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Where tradition meets science: microbial diversity and bioactive compounds in Armenian fermented milk products

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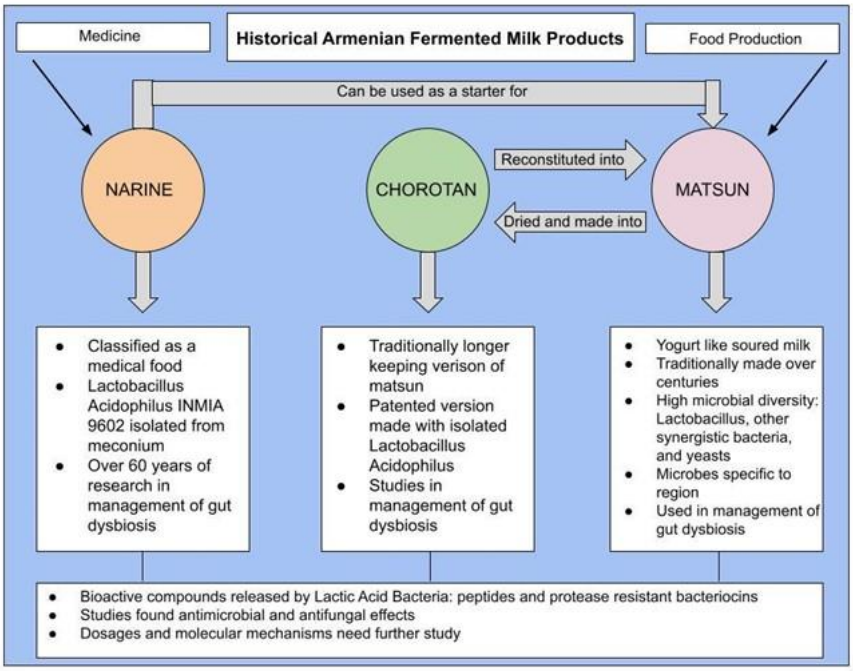
ABSTRACT

Armenia has a rich history of medicine and fermented foods. Fermented milk products are enjoyed both as a gustatory pleasure and a digestive remedy. Matsun is a traditional Armenian fermented milk product with historico-cultural roots in ancient subsistence and medical practices. Unlike commercial yogurt, it is made through serial inoculation and consists of a large microbial diversity honed through centuries of human selection. Also made from matsun is choratan, a long-keeping dried version of matsun that can be reconstituted into a creamy base. Narine is the commercial name of Lactobacillus acidophilus INMIA 9602, a bacterial strain endemic to the microbiome of Armenian newborns that is often reconstituted in milk and used as a medical food. Both choratan and Narine have been used in clinical trials for the management of symptoms related to gut dysbiosis. The review of cell cultures and animal trials revealed matsun as a rich source of probiotics with antimicrobial, antifungal, and radioprotective activity due to the peptides released and protease resistant bacteriocins produced. Clinical studies are needed to confirm the effects of combined strains in the human microbiome and establish dosages. Choratan as an isolated strain from matsun showed some effect on microbiome imbalance, but more studies are needed to confirm the results. Narine is well-studied in several preclinical and small clinical trials and accepted as a medical food. For future functional food consideration, replications of clinical trials, and large scale epidemiological and aftermarket studies are needed.



Keywords: Matsun, Choratan, Narine, History of Armenian Medicine, functional foods, bioactive compounds, Lactobacillus acidophilus INMIA 9602

INTRODUCTION

The probiotics in yogurt have been widely studied [1]. However, commercial yogurt is commonly made with strains isolated from Bulgarian yogurt in the early 20th century [1]. In recent years, interest is increasing in studying traditional milk products made through serial inoculation without laboratory starters.

Matsun is a traditional fermented milk product from Armenia eaten as a dietary staple, but also known as a digestive remedy. Versions of matsun are made throughout the Caucasus. The region has become so well known for its yogurt-like fermented dairy that Georgian matsoni is labeled Caspian Sea Yogurt in Japan, and advertised for its digestive benefits and relationship to human longevity. It is made with cow, goat, sheep, or a mixture of milks, pasteurized and inoculated with a previous batch of matsun [2]. Because it is still made in this traditional style, it maintains a consistent microbial makeup throughout time that is characteristic of its region [2,3]. With its unique microbial composition, matsun has potential for future functional food with further study. The Functional Food Center proposed the definition of functional food as “natural or processed foods that contain biologically-active compounds, which, in defined, effective, non-toxic amounts, provide a clinically proven and documented health benefit utilizing specific biomarkers, to promote optimal health and reduce the risk of chronic/viral diseases and manage their symptoms'' [4]. Isolates of beneficial bacteria originating from matsun have been investigated in the early stages of functional food research.

Choratan, a dried concentrate of matsun, is documented as a bioactive food supplement [5]. Studies have shown some promise in treating digestive disorders

though claims of contributing to longevity have not been conclusive [5].

Narine, an isolated strain of acidophilus from the human colon sometimes used as a yogurt starter, has been widely studied as a potential functional food starter and medical food [3, 6].

The purpose of this review is to explore the literature available about matsun (and chortan), establish it as a unique food, and evaluate its potential in functional food research. The rich history of fermentation and medicine in Armenia have influenced the human culture in which it is made and the microbial cultures of which it is composed. Environmental and anthropogenic factors contribute to the unique makeup of matsun, therefore it is imperative to preserve the folk foodways in which they arose and the microbial diversity it contains [3]. This microbial diversity may be investigated in the treatment of microbes as bioactive molecules targeted to manage specific pathologies. Isolates of some Armenian microorganisms, such as those in Narine and Choratan, have been investigated over the decades and can serve as a foundation for future studies in matsun microbial research.

Research Methods: Scientific and historic articles compiled for this review were found by conducting searches for yogurt, matsun, Armenian dairy, Narine probiotic, and Armenian medicine in Pubmed and Google Scholar. Articles concerning yogurt were used in regard to the history of fermentation, bioactive molecules of fermented milk, and when matsun or Armenia were also included. Popular Armenian cooking blogs and commercial Narine websites were also analyzed for examples of culinary uses of matsun and Narine. Functional Food definitions were researched using The Functional Food Science Journal website.

History of Armenian Medicine: Armenian medicine was highly acknowledged in the ancient world. While many texts have been lost in the wake of countless wars and political and territorial changes, there is evidence in historical medical texts that Greek, Persian, and Armenian scholars influenced and expanded each other's work [7]. Armenian medicine has its roots in folk medicine practiced by the Armenians before Christianity became the state religion in 301 AD. As early as 260, hospitals for leprosy were built [8]. Ancient writers including Herodotus, Strabo, Xenophanes, Tacitus, Pliny the Elder and Dioscorides described Armenian remedies, and herbs from the Armenian Highland were exported to the East and West [8]. Armenian medicine made use of medicinal plants, minerals, animals, and mixed compounds thereof, which were endowed with antitoxic, antisclerotic, and fermentative properties [8].

