

## Probiotics: History and Evolution

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### Introduction: Probiotics and Fermentation

Probiotics are viable microbial species, which are ingested for the purpose of altering the gastrointestinal flora in a manner, which confers health benefits. Currently available probiotic products include a wide array of bacterial and fungal species which are consumed in a variety of preparations. The use of microbials originated (unintentionally) centuries ago when people first noted the beneficial health effects of eating fermented foods. Modern probiotic-containing foods and products are the direct derivatives of these early fermented foods. The use of fermented milk and yogurt are the part of human history and their role has been with humanity, to date, between legends and historical data [1]. The present review outlines the origins of probiotic-containing foods and our subsequent refinement of these biologic agents.

Fermentation is the metabolic process by which an organism converts a carbohydrate, typically starch or a sugar, into an alcohol or an acid. These metabolic byproducts lower pH and have a host of other effects that prevent spoilage of fermented foodstuffs. The term fermentation is derived from *fermentum*, the Latin word for boiling. The name came from the observation that mixtures of crushed grapes kept in large vessels produced bubbles, as though they were boiling. While no one knows precisely when man began to use the fermentation process it is agreed that it is an ancient tool for preserving foods. Many believe the only older method of food preservation is dehydration. There is strong evidence to suggest that the art of fermentation originated in the great Indus Valley civilization. Several artifacts suggest that fermentation was known from the ancient times in Egypt and the Middle East [2]. The earliest recordings of fermentation date back as far as 6,000 B.C. in the Fertile Crescent region of lower Mesopotamia between the Tigris and Euphrates rivers [3]. Traditional Egyptian fermented milk products, Laban Rayeb and Laban Khad, were consumed as early as 7000 BC [4].

While serendipity probably played a major role in the genesis of fermentation, the process became popular not only because it preserved food, but also because it provided a variety of tastes and may have improved digestion or had other perceived beneficial effects. It was propagated through subsequent generations in the form of oral communication. By the middle ages, people were consuming a wide variety of fermented foods and drinks depending on raw materials, environmental conditions, and local taste preferences (Table 1).

### Fermented Milk

Man began domesticating animals in Asia and/or northeast Africa somewhere between 8,000 and 5,000 B.C. The Vedic hymns of India, written before 2,000 B.C., indicate that Hindu people used fermented milk products in their diet since prehistoric times [5]. Between 2,000 and 3,000 B.C. a multitude of other civilizations (the Egyptians, Greeks and Romans) left many records to indicate that milk, cheese, and butter were commonly used [6]. As an example, Sumerians crossed expanses of deserts with milk carried in bags made from the stomachs of sheep. The enzymes present in the stomach wall fermented the milk into

curd which improved the taste and shelf-life. The Bible, dated to the thirteenth century B.C, reports that "Abraham offered to God, showed in an oak wood, fermented milk" (Genesis 18, 1-8). During this time almost every civilization regularly ingested fermented milk products for its taste and health benefits. Geographic separation and cultural differences resulted in a variety of names used to describe these similar compounds (Table 2). Credited with saying "All disease begins in the gut" the Greek physician Hippocrates considered fermented milk both a food product and a medicine with the potential to cure intestinal disorders. Plinius, the Roman historian, stated that fermented milk products could be used for treating gastroenteritis [7].

### Fermented Vegetables

Nearly every civilization has developed food fermentation of some type. The peoples of Japan, China and Korea have relied heavily on fermentation as a pickling agent for cabbage, turnip, eggplant, cucumber, onion, squash and carrots over the centuries. Records in China document that cabbage has been fermented for over 6,000 years.

Commonly Used Fermented Foods
Bread
Milk and Cheese
Vegetables
Beer and Wine
Sausage
Chocolate
Soy sauce

Table 1: Different fermented food used in various civilizations.

Fermented Milk Product	Country
Kumiss	Mongolia
Kefir	Balkan
Taettemjolk	Scandinavia
Zabadi	Egypt
Doogh	Iran
Dahi	India
Koumiss	Russia
Cieddu	Italy

Table 2: Different names given to fermented milk in various parts of the world.

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Fermented vegetables were regularly provided to Chinese workers during the construction of the Great Wall of China (around 300 B.C.) to promote their health and well-being [8]. Several Roman texts document consumption of sauerkraut – a lacto-fermented cabbage – describing both its “delicious taste” and its medicinal properties. The Roman Emperor Tiberius regularly carried sauerkraut on his long voyages to prevent intestinal disorders. Nearly 2,000 years later, Captain James Cook and his crew similarly consumed sauerkraut on their long voyages to prevent illness (scurvy) [9].

## Bread

The first records of bread-making are contained in ancient Egyptian hieroglyphs [3]. Egyptians discovered that if dough was left untreated for several hours prior to baking, the resulting bread became airy and lighter. They attributed this phenomenon to a divine process rather than fermentation [3]. As Egyptians conquered more lands and expanded their empire this practice spread to other cultures. The Romans are known to have used yeasts collected from wines to make bread from fermented dough. Similarly, leaven – referred to repeatedly in the Bible – was a soft, fermented dough-like medium.

## Beer and Wine

Between 9,000 and 7,000 B.C. the nomadic life of the hunter-gatherer societies evolved into the more settled life of farmers. Many historians believe that brewing beer and wine originated during this period as a result of the first domestic cereal crops [2]. The earliest evidence that beer was produced and consumed comes from China more than 7,000 years ago. The archaeological record shows that as early as 4,000 B.C. yeast was used both as a leavening agent and for brewing ale in Egypt [2]. Centuries later, the Greeks and Romans are known to have used starter cultures to inoculate fresh fruit juice for fermentation [3].

