Role of Food Material Properties and Disintegration Kinetics in Gastric Digestion – A quest for foods for healthy benefits

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1 Introduction

The quest to manufacture foods for healthy benefits is an underpinning goal of the modern food industry. Food processing has evolved to carry out steps for the controlled destruction of natural food structures. These steps facilitate separation of valuable components from the original matrix in which they are embedded. The separated ingredients are then converted into recognizable processed foods with desirable textural and sensorial properties by application of one or more processing steps (Aguilera and Stanley, 1999). Recent evidence indicates that how the food structure breaks down during gastric digestion significantly affects the rate of uptake of nutrients in the gastrointestinal (GI) tract (Armand et al., 1999; Jarvi et al., 1995). Therefore the knowledge and any capability to predict how a food may disintegrate in the stomach are important for developing new food products with novel health benefits. Understanding the post-ingestion food behavior and the knowledge of the availability of nutrients and their uptake kinetics can guide food processors to select appropriate ingredients and processing conditions at the time of manufacture.

The focus of the current research is on understanding this admittedly complex subject, namely, the breakdown of a food in the human stomach. Nutrient absorption in the intestines is a topic for future study. From an engineering perspective, the human stomach is a receptacle, a grinder, a mixer and a pump that controls the digestion process. One of its major functions is to reduce the size of solid particulates and fat globules. The digestion process has been well studied in terms of secretion of gastric fluids, enzymatic breakdown of fats, proteins and carbohydrates, and molecular and ionic transport across the intestinal epithelium. However, there remains a notable lack of understanding about the food disintegration kinetics and the extraction of small molecules from complex food structures in the gastric environment. Furthermore, how the changes in food texture and microstructure (that define the material properties) resulting from various food processing affect gastric disintegration of foods is lacking.

Fortunately, considerable research done in the nutrition, medical and pharmaceutical field during the last 30 years provides useful information to initiate this research with a focus on foods. In the following subsections, some of the key studies done in these areas are reviewed with relevance to the current research.

1.1 Food disintegration in the human stomach

1.1.1 Gastric digestion of food and stomach motility

Digestion begins with chewing food in the mouth. Mastication reduces the particle size, hydrates and lubricates the food by mixing it with saliva. The size of particles resulting from mastication depends on the food texture. After chewing, solid food is transformed into a bolus made up of particles with a median particle size up to 3 mm (Peyron and others 2004; Jalabert-Malbos and others 2007). The bolus is transported through the esophagus to the stomach by the mechanism of peristalsis. Gastric juice is secreted from glands lining the stomach contains gastric acid, bile salts and digestive enzymes. The gastric juices penetrate and dilute the food

bolus. The proximal part made of fundus and body **(Figure 1**) acts as a reservoir for undigested material, responsible for the emptying of liquids, while the distal stomach (antrum) is the grinder, mixer, siever of solid food, and acts as a pump for gastric emptying of solids by propelling actions (Urbain and others 1989; Arora and others 2005).

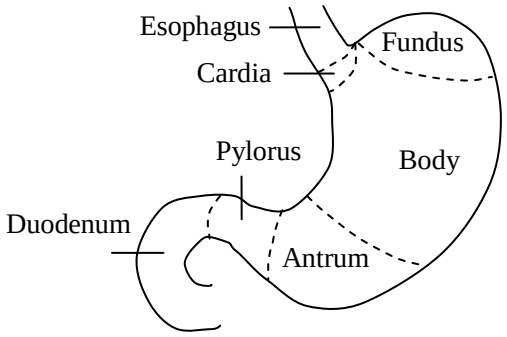

Figure 1. Diagram of the stomach showing different regions

The pattern of stomach motility is distinct in the fasting and fed states. There is a multi phase movement in fasting state and continuous movement in fed state. Upon ingestion of a mixed meal, peristaltic waves originate from the stomach wall and spread towards the antrum, mixing and forcing the antral contents towards the pylorus. As the peristaltic wave reaches the pylorus, the contraction width increases and indentations deepen, often virtually occluding the antral lumen, a process referred to as "terminal antral contraction" (Bilecen and others 2000; Schulze 2006). Meanwhile, the pylorus contracts and the sphincter narrows, so that the pyloric opening is small on the arrival of the peristaltic wave. The chyme is thus squirted back into the stomach, an action called retropulsion. Repeated propulsion, grinding and retropulsion reduce the size of food particles into a softer consistency in a suspension form. Antropyloric contractions occur and the pylorus partially open causing a "sieving effect", in which liquids and small particles (<1 - 2 mm) flow continuously from the stomach into the duodenum, while the indigestible particles greater in size than the pyloric opening are retropelled and retained in the stomach. Thus the activity in the stomach is more than simply mixing its contents. When the meal has finished emptying from the stomach, the fasting motility pattern is resumed, during which indigestible large objects are emptied (Schwizer and others 2006; Dressman 1986).

