Bring Back the Fat in Dairy

- To limit saturated fat intake, the most recent edition of the Dietary Guidelines for Americans advises eating low-fat and non-fat versions of dairy foods.
- A growing body of scientific research suggests dairy fats can have positive effects on heart health and the risk for other chronic diseases.
- A new study of over 30,000 post-menopausal women found that a higher intake of dairy, regardless of fat content, was associated with lower blood triglycerides, LDL cholesterol, glucose, insulin, and two markers associated with inflammation.
- Data from this large cross-sectional study suggest dairy-derived saturated fats are beneficial for heart health, chronic inflammation, and glucose metabolism.

Fashion trends from the 1990s may be making a comeback, but 1990’s dietary trends should definitely stay out of style. In that decade, fat was a four-letter word and non-fat and low-fat versions of foods were promoted over their full-fat counterparts, with the hope of improving heart health and reducing waist lines. We now know that trading fat for carbohydrates did not make Americans healthier (or thinner), but old habits die hard. Thirty years later, the influence of this fat-free mania on food choices and dietary recommendations is still evident. The most recent edition of the Dietary Guidelines for Americans [1] recommends non-fat and low-fat milk, yogurt, and cheese to limit saturated fat intake. But far from clogging arteries and increasing cholesterol, a growing body of scientific studies [2–7] suggests dairy-derived saturated fats could be beneficial for cardiovascular health.

The most recent vindication for dairy fats comes from data collected as part of the Women’s Health Initiative, one of the largest studies to address risk factors for cardiovascular disease. Detailed dietary data and blood samples were collected from over 35,000 post-menopausal women aged 50–79 from across the United States to test the hypothesis that dairy foods are associated with blood biomarkers commonly used to assess risk for cardiovascular disease and diabetes [8]. These included markers for lipid metabolism (total triglycerides, low-density lipoprotein, high-density lipoprotein, and total cholesterol), inflammation (C-reactive protein, IL-6, IL-10, and TNF-α), and glucose metabolism (glucose and insulin-related factors) [8].

Eating more dairy, including full-fat milk, cheese, and yogurt, was associated with a favorable biomarker profile. Going against the dogma that saturated fats are bad for heart health, higher intakes of full-fat dairy, cheese, and yogurt were associated with lower levels of blood triglycerides. And women with higher intakes of total dairy (all levels of fat), low-fat dairy, total cheese, and total yogurt also had lower levels of glucose, insulin, and two markers of inflammation (C-reactive protein and IL-6) [8].

Of all the dairy foods included in the analysis [8], yogurt seemed to have a unique influence on biomarker profiles. Increased yogurt consumption was associated with the largest percentage decrease in blood glucose, insulin, C-reactive protein, and IL-6 concentrations [8], supporting previous research on the protective effects of yogurt on inflammation and diabetes. Additionally, yogurt intake—of all fat levels—was associated with an increase in high-density lipoprotein (HDL) cholesterol, and a decrease in total
triglycerides and low-density lipoprotein (LDL) cholesterol. (For those needing a quick recap on cholesterol, LDL are proteins that move fat into the walls of the arteries and can lead to plaque, whereas HDL remove fats from the artery walls. Generally speaking, higher LDL increases the risk for cardiovascular disease, whereas lower LDL and lower triglycerides decrease the risk).

These additional effects of yogurt compared with other dairy foods are, at least in part, because yogurt is fermented and contains probiotic bacteria, like Lactobacillus. As yogurt is digested, these beneficial bacteria increase the concentration of biologically-active proteins, which then, in turn, could potentially influence physiological processes like glucose metabolism, lipid metabolism, and inflammatory reactions [9].

Cheese, another fermented dairy food, was also associated with favorable profiles [8]. Looking at just yogurt and cheese, one could argue that fermented dairy might offer health benefits despite their saturated fat content. But the finding that full-fat dairy intake was associated with lower triglycerides, as well as lower insulin and glucose concentrations, suggests that dairy-derived saturated fats could actually be mediating these associations [8] rather than simply riding the coattails of probiotics or other nutrients in dairy.