## Defining Probiotics

The connection between fermented foods, bacteria, and health originated with the foundation of the discipline of microbiology. In 1680, van Leeuwenhoek, used his newly built microscope to observe yeast cells in fermenting beer [10]. Because he never made an association between the presence of these yeast cells and the process of fermentation his observations were forgotten. In the late 1700's Lavoisier, a founder of modern chemistry, delineated the process of transformation of sugars to alcohol and carbon dioxide. He described this phenomenon of alcoholic fermentation as ‘one of the most extraordinary in chemistry’. However, he erroneously wrote that yeast played a physical rather than a chemical role in this process. In the 1840's, Theodor Schwann and Charles Cagniard-Latour suggested a possible association between the growth of yeast and the process of alcoholic fermentation. It was the great French chemist Louis Pasteur who definitively concluded that lactic acid fermentation was initiated by microorganisms based on his investigations. Pasteur originally defined fermentation as ‘respiration without air’ and stated, “*I am of the opinion that alcoholic fermentation never occurs without simultaneous organization, development, and multiplication of cells. If asked in what consists the chemical act whereby the sugar is decomposed, I am completely ignorant of it*”. Pasteur published his seminal results in a preliminary paper in 1857 and in a final version in 1860, which was titled “*Mémoire sur la fermentation alcoolique*” [11].

In 1899 Henry Tissier isolated *Bifidobacteria* from the stools of breast-fed infants. He found that they were a predominant component

of the intestinal flora in healthy humans and later recommended the administration of *Bifidobacteria* to infants with diarrhea [12]. Ilya Ilyich Metchnikoff, a Russian scientist, in the beginning of early 20<sup>th</sup> century linked the health and longevity of Bulgarian peasants with their heavy ingestion of yoghurt which contained large quantities of *Lactobacillus* species. In 1895, Metchnikoff became the director of the Pasteur Institute after Louis Pasteur's death. In 1908 he received the Nobel Prize in Medicine for his contributions to immunology – much of which stemmed from his investigations regarding ingestion of living organism. In 1907, Metchnikoff wrote his famous text, “*The Prolongation of Life*” based on his findings. This book is the first scientific description of the potential to improve human health through eating substances, which favorably alter the gastrointestinal microflora – a concept now widely accepted as the probiotic principle.

In 1907, a German chemist named Eduard Buchner received the Nobel Prize for proving that enzymes in yeast cells cause fermentation. Arthur Harden and Hans Euler-Chelpin received the Noble Prize in 1929 for elucidating how such enzymes cause fermentation. Probiotic therapy took a major step towards reality in 1930 when the Japanese microbiologist Minoru Shirota first discovered bacterial flora that survived passage through the gut after ingestion. Shirota was subsequently able to isolate and cultivate what is now known as *Lactobacillus casei* strain *shirota*. These efforts led to the first fermented bacteria-containing drink, which was commercially marketed as Yakult in 1935 – a product that continues to be manufactured and sold worldwide today.

The term *probiotic* is derived from Latin (pro) and Greek (bios) meaning literally “for life” [13]. It was first used by Kollath in 1953 to generically describe various organic and inorganic supplements that were believed to have the ability to restore the health of malnourished patients [14]. In 1954, the German researcher Ferdinand Vergin proposed the term *probiotika* to describe “active substances that are essential for a healthy development of life”. Lily and Stillwell published an article in Science in 1962 wherein they expanded the definition of probiotics to include “the anaerobic bacteria that are able to produce lactic acid and stimulate the growth of other organisms [15]. Parker in 1974 proposed that the term probiotic should include not only microbial organisms but also other substances that contributed to intestinal microbial balance [16].

Our current usage of the term probiotic was proposed by Roy Fuller who deleted “other substances” from the definition and defined probiotics as “live microbial feed supplements which beneficially affects the host animal by improving its intestinal microbial balance [17]. Our current definition of probiotics was formulated in 2001 by FAO/WHO as “live microorganisms which, when administered in adequate amount, confers health benefit to the host”. In 2002 FAO/WHO subsequently drafted guidelines regarding the evaluation of probiotics in various food products. Prebiotics are indigestible food ingredients that selectively promote the growth or activity of beneficial bacteria, thereby benefiting the host [18]. Synbiotics are combinations of probiotics and prebiotics designed to improve the survival of ingested microorganisms and their colonization of the intestinal tract [18].

## Commercialization of Probiotics

In 1906, “Le Fermente” a French Society began marketing a fermented milk product (Lactobacilline) containing *Streptococcus thermophilus* and *Lactobacillus delbruekii*. In 1919, Isaac Carasso similarly began commercial production of yogurt in Spain. It is unclear that these products contained living organisms and, if so,

whether these organisms were able to survive transit through the upper gastrointestinal tract. Accordingly, Yakult (described above) fermented milk is commonly cited as the first commercially available probiotic.

In the earlier part of last century, focus was on the use of fermented milk with probiotics to take care of intestinal infections. Gradually focus has shifted to survival of these bacteria in the gastrointestinal tract and the carrier food to have their beneficial effect on the host [19,20]. From the late 1930's onward, interest in probiotics gradually decreased as a result of the pressures of the Great Depression, World War II, and the discovery and proliferation of various antibiotics. However, global trends from the 1980's to the present have included increasing antimicrobial resistance, limited pharmaceutical research and development in infectious diseases, skyrocketing costs for new antibiotics, and discrepancies in availability and/or utilization of routine infection prevention measures. Accordingly, interest in probiotics has again increased as it is widely viewed as a non-antibiotic strategy to prevent and potentially treat a variety of infections. In 1994, passage of the Dietary Supplement Health and Education Act (DSHEA, see below) led to dramatic growth in the sales of products marketed as probiotics. This legislation allowed these agents to be marketed as dietary supplements without the rigorous requirements necessary to approve prescription drugs. Since this time, marketing and sales of probiotic products in the United States has grown exponentially. The global market of probiotic ingredients, supplements and food was \$14.9 billion in 2007 and is expected to reach \$19.6 billion in 2013. This represents a compound annual growth rate of 4.3 % [21].

