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A review on the relationship between food structure, processing and bioavailability

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ABSTRACT

This review highlights the effects of processing and food matrix on bioaccessibility and bioavailability of functional components. Human digestive system is reviewed as an element in bioavailability. Methods for bioaccessibility and bioavailability determination are described. Information about the location of functional compounds in the tissue is presented to portray the matrix information. Research data on the effects of food matrix and processing on bioaccessibility and bioavailability are summarized. Finally, trends in the development of functional component delivery systems are included.

Keywords functional foods, nutraceuticals, phytochemicals, bioaccessibility

INTRODUCTION

Scientific evidence links diet and some diseases like cardiovascular disease and some type of cancers (Rao, 2004; Verhagen et al., 2004; Parada and Aguilera, 2007). Fruits and vegetables are good sources of potentially bioactive compounds known as phytochemicals as well as vitamins, minerals, and fiber. Phytochemicals are not considered as nutrients but considered to have disease prevention potential. The market and eventually the research trend for functional foods which provide health benefits beyond basic nutrition are on the rise. Figure 1 illustrates the increase in the number of research articles published related to functional foods over the years. Articles with the key words functional food and bioavailability show an increasing trend after 1990s while the key word nutraceutical shows an increasing trend after the second half of 1990s which is after the introduction of the word to the literature. There is a growing interest in improving the knowledge on the dissolution and absorption mechanism of particular food components by body. This requires understanding the physiochemical basis of mastication, ingestion, digestion, and absorption of particular food components (McClements et al., 2008).

Interaction of foods with the human body is extremely complex, involves different physicochemical and physiological processes, which depend on the composition, properties, and structure of the initial food, the characteristics of the individual consuming the food, and various other factors like time of consumption and previous food consumed (McClements et al., 2008). The natural food matrix may influence the release and the absorption kinetics of some components in the digestive tract. For functional compounds to be effective on the human health

they should be available and then defined portion of it should be absorbed by the digestive tract. The bioavailability or the proportion of the ingested nutrient that is delivered to the blood stream for its intended mode of action is more important than the total amount present in the original food (Parada and Aguilera, 2007; Colle et al., 2010a).

Nutrients can be bound to plant organelles such as carotenoids in carrots or entrapped in a complex macromolecular matrix of swollen starch granules and protein such as isoflavones in baked products (Parada and Agilera 2007). Food matrix, natural or the one formed during processing, may affect the release of some food components in the digestive system. As an example, oils in nuts which have strong structure may not be absorbed fully in the digestive truck. It is known that increasing the oil content and destruction of the natural food matrix increases the absorption of carotene in the body (Vasquez-Caicedo et. al, 2007; Yonekura and Nagao, 2007). Bioabsorption of carotenes are higher in supplement tablets than that are buried in the natural matrix of fruits and vegetables (Yonekura and Nagao, 2007). Beta carotene enters the blood plasma faster if carrots are consumed as carrot juice or cooked carrots. Mastication and enzymes in the stomach may not be enough to break the structure of the carrot's strong cell structure to release beta carotene. Only antioxidant released from the food matrix by the action of digestive enzymes (small intestine) and bacterial microflora (large intestine) are bioaccessible in the gut and therefore potentially bioavailable (Saura-Calixt et al., 2007). Hence, it is important to know the disintegration of solid foods in human stomach to assess the bioavailability of nutrients in the gastrointestinal tract (Kong and Singh, 2008).

Bioaccessibility and bioavailability of each antioxidant are not same, and the highest concentrations of active metabolites in target tissues does not necessarily come from the

antioxidant that have the highest concentration in the ingested fruit (Palafox-Carlos et al., 2011). Fruit antioxidants are commonly mixed with macromolecules such as carbohydrates, lipids and proteins to form a food matrix (Palafox-Carlos et al., 2011). Effective delivery of nutrients in the gastrointestinal track for the health require new generation of foods designed with the combined knowledge of food scientists, engineers, sensory scientist, nutritionists, medical researchers, and psychologists (McClements et al., 2008; Norton et al., 2007). There are several reviews to acknowledge that the knowledge of several disciplines is necessary to understand the relationship between structure, processing and bioavailability for designing the next generation foods for the health benefit. Table 1 summarizes some of the reviews and their intention on the interactions. The aim of this review is to combine the information on the interaction between the ingredients, food structure, processing and human digestive system for designing functional foods for the health benefit. Research data on the effects of food structure and processing on bioavailability are summarized.

