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Fermented dairy
exploring the health benefits

Summary points

- Fermented dairy products, such as cheese, yogurt and kefir, have long been recognised for their health benefits. They are produced by the microbial fermentation of milk and several hundred varieties exist depending on the initial substrate, the microorganisms present and the conditions employed. This gives rise to a variety of textures, flavours, bioactive compounds and an enhanced nutritional composition.
- The molecules that impart the physiological effects of fermented dairy include vitamins, conjugated linoleic acid, oligo and exopolysaccharides, gamma-aminobutyric acid, short-chain fatty acids and bioactive peptides. Consumption of some of these foods can still have a beneficial impact on the gut microbiome, even when there are no live microbes remaining in the food itself. For example, fermentation of lactose results in the formation of prebiotic oligosaccharides, which can stimulate beneficial bacteria in the large intestine.
- Most of the health benefits related to fermented dairy are mediated by modulating immune responses such as inflammation and pathogen defence, mainly through the gut microbiome. Consumption has been associated with reductions in immune dysfunction and pro-inflammatory states, which relate to cancer, type 2 diabetes, cardiovascular disease and obesity. In addition, live yogurt cultures can improve digestion of lactose in yogurt, which helps those with lactose intolerance to enjoy the benefits of dairy.
- Novel research on kefir has improved current understanding of the molecules that are produced during fermentation and their resulting biological impact. Food for Health Ireland researchers are currently exploring how such bioactives may improve glycaemic control and could, therefore, play a role in managing related conditions.

EDITORIAL

As part of the current trend towards fermented foods, there has been a surge in the popularity of various fermented milk products, such as kefir.

Fermentation of dairy has been practised for thousands of years and is one of the oldest methods of extending the shelf life of milk. Beyond this, associated health benefits have also been recognised and research continues to deepen the understanding of how these foods impact a range of health parameters.

In this edition of *DN Forum*, scientists from Food for Health Ireland (FHI) explore the role of fermented dairy in health, with an overview of the literature and a synopsis of some novel FHI research in this area. Research into fermented dairy forms one of the key pillars of the new FHI 3 project that was launched this year and is outlined on page 4.

We hope you enjoy this edition of *DN Forum* and look forward to any feedback or comments you wish to share: nutrition@ndc.ie

Dr Marianne Walsh
Nutrition Manager,
The National Dairy Council (NDC)

Health benefits of fermented dairy

Dr Veronica L. Peterson, Post-Doctoral Researcher, Teagasc Food Biosciences, Moorepark, Co. Cork and **Dr Paul D. Cotter**, Senior Principal Research Officer and Head of Department, Teagasc Food Biosciences, Moorepark, Co. Cork


Dr Veronica L. Peterson


Dr Paul D. Cotter

Introduction

Fermented dairy is a staple food for many cultures around the world. Indeed, the first record of fermented milk consumption in Ireland dates back to the Neolithic period[1]. The fermentation of milk began as a means of food preservation by converting carbohydrates, particularly lactose, to lactic acid, which prevents the growth of spoilage- and disease-associated microorganisms. The safe and frequently health-associated lactic acid bacteria (LAB), such as the bacterial genera *Lactobacillus*, *Leuconostoc* and *Streptococcus*, are responsible for this conversion and are typically the dominant microorganisms in dairy fermentations[2]. Common commercial fermented dairy products available in Europe include cheese, yogurt, kefir, buttermilk, sour cream and crème fraîche. Through this microbial fermentation of milk products, many health-promoting molecules are released, such as vitamins, bioactive peptides and fatty acids.

The health benefits from consuming fermented dairy products have been recognised for some time; in the early 1900s, Élie Metchnikoff was one of the first scientists to suggest that yogurt may have health benefits, based on observations of increased longevity in certain Bulgarian populations that consumed high levels[3]. Research has focused on exploring this phenomenon with the aim of understanding the mechanisms and harnessing the bioactive molecules for their potential use as functional ingredients. Additionally, the growing research of the gut microbiome and its role in health has reinvigorated investigations of the potential biotherapeutic capability of 'live' fermented dairy products[2,4].

