Review

Individual Differences in Susceptibility of Dietary Emulsifiers

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Review

Individual Differences in Susceptibility of Dietary Emulsifiers

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Abstract

Dietary emulsifiers, common in processed and ultra-processed foods, improve food texture and shelf-life but may affect gut health by interacting with the microbiota and intestinal barrier. While emulsifiers have long been considered safe, growing evidence links their presence in ultra-processed foods to chronic disease risk. This review aims to evaluate the current understanding of the factors and mechanisms underlying individual differences in intestinal mucosal susceptibility to dietary emulsifiers. A search of PubMed and Embase through February 2026 identified eight relevant studies. Overall, the available evidence indicates a heterogeneous and highly individualized host response to dietary emulsifiers. These differences appear to be strongly influenced by the gut microbiota and its functional properties, while animal studies further suggest that host factors such as sex-related differences in microbial composition may also contribute to variability in response. Importantly, not all emulsifiers have the same effects, underscoring compound-specific impacts on gut physiology. The findings demonstrate that sensitivity to dietary emulsifiers varies substantially between individuals, challenging the long-standing assumption that these additives are universally safe. Given the multifactorial nature of this susceptibility, particularly the role of the gut microbiota, future research should adopt an integrative approach that combines microbial profiling with host genetics, immune responses, and early-life exposures. Such efforts will be essential to identify at-risk individuals and to inform more personalized dietary recommendations aimed at preserving intestinal health and reducing disease risk. Importantly, there is a clear need for larger, well-powered studies that can validate and expand upon these initial observations.

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1. Introduction

With the global rise in processed and ultra-processed food consumption, the intake of food additives has also increased drastically. Western dietary patterns are associated with a growing prevalence of health-related conditions such as obesity, diabetes, inflammatory bowel disease (IBD), and other chronic illnesses linked to diet. Most dietary advice focuses on excessive calorie intake, high sugar consumption, or high fat intake. However, the potential role of dietary additives is often overlooked or largely ignored.

Dietary emulsifiers are widely used food additives in processed and ultra processed foods that help improve texture, stability and shelf-life of foods [1]. Although they are considered non-toxic due to minimal absorption in the gastrointestinal tracts, emerging evidence suggest that these compounds can directly interact with the gut microbiota [2,3] and the intestinal barrier [4], potentially promoting low-grade inflammation and contributing to chronic inflammatory diseases such as inflammatory bowel disease and metabolic disorder [5–7].

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Especially their additive components, disrupt gut homeostasis through multiple interconnected mechanisms that mirror key features of inflammatory bowel disease (IBD). These additives can alter the gut microbiota, weaken mucus and epithelial barrier function, trigger endoplasmic reticulum stress, and activate inflammatory pathways, together sustaining the chronic, self-amplifying inflammation seen in IBD [8].

The intestinal barrier is a complex, multilayered system that balances nutrient absorption with protection against harmful substances. It is composed of a single layer of epithelial cells linked by tight junctions, overlaid by a mucus layer secreted by goblet cells, and monitored by underlying immune cells [9]. The barrier is intimately connected with the gut microbiota, which supports barrier integrity, regulates immune responses, and maintains microbial homeostasis. Disruptions in the microbial composition creates dysbiosis and can compromise the barrier function [10].

Experimental animal studies have shown that several commonly used dietary emulsifiers may negatively affect intestinal health. These include carboxymethylcellulose (CMC), polysorbate-80 (P80), carrageenan, lecithin and mono- and diglycerides of fatty acids (MDGs). Among these, CMC, carrageenan and P80 currently appear to have the strongest evidence for potentially harmful effects on the gut, while the effects of other emulsifiers appear to be less pronounced. Studies suggest that these compounds can disrupt the intestinal barrier, alter microbial composition, and increase mucosal permeability, which may contribute to intestinal inflammation [11–13].