Mekhitar Heratsi, the founder of medieval Armenian medicine, studied the scientific heritage of Greek, Roman and Arab physicians as well as classical Armenian folk medicine. In the late twelfth century, Heratsi traveled all over Cilician Armenia studying malaria and trying experimental therapy at patients' bedsides. He wrote his book *Consolation of Fevers*, in the vernacular of Middle Armenian so that it was accessible to more people. Many of his medical terms are still used in Armenia today. His theory of mouldiness, used to describe contagion as originating from infectious mold in the blood, is strikingly similar to infection theory centuries later in Italy, recommending quarantine and social distancing measures [8]. He also described what are today considered social determinants of health in long term disease, such as emotional disturbances, over-exhaustion, malnutrition, unfavorable climatic conditions and emphasized diet, exercise and mood lifting activities for patients [8]. Amirdovalt Amatsiatsi expanded on

Heratsi and other scholars' works, also using Middle Armenian along with translations in the languages of several surrounding empires [7,8,9]. Written in 1492, in *Useless for the Ignorant,* Amatsiatsi described principles in experimental medicine recognizable in the scientific method today such as only testing a single medicine on a stable subject, observing and recording the results, increasing or decreasing based on results, taking into account variables like environmental temperature and disease progression, and repeated testing under similar circumstances to confirm results [7]. The information he recorded traveling to different countries, collecting herbal remedies, and practicing experimental medicine influenced the use of medicinal plants and dietary remedies in Armenia and surrounding Byzantium for centuries. These foundational works encouraged a culture of scientific investigation in health and disease management and served as a precursor to bacteriology.

In the late nineteenth century and early twentieth century, considerable interest was shown in bacteriology worldwide due to the work of Louis Pasteur. Influenced by rumors of longevity in Bulgaria, Stamen Grigorov isolated L. bulgaricus in 1905. Eli Metchnikoff proposed drinking bulgarian milk in order to colonize the intestine with beneficial bacteria. However, Rettger and Cheplin found that L. bulgaricus was transient in the intestine and could not be implanted. They proposed that L. acidophilus, native to the intestine and flourishing on the lactose present in milk, was the beneficial bacteria responsible for alleviating dysbiosis [10]. In his 1908 book, *Bacteria in Relation to Country Life,* Jacob Lipman observed that sour milk, curd, and butter were all made and consumed from matsun in Armenia [11]. He inferred even then that it was not just the isolated *Bacterium mazun* that contributed to health benefits, but the synergistic combination of specialized yeasts and other lactobacilli [11]. While early scientists contributed to the overall understanding of the role of beneficial microbes, or probiotics, in human health, the isolation of just a few studied microbes and standardization of starter cultures inadvertently changed the microbial landscape worldwide. Through the popularity of commercial yogurt and standardized starter cultures, traditional dairy fermentation knowledge receded and with it the microbial diversity that was honed over centuries. Fortunately, as the study of probiotics declined in the wake of antibiotic breakthroughs, researchers in Armenia, like Dr. Yerzinkian continued to study endemic microbiota. This research was conducted while Armenia was part of the USSR and geopolitics kept it from worldwide accessibility until Armenian independence in 1991. In 1993, Evrik Afrikian established the Microbial Depository Center, with the goal of studying the microbial diversity of the South Caucasus [12]. Today, researchers are interested in preserving heirloom cultures in parts of the world that still practice traditional milk fermentation and cheesemaking [13]. Fortunately, because of the Microbial Depository Center, Armbiotech already has a collection of matsun and cheese strains from different regions preserved, on which many of the studies reviewed are based.

History of Matsun: Ancient Armenia was at the center of early milk processing. Genetic analysis of zooarchaeological assemblages show a connection between modern cattle populations in Europe and Neolithic cattle populations in Syria, suggesting domestication of cattle likely originated in the Near East and spread to Europe in coastal communities [14,15,16]. Potsherds containing residue from processed milk found in Northwestern Anatolia are among the earliest evidence for milk production, before 6500 BC [17]. Artifacts found in the Armenian highlands dating to 5000 BC include churns and fermenting vessels with dairy residue, consistent with knowledge of processing milk

[3]. DNA analysis of dental calculus on individuals in the Caucasus found evidence of dairy consumption in the fourth millennium in the South Caucasus [18]. DNA also reveals a human migration pattern from the South Caucasus, evenly distributed from Armenia and Iran, northward previous to the spread of pastoralism [19]. Ancient Armenians possessed dairying knowledge that spread from the Eurasian steppes throughout Europe.

Soured milk has a vast literary history often repeated in yogurt histories. It was first recorded in religious texts. In the Christian Holy Bible, Moses is said to have preached that this was a gift from God to his people [20,21]. Many translations of Genesis 18:8 describe Abraham as presenting "curds and whey" as part of the meal he sets before three angelic messengers [20,21. It is also recorded in the Hindu Holy Vedas and on Sumerian clay tablets [20,21]. In 100 BC, Pliny the Elder describes "barbarous nations" as making a thickened milk from "an acrid kind of liquid with a pleasant flavor" [22]. The history of the word *yogurt* is often traced back to Turkish scholars in 1074 [20], however, the word *matsun* is also traced to the eleventh century, illustrating matsun's established history in regions tied to Ancient Armenia. Grigor Magistros (990-1058), an Armenian prince and scholar, wrote of "matzoon" in his Definition of Grammar, as deriving from the word for "sour" and "glue like" [23]. Matsun is made of cow, goat, sheep, or mixed milks that undergo pasteurization and lactic acid fermentation through backslopping, or inoculation with stable microbial populations from previous batches. In his 2008 ethnographic study of rural Armenian and Georgian households in *Milk Culture in Eurasia,* Masahiro Hirata posits that fermenting became specialized in Caucasus, the mountainous region containing Georgia, Armenia, Nagorno Karabakh (Artsakh), and Azerbaijan. By exploring regions in and around the archaeological center of milk production, Hirata illustrated how environmental conditions and local economies adapted milk technology. He concluded that historically, processes of fermentation from West Asia and coagulation from Bulgaria were both used in the Caucasus. Due to the mountainous terrain, both hot and cold environments influenced the fermentation process, resulting in a unique soured milk culture [24].

The Slow Food Foundation has placed matsun on its *Ark of Taste,* a catalog of traditional foods at risk of disappearing. They describe the process of making matsun as a fermentation of milk and meran, a mixture of dried cornelian cherry, wheat and rye. The milk is boiled with cattle intestine placed in gauze, a source of rennet, that is removed before cooling and fermenting under cover overnight [25]. Hirata describes a different process in his 2008 study, in which the dried stomachs of pigs that were fed the whey byproduct of cheesemaking, are used as a natural rennet, but households depending on cow or sheep use rennet from the local animals [24]. However, in fermentation of matsun, the starter was a teaspoon of the previous batch of matsun and incubation time depended on the consistency and flavor desired [24]. A shorter incubation time yielded a softer and less acidic matsun for serving to children [24]. Households ate matsun daily with meals [24], indicating matsun's importance in their diet.