Research into the beneficial health effects of fermented dairy products has indicated that they can reduce inflammation and modulate immune response[5,6]; reduce the risk of cardiovascular disease (CVD) and cancer[4,5,6]; protect the body against disease-causing microorganisms[2,5]; increase the nutritional value of milk and nutrient utilisation[5,6]; have a beneficial effect on hunger/satiety signalling hormones and metabolism[2,6]; and can promote a healthy brain and digestive tract[2,6], among other benefits (**Figure 1**). Bacterial strains associated with fermented dairy have been shown to confer seizure protection in animal models exploring the mechanisms that underly the neuroprotective effects of the ketogenic diet in refractory epilepsy[7]. Effectiveness of fermented dairy has also been demonstrated in models of weight loss and type 2 diabetes (T2D)[2,8].

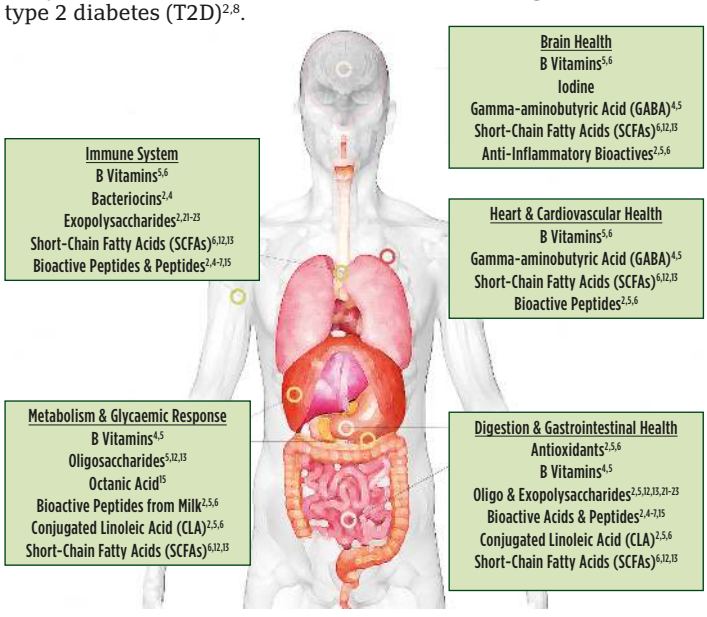

Figure 1: Components of fermented dairy and their associated health benefits.

This article gives an overview of fermented dairy, examining both the existing and emerging research around its impact on health.

Fermented dairy

The nature of fermented dairy products varies depending on the starting product used, which can include cream, whole or reduced-fat milk, or result from by-products of other dairy productions, as is the case for buttermilk. There are a wide range of fermented dairy products available globally, but for the purpose of this review, those that are most commonly consumed in Ireland, such as yogurt and kefir, are discussed here (cheese has been addressed in previous editions: Vol 6[2] and Vol 7[3]). Indeed, much of the fundamental knowledge about the health-promoting effects of fermented dairy comes from research on yogurt preparation and consumption[9]. Commercial yogurt is usually a simple culture of a few LAB, mainly *Lactobacillus spp* and *Streptococcus thermophilus*. However, there are a wide range of yogurt preparations available, each with variations in nutritional content and biotherapeutic potential. Buttermilk is a frequently fermented, side-product from butter production and is regarded as a low fat and high nutrient alternative to conventional milk. In Ireland, buttermilk is predominantly used in baked goods due to its high content of lactic acid that reacts with sodium bicarbonate, to create carbon dioxide in products such as soda bread.

Kefir is gaining popularity in artisanal and conventional Irish markets. Similar to Metchnikoff's observations of Bulgarian yogurt, consumption of kefir is traditionally associated with improved health and long life[10]. Kefir is a unique, fermented dairy product, in part due to its complex microbial composition, containing LAB and yeasts, as opposed to strictly bacterial dairy fermentations. Depending on the initial substrate, the microorganisms present, other ingredients and the conditions employed, different fermented dairy products produce a variety of textures, flavours and nutritional ingredients to suit a variety of tastes and dietary preferences.