THE HUMAN DIGESTIVE SYSTEM (INGESTION, MASTICATION, DIGESTION, AND ABSORPTION)

Digestion is mixing food with digestive juices, moving it through the digestive tract, and breaking down large molecules of food into smaller molecules. Digestive tract consists of the mouth, esophagus, stomach, small intestine, large intestine, and anus (Figure 2). The mucosa, lining inside theses organs, contains tiny glands that produce juices to help food digestion. The rhythmic, wave like contractions of organ walls due to layer of muscles called peristalsis can propel food and liquid through the system and also can mix the contents within each organ.

Digestion begins in the mouth and is completed in the small intestine. Most digested molecules of food, as well as water and minerals, are absorbed through the small intestine. Monomers formed during digestion are transported across the wall of the small intestine into the blood and lymph in the process of absorption (Fox, 2009).

Although during consumption all foods pass through a common unit operation (Figure 2), the gastrointestinal tract (GI), the process is the least understood of all the food processes (Norton et. al, 2006). Physical transformation of food matrices starts at the mouth, mastication considered the initial step of digestion of foods. Mastication is grinding food into small pieces and mixing them with saliva that contains enzymes to form a bolus so that the end product can be swallowed. Decreasing the size of the particles enlarges the surface area which is available for digestion and absorption. Reduction of the size of the foods during digestion leads to nutrient that are buried inside the food to come out and make it easy for body cells to absorb (Kong and Singh, 2008). During the digestion process flavoring compounds is released into the nasal cavity (Taylor and Linforth, 1996; Norton et al., 2006). Food bolus formed transported through the esophagus to the stomach by peristalsis mechanism (Kong and Singh, 2008).

Stomach behaves as a weakly mixed system in which the walls oscillate a small amount and cause some surface mixing and erosion. Acids and enzymes help breakdown of the food into small materials which can be absorbed into blood stream (Norton et al., 2006). Mouth and stomach are the major parts where foods are broken up to small pieces, on the other hand, small intestines are major site for nutrition absorption where the food is dissolved into the juices from the pancreas, liver and, intestine (Kong and Singh, 2008). Complete digestion time depends on food structure. Liquids are digested faster than semisolids or cellular structures (Norton et al.,

2006). Speed of the digestion depends on physiological events of the digestive track as well as the chemical and physical properties of the foods (Kong and Singh, 2008).

It is known that food processing conditions can affect or control the disintegration and dissolution steps of food digestion (Kong and Singh, 2008). Number of researchers are investigating food product microstructure design for in mouth behavior and delivery of molecular species (Norton et al., 2006). Other important stage is to understand the disintegration mechanism of solids foods in the stomach to be able asses the bioavailability of nutrients in the gastrointestinal tract (Norton et al., 2006; Kong and Singh, 2008). Additionally, physical properties of digesta may influence mixing, efficiency of digestion, and absorption within the lumen of the intestine (Lentle and Janssen, 2008).

BIOAVAILABILITY AND BIOACCESIBILITY

Bioaccessibility is defined as the amount of an ingested nutrient that is available for absorption in the gut after digestion (Colle et al., 2010a; Palafox-Carlos et al., 2011). Bioavailability is defined as the fraction of ingested nutrients that is available for utilization in normal physiological functions or storage in the body and includes nutrient accessibility (Duchateau and Klaffke, 2008; Van Buggenhout et al., 2010; Palafox-Carlos et al., 2011). The *in vivo* effects of antioxidants is not only function of their concentration but also function of their bioaccessibility and bioavailability after ingestion (Palafox-Carlos et al., 2011). Health claims for functional foods can only be made if the ingredient reaches the target site for the required physiological action (Duchateau and Klaffke, 2008).

It is important to investigate the bioaccessibility in the small intestine and release of the bioactive compounds from food matrix which can be a potential indicator of their absorption through intestinal barrier (Hervert-Hernandez et al., 2010). In recent years relationship between the food structure and nutrients's *in vitro* bioaccessibility and bioavailability (Lemmens et al., 2009) and *in vivo* bioavailability are receiving big attention. Food structure may hinder the bioaccessibility because nutrients are usually either inside the cell or connected to cellular structure (Karakaya and Yilmaz, 2007; Lemmens et al., 2009). Determination of bioaccessibility and bioavailability is important in the development of functional foods for the health benefit.