In their 2006 book, *Armenian Food: Fact, Fiction, and Folklore*, journalists Petrosian and Underwood describe matsun as a central pillar of Armenian identity and culture, citing its use in many lexical idioms [26]. They contend that every family had its own matsun making implements and that sharing meran was one way to unite Armenians living in the diaspora [26]. Famous midcentury Armenian Chef, Omar Khyam described a ritual in which emigrating Armenians dipped handkerchiefs into matsun and let it dry to be reconstituted later in their new homes [27]. This process, similar to the process of making a dried matsun product called choratan, highlights how important the consumption of matsun was in the past

and the ways in which making choratan adapted over time and circumstance. Historically, this affinity for matsun started the yogurt craze in America. In Massachusetts in the 1920s an Armenian couple, Rose and Sarkis Colombosian, delivered home cultured jars of milk in a wagon labeled, “madzoon” [28]. Rose started by making matsun in her kitchen. Popularity grew as recent immigrants and refugees found a taste of home and the Colombosians expanded their business into a creamery [29]. In the process of branding their matsun they shortened their name from Colombosian to Colombo as they felt it was easier for Americans to pronounce [28]. They also changed the name of their product to “yogurt” as Turkish was a common language in the local immigrant community that consisted of not only Armenians, but also Syrian, Lebanese, and Greek settlers [28,30]. By acclimating to American marketing pressures, matsun was hidden in the shadow of yogurt.

Dannon, invented in Spain by Isaac Carasso, a physician that used yogurt to treat dysbiosis, spread yogurt throughout Europe around the same time Colombo was gaining traction in America [1,20,21]. In the 1940s Dannon’s marketing in America ramped up, as Americans began associating yogurt with health. Offering smaller portions with sweet jams, Dannon catered to American tastes. Colombo would soon compete with their own flavored line. Because of the efforts of the yogurt industry in this time to market yogurt as tasty and healthy it grew into a multimillion-dollar business [31]. Yogurt went from a niche food targeted to the Middle Eastern diaspora to a symbol of European and American health foods [31]. Despite the commercial gains, yogurt, while widely consumed worldwide, is not eaten in the same quantities as matsun in the Caucasus where it is a common table accompaniment to any meal and forms the basis of other foods like breads, cakes, soups, and drinks.

Matsun is also traditionally used to make spas or tanapoor, a soup of cereal and matsun [32], that is derived from tan [33], a refreshing mix of water, cucumber, and mint [34]. Interestingly, mint is used in Traditional Armenian medicine for gastrointestinal disorders [35]. Naneh Israelyan describes mint as part of a holy quartet of herbs used to treat wide ranging illnesses in Armenian folk medicine. She also describes a combination of mineral water and matsun as a well-known remedy for diarrhea [9]. Peppermint oil has shown promise as treatment for irritable bowel syndrome (IBS) [36]. Tan is described as refreshing or thirst quenching in hot weather [26, 32, 34]. Recent studies have shown a correlation between heat waves and gastrointestinal distress in IBS, Infectious Gastroenteritis [37], and childhood diarrhea [38]. The gastronomic refreshment of tan overlaps with the traditional use of medicinal foods like matsun and mint for digestive issues and may have culturally evolved from historic medicinal uses in a hot environment. Table 1 indicates examples of foods that are derived from matsun.

Table 1. Foods Produced from Matsun

Food:	Processing/Additions:	Consumption Method:	Sources:
Butter	Churned	Spread on bread and used in cooking	[3], [24], [39]
Choratan	Whey Drained and Sun-Dried	Spread on bread or Reconstituted into matsun at a later date	[3], [24], [25], [39]
Tan	Mixed with water, cucumber, and herbs	Imbibed hot or cold depending on weather	[3], [26], [32], [34]
Tanapoor or Spas	Cooked with egg, grains, herbs, and flavorings	Eaten as soup	[32], [33]

Biodiversity of Matsun: Fermentation is thought to have arisen from the need to preserve food for storage, with lactic acid bacteria (LAB) inhibiting foodborne pathogenic bacteria and fungi. Before refrigeration, butter was made from matsun because of this longer preservation [3,24,39]. Traditional medicine also recognizes human health benefits to ingesting these LAB. Research into LAB isolated from Armenian dairy products has shown that particular strains exhibited strong antimicrobial activity, antifungal activity, and survived under gastrointestinal conditions.

In particular, L rhamnosus produced hydrogen peroxide, generating antibacterial activity in the presence of amylase and lipase. L. acidophilus and L. salivarius showed a strong rate of survival (30-30%) to intestinal stress even after previous gastric stress of pH 1.8. [40]. Strains isolated from Armenian salted cheese, L Rhamnosus BTK 2012 (MDC 9631), and dairy from the Nagorno Karabakh Republic, Streptococcus sp. K13 and Lactococcus sp 134, were tested on multi-drug resistant strains of pathogenic bacteria isolated from infected patients' body fluids. Ps. aeruginosa in particular was more sensitive to the probiotic strains than antibiotics [41]. Lactobacillus rhamnosus R-2002, L. delbrueckii subsp. lactis INRA-2010-4.2 and L. delbrueckii subsp. bulgaricus INRA-2010-5.2 were also found to inhibit fungal growth in vitro,particularly P. aurantioviolaceum and M. plumbeus [42]. The strongest antifungal activity was displayed by L. rhamnosus [42]. However, researchers also found that when combined with other LAB, L. rhamnosus lost some of its inhibitory effects, illustrating the importance of studying combined strains [42].

Multistrain probiotic concoctions are thought to enhance health benefits, and great care is taken to select strains that are compatible [1]. Matsun, through its centuries-long selection process, is already composed of compatible strains of microbes and synergistic yeast cultures [2,3]. A 2020 study comparing microbial strains isolated from matsuns in various regions in Armenia and Artsakh found that combining some strains increased antimicrobial activity compared to each strain alone [43]. For example, L. rhamnosus 2012's antibacterial activity against Salmonella typhimurium G 38 increased when paired with L. acidophilus 1991, L. paracasei 236, or E. faecium 64 [43]. Likewise, researchers found that in milk, LAB associations in time-spaced cultivation revealed a strong inhibitory effect against E. coli VKPM-M17, S. aureus MDC 5233, and B. mesentericus WT [44]. Co-cultivation of some strains may inhibit their antagonistic activity, however in MRS-Broth co-cultivation had high inhibitory effects against pathogens suggesting different growth mediums may have different effects [44]. These studies reveal the potential of combined bacterial strains in the management of microbiome imbalances.