Molecules produced by fermented dairy

Microbes involved in fermentations can be rudimentarily viewed as 'bags of enzymes', providing a means of controlled microbial growth, which produce compounds that preserve the food, change its taste and enhance the health benefits. Vitamins, conjugated linoleic acid (CLA), oligo and exopolysaccharides, gamma-aminobutyric acid (GABA), short-chain fatty acids (SCFAs), and bioactive peptides are all examples of molecules resulting from microbial fermentation of diary[11]. A summary of health benefits related to these molecules is outlined in **Table 1**.

CLA is created by LAB from unsaturated fats present in milk and confers health benefits, such as anti-inflammatory, antioxidant, and anti-atherosclerotic[2,5] properties. Additionally, CLA has been shown to have antihypertensive effects due to angiotensin-converting enzyme (ACE) inhibition[2,4]. A number of other dairy bioactives, such as GABA, have also been shown to have protective effects, including antihypertensive properties[4,5]. SCFAs include propionate (conjugate propionic acid), butyrate (conjugate butyric acid), and acetate (conjugate acetic acid). SCFAs have been linked to reduced inflammation[12] and reduced risk of human disease, such as colon cancer[13]. Essential B vitamins present in fermented dairy which are important for overall health include, B12, folate and other conjugates of folic acid, biotin and riboflavin[5,6].

The molecules produced in fermented dairy products reflect the microorganisms present[2]. LAB produce lactic acid while *Acetobacter* are predominantly involved in the production of acetic acid. *Lactobacillus*, as a frequently dominant LAB, is involved in lactic-acid production, as well as the production of carboxylic acids, esters and ketones. Lactic and acetic acids are the major acids present in dairy ferments and are also major contributors to ferment preservation, as these acids prevent growth of pathogenic bacteria[11]. *Propionibacterium spp.* produces propionate, CO_2 and

acetate. The yeast *saccharomyces* is predominantly attributed to the production of esters that contribute to flavour.
In addition to the health-associated compounds referred to above, some flavour molecules produced by the fermentation process are also beneficial to health. Curiously, several molecules associated with an unpleasant flavour are known to have health benefits. Octanoic, decanoic, and nonanoic acids are all associated with a 'goaty' or 'cheesy' smell[14]. Octanoic acid (also known as caprylic acid) is linked to satiety/hunger regulation, gastric emptying, weight loss, and is also used as an antimicrobial[15]. Decanoic (also known as capric or decylic acid) and nonanoic acid have been shown to exert the antiseizure effects associated with the clinical ketogenic diet, which is used for some patients with epilepsy[7].
Pleasant flavours are also produced from dairy fermentations. These include fruity flavours, such as pineapple (ethyl hexanoate and ethyl butanoate) and banana (3-methyl-butanol and 2-heptanone). Interestingly, 3-methyl-butanol is also one of the flavour components in the highly valued black truffle fungi.

Molecule Class	Molecule Name	Associated Health Benefits	Reference
Bioactive Acids	Lactic Acid	Antimicrobial, anti-inflammatory, antioxidant	[2, 5]
	Octanic Acid	Hunger/satiety regulation, antimicrobial	[15]
	Decanoic & Nonanoic Acid	Antiseizure	[7]
	Gamma-aminobutyric Acid (GABA)	Antihypertensive, Anxiolytic	[4, 5]
	Conjugated Linoleic Acid (CLA)	Anti-inflammatory, antioxidant, anti-cancer, cardiovascular health, immune regulation	[2, 5, 6]
Bioactive Peptides	Bacteriocins	Targeted defense from pathogens	[2, 4]
	Bioactive peptides from milk proteins	Antioxidant, immune modulatory, glycaemic & body mass regulation, nutrient absorption, cardiovascular health	[2, 5, 6]
Vitamins	Folic Acid and Folate, B12 (cobalamin), Biotin, Riboflavin	Nutrient utilisation, improved metabolism, glycaemic & body mass regulation, brain and cardiovascular health, essential nutrients for overall health	[5, 6]
Short-Chain Fatty Acids (SCFAs)	Butyrate, Acetate, Propionate	Anti-cancer, anti-inflammatory, gastrointestinal and brain health, reduced risk of cardiovascular disease (CVD)	[6, 12, 13]
Oligo & Exopolysaccharides	Exopolysaccharides	Immune regulation	[2, 21-23]
	Oligosaccharides	Promote healthy gut microbiome	[5, 12, 13]