The stomach contraction, particularly terminal antral contraction, imposes a considerable mechanical destructive force on food particulates and thus is crucial on the disintegration of solids. Researchers have measured contraction forces present in the stomach ranging from 0.2 N to 2 N (Vassallo and others 1992; Camillieri and Prather 1994, Kamba and others 2000, 2001).

1.1.2 Composition and rheology of gastric juice

Gastric juice contains 0.8-1 mg/mL pepsin and about 1.5 g/mL mucin (Vertzoni and others 2005; Dean and Ma 2007). In the fasted state, intragastric pH in healthy subjects is in the 1.3 –2.5 range. Eating can increase pH to a 4.5–5.8 range (Malagelada and others 1976). Typical gastric juice in the stomach is a viscous fluid with viscosity roughly in the range 10-2000 cP and density close to the density of water (Abrahamsson and others 2005; Marciani and others 2000). The fluid is non-Newtonian with pseudoplastic or shear-thinning behavior (Dikeman and Fahey 2006; Takahashi and Sakata 2002). Although ingestion of high viscosity meal will increase the apparent viscosity of the contents of the stomach, the effect is minimized as the stomach responds to high viscosity meal ingestion by rapid intragastric dilution causing a reduction of meal viscosity. Marciani and others (2000) reported that the zero-shear viscosity (obtained from the viscosity/shear rate profiles covering 30 shear rates 0.1 S^{-1} to 1000 s^{-1}) of a meal containing 1.5 g locust bean gum (LBG) /100 g fell from 11 to 2 Pa·s, and decreased to 0.3 Pa·s after 30 min.

1.1.3 Hydrodynamics of gastric flow and computational modeling

Fluid motion within the stomach is generated primarily by the gastric wall motion associated with antral contractile activity, pyloric opening and fundic contractions. The characteristic flow velocity is established by the propagation speed of the antral contraction waves (2-3 mm/s) (Kwiatek and others 2006; Bilecen and others 2000; Pal and others 2004). Abrahamsson and others (2005) suggested that the fluid flow is laminar with a Reynolds numbers in the order of 0.01-30. When food bolus enters the stomach, the breakdown of the bolus is by a process of elution (Marciani and others 2001).

Computational modeling has been used to construct flow paths for fluids and particles in the fluid motion, determine fluid forces in the fed stomach, and evaluate the stresses on drug tablets (Pal and others 2003, 2004, 2007; Schulze 2006; Abrahamsson and others 2005). Pal and others (2003, 2004) developed a two-dimensional computer model of the human stomach with the "lattice-Boltzmann" method. The model demonstrated that antrum contraction waves are central to gastric mixing. The strongest fluid motion is around the lumen occlusion, where the retropulsive jet is generated by contractions in the antrum, with jet velocity up to 7.5 mm/s.

1.1.4 In vitro and in vivo study of gastric digestion

In vivo approaches for investigating food disintegration in the GI tract are conducted by a feeding study, and acquiring the digesta samples using naso-gastric and naso-jejunal tube. The fluid digesta samples are aspirated from the stomach and upper small intestine or the terminal ileum (Marciani and others 2000). These samples may be analyzed for size of food particulates and rheological properties such as density and viscosity. Various instruments and techniques have been developed in the last two decades to study digestive process in the upper GI tract. Techniques such as intubation techniques, scintigraphy, ultrasonography, and magnetic resonance imaging (MRI) are commonly applied for evaluating gastric motility, accommodation, emptying and intragastric processing of food.

A limited number of *in vitro* GI tract models are currently available for nutrition, toxicology, pharmacology and safety assessments. TNO intestinal model (TIM), developed at TNO Nutrition and Food Research (Zeist, The Netherlands), is a commercialized dynamic GI tract model used in pharmacological and food testing for human and animal trials. It is designed to mimic the human physiological conditions in the stomach and small intestine, including simulation of pH changes, temperature, peristaltic movements, secretion of digestion enzymes, bile and pancreatic juices, and absorption of digested products. TIM has been used to evaluate bioaccessibility of nutrients (Verwei and others 2003), viability of the probiotic intake (Krul and others 2001), and assess drug dissolution and release under various physiological GI conditions and study drug-food interactions (Souliman and others 2006, 2007).