Milk fats are biologically different from those found in bacon or biscuits. Fats in milk are packaged in membrane-bound bubbles called globules (and are referred to as the milk fat globule membrane, or MFGM). Dairy fatty acids within the MFGM are shorter in carbon chain length relative to fatty acids from other animal fats, which could positively affect cholesterol by raising HDL levels [10, 11]. And new research suggests the MFGM interacts directly with microorganisms in the gut [12], which could then influence human physiology in much the same way as probiotics from fermented foods.

It seems counterintuitive that saturated fats could be heart healthy. After all, we have been inundated with dietary advice to limit or avoid them for decades precisely because of their association with cardiovascular disease. But it might be time for dietary advice to join the 21st century and focus on the biological effects of foods rather than nutrients.

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New Processing of Dairy Milk Yields Drug Delivery Vehicles

- Exosomes are small, membrane-enclosed vesicles produced by cells that can withstand digestion and pass the blood brain barrier.
- Pharmaceutical industries have a strong interest in exploring exosomes as drug delivery vehicles.
- Dairy milk contains a high concentration of exosomes, but purifying the extracellular vesicles and scaling up production has proven challenging.
- Scientists have described a new-and-improved scalable method of distilling exosomes from dairy milk.
- The new method has a 12.5% exosome extract return from starting volume, or roughly a cup of exosomes for every gallon of milk.

Dairy could a have a surprising new role to play in biomedicine and pharmacology. Over the past few years, researchers have shown a surging interest in exosomes [1–3], tiny membrane-bound vesicles that carry molecules from cell to cell. Scientists are hopeful that these cellular bubbles could serve as the ideal drug delivery vehicle. In a new paper, researchers have described an improved method for distilling an impressive number of exosomes from a cheap and widely available product—cow’s milk [4].

“Imagine instead of getting a vaccine shot, your nurse hands you a milkshake,” says Rob Gourdie, a biomedical researcher at the Virginia Polytechnic Institute, when describing the myriad medical possibilities with exosomes as a drug courier. “Another milkshake may contain exosomes loaded with a therapeutic peptide designed to protect internal organs such as the heart from myocardial infarction.”

Exosomes are a type of extracellular vesicle that regularly bleb off cell membranes in most animal cells. These lipid-bound packages, between 50 and 150 nanometers in diameter, ferry particles such as lipids, proteins, and nucleotides between cells [5]. Until relatively recently, scientists didn’t pay much regard to this cellular packaging, but in 2007, these vesicles were discovered to transfer genetic material that alters gene expression in cells [6]. That’s when biomedical researchers began to realize the potential of exosomes in drug delivery; the vesicles can be ingested and survive in vivo, and they are able to pass the blood-brain barrier, a protective barrier that prevents pathogens or unwanted chemicals from entering the brain [7]. Although the blood-brain barrier has a critical function in protecting the organ, it has posed a serial challenge for pharmacologists trying to deliver medication to the brain.

Body fluids such as blood, lymphatic fluid, urine, and milk contain abundant supplies of exosomes, but distilling exosomes from dairy milk has a few challenges [8]. “Exosomes are abundant in cow’s milk, yet they’re difficult to isolate from other milk proteins and lipids,” says Gourdie.

Prior to the new method described in the journal Nanotheranostics, exosomes were largely extracted from milk using a method called ultracentrifugation [4]. Essentially, the multi-step process involves spinning small volumes of a solution in a centrifuge for long periods of time, which makes larger molecules sink to the bottom of the solution. However, this process faces two main challenges—milk proteins called caseins form blobs that are very difficult to separate from the exosomes, which contaminates the purity of the exosome solution; and the centrifugation process is difficult to scale up, as only small quantities of milk can be centrifuged at a time [4].
Through trial-and-error, Gourdie and his research team greatly improved upon the distillation methods already in use. Most notably, they added a novel step called chelation that uses positively charged calcium ions to solubilize caseins and other contaminating proteins. In the ultracentrifugation method of extracting exosomes, this improved method yielded roughly 75 milligrams of exosome concentrate for every liter of dairy milk, or a 7.5% return from the starting volume [4].

Although adding a chelation step was able to clean out the pesky proteins, the scalability problem still remained. That’s why a chelation step was also added to a different exosome extraction method called tangential flow filtration (TFF), which works more like a molecular sieve to filter out particles of a desired size. A new and improved TFF method gave 12.5% exosome extract return from starting volume, or roughly a cup of exosomes for every gallon of milk [4]. “For the first time, we’ve charted a path toward the industrial scalability of exosome purification for oral drug delivery,” says Gourdie about the TFF chelation method.

