Effects of food emulsifiers on gut microbiota

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Abstract: Food emulsifier is mainly used in processed food, which involves the production and use and food safety issues. In recent years, more and more people suffer from metabolic diseases, which makes people begin to pay attention to them and study them in depth. In this paper, the relationship between food emulsifier and human gut microbiota is described in detail, and the relationship between gut microbiota and some common metabolic diseases and diet is introduced. Through the study of food emulsifier and gut microbiota, it is found that some food emulsifiers will change the gut microbiota and make it disordered; others are beneficial to their metabolic function. At the same time, some research experiments show that the results of food emulsifier acting on gut microbiota are different, indicating that the influence of food emulsifier on gut microbiota still needs to be further explored.

1. Introduction

Emulsifier is a class of food additives. The State Food and Drug Administration (SFDA) calls it "emulsifier or emulsifier salt". We often see it in the ingredients list of milk, ice cream, butter, pastries and soy sauce[1]. The characteristic of emulsifiers is that they have the ability to absorb the interface, especially the adsorption performance of the water / oil interface. There are many quantities and types of food emulsifiers, among which the most widely used are two synthetic emulsifiers (polysorbate-80 and carboxymethyl cellulose.

Gut microbiota is the largest microbial community in the human body, and they are closely related to the physiological functions of the host. Some studies have shown that dysbiosis of gut microbiota may contribute to the onset and development of metabolic diseases such as obesity, diabetes, and hypertension. Food emulsifiers were usually considered harmless in the earlier years ago. In recent years, with people's increasing attention to health, a variety of food additives are also concerned about the safety. Some food emulsifiers have been shown to cause the translocation of pathogenic microorganisms within the intestinal epithelial barrier, which in turn triggers intestinal inflammation and greatly increases the risk of disease. Therefore, investigating the impact of food emulsifiers on the intestinal microbiome contributes to understanding the connection between the gut microbiota and metabolic disorders, and provide new ideas and methods for the prevention and treatment of metabolic diseases[2, 3].

The author ntroduces some food emulsifiers which are widely used in daily life, understands their roles in food processing, and evaluates, analyzes and expounds their safety. Secondly, based on the systematic literature search, the gut flora was reviewed, including the characteristics of the gut microbiota, gut microbiota and common metabolic diseases and dietary structure. Consequently, an examination was conducted into the possible effects that food emulsifiers have on the gut microbiome.

2. Method

From the establishment of the subject to date, the main use of PubMed, Elsevier SD and Web of Science three databases to carry out a systematic literature search. The search was limited to: ("gut microbiota") & ("emulsifier", "carboxymethylcellulose", "lecithin", "polysorbate 80") & ("type I and type II diabetes", "obesity", "intestinal inflammation"). In addition, the association search of the eligible experimental studies was also conducted to find the original and additional references.

3. Common food emulsifiers

Table 1. Some common additives in daily food

Name of the species	Using in the product
Sodium Carboxymethylcellulose	Breads, biscuits, cakes, ice cream, margarine, jam, fruit syrup, gravy, egg products, cheese products
Polysorbate 80	Breads, cakes, ice cream, frozen desserts, pickles, salad dressing, shortenings, chocolate
Lecithin	Baked goods, chocolate, candy, ice cream, instant cocoa beverages, powdered milk, margarine, shortenings, macaroni and noodles

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Mono- and di-glycerides	Breads, cake, pasta, breakfast cereal, cream, milk products, cheese products, dried fruits and vegetables, jam, jelly, cocoa, chocolate, mustard, margarine, low-fat spreads, soup, broths, flavored drinks
Stearoyl lactylates	Waffles, pancakes, icing, dehydrated potatoes, snack dips, pudding, milk or cream substitutes, cheese substitutes, sauces and gravy
Sucrose esters	Sugar confectionery, chewing gum, sauce, soup, dessert, ice cream, milk-based beverages, cereal, supplements, coffee whitener
Polyglycerol polyricinoleate	Bread, cake, pastries, cereal, energy bars, nut spreads, rice snacks, popcorn, chocolate, margarine, cream, honey, sports drinks, dressings and vinegar

From Table 1, there are more than 100 kinds of food additives and emulsifiers allowed in daily life. In this part, only three common kinds of food emulsifiers are introduced.