BIOAVAILABILITY AND BIOACCESIBILITY DETERMINATION METHODS

Bioavailability and bioaccessibility of nutrients determined by *in vivo* or *in vitro* methods. *In vivo* methods provide direct data because it involves human or animal subjects. Usually a response is measured after the consumption of a certain dose of a nutrients and the changes of its concentration in the blood plasma measured with time. Another method is to measure the concentration of the nutrient in the blood plasma through an extended period of constant consumption of a specific food (Parada and Aguilera, 2007). Although human studies are the most appropriate approach as animal studies for investigation of bioavailability, they are ethically questionable (Biehler et al., 2011). In addition, variability in the physiological state of the individuals and possible interaction of the nutrient with other components in the diet are drawbacks of *in vivo* studies (Parada and Aguilera, 2007). Rapid, low-cost and with no ethical constraint alternative is *in vitro* model which simulates gastro intestinal passage. *In vitro*

techniques also improve accuracy and reproducibility (Kong and Singh, 2008). Nutrient *in vitro* bioaccessibility, which is the amount of nutrient released from food products, is the starting point for investigating nutrient bioavailability (Lemmens et al., 2010). Bioaccessibility is determined if only digestion process is simulated, bioavailability is determined when both digestion and absorption process is simulated and the measured response is the concentration of the desired component in the final extract for both simulation procedures (Parada and Aguilera, 2007). The digestion process is simulated by using commercial digestive enzymes under controlled conditions (Figure 3). Gastric digestion is simulated by pepsin- HCL digestion, followed by pancreatin digestion with bile salts (to simulate the conditions in the small intestine). Absorption step can be simulated with Caco-2 cells cultures, where Caco-2 cells is the short name of polarized human colon carcinoma cells line (Verwei et al., 2005; Parada and Aguilera, 2007).

There are number of *in vitro* gastrointestinal tract models available for nutrition, toxicology, pharmacology and safety assessments (Parada and Aguilera, 2007; Kong and Singh, 2008; Tharakan et al., 2010). There are two types of models, static and dynamic (Parada and Aguilera, 2007; Kong and Singh, 2008). The static models usually include peptic hydrolysis of homogenized food at pH 1.5 for 1-2 hr while stirring at 37°C (Kong and Singh, 2008). Dynamic models simulates the physical and physiological events that occur *in vivo* including simulation of pH changes, temperature, peristaltic movements, secretion of digestive enzymes, bile and pancreatic juices, and absorption of digested products (Parada and Aguilera, 2007; Kong and Singh, 2008;). The dynamic models are particularly useful where the physical condition like particle size and viscosity of the digesta changes over time and temporal effect like mixing,

diffusion and formation of colloidal phases are considered (Parada and Aguilera, 2007). It is important to predict the release of nutrients from food matrices under simulated gastrointestinal conditions to define which food matrix is the most suitable for which nutrient (Tedeschi et al., 2009).

EFFECT OF PROCESSING AND FOOD STRUCTURE ON BIOACCESSIBILITY AND BIOAVAILABILITY

Food products are usually structurally complex and this structure and its breakdown in the mouth determines the taste, texture and eating pleasure (Norton et al., 2006; Norton et al., 2007). Microstructure of foods or the food matrix plays an important role in the release and absorption of the nutrients and allergic compounds (Norton et al., 2007; Parada and Aguilera, 2007; Kong and Singh, 2008; Aherne et al., 2010). Grinding, fermentation and/or mild heat treatments break the cellular structure of the plants. Food matrix that is formed during processing and other components that are taken together with the food affects the kinetics of absorption kinetics in the digestive system. Degradation of the nutrient matrix complex or transformation to more active molecular structure may increase the bioavailability (Parada and Aguilera, 2007). Therefore, understanding food matrix and matrix structuring to increase the nutrient availability is an important area to investigate (Parada and Aguilera, 2007).

