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Hypothesis review: The direct interaction of food nanoparticles with the lymphatic system

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Abstract

Besides digestion and assimilation, there are other modes of direct interaction between food and human body. As it is known, the mucosal layer of the digestive tract interfaces with food after the digestion process. It has been demonstrated to uptake the micro- and nanoparticles via mucosa-associated lymphatic tissues (MALT). On the other hand, food is a typical polydisperse system and contains micro- and nanoparticles with different sizes and properties. Accordingly, it is hypothesized that food nanoparticles can directly interact with MALT and more specifically with the support of the preliminary experimental data from our research, that antioxidant nanoparticles can interact with the lymphatic vessels. This kind of interaction would be of great physiological importance. The confirmation of the hypothesis will establish a significant and novel approach to understand food system and provide answers to currently incomprehensible phenomena such as the biological functions of phytochemicals with low bioavailability.

Keywords: Food nanoparticles; Uptake; Intestinal mucosa; Lymphatic

1. Relationship between food and human body

There are many approaches to understand the relationship between food and human body. As elucidated by nutrition science, food is indispensable to life because of its role as the source of nutrients which are essential to support life and sustain growth. It is also a very important mean to maintain health and wellness, which has been scientifically demonstrated by ever increasing evidence in recent years. What is known more as common sense than scientific knowledge is that food is an important provider of sensory pleasure for human beings [1,2].

When food is considered as either the nutrient provider or a health keeper, it is known to be firstly physically, chemically, and biochemically broken down into the constituents and then be assimilated in the form of molecules which are subsequently circulated to organs, tissues and cells all over the body. One interaction mode of food with the body, already deeply studied, is degradation of intact food to polymers and molecules to interact with cells [3]. There is also a mode of direct interaction of food with the body without passing through the circulation system. It is mostly investigated as the sensory aspect of food. Free molecules can directly interact with cells to generate sensations, such as volatile molecules interact with cells of the olfactory organ resulting in sensory odors [4], and capsaicin binds to the heat-activated calcium channel protein on the heat sensing neuron to generate heat [5]. Otherwise, processing of food in the mouth contributes significantly to the sensory perception, which is one of the very few cases studied so far of non-molecular direct interaction of food with the body [6].

2. Interaction of food with human body via digestive tract mucosa

Referring to the interaction of food with human body, the digestive tract and the skin – the two major interfaces of human

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body interacting with external substances are discussed. The digestive tract and the skin are significantly different in their functions and structures due to the fundamental difference of the substances they are interfaced with. The former is a barrier and insulation, and functions as the first line of defense against the external harmful factors [7]. Whereas the latter is covered with a thin layer of permeable mucus rather than the tough and waterproof stratum corneum [8], the uppermost layer of the skin. Different from the substances the skin may be exposed to, those passing through the digestive tract can be anything but harmful. Different structures are ingeniously devised for different modes of interface with external substances. Apparently, the mucosal layer of the digestive tract functions not as insulation but facilitation of the interaction between food and the body in both digestion and assimilation course. The process is that food is firstly masticated and broken down in the mouth and then goes through various proteolysis in the stomach and further digestion and principle absorption in the intestine. Considering the interactive nature of mucosal layer and complex components of food before and after digesting process, there may be some other direct non-molecular interactions besides the known processes, which require further investigations.

Digestion imparts constant changes in the digestive tract thus mucosal layers in different sections of the tract are highly specialized, in order to carry out different interactions with ever changing food materials. A histological feature characterized by the mucosa layer from mouth to colon is the heavily populated with lymphoid cells and densely aligned lymphatic vessels. Mucosa-associated lymphoid tissues (MALT) are scattered along the wet mucosal linings throughout the digestive tract. Those surfaces constitute the most extensive immune barrier against pathogens [9]. Meanwhile, they are also the very venue for the direct interaction between the body and the external substances. This type of direct interaction will lead to the uptake of certain external substances, i.e. lipids, which are absorbed by human body through lymphatic system located in the intestinal tract.

3. Uptake of nanoparticles by digestive tract

Besides low molecular weight compounds, natural or synthetic micro- and nanoparticles can also be uptaken through the mucosa of the digestive tract. They can pass through the epithelial layer of digestive tract and passage into lymphatic vessels and lymph nodes and then deliver to various locations of the body. The earliest evidence of nanoparticle uptake was obtained from the observation that raw starch fed to rats was absorbed across the gut mucosa [10]. As a matter of fact, particles with different sizes ranged from nanometers to micrometers, natural or synthetic, metallic or organic, have been found to be uptaken across the mucosal layer of the digestive tract into the lymphatic system or blood [11]. Particles are transported across the epithelial mucus via one of the three possible routes identified, including paracellular penetration, endocytosis and uptake via mucosa-associated lymphoid tissues (MALT) depending on different sizes [12,13], surface charges [14], hydrophobicity level [15,16] and other factors [17]. The process is not only considered as a regular process [18,19], but also a promising novel approach to efficiently facilitate drug and vaccine delivery [20,21]. However, at present little is comprehensively understood about that the biological impact micro- and nanoparticles can generate when they are transported across the mucosal epithelia into the lymphatic system or further to visceral organs and tissues of the body.

4. Food nanoparticles

If food system contained micro- or nanoparticles with certain sizes and characteristics, which can be uptaken via lymphatic tissues of the digestive tract mucosa, they may possibly be uptaken in the same way. Hardly any substances can be better candidates than food as versatile micro-and nanoparticle providers for mucosal uptake. Food raw materials contain diverse compositions from free molecules to insoluble polymers, heat sensitive to insensitive proteins and hydrophilic to hydrophobic chemicals. They not only construct functional animal or plant bodies but also form the polydisperse system of food including solution, colloid, emulsion, foam, gel, etc. [22]. Processing such as heating, mechanical treatment and fermentation of food materials can accelerate chemical and physiochemical interactions between various compositions, resulting in even more diverse dispersions [23]. As a course of diminution, physical process, such as mixing with saliva or mastication of food, can possibly bring about more changes in dispersions besides biochemical process, i.e. enzymatic degradation. Therefore, the prominently diverse dispersions in raw materials together with further in vivo processing can possibly render food system containing micro-and nanoparticles of diverse properties. These micro- and nanoparticles are completely eligible to react with versatile mucosa linings of digestive tract.

The in vitro processing of food materials is different from the in vivo processing mentioned above and is also a course of food nanoparticles production. An insight into how processing generates food nanostructures has been gained from our recent work on soup [24]. Technically speaking, soups are products of boiling water and an extract of food materials, either animal or plant origin. It is found that only a certain substances actually migrate from the solid phase into the aqueous phase upon boiling water extraction. Besides water-soluble small molecules, lipid proteins in animal food materials and glycated protein in herbs resulted from Maillard reaction are found to migrate into soup, both of which can assemble into nanoparticles, respectively. Preliminary results indicate that those nanoparticles play a key role in maintaining biological activities of corresponding soups which are known as folk remedies [25]. Among all types of nanoparticles in a food system, only those which are physically and chemically stable can be expected to carry out meaningful reactions. Furthermore, nanoparticles obtained under harsh conditions, i.e. boiling water extraction, show outstanding physiochemical stable features and are likely to interact with mucosa layers, resulting in possibly reproducible impacts and endowing the food system with unique characteristics.

In a word, nothing is interfacing with the mucosal linings of digestive tract more than food, which is proved to be a