### United States (U.S.) Regulation of Probiotics

Probiotics can be marketed in several different ways in the U.S. depending on their intended usage. They can be marketed as foods, medical foods, dietary supplements or drugs. Each of these categories has unique requirements in terms of formulation, scientific documentation, and/or FDA approval. In most cases, probiotics are marketed as either a dietary supplement (e.g., products in pill form) or as a food substance (e.g., yogurt). Several of probiotic organisms including *Lactobacillus acidophilus*, *Streptococcus thermophilus*, and *Bifidobacterium lactis* have "generally recognized as safe" (GRAS) status, meaning that they are permissible additives in food substances. Similarly, these species and many others are contained in products marketed as dietary supplements, which are regulated via the afore-mentioned DSHEA. This legislation allows these products on the market without any pre-marketing approval. However, manufacturers are responsible for collecting data about adverse events that are reported. Manufacturers marketing probiotic-dietary supplements dietary supplements are also not permitted to make therapeutic claims. Those that do make medical claims are considered to be drugs in the eyes of FDA regulators. Current FDA guidelines state that if any agent (including probiotics) is ingested for the purpose of curing, mitigating, treating, diagnosing or preventing disease, it is classified as a "drug" and must undergo the regulatory process similar to any new pharmaceutical [22].

While such regulatory oversight is intended to ensure patient safety, it may not be entirely aligned with public desires. A recent qualitative study of U.S. consumers' perceptions of therapeutic probiotic agents confirms that patients expect rigorous federal regulations regarding accurate labeling and the evaluation of efficacy and safety endpoints [23]. However, study respondents also called for limited involvement by pharmaceutical companies, wide-spread access, and low costs. These observations suggest that from probiotics' origins as home-brewed fermented milk products to our present-day commercially

manufactured supplements, our understanding and acceptance of these agents has evolved to where we want our (probiotic) cake and to eat it too.

### Current role of Probiotics in Various Diseases

Probiotics seems to have a promising role in either shortening the duration or prevention of infections. Several laboratory studies and clinical trials are being conducted to evaluate the safety and efficacy of probiotics in several diseases. One of the biggest challenges we encounter now in probiotics is extrapolating the immunomodulatory effects found on laboratory studies with the outcomes in human trials. Multiple factors like genetics, microbial diversity etc play a role in the discrepancies between the laboratory studies and clinical trials. With meta-analysis of strain-specific clinical trials, the role of probiotics has been evolving.

#### Antibiotic-associated Diarrhea (AAD)

Antibiotics have shown to alter the intestinal microbiota of the host leading to decrease in amylolytic activity, [24] decreased short chain fatty acid production and increased proteolytic activity [25]. Several probiotic organisms have been studied in various clinical trials in children and adults to prevent or decrease the AAD. With increasing number of strain-specific clinical trials, a strain-specific meta-analysis of randomized clinical trials testing the efficacy of *S. boulardii* in preventing AAD, showed *S. boulardii* was significantly protective for AAD [26]. The number needed to prevent one case of AAD was 10.2. *Lactobacillus rhamnosus* GG (LGG) has showed benefit over the placebo or no treatment in several randomized control trials [27-30] in preventing antibiotic-associated diarrhea in children and adults.

#### *Clostridium difficile* (*C. difficile*) infection (CDI)

Probiotics have been studied in prevention, and treatment of *Clostridium difficile* infections (CDI) and recurrent CDI. In *in vitro* studies, *Saccharomyces boulardii* (*S. boulardii*), a probiotic yeast has shown to degrade *C. difficile* toxin A and B [31] and increase in anti-toxin secretory IgA levels [32]. *Lactobacillus rhamnosus* GG (LGG) has shown to increase the expression of mucins [33] and decrease the bacterial adherence [34]. With CDI or *C. difficile* toxin acquisition as primary or secondary outcome, several randomized controlled trials have been done [35-42]. None of them except one trial [42] has shown a statistically significant decrease in CDI or *C. difficile* toxin acquisition. In a randomized controlled trial on patients with recurrent CDI, high dose vancomycin (2g/d) with probiotics (*S. boulardii*) has shown a statistically significant reduction in recurrence rate compared with low dose vancomycin or metronidazole with probiotics [43].

#### Necrotizing Enterocolitis (NEC)

Bacterial colonization patterns are important in the pathogenesis of NEC since preterm infants of mothers receiving broad-spectrum antibiotics prenatally or preterm infants receiving antibiotics directly postnatally have been found to have higher risk for Necrotizing Enterocolitis due to a change in the intestinal microbiota [44,45]. Several meta-analysis [46-49] have shown to reduce the relative risk of NEC and death when *Bifidobacterium spp.* and *Lactobacillus acidophilus* are used prophylactically in neonates with birth weight <1500 gms. Among neonates with birth weights <750 gms, there was an increase in the risk of sepsis with the use of probiotics [50].