1.1.5 Mechanism of gastric emptying of solid foods

Numerous studies on gastric emptying have been conducted in the area of medical and nutritional research, focusing on food emptying time by using mostly scintigraphy and stable isotope breath test methods (Lee and others 2001).The rate of food disintegration in stomach is a key factor influencing emptying rate and subsequently affecting absorption of nutrients in the intestine. Faster disintegration and emptying of drug tablets is responsible for the faster absorption of drug ingredients in the intestine (Kelly and others 2003).

Gastric emptying results from the net effects of propulsive forces within the stomach and the resistance to flow offered by the narrowed gastroduodenal junction. The emptying rate is determined by the balance between driving and resistive forces (Vassallo and others 1992;

Schulze 2006). Liquid meals empty from the stomach according to first order kinetics, i.e. the speed is directly proportional to the volume present in the stomach (**Figure 2**).

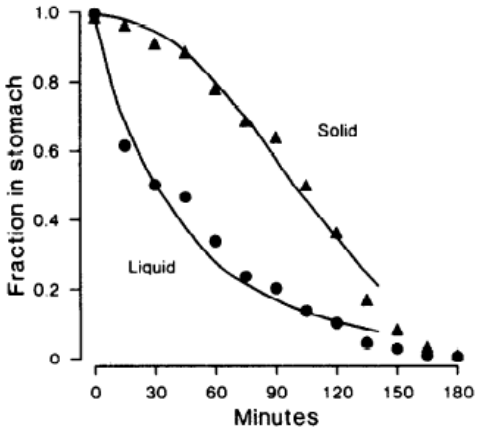

Figure 2. Gastric emptying data for a solid and liquid meal in a healthy volunteer. Data fitted with curves using power exponential model (Camilleri and others 1985)

The gastric emptying rate of solids, as indicated by the fraction of meal retention in the stomach vs. time, shows a biphasic pattern: a lag phase during which little emptying occurs, followed by a linear emptying phase during which solid particles empty from the stomach by mainly zero-order kinetics, i.e. independent of gastric volume (**Figure 2**) (Siegel and others 1988). The stomach empties solids completely over approximately 3 – 4 hours. Mathematical models have been proposed for evaluating gastric emptying rate, as indicated by fraction of food retention vs. time. For this purpose, Siegel's modified power exponential curve (Siegel and others 1988) is:

$$y(t) = 1 - (1 - e^{-kt})^{\beta} \quad (1)$$

where y(t) is the fractional meal retention at time t in minutes, *k* is the gastric emptying rate per minute, and β is the extrapolated y-intercept from the terminal portion of the curve.

1.1.6 Food (meal) properties affect emptying

Gastric emptying is so controlled that about 2 – 4 kcal/min (8.4–16.8 kJ/min) caloric content is delivered to the duodenum through a negative feedback mechanism mediated by the duodenal receptors. Meals with similar energy content are emptied from the stomach at similar rates (Faas and others 2002; Gentilcore and others 2006; Hellström and others 2006). In this context, meal calories, compositions and size are important for gastric emptying. Meals of larger weight and kcal content are associated with longer emptying time for both solids and liquids (Horowitz and others 1986; Hadi and others 2002). Among the major components of foods, fat is emptied more slowly than carbohydrates and proteins due to its high caloric density. Increasing the viscosity of liquid meals delays gastric emptying and increases satiety (Benini and others 1995). The physical properties such as size, density, texture and microstructure of the food are important in determining how easily it can be fragmented in the stomach.

Food processing (during manufacturing or cooking) modifies physical and chemical properties of food, and thus influences the release and uptake of nutrients from the food matrix. Comminution reduces food size that significantly improves gastric emptying rates and nutrient absoption (Pera and others 2002). A digestion study, using an *in vitro* system, showed that 3% of the carotenoid content was released from raw carrots, while 21% was released from the homogenized (pulped) carrots (Hedrén and others 2002). Heat treatment significantly improves bioavailability of carotenoid and lycopene in vegetables (Yeum and Russell 2002).