3.1. Carboxymethyl cellulose

Carboxymethylcellulose (CMC) is a type of anionic cellulose, using alternative base and acid-base reaction extraction, to produce a high viscosity aqueous solution, used as a specific functional component of various reprocessed foods. The carboxymethyl cellulose, which has thickening properties, is widely used in ice-cream, low-fat, gluten-free and bakery products[4, 5]. Moreover, carboxylylcellulose is an effective stabilizer of tartrate-unstable red wines and plays an important role in stabilizing tartrate-unstable wines[6]. However, the amount of carboxyylcellulose still needs to be controlled, and after safety assessment, the guiding value of daily intake is recommended to be 660-900 mg / kg body weight.

3.2. Polysorbate 80

Polysorbate 80 is one of the most commonly used polysorbates. It is made up of sorbitol Polyethylene glycol fatty acid esters, of which monooleate is the main component. Polysorbate 80 is widely regarded as an important auxiliary material for various drugs and food because of its characteristics, such as good surface activity, high biocompatibility, good emulsification, good stability, good wetting, good wettability and low cost. It acts as a defoamer or emulsifier in food production and is approved by the US Food and Drug Administration can be used in certain foods with a proportion of no more than 1 per cent. As a food emulsifier, it is commonly used in milk-derived products to improve yogurt bacteria with probiotic properties and improve their adhesion and survival rate[7, 8].After assessing the safety of polysorbate 80, JECFA recommended a safe intake (ADI) of no more than 25 mg each kg BW and each day.

3.3. And the lecithin

Lecithin is a mixture or fraction of phospholipids obtained by physical means from animal or plant ingredients, and in the latest assessment of lecithin, the main source of lecithin was identified as soybean, while others include plant sources such as corn, rapeseed, sunflower and cottonons, and egg yolk of animal sources. The European Commission Food Science Committee (SCF) (European Commission, 1982,1997) has assessed that the food emulsifier lecithin is safe for use in food. Lecithin is not required to limit daily intake, and a fine-grained assessment of its use in foods found no problems in those over 1 year of age[9, 10].

In conclusion, this part introduces three common food emulsifiers, explaining the role and passage of these three common food emulsifiers and the safety of these three common food emulsifiers. This seems to be at odds with the scientific community's long-held view that food emulsifiers have extremely negative effects. Therefore, next, we will describe and introduce the gut microbiota, and evaluate the relationship between food emulsifiers and the healthy state of the gut microbiota.

4. A review of the gut microbiota

4.1. gut microbiota

Gut *microbiota* is a diverse microbial ecosystem. There are many microorganisms in the animal gut, such as bacteria, viruses, archaea, unicellular eukaryotes, and so on. They are collectively known as gut microbiota, which are closely related to the health of individuals[11]. There are many types and quantities of the gut microbiota, and our human gut flora is a very complex ecosystem. The human gut harbors about 1,000 different bacteria, with about 150 times the number of total human genomes[12].The gut microbiota can affect the metabolism of organisms.. Its composition and function are not static and are influenced by dietary characteristics such as the type, amount and composition of lipids[13]. Dystregulation of gut microbiota will change its structure, composition, quantity and proportion, destroy the immune function of the lung, leading to disease susceptibility, the weakening of intestinal barrier function, make toxic bacterial metabolites into the circulatory system, and then accelerate the development of low-grade inflammation throughout the body. In addition, because the gut microbiota is considered a metabolic "organ", gut microbiota changes may lead to the relationship between the bacteria and the host, leading to metabolic disorders, metabolic syndrome (metabolic syndrome, MetS)[14], may be one of the predisposing factors for cardiovascular diseases such as hypertension, coronary heart disease and heart failure, as well as obesity, type I/II diabetes and IBD[15].

4.2. Gut microbiota and metabolic diseases

From the literature and reports published in these years, it can be seen that the relationship between metabolic diseases and gut microbiota has been explored more and more. In this section, we focus on the relationship between the gut microbiota and three common metabolic diseases.

4.2.1. Gut microbiota with type Ⅰ/Ⅱ diabetes mellitus

Diabetes is a chronic metabolic disease, the main clinical manifestation is the blood glucose index remained high for a long time, mainly autoimmune type I diabetes mellitus (T1D) and insulin-resistant type II diabetes mellitus (T2D)[16], With a high prevalence worldwide, it has become a common public health problem. Recent studies reveal that the gut microbiome plays a substantial role in the development of diabetes, and a correlation exists between them[17]. The composition of gut microbiota in patients with type I diabetes (T1DM) or type II diabetes (T2DM) changes, which may lead to intestinal leakage, antigen free entry into the digestive circulation system, trigger immune chain reaction, damage to pancreatic islet cells or cause metabolic disorders[18].

