intuitive to reason that the gastric filling will result in a pressurization of the stomach since there is alternative route for escape, resulting in developing of a high pressure zone in the manometry. Fortunately, this does not happen in physiology, since the tensile or stretch sensors in the gastric wall deals with the problem by sensing the distention of the lumen during the gastric filling of meal [2,3]. Gastric accommodation is a reflex response of the stomach to ensure that the gastric pressure never exceeds beyond a threshold pressure that is inconvenient to the subject [4]. Similarly, on detection of fats, the intestine shows a preference to elicit the segmental contractions over propulsive contractions in a way to drive emulsification and increase the rate of hydrolysis of the fat. Fat sensing is chemical in nature and chemo-specific neurons relay the information to ENS/CNS to trigger events for dealing with digestion of fats; involves changing the motility patterns.

Clinical studies report indicate presence of numerous reflex mechanisms in the gut such as vago-vagal reflex, ileal brake. Indeed, reflex form an integral part of the digestive system in homeostasis. Intestinal motility patterns are, in turn, governed by the gut-brain axis and involve participation of sensory and motor neurons (both Central (CNS) and Enteric Nervous System (ENS)), Interstitial Cells of Cajal (ICC), endocrine or paracrine factors of relevance to secretory glands/mucosal cells, and smooth muscle fibers. These components interact with each other and regulate the digestion via feedback. Essentially such integrity ensures that the digestion occurs at a near physiology that is flow rate (rate of gastric emptying) limited by the amount of calories the intestine can process (~2-3kcal/min) [5]. The intestine constantly relays a huge amount of sensory information to the CNS as part of the reflex mechanism to regulate the digestive process. According to Professor Wood [6], "Reflexes are declared, historically, to be the underpinnings of Enteric Nervous System (ENS) control of gastrointestinal motility." Of these processes, the mechanics play a major role in digestion by providing for mixing, grinding and transport function through peristalsis. The flow in the intestine is viscous dominated; suggesting that the forces developed in the intestine is majorly used to overcome the viscous resistance. The regime of intestinal flow can be estimated as follows-for a fluid (such as mango juice) of viscosity in the range of 1000 times that of the water of 1Pa·s, velocity of 1cm/s, tube diameter of 2cm, density of 1kg/cm^3, and the ration of radial to axial length scale as 0.1, then the Reynolds number can be calculated as equal to 0.02. Presuming that the viscosity of the fluid can be higher than 1Pa·s, the Reynolds number can decrease to a much lower value. Flow regime may vary significant from one segment to the other segment from as low as 1cP (equivalent to water) to highly viscous fluid as in large intestine. Depending on the nature of intestinal secretion, the fluid properties may differ and assume characteristics of Newtonian or non-Newtonian (pseudo-plastic or dilatant). Under normal digestion, the solid foods ingested are already disintegrated to less than 1-3mm in size by the gastric peristalsis; hence the intestinal contents are no larger than the critical dimension. Literature data suggests that the digestive system demarcates the processing of meal based on particle size by having the stomach to grind larger particles facilitated by acidolysis and intestine to mix with the digestive juices and disintegrate to the molecular level for absorption. Hence the motility patterns of the gut segments are tuned to establish the physiological function [1].

Flows resulting from circular contraction or peristalsis have been extensively studied preferably due to adoption by various biological systems such as blood vessels, ureter, and alimentary canal. Pal et al. [7] have demonstrated that the gastric peristalsis (model studied for CC alone) develop higher shearing in the lumen to physically break and shear the solid food [7]. Experimental studies of bead disintegration, visualized using Magnetic Resonance Imaging (MRI), supports the grinding function of the distal stomach [8]. Studies of relevance to the Local Longitudinal Shortening (LLS) of the longitudinal muscles are rare. Clinical and in silico studies of LLS show that they are essential in forcefully pushing the bolus from intestine to the stomach through the lower esophageal sphincter (a valve that remains closed, normally) [9,10]. Suggesting that, the CC coordinates with the LLS to develop higher forces in the lumen to serve the purpose of mixing, grinding and transport of the contents. The author has investigated the flows resulting from intestinal peristalsis with LLS [11]. The study provides details as to how the intestine may take advantage of contractility to perform intestinal digestion in an optimal manner by varying contractility and rheology of the contents. Parametric variations studied were LLS spacing (0-0.5 units of length scale), wavelength (0.5-1.5 units of length scale), and degree of occlusion (0%-80%). For efficient pumping, the intestine, as we speculate, may utilize LLS as a strategy to reduce the power requirement of peristalsis (up to 15%) at higher occlusion (70%) while at lower occlusion the peristalsis with LLS is found to inefficient. Coordination of the LLS and CC is necessary to achieve the goal of power reduction, since the shortening of the muscles in the longitudinal direction concentrates more number of circular fibers in the region local to LLS [10]. Increasing wavelength of the wave has an effect of lowering the shearing forces and increase in flow rate and luminal velocity; a wavelength comparable to intestinal diameters is more preferred. Shearing forces can be elevated by increasing the occlusion of the wave. Higher shearing necessary means that the particles are under succumbed to higher deformation which is needed for mixing the food with duodeno-biliary-pancreatic secretions. Occlusion of the wave, however, may serve for dual purpose:

a. To participate in mixing and grinding, and

b. To propel the food. At higher occlusion, the contents are majorly pushed through the intestinal segment similar to that of a plug flow. Such flows are not uncommon and can be found during interdigestive phase where the muscles undergo rigorous contractions (as in MMC) to expel out any undigested food leftover. Since the intestinal contractility is highly variable, the clinical studies performed so far have limited our understanding on the mechanics of digestion.

The intestinal preference to motility is highly meal dependent [12]. For digesting a given meal, the intestine may chose a specific type of contraction among the contractility space to perform the digestion effectively. Based on the duodenal infusion studies of hydrochloric acid and fat, we speculate that the intestine prefers to elicit segmental contractions to help homogenize the chyme (meal containing acid) with intestinal juices. Mixing can be assisted by eliciting back and forth moving contractions (antegrade and retrograde contractions) that run for a short span of the intestine. Study shows that the mixing is highly sensitive to frequency and increase with the frequency [1]. Probably, stationary contractions at higher frequency facilitates mixing process in the duodenum to serve the purpose of emulsification and homogenization, while in the distal intestine they serve to increase the accessibility of the nutrients to the intestinal mucosa for absorption through flushing.

How Rheology Affects GI Physiology?

Rheology has been known to affect the GI physiology which includes-appetite control or satiety, glycemic response, rate of absorption, and transit. It is well documented in literature that solid and liquid foods are differentially processed by the stomach; while solid requires further breakdown to small particles before they can be emptied into intestine, liquid on the other hand does not need such process. While caloric value of the meal plays a key role in determining the rate of gastric emptying, it comes under the regime of chemical control digestion. Rheology refers to the fluid properties that identifies as to how the fluid flows upon application of pressure force and the nature of shearing that take place in the fluid. A fluid is characterized by its viscosity, shear stress and strain rate [13]. The challenge of performing the function of mixing and transport of the luminal contents through peristalsis can be appreciated by the following example. In mechanical design, choice of a pump for pumping fluid is made based on the rheological properties. For fluid that exhibit a constant viscosity over operational range shear rate or agitation, power ratings of the pump may be chosen on the basis of this constant viscosity. However, for fluid that is shows shear thinning behavior is easier to pump since the instantaneously viscosity reduces drastically at higher straining. While on the other hand, the fluid with shear thickening behavior show increasing viscosity for increased straining, which makes it much difficult to pump. Intestinal peristalsis also has to deal with the problem of viscous changing behavior of the fluid if they need to develop sufficient forces for developing flows for the purpose of mixing, grinding and transport.

Viscosity of the meal is an important factor for the rate of gastric emptying. For example, addition of locust bean gum, pectin or guar gum to the meal have reduced the rate of gastric emptying, however addition of water to this test meal has no influence on gastric emptying in healthy subjects [14]. Addition of dietary fibre to the liquid meal is found to delay the rate of gastric emptying and removal of the fibre has an effect of increasing the emptying [15]. Studies have demonstrated amount of glucose absorbed is slowed by meal rich in dietary gums and the effect is found to increase with increasing proportion of the dietary gum. It has been reasoned that the soluble fibres form viscous gel by absorbing water and hence influence the rate of gastric emptying and glucose absorption [16]. It is worth considering that gastrointestinal segments also modify the rheology of the meal through mixing with secretions [17]. Since the nature of meal (rheology) can modulate the digestive process, it therefore necessitates for the design of foods that can provide functionality as desired such as glycemic response and obesity control [18,19]. Alginate-antacid food formulations for managing gastroesophageal reflux disease have shown to be effective in preventing backflow of the gastric contents through forming a viscous barrier at the proximal stomach [20,21]. Design of functional foods play a key role in managing patients suffering from digestive disorders. Studies on mathematical modelling of a nutrient based feedback mechanism suggest two key points:

1. The rate of gastric emptying is linked to intestinal bioaccessability and

2. Rate of secretion affects the viscosity of the digesta [22]. Considering that the mean total surface area of small intestinal mucosa approximates to ~32m2 [23], the small intestinal peristalsis may play a significant role in regulating the absorption process through rheological behavior and contractility. It, therefore, gives us a huge opportunity to explore mechanisms leading to digestion and developing models to predict the rate of absorption, bioaccessability, and availability of nutrient in patients.

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