1.2 Limitations of the existing studies

Studies in medicine, pharmacy and nutrition have demonstrated that disintegration of food in the stomach is a complex process involving numerous variables, including stomach contraction forces, hydrodynamic flow, physical properties of foods such as texture and

structure, particle size, meal volume, calories, composition, and viscosity. These and related factors influence the time taken for food to be disintegrated and emptied from the stomach, and impact the efficiency of systemic delivery of the nutrients for absorption in the intestines.

Past studies on food digestion in stomach involved using scintigraphy or MRI methods to investigate the intragastric movement and distribution of bulk foods and its delivery from the stomach to intestine. However, information is scarce on the influence of hydrodynamic and mechanical forces present in stomach on food disintegration. Limited number of studies have been done on the changes of rheological properties of gastric juice and the hydrodynamics of the fluid with ingested meal and its implications on food digestion. *In vitro* digestion models need to be developed for detailed investigations of food disintegration kinetic as related to the hydrodynamic and mechanical contraction forces that are present *in vivo*. Most of the current GI models, including the TIM model, can not accurately simulate the actual fluid mechanics and the mechanical forces encountered *in vivo* in the human GI tract.

Studies are needed to explore how the food material properties such as texture and microstructure affect the gastric disintegration kinetic. Although some research has been conducted on the effect of food processing on food digestion and glucose response, in-depth investigation on the relationships between food processing and the resultant physical and chemical properties of foods, and subsequently its disintegration performance in the GI tract are lacking. In order to develop next generation of foods for health that provide targeted delivery of nutrients in the GI tract, a combined understanding of materials science, physical chemistry and biophysics is needed, along with the processing conditions undergone by a food that affects its structure (Norton and others 2007).

Computational fluid dynamics is an important technique for predicting flow field and stresses developed in a fluid contained in a vessel with moving walls, similar to a stomach. Pal et al. (2004) developed a two-dimensional numerical model to study the flow and stresses inside the stomach. While this was a pioneering study, description of a stomach with an axisymmetric 2D shape is over simplification. Future enhancements need to consider stomach to be a 3D shape with appropriate modeling of fluid flow. Furthermore, mechanical forces resulting from the grinding or crushing of GI contents and/or friction between food/drug products and the GI wall should be incorporated into computational models to accurately simulate the digestion process.

2 Preliminary Studies

2.1 Development of *in vitro* stomach system

The *in vitro* stomach system consists of a custom-built turntable and a jacketed glass chamber (**Figure 3**). Simulated gastric juice (pepsin 1g/L, mucin 1.5 g/L, NaCl 8.775 g/L, pH = 1.8) is loaded inside the chamber. The jacket layer is connected to a hot water bath to keep the gastric juice at 37 ˚C. Food sample is attached to the tip of a rigid stainless-steel holding wire. When the turntable is rotated, the hydrodynamic forces on the stationary sample are transmitted to a load cell. The force is recorded with a computer. This *in vitro* stomach system showed excellent repeatability. When three replicates of carrots were tested up to 120 min at room temperature, the coefficient of variation was less than 10%. Plastic beads (size: 3 mm, specific gravity: 1.03) were combined with gastric juice to simulate food particulates and create friction/impact force on food samples. The mechanical force applied to the tested foods can be adjusted by changing the concentration of beads and rotational speed of the turntable. The *in vitro* system is capable of simulating the *in vivo* stomach in terms of providing a wide range of

forces comparable to those reported *in vivo*. The system is also capable of creating periodic forces to mimic the repeated contractions evident in a stomach (Kong and Singh 2007).