#### Inflammatory Bowel Disease (IBD)

*Lactobacillus paracasei* demonstrated immunomodulatory effects



by reducing proinflammatory cytokines in the plasma of patients with Ulcerative Colitis (UC) [51]. *VSL#3* induces IL-10 and down regulates IL-12p40 production by lamina propria in patients with UC [52]. But none of the clinical trials [53-56] have been able to demonstrate any significant improvement in IBD symptoms in comparison with placebo. We need several large randomized controlled trials and meta-analysis to demonstrate the superiority of probiotics over placebo or anti-inflammatory agents like steroids. At this moment, there is no role of probiotics in the management of inflammatory bowel diseases either in induction or maintenance phase of remission.

### Irritable Bowel Syndrome (IBS)

IBS is one of the most common intestinal disorders in the industrialized and developing nations and incurs significant health care costs. Irritable Bowel Syndrome is defined by symptom criteria of chronic recurring episodes of abdominal pain or discomfort with altered bowel habits in the absence of organic disease [57]. In addition, sensations of bloating with and without visible abdominal distension, increased anxiety and several extraintestinal symptoms commonly occur [58]. Although several animal and human studies suggests alteration in gut microbiota in patients with IBS, it needs to be determined if it is a consequence or the cause [59]. Increased incidence of irritable bowel syndrome following gastroenteritis, [60] abnormal lactulose breath testing sec to small bowel bacterial overgrowth and intestinal inflammation suggests alteration in the intestinal microbiota [61] In a systematic review of several randomized controlled trials, *Bifidobacterium infantis* 35624 was the only probiotic to provide significant improvement in IBS symptoms [62].

### Acute Pancreatitis

Infectious complications are the most frequent and severe complications of acute necrotizing pancreatitis (AP) with a mortality rate up to 80% [63]. Bacterial translocation has been proven to be an important mechanism for the infectious complications in patients with acute severe necrotizing pancreatitis [64]. Several randomized controlled trials [65-70] have shown that probiotics with or without prebiotics have shown to reduce the infectious complications in patients with acute severe pancreatitis. Besselink et al. (PROPATRIA trial) conducted a multicenter, double blind, placebo-controlled clinical trial [71] that randomized 296 acute pancreatitis patients to receive 28 days of enteral probiotic therapy (multi-species probiotics preparation) or placebo. This study found no differences in infectious complication rates between the probiotic group and their placebo controls (30% vs. 28%). Nine patients developed bowel ischemia (8 died) in the probiotics group, whereas none developed this complication in the placebo group. Surprisingly, the mortality rate was significantly higher in probiotic-treated patients than in those given placebo (16% vs. 6%). This study has been criticized for the design and execution of the study like inappropriate blinding, insufficient reporting of serious adverse events, increase in the sample size after the study was initiated, changing the study population from 'severe pancreatitis' to 'predicted severe pancreatitis' and incorrect execution of the intention-to-treat analysis [72]. The patients in the Besselink group also received a higher number and more strains of probiotic organisms (six strains of probiotics vs. 1-4 strains of probiotics in other studies) and some of the patients were receiving pressors. Randomized controlled trials and meta-analysis have not demonstrated significant benefits of prophylactic antibiotics on patients with necrotizing acute pancreatitis.

### Ventilator Associated Pneumonia (VAP)

Ventilator-associated pneumonia (VAP) is a leading hospital-

acquired infection in the US [73]. It not only prolongs the duration of mechanical ventilation, length of stay in the intensive care unit (ICU) and possible recovery of the lung function [74] but also increases the risk of death by 2-10 fold [75,76]. The pathogenesis of VAP is complex but typically involves colonization of the aero digestive tract with pathogenic bacteria, formation of biofilms, and microaspiration of contaminated secretions [77,78]. Several randomized control trials have studied the use of probiotics in prevention of VAP, ICU mortality, ICU stay, and in hospital mortality as primary or secondary end point. A meta-analysis [79] of 12 randomized controlled trials found significant reductions in the rate of ventilator-associated pneumonia, ICU length of stay, and colonization of the respiratory tract with *Pseudomonas aeruginosa* but no significant reduction in ICU mortality, hospital mortality or hospital length of stay.

### Obesity and Insulin Resistance

The composition of the microbiota not only varies from person to person but also varies along the length of the gastrointestinal tract [80]. Genotype, confirmed on studies involving monozygotic twins, also plays an important role on the composition of the intestinal microbiota [81]. The most abundant phyla are *Bacteroidetes*, and *Firmicutes*, together representing 90% of the total microbiota [80]. Despite wide variability in species composition of the intestinal microbiota, functional gene profiles (microbiomes) are similar across healthy individuals [82,83]. Diet probably plays a pivotal role in influencing the composition of the intestinal microbiota. *Bacteroides* enterotype was associated with high dietary consumption of saturated fats and protein and *Prevotella* enterotype was associated with low protein and fat intake along with high ingestion of carbohydrates [84]. The change in the dietary calorie load was rapidly (within 3 days) associated with changes in the bacterial composition of the gut microbiota [85]. Significant decrease in fecal *Enterobacteriaceae* and sulfate reducing bacteria were noted in obese adolescents who experienced weight loss with low calorie diet and exercise program [86]. Surprisingly, roux-en-Y gastric bypass surgery for weight loss has been associated with increase in pathogenic gut bacteria and loss of beneficial species [87]. There is no consensus on the specific patterns of bacteria that are implicated in obesity and insulin resistance. Obesity is a state of chronic and low-grade inflammation with metabolic complications [88]. High fat diet has shown to increase gut permeability and increase in plasma lipopolysaccharide (a major component of the outer membrane of Gram-negative bacteria) levels suggestive of low-grade endotoxemia (metabolic endotoxemia) [89,90] along with an increase in the amount of total bacteremia, Gram-negative bacteria, and *E. coli* DNA in the ileal mucosa, blood and mesenteric adipose tissue (metabolic bacteremia) [91]. Metabolic endotoxemia correlates positively with fasting insulin levels, insulin resistance, and cholesterol and triglyceride levels in type 2 diabetic patients [92]. Effect of the innate immune receptor, the pattern recognition receptor Tlr5, on the structural microbial composition and development of insulin resistance has been revealed. In this study, [93]. Tlr5<sup>-/-</sup> mice exhibited hyperphagia, obesity and insulin resistance. Even lean Tlr5<sup>-/-</sup> mice had insulin resistance. Food restriction has prevented obesity but not insulin resistance. Transplantation of the gut microbiota from Tlr5<sup>-/-</sup> mice to a germ free wild type mice resulted in hyperphagia, obesity and insulin resistance [93]. Antibiotic treatment of Tlr5<sup>-/-</sup> mice ameliorated insulin resistance, obesity and hyperphagia [93]. This suggests a good relationship between intestinal microbiota, innate immune system and insulin resistance.

