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The Impact of Emulsifiers in Ultra Processed Foods on Intestinal Health, Exacerbating Non-alcoholic Fatty Liver Disease, and Intervention Strategies

Wenjing Xiao[1, *]

[1]College of Animal Science and Technology, Southwest University, Chongqing, China
*Corresponding author: xiao1215@email.swu.edu.cn

Abstract:

The damage of emulsifiers in super processed foods to intestinal health aggravates the impact of nonalcoholic fatty liver disease and intervention strategies. the incidence rate of nonalcoholic fatty liver disease remains high. Artificial emulsifiers (such as polysorbate 80 and carboxymethyl cellulose) are commonly used additives in the food industry. They can disrupt the diversity of gut microbiota, increase intestinal mucosal permeability, promote endotoxin entry into the bloodstream, activate the "gut liver axis", induce liver inflammation and lipid accumulation, and exacerbate the progression of non-alcoholic fatty liver disease. The research findings of this paper this article reviews the damage mechanism of emulsifiers on intestinal microbiota and intestinal barrier, elucidates their pathway of regulating the occurrence and development of non-alcoholic fatty liver disease through the "gut liver axis", and summarizes targeted intervention strategies such as improving diet and enhancing body metabolism, providing theoretical reference for the prevention and clinical management of non-alcoholic fatty liver disease.

Keywords: Ultra processed foods; emulsifiers; non-alcoholic fatty liver disease; gut microbiota.

1. Introduction

Ultra processed foods (UPFs) have the nutritional characteristics of high energy density and low nutrient density. They are ready to eat, delicious and palatable foods made by many complex industrial processes, adding sugar, oil, salt and a series of food additives such as essence, pigment, emulsifier, etc [1]. Food additives are a type of substance that is generally not consumed directly as food, but is added to food for a certain technical purpose, including but not limited to coloring agents, flavorings, preservatives, emulsifiers, etc [2]. In the era of rapid development in the food industry, the traditional dietary pattern characterized by unprocessed or minimally processed foods such as fresh vegetables and livestock meat is

gradually being replaced by various UPFs, and the global consumption trend of ultra processed foods is rapidly increasing [1]. Emulsifiers, as commonly used additives in UPFs, have the effect of improving the stability and texture of food. Although emulsifiers play an important role in the food industry, increasing research suggests that long-term intake of UPFs containing emulsifiers may have negative effects on human health, particularly on intestinal health and liver function.

As an important digestive and immune organ in the human body, the health status of the intestine directly affects overall health [2]. The gut microbiota is a complex, dynamic, and spatially heterogeneous ecosystem with core functions such as participating in the digestion and degradation of difficult to digest nutrients, regulating host energy metabolism, promoting the growth and development of various systems, and forming and maintaining immune capabilities [3]. The intestinal barrier is composed of intestinal epithelial cells, tight junction proteins, mucus layer, and intestinal microbiota, which together maintain the normal function of the intestine. Research has found that emulsifiers in UPFs can cause disruption of gut microbiota and disrupt the integrity of the intestinal barrier, thereby inducing activation of inflammation in intestinal tissue [2]. The liver is the central organ of human metabolism, and increasing evidence suggests that emulsifiers in UPFs are closely associated with the deterioration of intestinal health and the exacerbation of Fatty Liver Disease (FLD).

At present, the global incidence rate of FLD continues to rise, which has become a serious public health problem threatening human health. With the improvement of people's living standards, the number of FLD patients in China is constantly increasing. Surveys show that the prevalence of FLD among adults in China ranges from 15% to 47% [4]. Therefore, in-depth research on the impact of emulsifiers in UPFs on intestinal health and exacerbation of fatty liver, as well as intervention strategies, has important practical significance and clinical value. At the same time, further research and practice are needed on how to reduce the harm of emulsifiers to health through effective intervention measures, such as adjusting dietary structure and developing new food additives to replace emulsifiers. This article aims to comprehensively explore the mechanism by which emulsifiers in UPFs disrupt intestinal health and exacerbate fatty liver, based on existing research results. Corresponding intervention strategies will be proposed to provide scientific basis for the prevention and treatment of fatty liver and the improvement of public health.