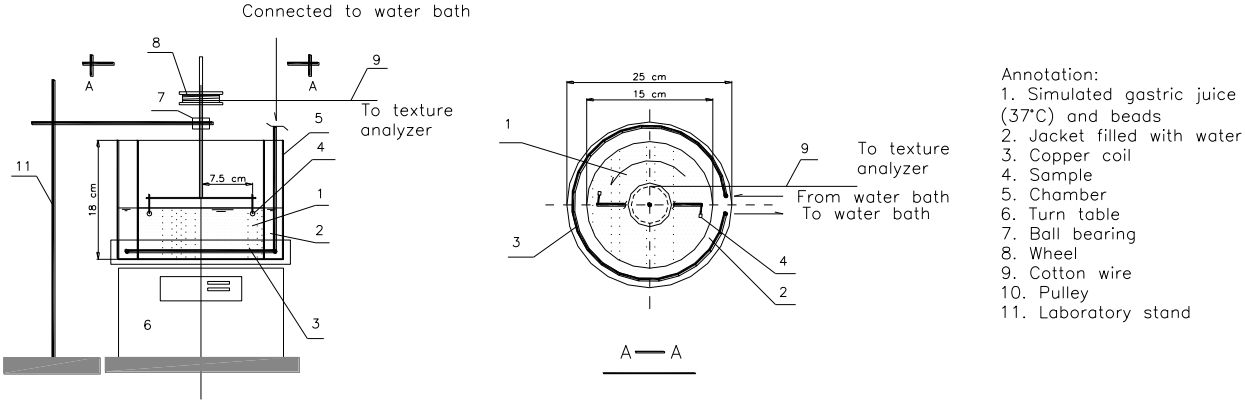

Figure 3. *In vitro* stomach system

2.2 Disintegration of selected foods in the *in vitro* system

We used the *in vitro* system to determine the disintegration of selected raw and processed foods. First, we examined the disintegration of foods during soaking in the simulated juice under static conditions. In general, no significant mass loss was obtained ($P > 0.05$) indicating that mechanical force is indispensable for food digestion.

We compared the disintegration of raw and cooked carrots (boiled for 2 min and 6 min, respectively) in the *in vitro* system subjected to different mechanical forces. Carrots were shaped into cylinders (6 mm diameter and length). **Figure 4** shows typical examples of the mass retention curve (W_t/W_0 vs. time) for raw and cooked (6 min) carrots. W_t and W_0 represent the initial sample weight and that after time t, respectively. Raw carrots exhibited the lowest disintegration rate. The mass retention ratio (W_t/W_0) showed a sigmoidal decrease with time, while carrots cooked for 6 min had the fastest disintegration with an exponential decay. The disintegration rate obtained for carrots cooked for 2 min is between the raw and 6-min-cooked carrots.

A good match was observed between the kinetics of food disintegration (**Figure 4**) and *in vivo* stomach emptying curves (**Figure 2**), i.e., the disintegration profile in the raw carrots is similar to the solid emptying curve (sigmoidal), while that for the carrots cooked for 6 min is close to the liquid emptying curve (exponential). The similarity between the disintegration and emptying curves indicate that the stomach emptying may be strongly affected by the food disintegration kinetics. Siegel's modified power exponential model (equation 1) was used to fit the disintegration data. **Figure 4** shows a good fit of the model with the *in vitro* data.

We also tested the disintegration of peanuts and almonds (raw, fried and roasted) in the *in vitro* system. For both almonds and peanuts, the order of the rate of disintegration was raw<fried<roasted (**Figure 5**).

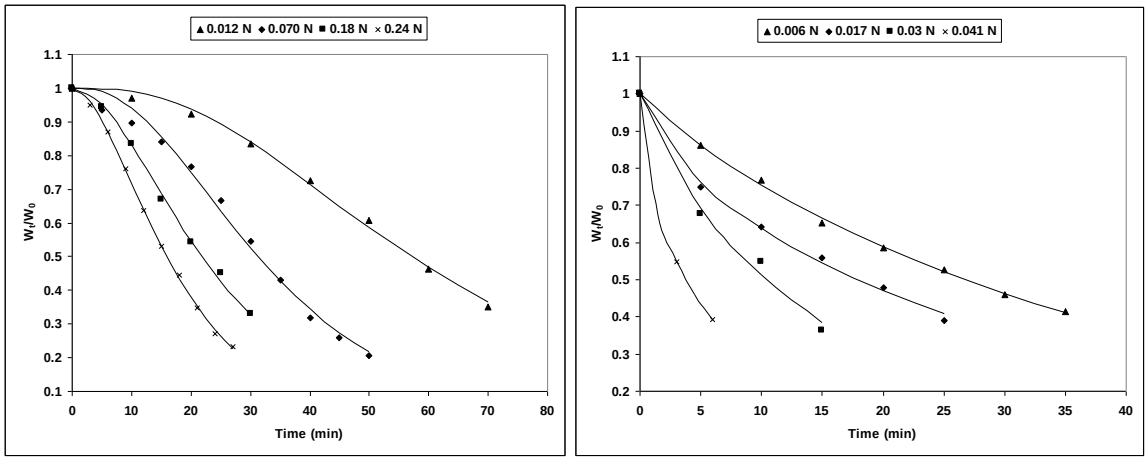

Figure 4. Mass retention data of raw carrots (left) and carrots cooked for 6 min (right) under different forces. Data fitted with modified power exponential model.