In addition, strains endemic to regions with naturally occurring radiation, such as the mountains of Armenia may have adaptive responses to radiation. Narine was used to treat digestive disorders related to radiation exposure after Chernobyl [3], but the protective properties of probiotics in radiation have yet to be fully explored. In a 2020 study, seventeen endemic Armenian probiotic lactobacilli including L. delbrueckii IAHAHI from matsun, were compared in the diets of Wuster rats exposed to radiation. All seventeen lactobacilli strains positively affected the survival and blood characteristics of irradiated rats in vivo. L. delbrueckii IAHAHI fed to rats before radiation showed no positive effects, but when fed after radiation the viability of irradiated rats increased [45]. It also lowered the rats' blood glucose levels, consistent with effects of the pronounced pyridoxine production of L. delbrueckii IAHAHI [45]. Further studies are needed to determine if human blood glucose may be affected in the same way, indicating potential use in type 2 diabetes patients [45].

Armenia's mountainous landscape provides a variety of environments, and traditional matsun making can vary depending on temperature, type of milk, type of recipe, and starter culture affecting the microbial composition in each region. The human selection of strain combinations over the centuries has the potential to address different pathogens. In Bokulich's Microbial Biogeography, different regions contained differing amounts of species. For example, matsun from Lori, Armenia contained the largest abundance of genus Enterococcus [2]. In a study of bacteria isolated from matsun in different regions, Tkhruni et al found that Enterococcus sp. 64 inhibited growth of pathogenic bacteria, Salmonella sp., E. coli sp., E. cloacae sp. 1, E. cloacae sp -2 and many studies found that antimicrobial properties of LAB are species specific [1, 43, 46]. Further study into the geography of matsun microbial content, at the species level, could provide insight into whether matsun from specific regions can be used in the management of specific conditions. Israelyan found that antimicrobial activity was more dependent on culturing conditions, ratio and temperature, than strain combinations alone. Ideal culturing conditions also lead to flavor perceived as "sweet" or "tasty" whereas the combinations with fewer antimicrobial effects were found to be "bitter" to human tastes [43]. Hirato noted that Caucasian cheese-making processes were carried out with extreme care in the control of temperature, the preparation of rennet, and the pursuit of flavor" [24]. Traditional production methods, shaped by human ingenuity and influenced by human taste, depended on these factors for matsun to be considered consumable and are consistent with the selection of ideal combinations of bacterial and yeast cultures.

Choratan: While making matsun is a method that arose from preserving milk, matsun can be preserved even longer in the practice of making choratan. Afrikian describes choratan as "dried on the bread, matsun" [3,39]. Hirata describes the process as draining the whey from matsun, rolling it into balls, and sun drying them. This can be reconstituted in warm water in seasons when milk is scarce [24]. Refrigeration has pushed this method closer to obsolescence, but Alexander Selimian recreated a bioactive supplement form of Choratan, marketed under the brand Vavigram, containing Lactobacillus acidophilus with the total amount of 2.5*107 per gram [5,47]. It is sold as a yogurt starter, sourdough starter, and animal feed and advertised as a competitor to Narine [47]. In a clinical trial one hundred forty-one patients with gastrointestinal, allergic, and diabetes mellitus II type diseases and 120 healthy patients were studied. Patients took their usual prescriptions for their clinical diagnoses and choratan was added. Choraton alone was prescribed for patients without clinical diagnoses. The dosage was 2-3 times (4-6g) a day for 8 weeks on average [5]. Both the dried and liquid forms of choratan suppressed bacterial growth in most samples. Fecal examinations occurred before and after administration of choratan and normal microflora increased, while pathogenic microflora decreased [5]. In a subjective survey of symptoms, the majority of patients experienced positive changes in their condition after taking Choratan, while 18% did not experience any difference and 5% experienced a worsening of their condition [5]. Patients in the healthy group and allergy group showed the most noticeable changes, and smaller changes within diabetes mellitus and gastrointestinal disease groups both bacteriologically and subjectively, suggesting that improvements were disease dependent [5].

Narine as a Matsun Alternative: Matsun is still made in the home in some communities, but this practice is disappearing as commercially prepared and mass-produced versions become more commonplace. In modern times and in the diaspora, matsun is sometimes made with commercial matsun, yogurt, and/or sour cream as starters [48]. A popular starter for homemade yogurt is Narine. Narine is considered a medical food, prescribed by doctors and sold in pharmacies as a freeze-dried live culture to treat gut dysbacteriosis from a variety of causes [49]. The freeze-dried strain can be used in capsule form or as a starter culture for yogurt. A prepared fermented milk version of Narine can also be found in pharmacies and is supplied to Armenian kindergartens and nursing homes as a nutrition supplement [49]. In a cross-sectional study of maternal knowledge and practices related to the management of childhood diarrhea, researchers found many mothers used Narine as a yogurt drink to treat childhood diarrhea [50]. Commercial formulations sold outside of Armenia often come with recipes for preparing Narine in milk as a yogurt starter [51] or using yogurt as a vehicle for Narine [52]. Fermented milk made from Narine is not called matsun on the label, though it competes for the same place at the table. Petrosian and Underwood noted the attitude that Narine is good for babies because it contains "the same familiar" matsun [26].

While Narine is often conflated with matsun as they are both used to manage digestive disorders, especially in infants [26], Narine is isolated from a strain endemic to the human colon, rather than the extracorporeal strains found in matsun. In the mid twentieth century, Dr. Yerzinkian, of the Institute of Microbiology within Armenia's National Academy of Sciences, isolated hundreds of strains of acidophilus, using ten in the treatment of bacterial dysentery in military hospitals in Yerevan, Armenia [53]. He isolated Lactobacillus acidophilus INMIA 9602 from his granddaughter Narine's meconium and found that this strain had antibiotic resistant, bile resistant, and acid resistant properties, and when Narine fell ill with intestinal infection a few years later, he used it to treat her, naming the probiotic formulation after her [3, 39, 54, 55, 56). The immune stimulating and modulating activities of Narine have been studied in many countries over the decades [3, 39]. As a vehicle for probiotics, it has been widely popular [26]. Narine produces an antimicrobial peptide, acidocin LCHV, that is responsible for its activity against a wide range of pathogens including meticillin-resistant Staphylococcus aureus (MRSA) and Clostridium difficile [57]. Researchers in Korea found Narine inhibited growth of C. sakazakii in vitro but did not find peptide LCHV and attributed the antimicrobial effect to acidity [58]. The same commercial manufacturers of Narine starters also sell a matsun starter, Karine, a combination of some of the lactobacillus found in matsun [51]. A 2003 study compared the antimicrobial activity of Narine, Karine, and matsun. Researchers cultured milk with each and strained the curds from the whey, using the whey to perform tests. All three exhibited antimicrobial activity against 16 pathogenic microbes, but Narine and Karine produced much higher effects than traditional matsun, attributed to their higher levels of L-lactic acid and its calcium and sodium salts [55]. Table 2 summarizes the probiotic effects of Narine, matsun, and choratan as demonstrated in the studies reviewed.