Carboxymethylcellulose (CMC) is a water-soluble anionic polymer widely used as a thickener and emulsifier in processed foods. In animal models, CMC exposure has been linked to increased bacterial density, altered microbial gene expression, and disruption of epithelial cell proliferation, contributing to intestinal inflammation [14,15]. Polysorbate-80 (P80) is a synthetic non-ionic surfactant used in sauces, soups, and dairy products. Studies in mice have shown that P80 can disrupt the gut microbiota and the mucosal lining, increasing susceptibility to chronic intestinal inflammation [11].

Other emulsifiers have also been associated with microbiota alterations. Carrageenans, a family of sulfated polysaccharides derived from red seaweed, have been shown in animal models to promote colonic inflammation and alter innate immune cell activity [16]. In addition, in vitro studies have demonstrated that exposure to carrageenans can result in substantial changes in microbiota composition and function, consistent with a shift toward a more pro-inflammatory microbial profile [17]. Another class of emulsifiers, mono- and diglycerides of fatty acids (MDGs), is commonly used in foods such as bread and infant formula. For example, glycerol monolaurate (GML), a widely used MDG, has been shown in animal studies to decrease levels of Akkermansia muciniphila while increasing Escherichia coli, changes that were associated with features of metabolic syndrome [18].

Not all emulsifiers affect the intestinal microbiota or gut barrier in the same way. For example, an ex vivo MiniBioReactor study showed that soy lecithin, one of the most commonly used emulsifiers, did not significantly alter the gut microbiota, whereas sunflower lecithin led to a significant increase in flagellin levels, a marker associated with pro-inflammatory potential [17]. These findings highlight that different emulsifiers can have distinct biological effects.

In addition, it is important to recognize that there can be interindividual variability in the response to emulsifiers. In other words, the effects of emulsifiers can differ substantially between individuals. This variability is consistent with observations for other dietary additives, such as fibers and non-nutritive sweeteners, where the extent of microbiota changes and inflammatory responses depends strongly on a person's baseline microbial composition [19,20].

Therefore, this review aims to evaluate the current understanding of the factors and mechanisms underlying individual differences in the intestinal mucosal susceptibility to dietary emulsifiers. The research question is: What is the current understanding of the underlying individual differences in intestinal mucosal susceptibility to dietary emulsifiers?

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2. Materials and Methods

PubMed and Embase were searched from inception to March 2026 using the patient, intervention, comparison, outcome (PICO) framework. For the population (P), human studies, animal models, and in vitro and ex vivo systems were included. The intervention/exposure (I) comprised dietary emulsifiers, for which the search terms "dietary emulsifier" and "food emulsifier" were used. A comparison (C) was not considered relevant to the research question.

The outcomes (O) of interest were factors indicating changes in the intestinal mucosa. These included: (1) alterations in gut microbiota composition, (2) inflammatory and immune markers, and (3) intestinal mucosal integrity. Search terms related to these outcomes included "intestinal mucosa," "intestinal barrier," "microbiota," and "intestinal inflammation." Synonyms and related terms for each PICO element were also included; the full search strategy is provided in the appendix.

All retrieved articles were imported into an Excel file, and duplicates were removed through manual screening. Articles were initially screened by title and abstract to assess relevance to dietary emulsifiers. Records from both databases were then combined into a single Excel file, and duplicates were removed again. The remaining articles underwent further screening through abstract review and full-text assessment based on the inclusion and exclusion criteria (Table 1). In addition, the reference lists of relevant review articles and included studies were screened to identify additional articles, which were reviewed using the same criteria.

Table 1. Inclusion and exclusion criteria.