“What’s remarkable is the quantity of extracellular vesicles they are able to produce,” says Joy Wolfram, a biomedical researcher at Mayo Clinic who was not involved in the study. “Isolating and manufacturing extracellular vesicles in a scalable manner has always prevented their translation into the clinic, but this paper shows a path to overcome those roadblocks.”

The new dairy exosome purification process could serve to be one key step in a budding branch of pharmacology.


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Anti-viral Properties of Human Milk Oligosaccharides

- Sugars found in human milk, called human milk oligosaccharides (HMOs), have been shown to protect against bacterial pathogens and viruses.
- A new review provides an overview of evidence that HMOs might protect against viruses common in pediatric ICUs, including norovirus and respiratory syncytial virus.
- The findings further highlight the benefits of breastfeeding in protecting infants, while also adding to the potential applications of HMOs.

A surge in viral infections this past summer caused more children to be hospitalized than usual, and it’s not all COVID-19 [1,2]. Other respiratory viruses, including respiratory syncytial virus, have been hitting kids hard, highlighting how vulnerable they can be to viral infections. So it’s a good thing that in addition
to providing nutrition, human milk can help protect against these diseases. Sugars called human milk oligosaccharides (HMOs) are abundant in human milk and are one of the human milk components that have been shown to have protective effects against a wide range of pathogens.

Many studies have shown how HMOs protect against bacterial pathogens, and Dr. Steven Townsend of Vanderbilt University wondered whether there was also evidence for their effects against viruses. “We know these compounds have activity against bacteria, so I told my students to start to figure out what’s known in the literature about their antiviral properties,” he says. In a new review article, Townsend and his co-authors present an overview of evidence that HMOs might also protect against several viruses [3]. “It turns out that these compounds do have some interesting antiviral properties,” he says.

Viruses recognize and bind to sugars in our body during infection, and the review article highlights several examples of human milk sugars functioning as a receptor decoy for viral binding and thus preventing viral infection [3]. “These compounds look like a lot of sugars that are on human surfaces, whether it’s in our saliva, on the mucus layer, in our eyes, or on our epithelium, and they become very potent decoy receptors,” says Townsend.

Townsend and his colleagues listed examples of binding between certain HMOs, such as 2-fucosyllactose and 3-fucosyllactose, and several viruses, including influenza, rotavirus, respiratory syncytial virus, human immunodeficiency virus (HIV), and norovirus, as well as evidence of such binding reducing viral infection [1–14]. They also found evidence of a role for HMOs in modulating the immune response, which can reduce infection by these viruses and also prevent necrotizing enterocolitis (NEC), an intestinal disease linked to viral infections [14–18]. Some studies have found disialyllacto-N-tetraose to be the most effective HMO in preventing NEC, although the underlying mechanism is still unclear [19,20].

High concentrations of HMOs present in breast milk have also been shown to reduce the risk of transmission of HIV to the infant through breastfeeding [13]. Researchers are also starting to look into whether SARS-CoV-2, the virus responsible for the COVID-19 pandemic, is transmitted through breastfeeding, and whether HMOs can serve as receptor decoys or have other protective effects against this virus [21].

The review article suggests that the antiviral properties of HMOs may be worth investigating further [3]. Researchers still don’t fully understand the specific structural basis for HMOs’ antiviral properties, and only a small number of known HMOs have been structurally characterized or evaluated for antiviral activity.

Figuring out ways to synthesize more HMOs would help researchers better study the link between their structure and their antiviral activity. “My group and others are figuring out ways to synthesize these compounds,” says Townsend. “I think if we’re careful and we’re smart, there are a lot of strategic applications for most of them,” he says.

The review highlights yet another way that human milk protects infants. “Breastfeeding is super powerful, and if you just go to the literature, you can see breastfed babies typically get sick far less than formula-fed babies, and HMOs are just a small part of that equation,” says Townsend. “Infant formula does not have HMOs, and there are companies that are trying to add them to formula, but they’re not adding 8 to 20 grams, so what we’re able to add at the moment is not even close to what moms can provide,” he says. So when it comes to protecting infants against infections, it seems like there’s no substitute for mother’s milk.