2. Overview of Ultra Processed Foods, Emulsifiers, and Fatty Liver

2.1 Overview of Ultra Processed Foods and Emulsifiers

UPFs are ready to eat and delicious foods made through a series of complex industrial processes such as hydrolysis, hydrogenation, and pre frying, and the addition of food additives. UPFs have the nutritional characteristics of high energy density and low nutrient density, and are found in various foods such as sugary drinks, ready to eat sauces, breakfast cereals, heated ready to eat foods, processed meat products, distilled spirits, etc. The above definition is taken from the 2019 NOVA Food Classification System, which is the most widely used food processing classification system globally and has been recognized by the Food and Agriculture Organization of the United Nations (FAO) [5].

Emulsifier is one of the important food additives. Emulsifiers can significantly reduce the interfacial tension between oil and water phases, forming a stable emulsion of immiscible oil and water, making food more delicate, soft, and smooth, enriching the variety and taste of food, and also extending the shelf life of food. The application range of food emulsifiers is extremely wide, covering almost all fields of food processing, from daily bread, cakes, ice cream, to industrial meat products, dairy products, etc. Its usage accounts for 50% of the total amount of food additives used. However, with the widespread application of food emulsifiers in food processing, their potential health risks have gradually attracted people's attention [2]. At present, the commonly used emulsifiers in China mainly include more than 40 types such as glycerides, carboxymethyl cellulose, Tween, carrageenan, soybean phospholipids, and rapeseed phospholipids. Sodium carboxymethyl cellulose and polysorbate 80 are also widely regarded as emulsifiers with inflammatory effects. Research has found that carboxymethyl cellulose and Tween have long-lasting harmful effects on the composition and function of the gut microbiota, and 18 other tested additives also have similar effects [6].

2.2 Overview of Fatty Liver

FLD is a type of disease characterized by liver cell steatosis and fat accumulation caused by various reasons. FLD is divided into alcoholic fatty liver disease (AFLD) and non-alcoholic fatty liver disease (NAFLD) based on long-term excessive alcohol consumption [7]. FLD is reversible and can mostly return to normal after changing lifestyle and dietary habits. However, if not diagnosed early and

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intervened in a timely manner, it may develop into cirrhosis or even liver cancer [4].

The research results show that UPFs are associated with chronic diseases such as obesity, cardiovascular disease, and inflammatory bowel disease [1]. Related studies have also confirmed that obesity and lipid composition are important risk factors for the progression of NAFLD. Obesity increases the all-cause mortality rate of NAFLD and also increases the liver specific mortality rate of NAFLD patients. The results obtained from these studies are that UPFs can affect or even worsen NAFLD [8].

3. The Destructive Mechanism of Emulsifiers on Intestinal Health

3.1 Effects of Emulsifiers on Gut Microbiota

Although the impact of food emulsifiers on changes in body mass is still controversial, their effects on gut microbiota have been fully confirmed by animal experiments [2]. Naimi et al. observed the degree of influence of emulsifiers on maintaining the human gut microbiota in vitro in a micro bioreactor array model. They studied 20 commonly used food emulsifiers and analyzed the gut microbiota density, composition, gene expression, and pro-inflammatory potential (bioactive lipopolysaccharides and flagellar proteins) on a daily basis. It was found that carboxymethyl cellulose and Tween 80 had long-lasting harmful effects on the composition and function of gut microbiota. At the same time, the study showed that various emulsifiers such as carboxymethyl cellulose, Tween 80, lecithin compounds, diacetyl tartaric acid mono (di) glycerides, and glycerol compounds can significantly reduce lactobacilli. In addition, relevant studies have found that carboxymethyl cellulose may also affect gut microbiota through other mechanisms. After administering 100 μ l of 2% carboxymethyl cellulose sodium solution to Interleukin-10 (IL-10) knockout mice, bacterial overgrowth occurred in the intestinal tract, causing the villous spaces to widen and bacteria to adhere more to the intestinal mucosa, migrating towards the glandular crypts, leading to intestinal inflammation. These results all indicate that regular and excessive intake of carboxymethyl cellulose may lead to an imbalance in gut microbiota, thereby promoting the occurrence and development of intestinal inflammation [6].