Inclusion criteria	Exclusion criteria
Experimental articles	Review papers (they were used to scan for more relevant papers)
Outcomes have to do with dietary emulsifiers	Does not discuss dietary emulsifiers
Mention of individualized susceptibility/ factors related to susceptibility/heterogeneity of outcomes/mechanisms that are related to susceptibility	No mention of individualized susceptibility/ factors related to susceptibility/heterogeneity of outcomes/mechanisms that are related to susceptibility
Article is available in full text	Article is not available in full text
Text is written in English	Text is written in another language
Articles show possible heterogeneity in data	Articles do not show possible heterogeneity in data

Following study inclusion, all selected articles were read in full and categorized according to their contribution to the research question. Studies were grouped based on the type of evidence they provided regarding susceptibility to dietary emulsifiers.

3. Results

Between January 2026 and March 2026 PubMed and Embase were searched. This was done using a search query with terms related to dietary emulsifiers, the intestinal barrier, sensitivity, genetics, and gut microbiota. The search identified a total of 494 articles. After initial screening of titles and abstracts for relevance to the research question and removal of duplicates, 76 articles remained. A few weeks later a second search was done with only the search terms 'dietary emulsifier' and 742 articles were found. These articles were also screened and an additional 17 articles were found.

All articles were entered into an Excel file, and the abstracts and the full texts, were examined in more detail. Twelve articles were selected based on the inclusion and exclusion criteria These articles were discussed and eight articles eventually seemed relevant for individual susceptibility to dietary emulsifiers (Table 2).

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When reviewing the articles relevant to the research question and examining the figures presented in their results, five studies demonstrate variability in responses to dietary emulsifiers [21–25]. Among these studies, three studies explicitly addressed this variability [21–23].

Table 2. Relevant articles and main findings.

Author, Year & Country	Sample/Population	Study Design	Variability measurement	Main findings
Kordahi et al., 2025. USA	Wild-type male mice N=60	Animal study	16S rRNA gene amplification and sequencing	CMC and P80 show variable effects on WT mice
Holder et al., 2019. USA	Mice N=6 (3 male and 3 female)	Animal study	16S rRNA sequencing	There are sex-specific differences in gut microbiota composition following emulsifier exposure
Rousta et al. (2021) USA	Mice N=3x7 to 8 mice	Fecal transplants	Shotgun metagenomic analysis (whole genome sequencing)	There is a variability in results of the effects of CMC and P80
Miclotte et al. (2020) Belgium	Fecal samples of human donors (N=10)	In vitro	16S rRNA gene amplicon sequencing	Some donors had consistently high susceptibility, some had some susceptibility, some low susceptibility
Rytter et al. (2025) France	Faecal samples from the 16 FRESH subjects (N=9 from the control group and N=7 from the CMC-exposed groups)	In vitro	MiniBioReactor Arrays	Microbiota functional markers rather than taxonomy alone are associated with emulsifier sensitivity
Wellens et al. (2025) Belgium	Humans N=60	Randomized placebo-controlled trial design	Within-group variation and fecal short-chain fatty acid concentration	There is within-group variation and interindividual variability in fecal short-chain fatty acid concentration over time
Chassaing et al. (2022) USA	Humans N=16	Randomized, controlled-feeding study	Intersubject variability in the response to CMC consumption	There is a clear difference in distance of bacteria from IEC, in fecal LPS and in Bray curtis distance between high sensitive and low sensitive individuals. There is no significant difference between changes of the fecal level of the inflammatory marker Lipocalin-2.
Daniel et al. (2024) USA	Humans N=16 IL-10 deficient mice	Randomized, controlled-feeding study	Intersubject variability in the response to CMC consumption	Genetics are not sufficient to account for inter-individual susceptibility to CMC in humans. Mice with microbiota from sensitive donors developed

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	intestinal inflammation. Mice with microbiota from insensitive donors were largely unaffected

Mouse Studies to Predict Human Responses

Kordahi et al. studied to which extent mucus-associated bacteria that encroach within the inner intestinal mucus layer are playing a direct role in driving chronic intestinal inflammation and associated metabolic dysregulations in their host when consuming P80 and CMC [24]. They found that dietary emulsifiers consumption alters microbiota composition and could induce a variable low grade intestinal inflammation that could be prevented by immunization with flagellin, a TLR5 agonist by inducing flagellin-specific IgA response. These studies were performed in wild-type mice, so it does not directly say something about interindividual effects in humans.