Secondary plant metabolites have been receiving attention as functional components due to their role in health promotion (van Boekel et al., 2010). Chemically, plant secondary metabolites can be divided into three groups: terpenes, phenolics, and nitrogen containing groups. The red, orange, and yellow carotenoids are tetraterpenes that function as accessory

pigments (Taiz and Zeiger, 2006). Glucosinolates, which are water soluble class of nitrogen containing secondary metabolites, are considered to be health promoting due to the isothiocyanates derived from them (Mithen et al., 2000; Jones, 2007; Jones, et. al., 2010; van Boekel et al., 2010). Isothiocanetes are breakdown products of glucosinolates hydrolyzation by the enzyme myrosinase when the plant tissue is damaged by food preparation or by chewing (Mithen et al., 2000).

Intracellular localization of nutrients implies that their accessibility is related by several structural elements (Lemmens et al., 2009). In order to understand the release of these functional components during digestion it would be important to know where they are located in the tissue and how processing affects the release of the compound. Table 2 illustrates the location of these group of secondary metabolites in the plant tissue and Table 3 summarizes the effect of processing on their bioavailability.

Several researchers emphasize that food processing is a value adding step (Karakaya and Yilmaz, 2007). It is known that grinding and cooking enhance the extraction of β-carotene from plant structure and enhance the bioaccessibility by destroying the cell wall structure (Parada and Aguilera, 2007; Bengtsson et al., 2010). Yonekura and Nagao (2007) claims that β-carotene level is higher in the plasma of the people who consumed cooked carrot compared to people consumed raw carrot. As quoted in Parada and Aguilera (2007) Rock et al. (1998) found that plasma of women who consumed cooked carrot and spinach contain three times more β-carotene compared to women who consumed raw vegetables. The bioavailability of beta-carotene is one order of magnitude higher when provided as a pure compound added to foods than when it is present naturally in foods (Hof et al., 2000). Hervert-Hernandez et al. (2010) found that with digestive

system enzymes up to 49 % of β-carotene can be released from the food matrix in the study where they have tested four hot pepper variety. Lemmens et al. (2009) observed that different heat treatments and different pretreatments affects the amounts of β-carotene and bioaccessible β-carotene in carrots. They observed that amount of bioaccessible β-carotene increases as the carrot tissue disintegrate (Lemmens et al., 2009). According to Tydeman et al. (2010) cell wall rupture prior to digestion is a requirement for carotene bioaccessibility in the upper intestine and heating does not enhance carotene release from intact cells of carrot tissue. Mechanical breakdown is more important for raw carrots than thermally processed carrots for β-carotene bioavilability (Lemmens et al., 2010).

Tiback et al. (2009) in one of their studies have shown that even though mechanical and heat treatment did not affect the lycopene content, extensive meshing and heat treatment affect the *in vitro* availability if the treatments are applied in sequence. It is known that lycopene bioavailability is higher for such as tomato paste, pure and sauce compared to raw tomato (Gomez-Romero, 2007; Roldan-Gutierrez, 2007). Aguilera (2005) stated that researchers have found that plasma reaction is 22-380 % higher for tomato paste compared to raw tomato for the same amount of lycopene. Release of lycopene from the cell structure in the tomato affects its availability and absorptivity in the digestive system (Parada and Aguilera, 2007). Cooking, heat, mechanical or enzymatic processing may make the lycopene more accessible by breaking the cellular structure and eventually destroying the bond with the tissue (Yonekura and Nagao, 2007). Release of carotenoids from vegetable tissue is due to cell structure disruption by food processing, it does not happen in the digestive system (Prada and Aguilera, 2007).

Various dietary factors have an effect on the bioavailability of carotenoids. The type of food matrix in which carotenoids are located is a major factor (Hof et al., 2000). It is recognized that the carotenoids are not actively absorbed by the gut but are absorbed passively along with lipids (Hof et al., 2000; Unlu et al., 2005). The bioavailability of β-carotene from vegetables in particular has been shown to be low (14% from mixed vegetables) compared with that of purified β-carotene added to a simple matrix (e.g., salad dressing), whereas for lutein, the difference is much smaller (relative bioavailability of 67% from mixed vegetables). Processing, such as mechanical homogenization or heat treatment, has the potential to enhance the bioavailability of carotenoids from vegetables (from 18% to a sixfold increase). Unabsorbable, fat-soluble compounds reduce carotenoid absorption, and interaction among carotenoids may also result in a reduced carotenoid bioavailability (Hof et al., 2000). According to Colle et al. (2010b) improved fiber network strength during high pressure homogenization reduce the bioaccessibility of entrapped lycopene in tomato pulp and, thermal treatment after homogenization did not improve the accessibility.