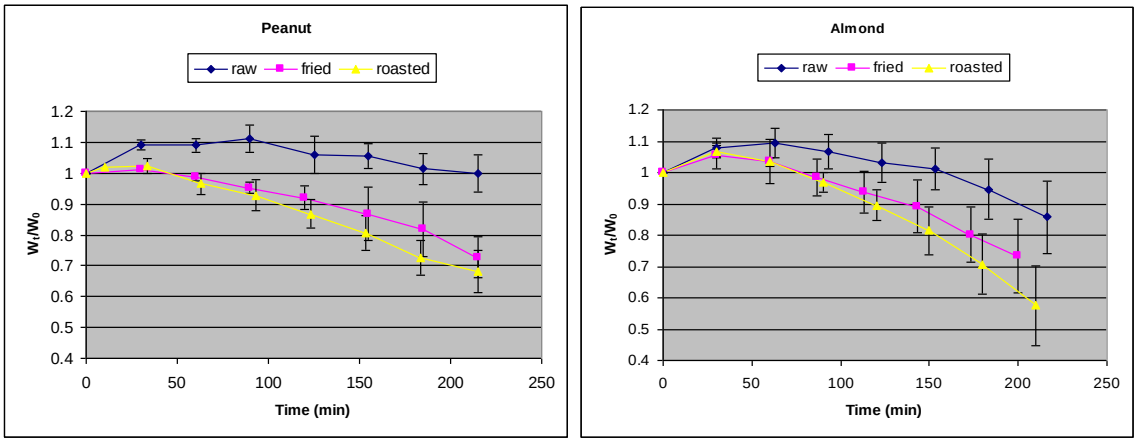

Figure 5. Mass retention data of peanuts (left) and almonds (right) in raw, fried and roasted state.

Using equation 1, we calculated the half-time ($t_{1/2}$) of weight loss of a food sample. Higher mechanical force, smaller size, and longer cooking time were all related with shorter $t_{1/2}$. Food structure and texture significantly affect disintegration. When subjected to 0.2 N mechanical force, the $t_{1/2}$ is ~ 20 min for raw carrots and >4 hr for peanut and almond.

2.3 Influence of food texture and microstructure on disintegration kinetics

From preliminary trials we found that the shape of the mass retention curve is either a sigmoidal decay (with an initial delay) or an exponential decay (**Figure 4**). These profiles are decided largely by the hardness of the foods during digestion and the extent of physical forces acting on the food particulates. Our study suggests that the kinetics of disintegration of food particulates is the result of a competition between surface erosion and tenderization. Surface erosion is defined as the wearing off of food surface by an impinging gastric fluid containing food solids during normal impact, friction, and shear forces acting on the surface of a food. The erosion rate is dependent mainly upon the strength of food matrix and the mechanical forces. The tenderization (texture softening) front starts from the sample surface, and gradually advances to the core of the food sample as a result of the liquid uptake. **Figure 6** shows a schematic illustrating the effects of surface erosion and tenderization on disintegration of a food particulate.

The textural change in the digested foods is a result of the change in the microstructure. We examined the microstructure of partially digested raw carrot in the *in vitro* system by viewing images of samples. Methelyne blue was added to gastric juice to demonstrate the tenderization front by forming a blue color in the water penetrated area where digestion occurred. **Figure 7A** shows penetration front separating the cross section into an unaffected core region (lighter) and the fully digested edge region (darker). **Figures 7A, 7B1, 7B2, 7C1** and **7C2** compare distinct structures between these two areas. Textural measurement indicated that the hardness in the digested area is significantly lower.

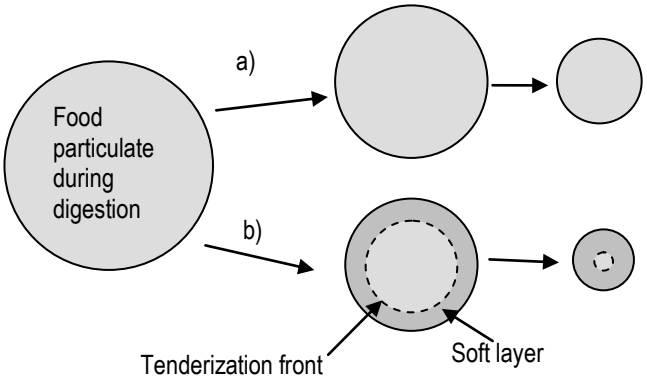

Figure 6. Food surface erosion and tenderization during food disintegration: a) surface erodes faster than the advance of the tenderization front, thus the food disintegration is not affected by texture change, leading to an exponential decay in mass retention; b) surface erosion is slower than tenderization, thus the texture softening promotes disintegration, resulting in a sigmoidal profile of mass retention.