In another study Holder et al. identified sex-specific differences in gut microbiota composition following emulsifier exposure [26]. In male mice, emulsifier consumption generally reduced the abundance of the Firmicutes phylum and the genera Oscillospira, Coprococcus, and rc4_4, whereas in female mice it reduced the abundance of Bacteroides, Sphingomonadales, Sphingomonas, and Ruminococcus. Consumption of the emulsifier CMC increased the abundance of Dorea in males and increased Anaeroplasma in females. P80 consumption increased the abundance of Bacteroides, Burkholderia, Clostridium, and Veillonella in males, and increased the relative abundance of the Proteobacteria phylum as well as the genera Clostridium and Burkholderia in females. The authors reported that emulsifier treatment altered anxiety-like behaviors in male mice and reduced social behavior in females. They also observed changes in the expression of neuropeptides involved in regulating feeding, as well as social and anxiety-related behaviors. Multivariate analyses further showed that CMC and P80 produced distinct clusters of physiological, neural, and behavioral effects in male and female mice. The translational ability to the human is complex, but in general indicate that these dietary emulsifiers might be a specific perturbant of the gut-brain axis and altered behavior that differ in male and female.

Human (Experimental and RCT) and Humanized Mice Experiments

Rousta et al., studied the effects of CMC and P80 on colitis [25]. This study used the IL-10 deficient mice model in which fecal transplants of pooled IBD patients demonstrate a variable effect of CMC and P80 on gut microbiota abundance and composition, the Shannon-index shows a variability in results of the effects of CMC. P80 shows less variability in effects. CMC has a detrimental effect on colonic inflammation, much greater than P80.

Using in vitro fecal samples from 10 human donors, Miclotte et al. found that the effect of emulsifiers on short chain fatty acid production, microbial community and flagellin levels varied substantially between individual donors [21]. Therefore, the authors decided to rank the donors based on their sensitivity and identified that there were donors that had consistently a high susceptibility, donors that had some susceptibility and some donors that had consistently a low susceptibility to emulsifiers. Of note, the emulsifiers, especially some new developed ones, generated to satisfy the clean label movement demonstrated notable anti-microbial effects, making them not suitable to use.

Rytter et al. used an in vitro microbiota model (MiniBioReactor Array) to replicate and predict how each donor's microbiota responds to emulsifiers [28]. They try to predict the donor's sensitivity using the individual's baseline gut microbiota. Donor microbiotas that were predicted (based on metagenomic signatures) to be CMC sensitive showed large perturbations when exposed to CMC. Microbiotas predicted to be insensitive did not. Therefore, taxonomic composition alone was insufficient. Because of this, the authors applied metagenomic analyses and identified 78 functional markers associated with emulsifier sensitivity, largely present in Clostridium, Dorea, Coprobacillus, and Escherichia genera. These markers reflected the presence of specific metabolic pathways. The

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authors therefore suggest that microbiota functional (metagenomic) makers rather than taxonomy alone are associated with emulsifier sensitivity.

To study the effects of the different emulsifiers in human randomized controlled trials are a way to reliable study the effectivity of the effects of dietary emulsifiers. Wellens et al. did a randomized trial to study the effects of five dietary emulsifiers on inflammation, permeability, and the gut microbiome [23]. The population had sixty healthy participants and got either carboxymethyl cellulose, polysorbate-80, carrageenan, soy lecithin, native rice starch, or no additives administered through brownies. Results of within-group variability in week 2 and week 6 is shown for fecal calprotectin, LBP and fractional excretion of lactulose and mannitol. Some variability can be seen in this figure. Also, fecal short-chain fatty acid concentration at week 6 shows interindividual variability in the results. The authors suggest in the discussion that part of their results can be explained by "personal susceptibility to emulsifiers" that "might drive personal responses to emulsifiers".