Cooking has an adverse effect on polyphenols, steam cooking which avoid leaching is preferable. Fruit peeling, dehulling of legumes and cereals can result in loss of some polyphenols. Cellular breakdown due to grinding of plant tissues may bring cytoplasmic polyphenol oxidase and phenol substances present in the vacuoles in contact and lead to oxidative degradation of polyphenols (van Boekel et al., 2010). According to Ortega et al. (2011) soluble dietary fiber enhanced the stability of the phenolic compounds during duodenal digestion phase of *in vitro* digestion method. Composition of the food matrix is a factor in stability and digestibility of polyphenols located in the food matrix (Ortega et al., 2011).

A functional ingredient has to be released from the product matrix into a molecularly dispersed state, either in classic solution or in micellar state. Functional ingredients only in the dispersed state can cross the gut wall. Release and dissolution depend on both molecular physiochemical properties of the ingredient and those of the entire product. The uptake of hydrophobic, poorly water soluble substrates are more complex. Compartmentalization strategies, like encapsulation, may offer solutions to problem; it should, however, stay in mind that encapsulates by themselves affect bioavailability through the changed dynamics of the uptake processes (Duchateau and Klaffke, 2008).

Microencapsulation is used to improve bioavailability, control the release kinetics, minimize drug side effects and musk the bitter taste of drug substances in pharmaceutical industry. In food industry its typical use is controlled release of flavorings and the production of foods containing functional ingredients such as probiotics and bioactive ingredients (Kuang et al., 2010). Nanotechnology or encapsulation can be used to enhance oral bioavailability of phytochemicals by changing the pharmacokinetics and biodistribution (Huang et. al, 2010). In order to incorporate functional components effectively in a food system, sophisticated encapsulation matrices have to be engineered. Those matrices should provide physical stability, chemical stability and should have precise control over the release of encapsulated components during mastication and digestion to optimize absorption. Bioactive compounds tightly bind to the food matrix, highly lipophilic result in poor absorption and limited bioavailability. In addition, they can be chemically unstable once they are extracted from plants or animal based sources. Therefore, a suitable delivery system becomes important like nanoemulsions, microemulsions and biopoylmeric nanoparticles (Weiss et al., 2008). Siddiqui et al. (2010)

introduced a new concept “nanochemoprevention”, which is sustained release of bioactive food components for cancer prevention. Their data in a study with a well known chemopreventive agent, epigallocatechin-3-gallate (EGCG), suggest that nano-EGCG shows 10 fold dose advantage over nanoencapsulated EGCG.

According to Lentle and Janssen (2010) digesta behaves as a non-Newtonian material, and apparent viscosity and fluid phase permeability changes along the human intestinal tract. In addition, bulk mixing inside the digestive system is affected by the changes in the flow behavior (Lentle and Janssen, 2008, 2010). Skilful use of nutritionally inert items that modulate physical properties inside the digestive system offers the opportunity to formulate foods with health promoting properties (Lentle and Janssen, 2010). As an example, liquid products can be made to self structure inside the GI by choosing hydrocolloids that are acid sensitive, such as alginate to slow the digestive process and stomach emptying (Norton et al., 2007).

Understanding the basics of the relationships between the food matrix, processing and active compounds and their performance in the digestive tract will lead to development of new generation functional foods for health benefit (Kong and Singh, 2008). Improvement of bioavailability of the biologically active compounds in the foods is important for development of food or health programs for public health (O'Sullivan et al., 2010).

CONCLUSION

In the review, current status and future trends on functional food development are noted. Advancement in the enhanced bioavailability of the functional components for the next generation of foods require deep understanding of the effects of processing and digestive system

on food matrix. It is necessary to evaluate how food structure and food processing affect bioavailability of nutrients and bioactive compounds. Processing methods could be altered or improved to enhance bioavailability. Furthermore, absorption mechanism of the components by the digestive system and, mechanics and physiology of digestive system need to be investigated in detail to be able to optimize the product design. Efficient delivery systems such as encapsulates or nano sized components should also be investigated to broaden the available systems for product development. In the end, all those combined knowledge can advance the development of functional foods with efficient use of resources.

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Table 1. Summary of selected reviews on bioavailability, structure, functionality and delivery systems.