Dairy Farming Is Getting a Big Data Boost

- Data sets from dairy farms are being cleaned, standardized, and integrated to create a suite of new tools to assist dairy farmers in decision making.
- Tools include calculating feed efficiency, determining nutritional groupings, detecting early onset for clinical mastitis, determining the financial value of a cow, and creating first lactation curves.
- Farmers will be able to easily access these customizable tools in a web platform or app.

Industries around the world are being swept up in a Big Data and AI revolution, and dairy is no exception. A new, multidisciplinary project called Dairy Brain is using big data analytics and AI to give the industry a technological boost. Dairy Brain, a collaborative project with the University of Wisconsin-Madison, is designing a web-based platform with a suite of smart tools informed by data analytics and AI that assists dairy farmers in management and decision making.
“The main idea of the Dairy Brain project is to collect data from farms, integrate all the data, and develop decision-supporting tools at different levels,” says Liliana Fadul-Pacheco, a research associate at the University of Wisconsin-Madison.

To start, Fadul-Pacheco and a multi-disciplinary team of collaborators collected data from a variety of sources, from the milking parlor to the Dairy Herd Improvement Association (DHIA), to genetics. They then set to work cleaning, standardizing, and integrating the information in a portion of the project called the Agricultural Data Hub. With these gargantuan quantities of data they then have been able to create a host of tools to assist dairy farm management [1].

“This type of data has been always there, but I think the nice thing about what we’re doing at Dairy Brain—the innovation part—is integrating everything,” says Fadul-Pacheco, explaining that while farmers have lots of raw data and statistics, they don’t necessarily have the time or expertise to analyze it. One of the early challenges, she says, is that streams of information historically have been kept separate and being able to link and standardize the data will lead to a more robust dataset that can train machine learning algorithms.

For example, Fadul-Pacheco says farmers may have feed data and milk production data, but the two might not be integrated in order to calculate feed efficiency, a ratio between the amount of feed a cow is consuming and her milk production. By integrating the two datasets, farmers can get quick and up-to-date feed efficiency statistics for their herds. Anomalies in feed efficiency could indicate to the farmer a possible issue with the feed or feeding regimen, for example.

And the feed efficiency calculator is just one simple tool created using dairy’s Big Data. Another tool has been created for nutritional group management. When feeding cows, farmers can group them by parameters such as lactation stage, age, or size, but a new algorithm can take all these factors into account and create the optimal groupings for the farmer [2].

Fadul-Pacheco is also building a machine-learning algorithm that can predict which cows might be at risk of developing clinical mastitis, an infectious disease of the mammary glands that causes visibly abnormal milk. The machine-learning algorithm can be trained on large datasets to scan for patterns and predictive variables that could be early indicators of the disease. The many variables and statistical biases in the data are a challenge to work around, and Fadul-Pacheco says, “The next steps right now are to have more data, continue training the algorithm, and maybe add some genetic variables” [3].

Another complex tool is designed to calculate the financial value of a cow. “If you have two cows and you need to sell one because you don’t have space, you need to decide which will be better in the future,” Fadul-Pacheco offers as a simple example. By considering variables such as productivity, health, and reproduction, Dairy Brain researchers can create an algorithm for estimating the net financial value of each cow in order to inform management decisions.

Another module, which Fadul-Pacheco says is still in the early stages of development, is calculating the first lactation curve for cows. Lactation curves are created when a cow gives birth and her milk productivity is graphed over time. Dairy farmers can create the curves for cows that have had at least one calf, as the data is extrapolated from their first birth. However, determining a first lactation curve for a cow is trickier. Data scientists are working on an algorithm to calculate this based on a cow’s siblings.

“It’s been challenge after challenge, but we’re getting there,” says Fadul-Pacheco, who expects Dairy Brain to be ready for use in the next year or two. Other aspects of Dairy Brain have included the
Coordinated Innovation Network (CIN) that guides the responsible use of data, and the Extension Program, which regularly collaborates with dairy farmer stakeholders on the design and practicality of tools. “There are tools that are coming that are super practical,” says Fadul-Pacheco.


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