Chassaing et al. showed that some individuals are more sensitive to CMC than others [22]. They performed a double-blind controlled-feeding study of the ubiquitous synthetic emulsifier CMC in which healthy adults consumed only emulsifier-free diets (n = 9) or an identical diet enriched with 15 g per day of CMC (n = 7) for 11 days. On average, bacterial-epithelial distance did not change over the course of the study in the control or CMC group. However, 2 individual subjects within the CMC group showed a marked reduction in this parameter, such that their biopsies showed bacteria in very close proximity to the epithelium following CMC exposure similar to observations made in patients with IBD. Their results suggest that some individuals may be prone to develop alterations in the host-microbiota interactions in response to CMC consumption. To examine this, they split the group into the 2 that were sensitive and 7 that were insensitive and compared these. This paper shows very clearly a difference in distance of bacteria from IEC, in fecal LPS and in Bray curtis distance between these two groups. It shows no significant difference between changes of the fecal level of the inflammatory marker Lipocalin-2 from day 0 to subsequent days.

Daniel et al. tried to explain the mechanisms of individual sensitivity to the observed dietary emulsifier CMC [27]. The Functional Research of Emulsifiers in Humans Corrected (FRESH) study, a randomized, double-blind, controlled-feeding assay, found significant changes in microbiota composition and fecal metabolome relative to control subjects. However, the response to CMC was very heterogenous. Specifically, 2 subjects were highly CMC sensitive in that they showed stark alterations in microbiota composition and developed microbiota encroachment, whereas other subjects were relatively insensitive to CMC. Therefore, they studied the mechanics of this sensitivity [27]. The authors initially hypothesized that variants in NOD2 and ATG16L1, two genes strongly associated with IBD risk, would be more prevalent in CMC-sensitive individuals. However, none of the CMC-sensitive participants carried NOD2 mutations, and ATG16L1 variants were equally distributed between CMC-sensitive and insensitive groups. To explore alternative genetic explanations, the authors assessed baseline intestinal gene expression using RNA sequencing. They found that overall gene expression profiles were nearly identical between sensitive and insensitive individuals. Therefore, the authors suggested that genetics are not sufficient to account for inter-individual susceptibility to CMC in humans, and that there are non-genetic or dynamic factors that may play a more important role.

After looking at genetic variation as a determinant of CMC-sensitivity, the authors transplanted fecal microbiota from CMC-sensitive and CMC-insensitive human donors into germ-free IL-10–deficient mice. Upon CMC exposure, mice colonized with microbiota from sensitive donors developed marked intestinal inflammation, including microbiota encroachment, immune cell infiltration, and tissue pathology. In contrast, mice receiving microbiota from insensitive donors were largely unaffected.

4. Discussion

This review included eight studies examining individual susceptibility to dietary emulsifiers. Understanding the mechanisms of susceptibility is particularly important given the widespread

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presence of dietary emulsifiers in Western diets. For example, a large cohort study by Chazelas et al. demonstrated that chronic exposure to food additives is common, with 48 additives consumed by more than 10% of participants, several of which have been linked to adverse health effects in experimental studies [29].

Across five studies, evidence consistently indicates a clear variation in sensitivity to dietary emulsifiers. Two studies demonstrated this effect in mice [21,24], while three studies reported similar findings in humans [22,23,27]. Miclotte et al. categorized sensitivity into three phenotypes following emulsifier exposure: high, intermediate, and low susceptibility [21].

Daniel et al. identified baseline gut microbiota as a key factor underlying this variability in susceptibility to dietary emulsifiers [27]. Supporting this, Rytter et al. showed that when baseline microbiota is incorporated into predictive models, it consistently emerges as the strongest predictor of individual responses to dietary emulsifiers [28].