Table 1: Molecules present in fermented dairy products and their associated health benefits

Overview of health benefits of fermented dairy

Pre-digestion

The enzymatic process of microbial fermentation releases molecules that are easily digested, including vitamins, peptides, and organic fatty acids. These enzymatic processes, carried out by bacteria before human consumption, allow easier digestion of nutrients in the gut, and also create bioactive peptides that bind to essential vitamins and trace elements to promote their absorption. Fermented dairy products are also well tolerated by those with lactose intolerance; thus, these products can provide the health benefits associated with dairy to those unable to consume the unfermented product. Furthermore, the European Food Safety Authority (EFSA) has approved the following health claim relating to yogurt with live cultures: 'Live yogurt cultures can improve digestion of yogurt lactose in individuals with lactose maldigestion'[16].

Beneficial fermented products

A considerable amount of research relating to fermented dairy products has shown that consumption of these products can reduce the risk of cardiovascular disease, associated with reduced cholesterol[2,4,6]. It has also been indicated that fermented dairy may modulate immunological responses[2,4,5]. This includes not only reducing inflammation, but also contributing to the development of an appropriate immune response against pathogens. Furthermore, consumption of fermented dairy products has been associated with reductions in immune dysfunction and pro-inflammatory states related to cancer, type-2 diabetes, cardiovascular disease, obesity and other diseases[2,5,6].
Microbes involved in the fermentation of dairy produce antimicrobial and antioxidant compounds that, in addition to protecting the food product from pathogens and toxins[2], can also protect the host. Antioxidants are molecules that neutralise reactive oxygen species (ROS), such as peroxides, to a more stable, less biologically harmful compound. Antimicrobial compounds are major contributors to food preservation and include bacteriocins[2]. Indeed, selective culturing and evolution of LAB have resulted in the production of safer and healthier food products.

Benefit of live biotherapeutic products in dairy ferments

Although the reported benefits associated with the use of some live biotherapeutics in fermented products is increasing, strict regulation is in place to ensure that these claims are thoroughly validated. Many commercial fermented dairy products undergo a process, such as pasteurisation, which kills the bacterial cultures responsible for fermentation, though live biotherapeutic (probiotic) strains may be added after this process. The EFSA has stated that "live biotherapeutics must survive the gastrointestinal (GI) tract and be resistant to gastric juices, bile, as well as being beneficial to the host, which includes being non-pathogenic, protecting against pathogens, and free of antibiotic resistance genes".
The consumption of fermented dairy can still have a beneficial impact on the gut microbiome, even if there are no live microbes present in the food product. For example, recent research has indicated that the beneficial effects of a ketogenic diet, when used as a clinical intervention to reduce the risk of neurodegeneration, may be mediated through the microbiome[17]. Molecules produced by dairy fermentation that are not immediately digested can go on to promote the growth of beneficial bacteria in the gut, such as *bifidobacterium* and *akkermansia*, which in turn influence host biological processes[2,18,19]. *Akkermansia muciniphila* inhabits the mucosal layer close to the intestinal tissue and its presence has been shown to have beneficial impacts on host health[7,17,20].
LAB fermentation of lactose results in the formation of prebiotic oligosaccharides, such as galacto-oligosaccharide. Such prebiotics in the GI tract are fermented by beneficial bacteria and lead to the production of the aforementioned SCFAs. Some of the anti-inflammatory and immune-regulatory effects from fermented dairy are linked to beneficial bacteria in the gut microbiome. Regulatory T cells modulate the immune system and are capable of producing an anti-inflammatory response. Research suggests that gut bacteria influence these immune regulatory cells in the intestine by a mechanism of action through polysaccharide A and SCFAs[12,21,22,23].