Narine in Clinical Trials Clinical trials of Narine have been conducted for many years but have not been easily accessible in the west (see references in 3,39,56,59). Afrikian reported that much clinical research over the years demonstrated that Narine stimulates the immune system through the interferon-NK system [3]. Recent clinical trials of Narine in the management of Familial Mediterranean Fever (FMF) have been largely spearheaded by Astghik Pepoyan. In the 2021 study, *The Effect of Immunobiotic/Psychobiotic Lactobacillus acidophilus Strain INMIA 9602 Er 317/402 Narine on Gut Prevotella in Familial Mediterranean Fever: Gender-Associated Effects*, twenty healthy volunteers and twenty FMF patients took a Narine probiotic capsule twice a day for 30 days. None of the participants had taken antibiotics, hormones, or chemotherapeutic agents in the month leading up to the study. The distribution of gut Prevotella in healthy people differed between healthy men and healthy women. Narine returned the gut microbiota to a healthy state in both male and female FMF patients [60]. Depression levels were also investigated revealing significant levels of depression in FMF patients in remission.There was a tendency of decreasing depression scores for the male FMF patients after treatment with Narine [60]. Researchers concluded that the gut microbiota of patients with FMF disease contain more Prevotella than healthy gut bacteria, which may play a role in depression and that Narine might be suggested to patients with FMF to improve gut microbiota abnormalities as well as depression [60].

In 2018, forty healthy volunteers with low levels of C. albicans in their gut microbiota were compared to 48 FNF-positive volunteers that were half C. albicans carriers in a double blind, partly randomized, placebo-controlled trial [54]. Narine capsules were prescribed to patients in each FMF group while the rest of the participants took a placebo capsule. Narine lowered the amount of C. albicans in the experimental group, while the placebo had no effect on the control group. Narine also reduced the abundance of Enterobacteriaceae and yeast in the gut of FMF patients [54]. In a smaller 2017 study, nine people with FMF and five healthy volunteers participated. The FMF-positive participants continued to take their regular medication. Narine was administered to FMF-positive study participants with low numbers of gut lactobacilli. Five participants received Narine, and four received an empty capsule. The predominant strain of E. coli isolated from FMF-positive participants grew significantly faster than strains isolated from healthy study participants before probiotics were administered [6]. After the Narine was administered, the growth of gut commensal E. coli isolated from FMF-positive study participants were similar to those of E. coli isolated from healthy volunteers, showing that Narine extended the preparatory growth phase of commensal E. coli in FMF-positive samples [6]. Narine also had a positive effect on FMF patients with high levels of C-Reactive Protein during remission [6]. Analyzing commensal E. coli growth as a biomarker, researchers concluded that Narine *Lactobacillus acidophilus INMIA 9602* Er-2 strain 317/402 can be used to develop therapeutic interventions aimed at restoring gastrointestinal tract immunity and integrity [6].

Table 2. Probiotic Effects of Matsun, Choratan, and Narine as studied

Fermented Dairy Type	Bacteria	Effects
Matsun	Lactobacillus rhamnosus	Antibacterial activity in the presence of amylase and lipase [40] Survived intestinal stress in vitro [40] Inhibited fungal growth in vitro [42] Inhibited growth of MDR bacteria in vitro [41]
Matsun	Lactobacillus delbrueckii	Inhibited fungal growth in vitro [42] Increased viability of rats exposed to radiation [45] Lowered blood glucose levels of rats exposed to radiation [45]
Matsun	Enterococcus sp 64	Inhibited growth of pathogenic bacteria in vitro [2]
Choratan	Lactobacillus acidophilus	Decreased pathogenic microflora in clinical trial [5] Increased normal microflora in clinical trial [5]
Narine	Lactobacillus acidophilus INMIA 9602	Antibacterial effects against pathogenic bacteria [55],[57] Returned microbial flora to normal state in FMF patients [60] Depression scores decreased in male FMF patients [60] Lowered the amount of Candida albicans in FMF patients [54] Extended the preparatory growth phase of E. Coli in FMF patients [6]

Functional Food Potential The historical use of matsun to treat digestive disorders suggests its potential as a functional food. The process of determining functional food (FF) status per the Functional Food Center is rigorous and includes many steps to ensure the safety and efficacy of FFs. The investigation of historical practices to determine use is only the first step. Determination of BCs, biological pathways, and biomarkers must also be determined. As a milk product, matsun contains BCs present in milk such as lipids, vitamins, lactoferrin, enzymes, caseins and whey proteins, immunoglobulins, cytokines, peptides and lactose and oligosaccharides [1,3]. The fermentation process inherent in making matsun allows for the release and bioavailability of protein derived peptides and digestive, coagulant and microbial enzymes [1]. Specifically, protease resistant bacteriocins are produced from matsun lactobacilli and inhibit the growth of MDR and pathogenic bacteria [3,39, 46, 61]. The preclinical studies reviewed suggest that matsun may be used in the management of gut dysbiosis in a range of diseases such as childhood diarrhea, H. pylori, foodborne illnesses, radiation sickness, and antibiotic resistant infection [3, 39-46, 55]. Furthermore, the distinct regional variations may determine distinct uses based on the natural endemic flora. Clinical studies are needed to determine effectiveness in the body, dosage and upper limits.

Traditionally, choratan is essentially dried matsun to be reconstituted as needed and contains the same microbial community as matsun. The clinically tested version of choratan contained a single isolated strain from matsun, rather than the naturally occurring combination of strains. While *L. acidophilus INMIA 9602* Er-2 strain 317/402 Narine is a scientifically isolated strain endemic to the human body, it is also dried, like Choratan, and reconstituted into a matsun like food. Because of the historical scientific practice of isolating strains, Narine is more common in clinical trials than whole matsun. The clinical trials of Narine and Choratan demonstrate the ability of specific doses of specific LAB

to inhibit growth of pathogenic bacteria and increase beneficial bacteria in the colon. Bacterial growth in stool samples were measured as biomarkers. While properties of isolated bacterial strains are numerous, more studies of combined strains or whole matsun are needed to establish molecular mechanisms of biological pathways using similar biomarkers.