Mechanistically, emulsifiers reduce the spatial separation between the gut microbiota and the intestinal epithelium. This results in bacterial encroachment into the mucus layer and increased exposure of epithelial and immune cells to microbial antigens [30]. While emulsifier exposure induces some taxonomic shifts in the microbiota, functional analyses indicate that susceptibility is more accurately predicted by microbial traits such as flagellin expression, motility, mucolytic activity, and pro-inflammatory signaling capacity [24,28].

This might explain why individual responses differ: the composition and functional characteristics of a person's gut microbiota largely determine how they react to emulsifiers. Some individuals harbor microbial communities that are more prone to inflammatory or disruptive responses, increasing their risk of intestinal inflammation or metabolic disturbances, while others remain relatively unaffected.

In addition to host–microbiota interactions, it also matters what type of emulsifier is consumed, since not all emulsifiers have the same impact. For example, suggests that while carboxymethylcellulose (CMC) and polysorbate 80 (P80) can have strong effects, others like soy lecithin may not significantly impact the gut microbiota [17].

Furthermore, biological sex can also contribute to variability in emulsifier susceptibility. Holder et al. reported sex-specific differences in microbiota composition and inflammatory responses to emulsifier exposure, with male and female mice exhibiting distinct bacterial taxa and immune profiles [26]. These findings suggest that hormonal and immunological differences between sexes may further contribute to individual responses to dietary emulsifiers.

Regarding host genetics, relatively few studies have examined the role of genetic predisposition in susceptibility to dietary emulsifiers. Variants in the NOD2 gene are well-established risk factors for Crohn's disease [31]. However, no significant association has been observed between NOD2 mutations and sensitivity to carboxymethylcellulose (CMC) in humans [27]. When further studying other genes and whether they could explain susceptibility to emulsifiers, Daniel et al. also found no correlation, thereby suggesting that genetic susceptibility to inflammatory bowel disease does not necessarily translate directly to susceptibility to dietary emulsifiers [27].

Beyond intrinsic host factors, environmental factors might also interact with dietary emulsifier exposure and should be considered in future research. A prospective study of first-degree relatives of individuals with Crohn's disease demonstrated that early-life and current environmental exposures influence future disease risk [32]. More broadly, environmental factors such as diet, smoking, urbanization, pollution, vitamin D status, and microbial exposures are known to interact with genetic susceptibility and dysbiosis to modulate inflammatory bowel disease risk [33].

A limitation of this review is that much of the available data is based on relatively small studies. As a result, findings should be interpreted with caution, as they may not fully capture the complexity and variability of individual responses to dietary emulsifiers. To strengthen the evidence base, there is a clear need for larger, well-powered studies that can validate and expand upon these initial observations. Such research will be essential to generate clinically relevant insights into individual

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susceptibility to emulsifiers and to better understand how these findings can be translated into meaningful dietary recommendations and health outcomes.

5. Conclusions

This scoping review demonstrates that sensitivity to dietary emulsifiers varies between individuals, challenging the long-standing assumption that these additives are universally safe. Growing evidence links the consumption of ultra-processed foods, often rich in emulsifiers, to an increased risk of chronic diseases. As most studies on this topic have emerged only recently, the field is still developing, but current findings highlight the importance of understanding why some individuals are more susceptible than others.

Given that this susceptibility is influenced by multiple factors, particularly the gut microbiota and its functional properties, future research should adopt an integrative approach. Combining microbial profiling with host genetics, immune responses, and early-life exposures will be essential to identify individuals at higher risk and to develop more personalized dietary recommendations aimed at maintaining intestinal health. Importantly, there is a clear need for larger, well-powered studies that can validate and expand upon these initial observations.

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Abbreviations

The following abbreviations are used in this manuscript:

IBD	Inflammatory bowel disease
PICO	patient, intervention, comparison, outcome

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