Title	Relationship
The role of dietary fiber in the bioaccessibility and bioavailability of fruit and vegetable antioxidants	Food matrix-bioavailability
Bioavailability and delivery of nutraceuticals using nanotechnology	Delivery systems-bioavailability
Microencapsulation as a tool for incorporating bioactive ingredients into food	Delivery system-bioaccessibility
Controlling lipid bioavailability through physicochemical and structural approach	Digestion mechanism- bioavailability
Structural design principles for delivery of bioactive components in nutraceuticals and functional foods	Delivery system-design principles
Structure-function relationships to guide rational design and fabrication of particulate food delivery systems	Delivery systems- bioavailability
Designing food structure to control stability, digestion, release and absorption of lipophilic food components	Structure-bioavailability
Solid lipid nanoparticles as delivery systems for bioactive food componenents	Delivery systems-structure
Physical characteristics of digesta and their influence on flow and mixing in the mammalian intestine: a review	Physical characteristics of digesta-bioavailability
Disintegration of solid foods in human stomach	Structure- bioavailability
Product compositon, structure and bioavailability	Structure - bioavailability
Understanding food structuring and breakdown: engineering approaches to obesity	Structure- bioavailability
Food microstructure affects the bioavailability of several nutrients	Structure-bioavailability
Product/process integration in food manufacture: Engineering sustained health	Structure-health
Polyphenols: food sources and bioavailability	Processing-bioavailability
The nutritional significance, biosynthesis and bioavailability of glucosinolates in human foods	Processing-bioavailability

Table 2. Selected secondary plant metabolites as micro nutrients and their location within the tissue.

Selected groups of functional compounds	Location	Source
Carotenoids (Several forms: β-caroten, lycopene and lutein)	Found either in the chloroplast membrane or in specialized plastids called chromoplasts	All photosynthetic organisms, like sweet potato, carrots, spinach, red pepper, kale, tomatoes and brocol
Polyphenols	Found as conjugates with mono and poly saccharides and proteins. Generally dissolved in vacuoles and the apoplast of plant cells	Almost all foods of plant origin
Glucosinolates (or mustard oil glycosides)	Stored in the intact plant separately from the enzymes that hydrolyze them, thus they can only come in to contact with these enzymes when the plant is crushed	In Brassica vegetables

Table 3. Selected functional compounds that processing or food matrix affects their bioavailability.

Functional compounds	Affected by	Reference
Carotenoids	Processing and inclusion of oil enhances bioavailability	Parada and Aguilera,
Polyphenols	Food matrix and background diet may affect bioavailability	Parada and Aguilera,
Glucosinolates	Processing may decrease the amount in the food	Mithen et al., 2000; J

Figure 1. Trend for the number of research articles published with the key words: Functional food, bioavailability and food and, nutraceuticals. Data are from ISI Web of Knowledge, Copyrigt 2011 The Thomson Reuters.