In a study on school children, [94] *Bifidobacterium spp.* number in fecal samples during infancy was higher in children who were normal

weight at 7 years than in children becoming overweight. This study suggests the aberrant gut microbiota composition precedes overweight. *Bifidobacterium spp.* is also present in higher numbers in normal-weight vs. overweight women and also in women with lower weight gain during pregnancy. The number of *Bifidobacterium spp.* has been shown to increase in the presence of inulin-type fructans with prebiotic properties [95]. Effect was seen within a few days and disappears in a week after the discontinuation. In a double-blind, randomized, placebo-controlled trial, [96] consuming 200 g/day of fermented milk with *Lactobacillus gasseri* SBT2055 (LG2055) for 12 weeks was associated with significant decrease in abdominal visceral and subcutaneous fat area, body weight and waist circumference as compared to fermented milk alone.

Gut microbiota seems to be a potential nutritional and pharmacological target for the management of obesity and insulin resistance. This is an exciting and rich area of investigation involving many fields like gastroenterology, immunology, endocrinology and microbiology.

## Summary

Probiotics are now being studied in various gastrointestinal and non-gastrointestinal disorders and its role has been slowly emerging over the last 2-3 decades. We need large randomized placebo-controlled single strain trials with standard dosing, formulation and duration of treatment in various diseases to get the consistent results. At this moment it is difficult to recommend any particular probiotic for a particular disease as the preparation and dosing may not be available commercially. The interaction of the gut microbiota with its host and mutual regulation has become one of the important topics of biomedical research. Their relevance in human diseases require much more research.