4.2.2. Gut microbiota and obesity

From Fig.1,obesity is a complex metabolic disorder phenomenon, which can be caused by genetic and non-genetic (such as environmental factors) and other factors together or alone[19]. Obesity is becoming more and more common worldwide, and its number and incidence are increasing year by year. In recent years, increasing evidence links obesity with gut microbiota. For adults, the characteristics of gut microbiota reflect the physiological characteristics and habits of individuals, including dietary preferences, lifestyle and metabolic status, and so on. By analyzing the characteristics of the gut microbiota, it may be possible to uncover the causes of metabolic disorders, including obesity. Children's gut microbiota is tending to mature, obesity and its causes in such people may affect their structure, and even their life[20, 21].

Fig 1. Plants affect weight loss through intestinal microflora.

4.2.3. Gut microbiota and inflammatory bowel disease

Chronic progressive inflammation of the gastrointestinal is the clinical manifestation of inflammatory bowel disease (IBD), in which Crohn's disease (CD) affects the colonic mucosa and ulcerative colitis disease (UC) affects the entire gastrointestinal tract, this leads to an increased risk of developing colon cancer. Different genetic, immune, and environmental factors may trigger inflammatory bowel disease (IBD). Recent observations have found that after the onset of IBD in patients, the gut microbiota is disturbed and multiple inflammatory responses occur at the gut barrier, resulting in impaired gut barrier integrity. This shows that the two are related. Under such adverse conditions, intestinal probiotics decrease due to weak competitiveness, resulting to increased pathogens, thus inducing the host immune response, and then these changes are reflected in the intestinal microecological destruction of intestinal epithelial function, which may also lead to the conversion of commercially available probiotics into pathogenic bacteria[22-24].

In short, this part introduces three metabolic diseases, understands how these three diseases are caused and elucidates the connection between gut microbiota and these three metabolic disorders, mainly focusing on the

relationship between three metabolic diseases and gut microbiota disorders. And from Fig. 2 and summarizing, this shows that metabolic diseases can have a direct impact on the intestinal microflora. In order to further explore whether food emulsifiers will have an impact on the status of the gut microbiota, let's look at the differences in daily dietary structure and the presentation of gut microbiota status in the following chapters.

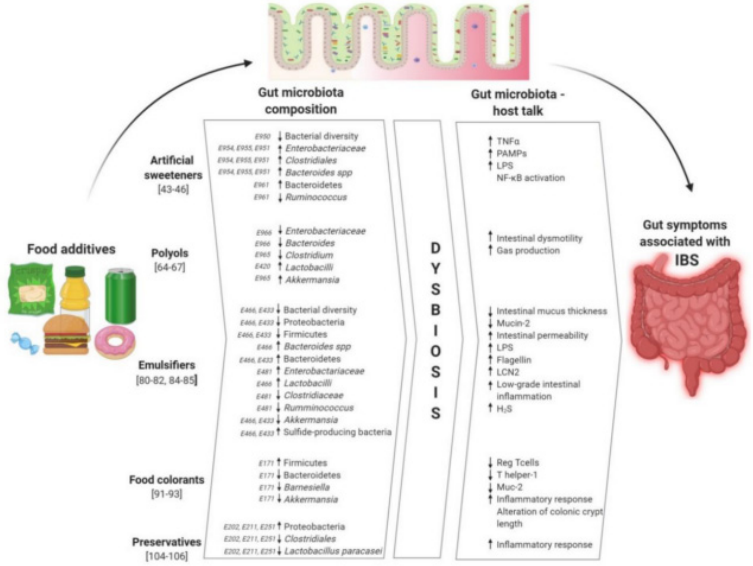

Fig 2. Food additives, gut microbiota, and inflammatory bowel disease (a non-exhaustive list of food additives).

4.3. Effect of diet on intestinal microflora

Daily Diet can regulate the status of gut microbiota, change its composition, structure, diversity and metabolism is closely related. Adjusting dietary strategies may potentially manipulate the diversity, composition, and stability of microorganisms. Therefore, a large number of dietary intervention trials have been conducted in the fields of nutrition and medicine, attempting to improve the host's condition and prevent disease by intervening in the gut microbiota ecology. According to the literature, dietary fiber and dietary compounds in dietary components contribute to the growth of gut microbiota, which can prevent cancer and promote human health. Among them, dietary compounds can interact with the intestinal microflora. The gut microbiota will metabolize dietary compounds, while dietary compounds can regulate their composition, structure, and function[25-27]. Dietary fiber is a kind of polysaccharide, from the chemical structure, it belongs to complex carbohydrates. It is neither absorbed by the gastrointestinal tract nor produces energy. But it will ferment under the influence of intestinal bacteria, producing SCFAs and other beneficial microbial metabolites. Dietary fiber is a source of nutrients for the gut microbiota and maintains the integrity of its barrier. There are experimental findings that in the absence of dietary fiber, the gut microbiota will use the mucus glycoprotein secreted by the host as a nutrient source, eroding the mucus barrier of the colon, resulting in increased epithelial access, prone to colitis, obesity, typeIIdiabetes and other metabolic disorders[28, 29]. Therefore, it can be concluded that diet can regulate mucosal barrier function, diet may participate in inflammatory response and immune function, and diet may help to shape the gut microbiotaand its metabolites[30].