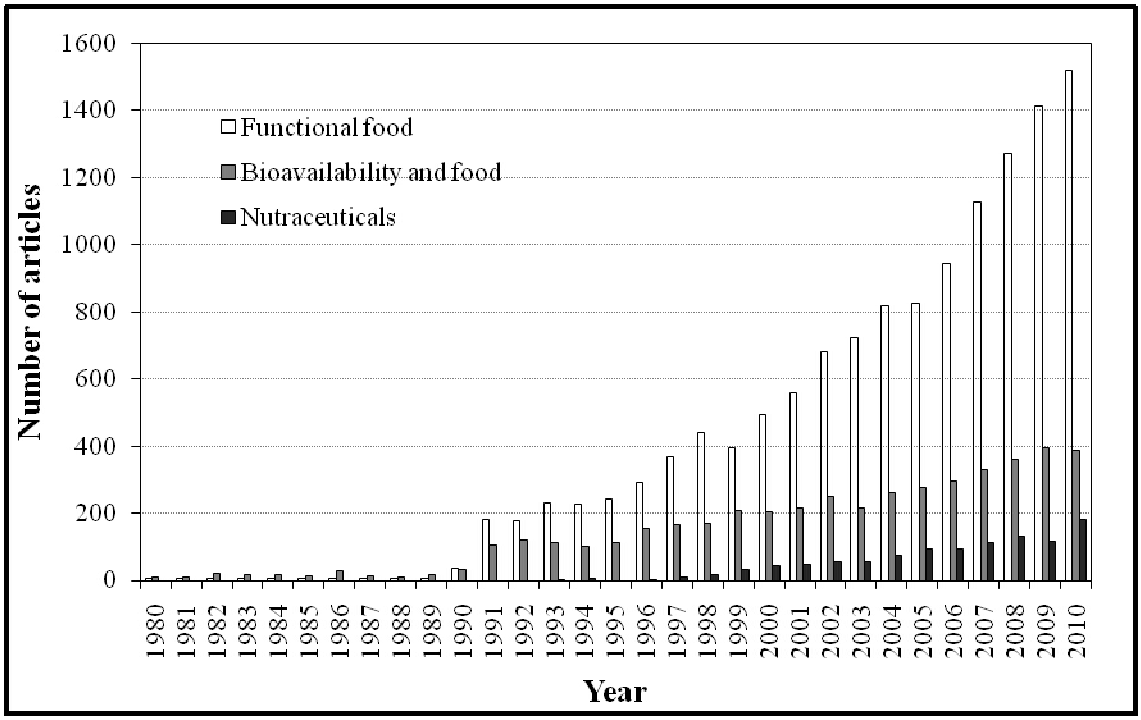

Figure 2. Schematic diagram of the digestive system.

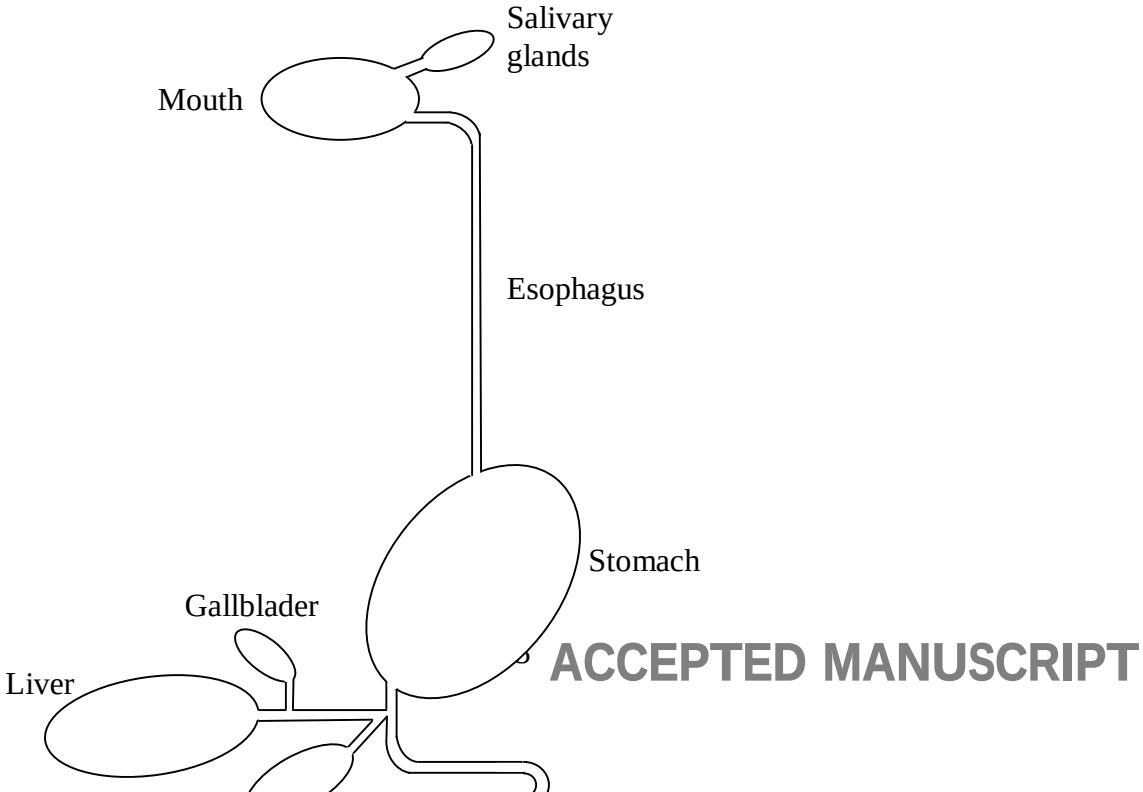

Figure 3. Diagram of an *in vitro* digestion method to determine bioavailability which uses Caco-2 cell culture to asses absorption step (adopted from Parada and Aguilera, 2007).