## References

- Perles C (1977) Le strategie alimentari nella preistoria In: Flandrin J-L, Montanari M (eds) Storiadell'alimentazione. Ed. Laterza, Roma-Bari:12-25.
- McGovern, PE (2009) Uncorking the Past: The Quest for Wine, Beer, and Other Alcoholic Beverages. University of California Press, Berkeley.
- Kenneth FK, Kriemhild CO (2000) Cambridge World History of Food: Vol 1 Cambridge University Press: Cambridge.
- Kosikowski F, VV Mistry (1997) Cheese and fermented milk foods-Origins and Principles, Westport CT USA.
- Max M (1900) Sacred Books of the East. The Colonial Press, New York.
- Breasted JH (1906) Ancient Records of Egypt. University of Chicago Press, Chicago.
- Suvarna VC, Boby UV (2005) Probiotics in Human Health: A Current Assessment. Current Science 88: 1744-1748.
- Yokotsuka T (1985) Fermented protein foods in the Orient, with emphasis on Shoyu and Miso in Japan', in B.J.B Wood. Microbiology of Fermented Foods, Elsevier Applied Science, London.
- Saloheimo P (2005) [Captain Cook used sauerkraut to prevent scurvy]. Duodecim 121: 1014-1015.
- Huxley A (1871) Discourses: Biological & Geological (volumeVIII): Yeast. Collected Essays.
- Pasteur L (1858) Mèmoire sur la fermentation appeleé lactique. Annales de Chimie et de Physique 3e. 52: 404-418.
- Tissier H (1906) Traitement des infections intestinales par la méthode de la flore bactérienne de l'intestin. Crit Rev Soc Biol 60: 359-361.
- Hamilton-Miller JM, Gibson GR, Bruck W (2003) Some insights into the derivation and early uses of the word 'probiotic'. Br J Nutr 90: 845.
- KOLLATH W (1953) [The increase of the diseases of civilization and their prevention]. Munch Med Wochenschr 95: 1260-1262.
- LILLY DM, STILLWELL RH (1965) PROBIOTICS: GROWTH-PROMOTING FACTORS PRODUCED BY MICROORGANISMS. Science 147: 747-748.
- Parker RB (1974) The other half of the antibiotic story. Anim Nut Health 29: 4-8.
- Fuller R (1989) Probiotics in man and animals. J Appl Bacteriol 66: 365-378.
- de Vrese M, Schrezenmeier J (2008) Probiotics, prebiotics, and synbiotics. Adv Biochem Eng Biotechnol 111: 1-66.
- Lourens-Hattingh A, Viljoen, BC (2001) Yogurt as probiotic carrier food. International Dairy Journ al 11:1-17.
- Roy D (2005) Technological aspects related to the use of bifidobacteria in dairy products. Lait 85: 39-56.
- Agheyisi R (2008) The probiotics market: Ingredients, supplements, foods, Report code: FOD035B, BCC Research, Wellesley, MA, USA.
- www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/UMC229175.pdf
- Harrison KL, Farrell RM, Brinich MA, Highland J, Mercer M, et al. (2012) 'Someone should oversee it': patient perspectives on the ethical issues arising with the regulation of probiotics. Health Expect .
- Meuller S, Saunier K, Hanisch C, Norin E, Alm L, et al. (2006) Differences in faecal microbiota in different European study populations in relation to age, gender, and country: A cross-sectional study. Appl Environ Microbiol 72: 1027-1033.
- Guigoz Y, Doré J, Schiffrin EJ (2008) The inflammatory status of old age can be nurtured from the intestinal environment. Curr Opin Clin Nutr Metab Care 11: 13-20.
- McFarland LV (2010) Systematic review and meta-analysis of *Saccharomyces boulardii* in adult patients. World J Gastroenterol 16: 2202-2222.
- Wenus C, Goll R, Loken EB, Biong AS, Halvorsen DS, et al. (2007) Prevention of antibiotic associated diarrhoea by a fermented probiotic milk drink. Eur J Clin Nutr 62: 299-301.
- Vanderhoof JA, Whitney DB, Antonson DL, Hanner TL, Lupo JV, et al. (1999) *Lactobacillus GG* in the prevention of antibiotic-associated diarrhea in children. J Pediatr 135: 564-568.
- Arvola T, Laiho K, Torkkeli S, Mykkänen H, Salminen S, et al. (1999) Prophylactic *Lactobacillus GG* reduces antibiotic-associated diarrhea in children with respiratory infections: a randomized study. Pediatrics 104: e64.
- Thomas MR, Litin SC, Osmon DR, Corr AP, Weaver AL, et al. (2001) Lack of effect of *Lactobacillus GG* on antibiotic-associated diarrhea: a randomized, placebo-controlled trial. Mayo Clin Proc 76: 883-889.
- Castagliuolo I, LaMont JT, Nikulasson ST, Pothoulakis C (1996) *Saccharomyces boulardii* protease inhibits Clostridium difficile toxin A effects in the rat ileum. Infect Immun 64: 5225-5232.
- Qamar A, Aboudola S, Warny M, Michetti P, Pothoulakis C, et al. (2001) *Saccharomyces boulardii* stimulates intestinal immunoglobulin A immune response to Clostridium difficile toxin A in mice. Infect Immun 69: 2762-2765.
- Mack DR, Michail S, Wei S, McDougall L, Hollingsworth MA (1999) Probiotics inhibit enteropathogenic *E. coli* adherence in vitro by inducing intestinal mucin gene expression. Am J Physiol 276: G941-950.
- Naaber P, Mikelsaar RH, Salminen S, Mikelsaar M (1998) Bacterial translocation, intestinal microflora and morphological changes of intestinal mucosa in experimental models of Clostridium difficile infection. J Med Microbiol 47: 591-598.
- McFarland LV, Surawicz CM, Greenberg RN, Elmer GW, Moyer KA, et al. (1995) Prevention of beta-lactam-associated diarrhea by *Saccharomyces boulardii* compared with placebo. Am J Gastroenterol 90: 439-448.
- Plummer S, Weaver MA, Harris JC, Dee P, Hunter J (2004) Clostridium difficile pilot study: effects of probiotic supplementation on the incidence of C. difficile diarrhoea. Int Microbiol 7: 59-62.
- Thomas MR, Litin SC, Osmon DR, Corr AP, Weaver AL, et al. (2001) Lack of effect of *Lactobacillus GG* on antibiotic-associated diarrhea: a randomized, placebo-controlled trial. Mayo Clin Proc 76: 883-889.
- Surawicz CM, Elmer GW, Speelman P, McFarland LV, Chinn J, et al. (1989)