Novel Irish research

Investigations of kefir

Novel Irish research led by Dr Paul Cotter has focused on the microbiology, metabolism and health benefits of milk products, including kefir as a representative fermented dairy product. Recently published work has shown that the flavour created by secondary molecules present in kefir is dependent on the microbes present in the original kefir grain and the stage of fermentation[14]. *Lactobacillus kefiranofaciens* is dominant at the early stages of fermentation and is associated with esters and ketones, which give cheesy and fruity flavours. *Leuconostoc mesenteroides* is more abundant in the later stages and is associated with acetic acid and 2,3-butanedione, which give vinegary and buttery flavours respectively[1]. Furthermore, it was demonstrated that certain kefir products are capable of reducing weight gain and associated biological measures in rodents fed a high fat diet[8]. Serum cholesterol was also improved in the rodent model[8]. This aligns with other research that kefir and kefir-derived peptides are capable of remediating fatty liver disease due to impairments in intestinal permeability related to obesity[2,4,6].

Metabolism and glycaemic response

Investigation of how gut microbes alter nutrient availability and host metabolism is one of the key aspects of understanding the role of fermented dairy in glycaemic control. Research into the metabolic effects of the gut microbiome has been explored in diabetes[24,25], body weight[24,25,26] and exercise[27,28]. Indeed, certain gut microbes are capable of influencing various metabolic pathways, including neutralisation of ROS[7], glycolysis and gluconeogenesis[19,24]. A new research programme by Food for Health Ireland has spearheaded investigations into the bioactive properties of fermented dairy and how these bioactives may be utilised to improve glycaemic control. This research aims to inform the dairy industry, so that functional products can be designed that could potentially play a role in the reduction of type-2 diabetes and obesity.

Conclusion

Fermented dairy has been an integral part of the human diet for thousands of years and evidence continues to support its place as a part of a balanced, healthy diet. Dairy fermentation results in the alteration of biomolecular characteristics of food through microbial-mediated enzymatic processes. LAB fermentation of milk results in enhanced nutritional value and production of bioactive compounds that confer health benefits. Novel research is underway to harness these health-promoting molecules and provide further understanding of the health effects.

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Launch of FHI 3

Food for Health Ireland has just launched the third phase of its research development, FHI-3. Involving a multi-location, multi-partnered, multi-disciplinary research centre, the aim of the work is to improve health through innovation in food, primarily dairy. The research focuses on key areas of health such as cardiovascular health, gut health, maternal health and healthy ageing. These are investigated under the categories of dairy fermentates, grass-fed dairy and cheeses.

For more information visit www.fhi.ie

New Resource

The National Dairy Council has produced a new consumer booklet on '*Common Dairy Myths*'. The booklet covers a range of topics, addressing misconceptions around nutrition, animal welfare, dairy processing and sustainability.

It can be downloaded from www.ndc.ie or a limited number of copies may be ordered by contacting hello@ndc.ie

Contact us...

The National Dairy Council (NDC)

The National Dairy Council
The Studio, Maple Avenue,
Stillorgan, Co. Dublin, Ireland
+353 (0)1 290 2451
info@ndc.ie | www.ndc.ie

NDCIreland @NDC_ie

Mission: To deliver real and unique value to Irish dairy farmers by protecting and promoting the image, quality, taste and nutritional credentials of Irish dairy produce to a wide variety of audiences in a clearly defined, focused and effective manner.

Food for Health Ireland (FHI)

Food for Health Ireland
Science Centre South,
University College Dublin
Tel: + 353 (0)1 716 2391
fhi@ucd.ie | www.fhi.ie

Food for Health Ireland @fhi_phase3

Mission: To leverage the world-class capabilities of the Irish academic partners, with the market expertise of the industry partners, into a pipeline of innovative, nutritional functional ingredients/products for the global food industry.