Through the deep understanding and analysis of the gut microbiota, we know that the gut microbiota can be disordered; understand that metabolic diseases are the direct cause of the gut microbiota disorder; understand that the dietary structure can affect the gut microbiota, promote its shaping. Since the diet contains food emulsifier components, This suggests a connection between the two. Hence, in the subsequent section, we will delve into and assess the influence of food emulsifiers on the gut microbiota.

5. Effect of food emulsifiers on the gut microbiota

Over the past 15 years, the gut microbiota has attracted much attention due to their potential effects on various metabolic functions. However, recent research show that the consumption of food emulsifiers has increased rapidly in the past half century, and the topic of the influence of food emulsifiers on the composition and function of the gut microbiota has gradually attracted attention[31-33].

At present, many processed foods are added with emulsifiers to achieve preservation, thickening, solidification and other purposes. People will unconsciously absorb these emulsifiers, and according to previous studies on the relationship between food emulsifiers and the environment of the gut microbiota, both carboxymethylcellulose and polysorbate 80 can affect the composition and function of the gut microbiota. After many studies summarized, it was found that carboxymethyl cellulose and polysorbate 80 could significantly alter the microbiome diversity, increase the levels of Proteus and E. coli, and reduce Bacteroides and Clostridium spp. Alternatively, over time, carboxymethylcellulose and polysorbate 80 were found to cause the intestinal mucosal layer to become thinner than

before and more sensitive to exogenous compounds. The thinning of the mucosal layer can lead to bile acids and its complex difficult soluble bile acid permeability increase, lead to the change of bile acid spectrum and bile acid metabolism abnormalities, thus stimulate the gut microbiota become more toxic. To augment their motility and facilitate colonization of the epithelium, these microorganisms exhibit a greater capacity to adhere to the intestinal mucosa, penetrating deeply into the crypts. This enhancement of intestinal permeability intensifies the dissemination of inflammation, subsequently transforming the gut microbiota function into a proinflammatory state that predisposes individuals to metabolic syndrome and intestinal inflammatory diseases. Certainly, food emulsifiers are known to influence the structure and functionality of gut microbiota in a positive manner. For instance, they can lead to a decrease in the relative presence of the Clostridium order, particularly the Faecalibacterium genus, as well as the verrucosis microsporidian associated with Ackermania, a genus recognized for its anti-inflammatory effects. And, Research indicates that carrageenan influences the intestinal microbiome by diminishing the presence of the pro-inflammatory mucin-degrading bacterium Akkermansia muciniphila. However, some additives (such as lecithin) have not been found to have a significant effect on the gut microbiota.

6. Summary and Outlook

This paper collects the contents of common food emulsifiers in processing, production and safety of common food emulsifiers, and systematically discusses the gut microbiota from three dimensions: the meaningful nature of the gut microbiota, common metabolic diseases and diet. When evaluating the effect of food emulsifiers on gut microbiota, it is found that many studies show that several food emulsifiers will exacerbate the development of metabolic and inflammatory diseases through regulation and gut microbiota, while some food emulsifiers also have the function of preventing the disorder of gut microbiota. Some studies have even found differences in the results that even the same food emulsifier will act on the gut microbiota. The influencing factor for this result may be due to the different concentration of emulsifier; other components in the food, such as protein, carbohydrates, fat, etc., which may also affect the gut microbiota. When food contains multiple ingredients, the effect of emulsifier may be influenced by other components; the response to the same emulsifier may be different. In addition, factors such as individual physiological status and dietary habits may also affect the composition and function of the gut microbiota. Obviously, the effects of food emulsifiers on the intestinal microbiota still require continuous observation and research.

In the future, it is hoped that more studies will reveal the specific effects of food emulsifiers on gut microbiota, can further reveal the causes of metabolic diseases and find a convenient way to observe the changes of gut microbiota. And, the influence degree of food emulsifier on gut microbiota was evaluated in depth, and it was included in the safety evaluation standard of food safety.

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