- Prevention of antibiotic-associated diarrhea by *Saccharomyces boulardii*: a prospective study. *Gastroenterology* 96: 981-988.
39. Lewis SJ, Potts LF, Barry RE (1998) The lack of therapeutic effect of *Saccharomyces boulardii* in the prevention of antibiotic-related diarrhoea in elderly patients. *J Infect* 36: 171-174.
40. Kotowska M, Albrecht P, Szajewska H (2005) *Saccharomyces boulardii* in the prevention of antibiotic-associated diarrhoea in children: a randomized double-blind placebo-controlled trial. *Aliment Pharmacol Ther* 21: 583-590.
41. Can M, BeÄYirbellioglu BA, Avci IY, Beker CM, Pahsa A (2006) Prophylactic *Saccharomyces boulardii* in the prevention of antibiotic-associated diarrhea: a prospective study. *Med Sci Monit* 12: P119-22.
42. Hickson M, D'Souza AL, Muthu N, Rogers TR, Want S, et al. (2007) Use of probiotic *Lactobacillus* preparation to prevent diarrhoea associated with antibiotics: randomised double blind placebo controlled trial. *BMJ* 335: 80.
43. Surawicz CM, McFarland LV, Greenberg RN, Rubin M, Fekety R, et al. (2000) The search for a better treatment for recurrent *Clostridium difficile* disease: use of high-dose vancomycin combined with *Saccharomyces boulardii*. *Clin Infect Dis* 31: 1012-1017.
44. Cotten CM, Taylor S, Stoll B, Goldberg RN, Hasen NI, et al. (2009) Prolonged duration of initial empirical antibiotic treatment is associated with increased rates of necrotizing enterocolitis and death for extremely low birth weight infants. *Pediatrics* 123: 58-66.
45. Kenyon SL, Taylor DJ, Tarnow-Mordi W; ORACLE Collaborative Group (2001) Broad-spectrum antibiotics for preterm, prelabour rupture of fetal membranes: the ORACLE I randomised trial. *ORACLE Collaborative Group. Lancet* 357: 979-988.
46. Alfaleh K, Bassler D (2011) Probiotics for prevention of necrotizing enterocolitis in preterm infants. *Cochrane Database Syst Rev* 3: CD005496.
47. Deshpande G, Rao S, Patole S (2007) Probiotics for prevention of necrotising enterocolitis in preterm neonates with very low birthweight: a systematic review of randomised controlled trials. *Lancet* 369: 1614-1620.
48. Mihatsch WA (2008) Probiotika bei Frühgeborenen. *Monatsschr Kinderheilk* 156: 1070-1075.
49. Hammerman C, Kaplan M (2006) Probiotics and neonatal intestinal infection. *Curr Opin Infect Dis* 19: 277-282.
50. Lin HC, Hsu CH, Chen HL, Chung MY, Hsu JF, et al. (2008) Oral probiotics prevent necrotizing enterocolitis in very low birth weight preterm infants: a multicenter, randomized, controlled trial. *Pediatrics* 122: 693-700.
51. Federico A, Tuccillo C, Grossi E, Abbiati R, Garbagna N, et al. (2009) The effect of a new symbiotic formulation on plasma levels and peripheral blood mononuclear cell expression of some pro-inflammatory cytokines in patients with ulcerative colitis: a pilot study. *Eur Rev Med Pharmacol Sci* 13: 285-293.
52. Ng SC, Plamondon S, Al-Hassi HO, Kam MA, Knight SC, et al. (2008) M<sub>1202</sub> Effective probiotic treatment (VSL#3), but not placebo, in acute ulcerative colitis is associated with downregulation of inflammatory intestinal dendritic cells. *Gut* 57 (suppl 1): 96.
53. Rembacken BJ, Snelling AM, Hawkey PM, Chalmers DM, Axon AT (1999) Non-pathogenic *Escherichia coli* versus mesalazine for the treatment of ulcerative colitis: a randomised trial. *Lancet* 354: 635-639.
54. Schultz M, Timmer A, Herfarth HH, Sartor RB, Vanderhoof JA, et al. (2004) *Lactobacillus GG* in inducing and maintaining remission of Crohn's disease. *BMC Gastroenterol* 4: 5.
55. Bousvaros A, Guandalini S, Baldassano RN, Botelho C, Evans J, et al. (2005) A randomized, double-blind trial of *Lactobacillus GG* versus placebo in addition to standard maintenance therapy for children with Crohn's disease. *Inflamm Bowel Dis* 11: 833-839.
56. Marteau P, Lémann M, Seksik P, Laharie D, Colombel JF, et al. (2006) Ineffectiveness of *Lactobacillus johnsonii* LA1 for prophylaxis of postoperative recurrence in Crohn's disease: a randomised, double blind, placebo controlled GETAID trial. *Gut* 55: 842-847.
57. Longstreth GF, Thompson WG, Chey WD, Houghton LA, Mearin F, et al. (2006) Functional bowel disorders. *Gastroenterology* 130: 1480-1491.
58. Moayyedi P, Ford AC (2011) Symptom-based diagnostic criteria for irritable bowel syndrome: the more things change, the more they stay the same. *Gastroenterol Clin North Am* 40: 87-103.
59. Rhee SH, Pothoulakis C, Mayer EA (2009) Principles and clinical implications of the brain-gut-enteric microbiota axis. *Nat Rev Gastroenterol Hepatol* 6: 306-314.
60. Porter CK, Gormley R, Tribble DR, Cash BD, Riddle MS (2011) The Incidence and gastrointestinal infectious risk of functional gastrointestinal disorders in a healthy US adult population. *Am J Gastroenterol* 106: 130-138.
61. Shah ED, Basseri RJ, Chong K, Pimentel M (2010) Abnormal breath testing in IBS: a meta-analysis. *Dig Dis Sci* 55: 2441-2449.
62. Brenner DM, Moeller MJ, Chey WD, Schoenfeld PS (2009) The utility of probiotics in the treatment of irritable bowel syndrome: a systematic review. *Am J Gastroenterol* 104: 1033-1049.
63. McFadden DW (1991) Organ failure and multiple organ system failure in pancreatitis. *Pancreas* 6 Suppl 1: S37-43.
64. Cicalese L, Sahai A, Sileri P, Rastellini C, Subbotin V, et al. (2001) Acute pancreatitis and bacterial translocation. *Dig Dis Sci* 46: 1127-1132.
65. Oláh A, Belágyi T, Issekutz A, Gamal ME, Bengmark S (2002) Randomized clinical trial of specific *Lactobacillus* and fibre supplement to early enteral nutrition in patients with acute pancreatitis. *Br J Surg* 89: 1103-1107.
66. Qin HL, Zheng JJ, Tong DN, Chen WX, Fan XB, et al. (2008) Effect of *Lactobacillus plantarum* enteral feeding on the gut permeability and septic complications in the patients with acute pancreatitis. *Eur J Clin Nutr* 62: 923-930.
67. Oláh A, Belágyi T, Pótó L, Romics L Jr, Bengmark S (2007) Synbiotic control of inflammation and infection in severe acute pancreatitis: a prospective, randomized, double blind study. *Hepatogastroenterology* 54: 590-594.
68. Li YM (2007) Adjuvant therapy for probiotics in patients with severe acute pancreatitis: An analysis of 14 cases. *Shijie Huaren Xiaohua Zazhi* 15: 302-304.
69. Karakan T, Ergun M, Dogan I, Cindoruk M, Unal S (2007) Comparison of early enteral nutrition in severe acute pancreatitis with prebiotic fiber supplementation versus standard enteral solution: a prospective randomized double-blind study. *World J Gastroenterol* 13: 2733-2737.
70. Wu XG, Zhang QC (2009) Adjuvant therapy for probiotics in patients with severe acute pancreatitis with hepatic lesion: an analysis of 27 cases. *Clin Med* 29: 51-52.
71. Besselink MG, van Santvoort HC, Buskens E, Boermeester MA, van Goor H, et al. (2008) Probiotic prophylaxis in predicted severe acute pancreatitis: a randomized, double-blind, placebo-controlled trial. *Lancet* 371: 651-659.
72. Sheldon T (2010) Dutch probiotics study is criticised for its "design, approval, and conduct". *BMJ* 340: c77.
73. American Thoracic Society; Infectious Diseases Society of America (2005) Guidelines for the management of adults with hospital-acquired, ventilator-associated, and healthcare-associated pneumonia. *Am J Respir Crit Care Med* 171: 388-416.
74. Safdar N, Dezfulian C, Collard HR, Saint S (2005) Clinical and economic consequences of ventilator-associated pneumonia: a systematic review. *Crit Care Med* 33: 2184-2193.
75. Craven DE, De Rosa FG, Thornton D (2002) Nosocomial pneumonia: emerging concepts in diagnosis, management, and prophylaxis. *Curr Opin Crit Care* 8: 421-429.
76. Chastre J, Fagon JY (2002) Ventilator-associated pneumonia. *Am J Respir Crit Care Med* 165: 867-903.
77. Kollef MH (2005) What is ventilator-associated pneumonia and why is it important? *Respir Care* 50: 714-721.
78. Kollef MH (2004) Prevention of hospital-associated pneumonia and ventilator-associated pneumonia. *Crit Care Med* 32: 1396-1405.
79. Liu KX, Zhu YG, Zhang J, Tao LL, Lee JW, et al. (2012) Probiotics' effects on the incidence of nosocomial pneumonia in critically ill patients: a systematic review and meta-analysis. *Crit Care* 16: R109.
80. Candela M, Maccaferri S, Turrone S, Carnevali P, Brigidi P (2010) Functional intestinal microbiome, new frontiers in prebiotic design. *Int J Food Microbiol* 140: 93-101.
81. Zoetendal EG, Akkermans AD, Akkermans-van Vliet WM, deVisser JA, de Vos WM (2001) The host genotype affects the bacterial community in the human gastrointestinal tract. *Microb Ecol Health Dis* 13:129-134.