Determining an appropriate vehicle is another important step in the marketing of functional food. The adoption of Narine as a yogurt starter illustrates the adaptability of yogurt as a vehicle for probiotic delivery. Matsun, as a food similar to yogurt, may serve as an easy to incorporate vehicle for delivering the probiotics and peptides it contains. Yogurt has been intensively studied, but no standard dosage is yet available, though specific amounts of viable bacteria, such as the 1.5 x 10^8 used in Narine studies, are recommended [6,45,54,60]. Further complicating this, yogurt is consumed in varying amounts depending on the human culture in which it is consumed. In the United States, for example, yogurt is often consumed as a sweetened breakfast or dessert item, to be eaten once per day. However, in the Caucasus, yogurt, or matsun, is typically consumed more often. The disparity in amounts consumed might lead to different results in different populations so consumption must be considered as a factor when planning epidemiological and aftermarket studies. Because the ratios of LAB in fermentation affect the taste [43], it may not be feasible to increase them in a standard serving, but rather encourage more servings or culinary uses to aid in ingesting effective amounts. In FF science, it is important to establish a dosage, or "critical amount of BCs that create a chain reaction in the body that leads to health benefits for those that consume it" and to establish the upper limit in which BCs have no adverse effects on most people [62]. No studies found in this review found adverse effects of LAB consumption, however, it is an area in need of further research to ensure the safe limits are known and varied ingestion patterns of mixed populations must be considered. Armenian cookbooks and blogs have numerous recipes containing matsun, illustrating the ease with which people can adapt to using surpluses of a long-lasting food, like matsun, but also how it can be incorporated into the diet in many forms. Tradition suggests that certain pairings, like the mint in tan, may increase the effectiveness of matsun. Food combinations that boost microbial growth or effectiveness and therefore the critical amount of BCs delivered are another area in need of further research.Figures 1-3 are examples of matsun and foods derived from it: choratan and tanapoor.

Figure 1. Image of Homemade Matsun Produced in June 2022, San Diego, CA. Photo courtesy of Danik Martirosyan.

Figure 2. Image of Traditionally Made Choratan [63].

Figure 3. Traditional Armenian Dish, Spas or Tanapoor, with Matsun, Egg, Wheat, and Herbs [64]

CONCLUSION

The cultural evolution of matsun making and its uses in traditional medicine for digestive disorders illustrate a rich history in which culinary and medical practices overlap. By examining traditional foodways and ancient medicine, researchers can find valuable sources of BCs for use in disease management and overall health. The everyday use of foods purported for health benefits can also provide insight into effective vehicles for delivering these health benefits. In making and consuming matsun, Armenians have preserved a centuries long selection of beneficial bacteria, passing health benefits to future

generations and affecting scientific research in probiotics today.

Isolated bacterial strains derived from matsun have illustrated the potential for management of digestive symptoms, but clinical trials are needed to confirm the interactions in the human body and establish effective dosages. The use of L. acidophilus isolated from Choratan in a clinical trial, effectively dried matsun, demonstrated the ability to establish an effective dose and illustrated the potential of LAB to inhibit pathogenic bacterial growth in the colon. However, more trials are needed to confirm this and disentangle the effects among different disorders. Studies concentrated on specific disorders, such as done in the Narine FMF trials may reveal more information about the biological pathways involved. The isolation of individual bacteria from matsun in studies may obscure the effects of the selective combinations of bacteria and yeast already present through controlled serial inoculation.The collection of regional matsun varieties and the analysis of their microbial composition illustrates matsun as a rich source of probiotics. Continued collection of traditionally made matsun and choratan may provide sources of previously understudied microbial strains. Preclinical trials are needed to confirm potential benefits of regional variations and newly uncovered strains. Whole matsun feeding trials could further shed light on the potential benefits of selectively combined microbial strains on human health. Further examination into the effects of additional ingredients combined with matsun have the potential to reveal the ways in which food combinations can affect probiotic ingestion.

Narine has been studied for over fifty years with demonstrated effects on the management of gut dysbiosis. This intense study has led to established dosages and marketing as a dietary supplement. For these reasons, Narine is a good candidate for a FF product, however, molecular mechanisms need to be investigated and epidemiological and aftermarket studies are needed to evaluate effectiveness in populations. Large-scale retrospective cohort studies in a specific pathology, such as FMF or IBD, could be used to evaluate the correlations between *L. acidophilus INMIA 9602* Er-2 strain 317/402 Narine intake and the effect on commensal gut flora over time. Narine is sold both as a powdered probiotic strain in capsules and as a reconstituted mixture of probiotics and milk, however, clinical studies used only the capsule form. Observational analysis of the vehicles chosen, Narine powder capsules or reconstituted, in aftermarket study and stool analysis for the effectiveness of each for dose delivery can shed light on the ways in which people choose to consume functional foods and the effectiveness of the different forms in which Narine is marketed and available. The replication of clinical trials in more countries could also aid in further confirming Narine's functional status.

Abbreviations: BC bioactive compound**,** FF functional food, FMF Familial Mediterranean Fever, IBS Inflammatory Bowel Syndrome, LAB lactic acid bacteria, MDR multidrug resistant, MRSA Methicillin-resistant staphylococcus aureus

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Author's Contributions:

The idea of tracing the history of medieval Armenian dietary remedies to modern use was conceived by DM and discussed with KG. KG conducted exploratory research on medieval Armenian diets and suggested a review of matsun. KG collected and reviewed articles and wrote the manuscript. DM advised, participated in reviewing articles and editing the manuscript.