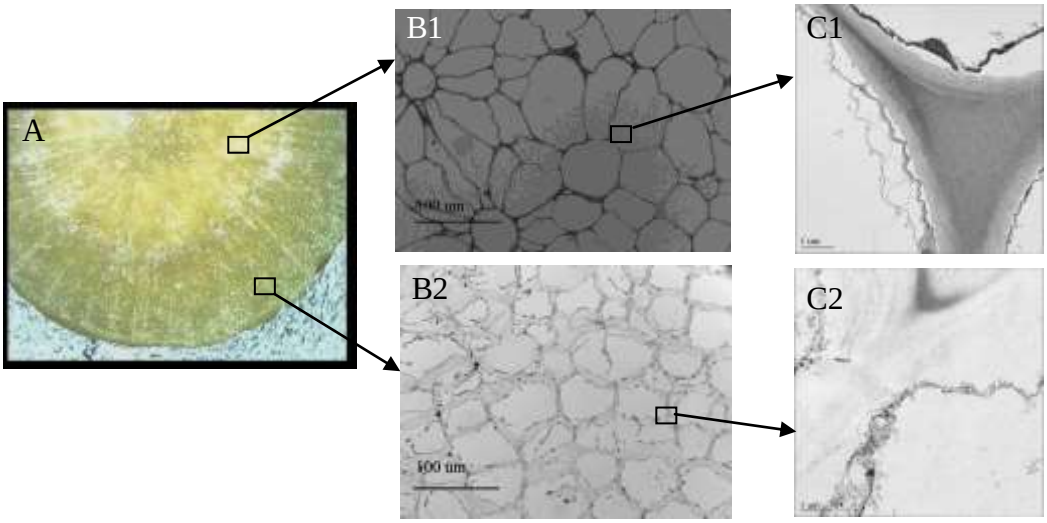

Figure 7. Changes in the microstructure of digested carrots. A: Image showing cross section of partially digested cylindrical carrot sample (dia: 3mm) with front line of water penetration (colored by methylene blue); B1, B2: Light microscopy images showing the undigested central region and the severely digested edge region; C1, C2: TEM images showing intact cell wall in the central region (C1) and damaged cell wall in the edge region (C2).

2.1 Effect of food ingestion on rheological properties of gastric juice

We determined the influence of ingestion of carrots on the rheology of simulated gastric juice. Twenty gram carrot cubes (3mm), raw and cooked for 2, 4 and 6 min, were added into simulated gastric juice in a 50 mL cup, and mixed at 37˚C for 2 hr at 75 rpm. After mixing, a

Coaxial rheometer (Haake) was used to measure the stress with a Vane probe (FL22, 4 wings) at shear rates between 0-100 1/s. Significant differences in the viscosity of mixture were observed. The data fitted the Power-law flow equation: $\sigma = K \cdot \gamma^n$ where σ is the shear stress (Pa), γ the shear rate (s^{-1}), *K* the consistency coefficient ($Pa.s^n$), and n the flow behavior index (dimensionless). Calculated parameters are shown in **Table 1**. The results show a pseudoplastic behavior (n<1, shear thining) in the mixture, confirming previous reports (Dikeman and Fahey 2006). However, the shear thickening effect is also shown in the mixture with carrots cooked for 4 and 6 min (n>1). We found that the *K* and *n* values have a good linear and exponential relationship with the hardness of carrots, respectively.

Table 1. Power-law equation parameters for gastric mixture

Carrot samples used in the mixture	K ($Pa.s^n$)	n	R^2	Shear rate (1/s)
raw	10.51	0.629	0.77	2-100
2 min boiled	4.444	0.763	0.80	2-100
4 min boiled	0.660	1.066	0.93	2-100
6 min boiled	0.458	1.128	0.93	2-100

Our results showed that the food disintegration rate significantly decreased with an increase in the viscosity of gastric juice, probably due to a viscous film that formed on the food surface that reduced the influence of surface forces.