3.2 Exploration of Emulsifier Induced Intestinal Inflammation

The damage of inflammation to the intestine has been extensively studied, and the pro-inflammatory effect of emulsifiers has been confirmed in many in vitro and animal experimental models [2]. Related studies have found that regular and excessive intake of carboxymethyl cellulose may lead to an imbalance in gut microbiota, thereby promoting the occurrence and development of intestinal inflammation [6]. Researchers fed mice with two commonly used emulsifiers mixed into their food, including polysorbate 80 and carboxymethyl cellulose. After extensive digestion of emulsifiers, changes in the composition of gut microbiota were observed, which further promoted inflammation. The altered microbiota has a stronger ability to digest and penetrate the dense mucus layer of the intestine, and leads to the expression of more flagella and lipopolysaccharides in bacteria, which can activate the immune system and activate the expression of pro-inflammatory genes. In mice with pre-existing immune system abnormalities, changes in gut microbiota can lead to chronic colitis. On the contrary, in normal immune system mice, changes in microbiota mainly induce mild intestinal inflammation and metabolic syndrome, characterized by increased food consumption, obesity, hyperglycemia, and insulin resistance [9].

It is worth mentioning that although there is sufficient epidemiological evidence to prove that the intake of UPFs by the population is positively correlated with the incidence of inflammatory bowel disease (IBD) [2]. However, in fact, in addition to emulsifiers, food additives such as preservatives, antioxidants, colorants and various synthetic essence are also added during the secondary processing of food. However, due to limitations in experimental samples and ethical requirements, it are still unable to determine whether the inflammatory effects it produces are entirely attributed to emulsifiers, and further improvement in experimental methods and conditions is needed for verification.

4. The Main Role of Impaired Intestinal Health in Exacerbating NAFLD

4.1 Intestinal Health Damage Exacerbates Liver Damage

At present, the etiology of NAFLD in clinical practice is not fully understood, but a large number of studies have confirmed that gut microbiota and intestinal inflammation play important roles in the occurrence, development, and prognosis of non-alcoholic fatty liver disease. In the intestine, probiotics and pathogenic bacteria such as Escherichia coli and Enterococcus maintain the balance of gut microbiota. Pathogenic bacteria have the ability to disrupt the intestinal mucosal barrier, while probiotics can

maintain intestinal mucosal safety. When the number of pathogenic bacteria increases and the number of probiotics decreases, the gut microbiota is disrupted, which can induce intestinal inflammation and damage the intestinal mucosal barrier [10]. Related studies have shown that when NAFLD patients experience an imbalance in gut microbiota and damage to the intestinal barrier, endotoxemia can stimulate the release of a large amount of inflammatory factors, triggering an inflammatory response within the liver and exacerbating the damage to liver cells [11]. At the same time, by damaging the liver through the gut liver axis pathway, the condition of NAFLD patients will also worsen, ultimately leading to liver function damage [10]. Relevant evidence also indicates that during the occurrence and development of NAFLD, due to the destruction of the intestinal mucosal barrier, intestinal permeability increases, and a large amount of harmful substances such as intestinal bacterial metabolites and components enter the liver through the portal vein. They will exacerbate the inflammatory response, oxidative stress, and lipid accumulation of the liver, thereby further exacerbating the degree of damage and fibrosis process of NAFLD [12].

4.2 Intestinal Health Impairment Leads to A Vicious Cycle of Metabolic Disorders

Metabolic syndrome (MS) is a complex metabolic abnormality syndrome characterized by obesity and insulin resistance (IR) [3]. Lipopolysaccharide (LPS) low-grade inflammation is the core of metabolic diseases such as obesity and insulin resistance, and obese individuals are in a mild chronic inflammatory state. After the death and dissolution of intestinal bacteria, LPS is released into the bloodstream to form metabolic endotoxemia, promoting the infiltration of inflammatory cells and the production of inflammatory factors in the adipose tissue of obese individuals. At the same time, gut microbiota can also activate the endocannabinoid system, increase intestinal permeability, raise plasma LPS levels, and exacerbate intestinal barrier disruption. LPS produced by gut microbiota imbalance can activate Xanthine Oxidase (XO) activity, which plays an important role in the mechanism of hyperuricemia [13], high uric acid can induce lipid metabolism disorders through IR, leading to fatty liver [4]. In pathological obesity, the increase in the tension of the cannabinoid system and LPS levels exacerbates the imbalance of fat production, leading to a vicious cycle [13].