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REFERENCES

1. Baek, Young and Lee, Byong. Probiotics and Prebiotics as Bioactive Components in Dairy Products. 2009; DOI: 10.1002/9780813821504.ch12.
2. Bokulich NA, Amiranashvili L, Chitchyan K, et al. Microbial biogeography of the transnational fermented milk matsoni. Food Microbiology. 2015;50:12-19. DOI:10.1016/j.fm.2015.01.018
3. Afrikian E. Studies of lactic-acid bacteria in Armenia with emphasis on radioprotective properties. Environmentalist. 2012;32(2):256-268. DOI:10.1007/s10669-012-9387-4
4. Martirosyan D, Lampert T, Ekblad M. Classification and regulation of functional food proposed by the Functional Food Center. *Functional Food Science*. 2022;2(2):25-46. DOI:10.31989/ffs.v2i2.890
5. Kalikyan Z, Avagyan V, Abrahamyan A, Vardanyan L, Selimyan A, Avagyan M. Armenian fermented milk product Choratan and its influence on gut microbiota in health and pathology. *Bioactive Compounds in Health and Disease*. 2018;1(5):60. DOI:10.31989/bchd.v1i5.562
6. Pepoyan A z., Balayan M h., Manvelyan A m., et al. Lactobacillus acidophilus INMIA 9602 Er-2 strain 317/402 probiotic regulates growth of commensal Escherichia coli in gut microbiota of familial Mediterranean fever disease subjects. *Letters in Applied Microbiology*. 2017;64(4):254-260. DOI:10.1111/lam.12722
7. Gurunluoglu A, Gurunluoglu R, Hakobyan T. A medieval physician: Amirdovlat Amasiatsi (1420–1495). *J Med Biogr*. 2019;27(2):76-85. DOI:10.1177/0967772016682726
8. Vardanyan S. The medical heritage of medieval Armenia. Its theoretical and practical value in the light of modern science. *The New Armenian Medical Journal.* 2007;1:15-27. Accessed August 19, 2022. https://www.ysmu.am/website/documentation/files/51d6e579.pdf
9. Israelyan N. Fecund Earth: Health and History Traditions in Armenia. *Fourth World Journal*. 2019;17(2):92-105.
10. Kulp WL, Rettger LF. Comparative Study of Lactobacillus acidophilus and Lactobacillus bulgaricus. *J Bacteriol*. 1924;9(4):357-395.
11. Lipman JG. *Bacteria in Relation to Country Life*. Macmillan; 1908.
12. The Microbial Depository Center at Armbiotechnology. [SCIENTIFIC AND PRODUCTION CENTER "ARMBIOTECHNOLOGY" NAS RA] Retrieved June 28, 2022.
13. Heirloom Microbes. Warinner Group. Published July 2, 2017. Accessed June 27, 2022. http://christinawarinner.com/research-2/research-h/
14. Edwards CJ, Bollongino R, Scheu A, et al. Mitochondrial DNA analysis shows a Near Eastern Neolithic origin for domestic cattle and no indication of domestication of European aurochs. *Proceedings of the Royal Society B: Biological Sciences*. Published online April 3, 2007. DOI:10.1098/rspb.2007.0020
15. Curry A. Archaeology: The milk revolution. *Nature*. 2013;500(7460):20-22. DOI:10.1038/500020a
16. Zeder MA. Domestication and early agriculture in the Mediterranean Basin: Origins, diffusion, and impact. *Proc Natl Acad Sci U S A*. 2008;105(33):11597-11604. DOI:10.1073/pnas.0801317105.
17. Evershed RP, Payne S, Sherratt AG, et al. Earliest date for milk use in the Near East and southeastern Europe linked to cattle herding. *Nature*. 2008;455(7212):528-531. DOI:10.1038/nature07180
18. Scott A, Reinhold S, Hermes T, et al. Emergence and intensification of dairying in the Caucasus and Eurasian steppes. *Nat Ecol Evol*. 2022;6(6):813-822. DOI:10.1038/s41559-022-01701-6
19. Wang C, Reinhold S, Haak W, et al. Ancient human genome-wide data from a 3000-year interval in the Caucasus corresponds with eco-geographic regions | Nature Communications. Accessed June 27, 2022. https://www.nature.com/articles/s41467-018-08220-8
20. Ozen M, Dinleyici EC. The history of probiotics: the untold story. *Beneficial Microbes*. Published online January 9, 2015. DOI:10.3920/BM2014.0103
21. Fisberg M, Machado R. History of yogurt and current patterns of consumption. *Nutrition Reviews*. 2015;73(suppl_1):4-7. DOI:10.1093/nutrit/nuv020
22. Elder.) P (the. *The Natural History of Pliny*. H. G. Bohn; 1855.
23. Nicholas Adontz, Նիկողայոս Ադոնց. *Dionisii Trakiiskii i armyanskie tolkovateli [Dionysius Thrax and His Armenian Commentators]*. Accessed June 27, 2022. http://archive.org/details/adontz-1915-dionysius-thrax-russian
24. Hirato M. *Milk Culture in Eurasia*. Accessed June 27, 2022. https://link.springer.com/book/10.1007/978-981-15-1765-5 ch.7, 8.
25. Matsun - Arca del Gusto. Slow Food Foundation. Accessed May 19, 2022. https://www.fondazioneslowfood.com/en/ark-of-taste-slow-food/matsun/
26. Petrosian I, Underwood D. *Armenian Food: Fact, Fiction & Folklore*. Lulu.com; 2006.ch16.
27. James F. Yogurt: Its Life and Culture. *Expedition*. 1975;18(1):32-38.
28. Meet the Family Making Yogurt with a Healthy Serving of Armenian Culture. The Armenian Weekly. Published December 6, 2018. Accessed April 24, 2022. https://armenianweekly.com/2018/12/06/meet-the-