2.2 Computational flow modeling of flow field in a human stomach

We have developed a 3-D computational model of human stomach to simulate the unsteady flow field generated inside human stomach due to the movement of contraction waves. The model used the Navier-stokes equations for fluid flow with deforming boundary walls. Fluent 6.2.16, a CFD solver, was used to solve the flow equations. The model demonstrated that as the antral contraction wave (ACW) moves towards the pyloric valve, a retrograde jet flow is created (**Figure 8**). Maximum fluid velocity was observed near the occlusion area of the ACW closest to pylorus and the strain rate was higher at those locations (**Figure 8**).

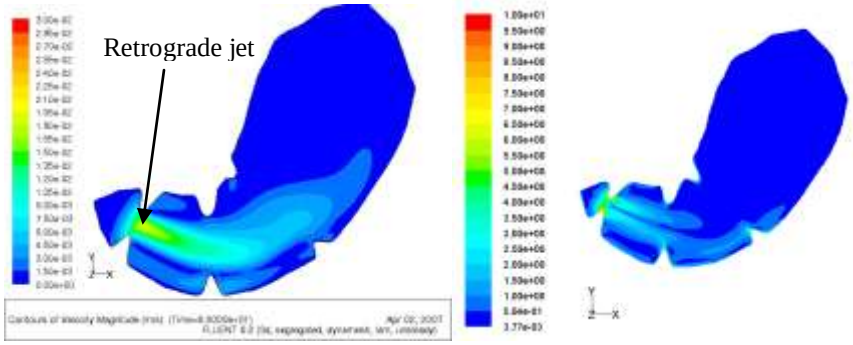

Figure 8. Contours of velocity (left) and strain rate (1/s) (right) inside the model stomach

3 OBJECTIVES

3.1 Objectives

The long term goal of the current study is to gain an understanding of the link between food material properties obtained at the manufacturing stage and the disintegration kinetics of the food in the human stomach. To accomplish this goal, the following objectives are being addressed:

1) Develop an *in vitro* stomach model for detailed investigations of food disintegration kinetics as related to the influences of hydrodynamic and mechanical contraction forces that are present *in vivo*.

2) Explore the relationships between food material properties including texture and microstructure and the disintegration kinetics for several raw and processed food products.

3) Study the changes in the rheological properties of gastric juice when mixed with foods and the influence of such changes on food disintegration.

4) Predict the flow field in a human stomach using mathematical modeling, quantitatively elaborating velocity vectors, shear stresses, retrograded and vortical flow due to peristaltic wall motion, and combine the experimental results of disintegration kinetics and the calculated flow field to develop computational model of gastric digestion.

5) Seek relationships of how food properties obtained during manufacturing influence food disintegration and nutrient delivery in the GI tract.

4 Significance of Research

This research is aimed at determining the kinetics of disintegration of different types of foods in the stomach as affected by realistic physiological conditions and food material properties. This study will provide the scientific basis for how food's microstructure and texture influence disintegration, and the interactions between food disintegration and the rheology of gastric contents. Findings from this research will provide an improved understanding of the interaction of the food matrix and active ingredients during gastric digestion. The computational modeling of the human stomach will predict the kinetics of disintegration of a food matrix under known physiological conditions of the stomach. These findings should provide new information for the food processing industry to develop structured foods for healthful benefits and develop strategies for controlled release of food nutrients at desired sites in the GI tract.

The anticipated information will enhance understanding of the stomach emptying of foods to develop approaches to control it. Control of gastric emptying is essential for ensuring optimal digestion. The rate of food disintegration in the stomach appears to be a key factor influencing emptying rate and subsequently affecting absorption of nutrients in the intestine. The potential for modulation of the rate of gastric emptying to control obesity and diabetic patients is now being explored vigorously by the pharmaceutical industry (Rayner and others 2001). Our preliminary results imply that gastric emptying of solid foods may be controlled by manipulating the texture such as hardness at the manufacturing and cooking stage. An enhanced understanding of food disintegration in the stomach and its relationships with material properties of foods may help different clinical settings through the design of specific food formulations and microstructures.

Study of gastric disintegration of foods should also help our understanding of the interactions between food and drugs during digestion. The disintegration activity of a drug is substantially affected by the presence of food components. Thus the understanding of food disintegration should help improve the control of drug dissolution in stomach.

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