82. Wu GD, Chen J, Hoffmann C, Bittinger K, Chen YY, et al. (2011) Linking long-term dietary patterns with gut microbial enterotypes. *Science* 334: 105-108.
83. Turnbaugh PJ, Hamady M, Yatsunenko T, Cantarel BL, Duncan A, et al. (2009) A core gut microbiome in obese and lean twins. *Nature* 457: 480-484.
84. Wu GD, Chen J, Hoffmann C, Bittinger K, Chen YY, et al. (2011) Linking long-term dietary patterns with gut microbial enterotypes. *Science* 334: 105-108.
85. Jumpertz R, Le DS, Turnbaugh PJ, Trinidad C, Bogardus C, et al. (2011) Energy-balance studies reveal associations between gut microbes, caloric load, and nutrient absorption in humans. *Am J Clin Nutr* 94: 58-65.
86. Sotos M, Nadal I, Marti A, Martinez A, Martin-Matillas M et al. (2008) Gut microbes and obesity in adolescents. *Proc Nutr Soc* 67: E20.
87. Zhang H, DiBaise JK, Zuccolo A, Kudrna D, Braidotti M, et al. (2009) Human gut microbiota in obesity and after gastric bypass. *Proc Natl Acad Sci U S A* 106: 2365-2370.
88. Trayhurn P, Wood IS (2005) Signalling role of adipose tissue: adipokines and inflammation in obesity. *Biochem Soc Trans* 33: 1078-1081.
89. Amar J, Burcelin R, Ruidavets JB, Cani PD, Fauvel J, et al. (2008) Energy intake is associated with endotoxemia in apparently healthy men. *Am J Clin Nutr* 87: 1219-1223.
90. Brun P, Castagliuolo I, Di Leo V, Buda A, Pinzani M, et al. (2007) Increased intestinal permeability in obese mice: new evidence in the pathogenesis of nonalcoholic steatohepatitis. *Am J Physiol Gastrointest Liver Physiol* 292: G518-525.
91. Amar J, Chabo C, Waget A, Klopp P, Vachoux C, et al. (2011) Intestinal mucosal adherence and translocation of commensal bacteria at the early onset of type 2 diabetes: molecular mechanisms and probiotic treatment. *EMBO Mol Med* 3: 559-572.
92. Creely SJ, McTernan PG, Kusminski CM, Fisher fM, Da Silva NF, et al. (2007) Lipopolysaccharide activates an innate immune system response in human adipose tissue in obesity and type 2 diabetes. *Am J Physiol Endocrinol Metab* 292: E740-747.
93. Vijay-Kumar M, Aitken JD, Carvalho FA, Cullender TC, Mwangi S, et al. (2010) Metabolic syndrome and altered gut microbiota in mice lacking Toll-like receptor 5. *Science* 328: 228-231.
94. Kalliomäki M, Collado MC, Salminen S, Isolauri E (2008) Early differences in fecal microbiota composition in children may predict overweight. *Am J Clin Nutr* 87: 534-538.
95. Gibson GR, Roberfroid MB (1995) Dietary modulation of the human colonic microbiota: introducing the concept of prebiotics. *J Nutr* 125: 1401-1412.
96. Luoto R, Kalliomäki M, Laitinen K, Isolauri E (2010) The impact of perinatal probiotic intervention on the development of overweight and obesity: follow-up study from birth to 10 years. *Int J Obes (Lond)* 34: 1531-1537.

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