family-making-yogurt-with-a-healthy-serving-of-armenian-culture/

29. MHS Collections Online: Colombo Yogurt 8-ounce container. Accessed April 28, 2022. http://www.masshist.org/database/205
30. "Colombo" Yogurts - How Armenian Matsun Conquered America. Phoenix Tour Armenia. Published January 15, 2022. Accessed June 10, 2022. https://phoenixtour.org/blog/colombo-yogurts-how-armenian-matsun-conquered-america/
31. Gurel P. Live and Active Cultures: Gender, Ethnicity, and "Greek" Yogurt in America. *Gastronomica*. 2016;16(4):66-77.
32. Tanapoor - Spas - Yogurt Soup - Heghineh.com Armenian Cuisine. Accessed June 27, 2022. https://heghineh.com/spas/
33. Spas-Armenian Yogurt Soup. Phoenix Tour. [Spas - Armenian yogurt soup (Tanapoor) | Phoenix TourArmenia] Retrieved June 28, 2022.
34. Ushakova AM. Tan - Armenian Yogurt Drink. MariaUshakova.com. Published July 2, 2014. Accessed June 27, 2022. https://www.mariaushakova.com/2014/07/tan-armenian-yogurt-drink/
35. Davtyan S. The Armenian Plant Names ananux and nni, and Persian na'nā' and nānxvāh. *Journal of Near Eastern Studies*. 2019;78(1):113-117. DOI:10.1086/702191
36. Khanna R, MacDonald JK, Levesque BG. Peppermint oil for the treatment of irritable bowel syndrome: a systematic review and meta-analysis. *J Clin Gastroenterol*. 2014;48(6):505-512. DOI:10.1097/MCG.0b013e3182a88357
37. Manser CN, Paul M, Rogler G, Held L, Frei T. Heat waves, incidence of infectious gastroenteritis, and relapse rates of inflammatory bowel disease: a retrospective controlled observational study. *Am J Gastroenterol*. 2013;108(9):1480-1485. DOI:10.1038/ajg.2013.186
38. Xu Z, Liu Y, Ma Z, (Sam) Toloo G, Hu W, Tong S. Assessment of the temperature effect on childhood diarrhea using satellite imagery. *Sci Rep*. 2014;4:5389. DOI:10.1038/srep05389
39. Afrikian EG. Biological and Practical Aspects of Lactobacteria from National Food Matsoon. *Electronic Journal of Natural Sciences*. 2009;12(1):16-23.
40. Movsesyan I, Ahabekyan N, Bazukyan I, et al. Properties and Survival Under Simulated Gastrointestinal Conditions of Lactic Acid Bacteria Isolated from Armenian Cheeses and Matsuns. *Biotechnology & Biotechnological Equipment*. 2010;24(sup1):444-449. DOI:10.1080/13102818.2010.10817880
41. Israyelyan A, Karapefyan K, Thruni F, et al. Sensitivity of different pathogens to biological antimicrobial agents. Accessed May 5, 2022 https://cyberleninka.ru/article/n/sensitivity-of-different-pathogens-to-biological-antimicrobial-agents/viewer
42. Bazukyan I, Matevosyan L, Toplaghaltsyan A, Trchounian A. Antifungal activity of lactobacilli isolated from Armenian dairy products: an effective strain and its probable nature. *AMB Expr*. 2018;8(1):87. DOI:10.1186/s13568-018-0619-y
43. Israyelyan A, Karapetyan K, Arstamyan L, Alexsanyan L. Interaction of Lactic Acid Bacteria under Different Conditions of Combined Growth. *Biol Bull Russ Acad Sci*. 2021;48(3):290-295. DOI:10.1134/S1062359021030079
44. Matevosyan L, Bazukyan I, Trchounian A. Antifungal and antibacterial effects of newly created lactic acid bacteria associations depending on cultivation media and duration of cultivation. *BMC Microbiology*. 2019;19(1):102. DOI:10.1186/s12866-019-1475-x
45. Pepoyan AZ, Manvelyan AM, Balayan MH, et al. The Effectiveness of Potential Probiotics Lactobacillus rhamnosus Vahe and Lactobacillus delbrueckii IAHAHI in Irradiated Rats Depends on the Nutritional Stage of the Host. *Probiotics & Antimicro Prot*. 2020;12(4):1439-1450. DOI:10.1007/s12602-020-09662-7
46. Tkhruni FN, Karapetyan KJ, Danova ST, Dimov SG, Karimpour FA. Probiotic properties of endemic strains of lactic acid bacteria. *Journal of BioScience & Biotechnology*. 2013;2(2):109-115.
47. Selimian DA. New Approach to the Significant Reduction of Green House Gases (GHG) in Pork and Poultry Production. *IOSR-JAVS*. 2013;2(2):18-22. DOI:10.9790/2380-0221822
48. Armenian Yogurt - Մերած Սածուն - Armenian Cuisine. Heghineh.com. Published October 20, 2015. Accessed June 27, 2022. https://heghineh.com/armenian-yogurt/
49. Scientific And Production Center "Armbiotechnology" NAS RA. [https://armbiotech.am/en/products/narine-dietary-lactic-acid-product]. Accessed June 27, 2022.
50. Papikyan, S. *The Association of Maternal Knowledge and Management With Prevalence and Duration of Childhood Diarrheal Disease in Yerevan*. [Dissertation]. Yerevan: American University of Armenia; 2009.
51. Narum. Narum Sour Milk, 5 sachets. Sklep z probiotykami Narine, opinie | Producent Narum Polska. Accessed June 27, 2022. https://mynarum.com/en/narum-sour-milk--5-sachets,76,72.html
52. Pure Narine | Health & Wellness Partners Inc. Published July 9, 2018. Accessed June 27, 2022. https://hwpartners.co.jp/en/product/pure-narine/
53. Harutyunyan N, Kushugulova A, Hovanissyan N, Pepoyan A. One Health Probiotics as Biocontrol Agents: One Health Tomato Probiotics. *Plants*. 2022;11:1334. DOI:10.3390/plants11101334
54. Pepoyan A, Balayan M, Manvelyan A, et al. Probiotic Lactobacillus acidophilus Strain INMIA 9602 Er 317/402 Administration Reduces the Numbers of Candida albicans

and Abundance of Enterobacteria in the Gut Microbiota of Familial Mediterranean Fever Patients. *Front Immunol*. 2018;9:1426. DOI:10.3389/fimmu.2018.01426

55. Martirosyan AO, Mndzhoyan ShL, Charyan LM, Akopyan LG, Nikishchenko MN. Antimicrobial Activity of Lactic Acid Bacteria from Sour Milk Products Narine, Karine, and Matsun. *Applied Biochemistry and Microbiology*. 2004;40(2):178-180. DOI:10.1023/B:ABIM.0000018922.03283.b9
56. Narine's Allure. Health and Wellness Partners Inc. [NARINE'S ALLURE | Health & Wellness Partners Inc. (hwpartners.co.jp)]. Accessed June 28, 2022.
57. Mkrtchyan H, Gibbons S, Heidelberger S, Zloh M, Limaki HK. Purification, characterisation and identification of acidocin LCHV, an antimicrobial peptide produced by Lactobacillus acidophilus n.v. Er 317/402 strain Narine. *International Journal of Antimicrobial Agents*. 2010;35(3):255-260. DOI:10.1016/j.ijantimicag.2009.11.017
58. Charchoghlyan H, Kwon H, Hwang DJ, Lee JS, Lee J, Kim M. Inhibition of Cronobacter sakazakii by Lactobacillus acidophilus n.v. Er2 317/402. *Korean J Food Sci Anim Resour*. 2016;36(5):635-640. DOI:10.5851/kosfa.2016.36.5.635
59. Research Sector of LActic Acid Bacteria. Armbiotech. [SCIENTIFIC AND PRODUCTION CENTER "ARMBIOTECHNOLOGY" NAS RA]. Accessed June 28, 2022.
60. Pepoyan AZ, Pepoyan ES, Galstyan L, et al. The Effect of Immunobiotic/Psychobiotic Lactobacillus acidophilus Strain INMIA 9602 Er 317/402 Narine on Gut Prevotella in Familial Mediterranean Fever: Gender-Associated Effects. *Probiotics Antimicrob Proteins*. 2021;13(5):1306-1315. DOI:10.1007/s12602-021-09779-3
61. Tkhruni FN, Aghajanyan AE, Balabekyan TR, Khachatryan TV, Karapetyan KJ. Characteristic of Bacteriocins of Lactobacillus rhamnosus BTK 20-12 Potential Probiotic Strain. *Probiotics Antimicrob Proteins*. 2020;12(2):716-724. DOI:10.1007/s12602-019-09569-y
62. Martirosyan D.M., Sanchez S.S. Establishment of dosage of bioactive compounds in functional food products. Functional Food Science 2022; 3(2): 79-93. DOI: https://doi.org/10.31989/ffs.v2i3.915
63. Ciga. Assortment of Kashk, Qurut, Chortan, Qurt, Aaruul at the market, a type of hard cheese in Central Asia and Middle East. Shutterstock. https://www.shutterstock.com/image-photo/assortment-kashk-qurut-chortan-qurt-aaruul-1439767118. Accessed August 21,2022.
64. Frantic00. A traditional Armenian dish is spas soup made from fermented yogurt or matzoon with egg yolk and wheat. Helps to cope with a hangover. Shutterstock. https://www.shutterstock.com/image-photo/traditional-armenian-dish-spas-soup-made-2067373862. Accessed August 22, 2022.