Multiple studies have confirmed that, Body Mass Index (BMI), Triglycerides (TG), low-density lipoprotein cholesterol (LDL-C) and other indicators are closely related to the risk factors of fatty liver. Obesity and dyslipidemia can lead to abnormal accumulation of triglycerides in the liver. High blood sugar not only enhances insulin resistance (IR), but also stimulates insulin secretion, prompting the liver to synthesize more triglycerides and diglycerides (VLDL-C), ultimately leading to elevated triglyceride levels and accumulation in the liver, forming fatty liver. Conversely, fatty liver can exacerbate insulin resistance, forming a vicious cycle [4]. With the continuous deepening of research on metabolic syndrome, the academic community has gradually reached a consensus that the fundamental cause of metabolic syndrome may be chronic low-grade inflammatory response. Changes in lifestyle habits and environmental factors may alter the types, distribution, and proportion of gut microbiota, thereby affecting the concentration of metabolic products and intestinal permeability, leading to more inflammatory factors entering the bloodstream and inducing metabolic disorders [13].

5. Intervention Strategies for Emulsifier Related Fatty Liver

In daily life, consuming reasonable, moderate, or even less emulsifiers is the most direct intervention method. Patients should prioritize natural, unprocessed, or lightly processed foods such as fresh vegetables, fruits, whole grain lean meat, fish and shrimp, and plain nuts, which are almost free of artificial emulsifiers. When purchasing packaged food. Carefully review the ingredient list and avoid products containing common artificial emulsifiers such as polysorbate 80 and carboxymethyl cellulose (such as some pastries, fried foods, fast food soups, etc.). In addition, basic habits and adjustments can also help the liver restore metabolic function and alleviate inflammatory reactions. Patients can engage in moderate intensity aerobic exercise (such as brisk walking, jogging, swimming) every week to improve metabolism, which not only reduces liver fat content but also improves insulin resistance. It is worth mentioning that quitting smoking and drinking, as well as controlling the weight of overweight individuals, are also good ways. At the same time, it can also prevent the occurrence of diseases by regularly monitoring liver function and liver status, and if necessary, medical interventions can be used to assist. During regular check ups, liver function, blood lipid, blood glucose testing, as well as liver ultrasound examination should be performed to evaluate the degree of liver fat accumulation and damage.

6. Conclusion

Existing research has shown that artificial emulsifiers in UPFs, such as polysorbate 80 and carboxymethyl cellulose, exacerbate the occurrence and development of NA-

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FLD through the "gut liver axis" pathway by disrupting the integrity of the intestinal barrier and inducing dysbiosis of the gut microbiota. Specifically, emulsifiers can reduce the expression of intestinal tight junction proteins, leading to the entry of endotoxins into the bloodstream and activating liver inflammatory responses; Simultaneously altering the composition of gut microbiota (such as reducing beneficial bacteria and increasing pro-inflammatory bacteria), affecting liver lipid metabolism through metabolism, and promoting fat accumulation in liver cells. The current intervention research focuses on reducing emulsifier intake, improving human metabolism, and medical interventions, confirming that it can alleviate intestinal damage and liver steatosis, providing key evidence for the "gut liver" association in the study of NAFLD mechanisms.

Future research needs to further clarify the specific mechanisms by which different emulsifiers regulate the gut liver axis, and combine single-cell sequencing, metabolomics, and other technologies to analyze key signaling pathways; Simultaneously exploring personalized intervention plans, such as customizing probiotic combinations for different gut microbiota subtypes, or developing natural safe food additives that can replace artificial emulsifiers. In addition, it is necessary to further verify the clinical translational value of gut microbiota intervention in the prevention and treatment of emulsifier related NAFLD, providing new targets and practical basis for precise prevention and control of NAFLD.

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