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Review

Got Whey? Sustainability Endpoints for the Dairy Industry through Resource Biorecovery

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Abstract: Whey has applications in food, beverages, personal care products, pharmaceuticals, and the medical sector. However, it remains a massive dairy residue worldwide (160.7 million m^3 $year^{-1}$), with high organic and nutrient loads. About 42% is used for low-value products such as animal feed and fertilizers or is even directly discharged into water streams, leading to ecosystem damage via eutrophication. We reviewed the uses and applications of cheese whey, along with associated environmental impacts and innovative ways to mitigate them using affordable and scalable technologies. Recycling and repurposing whey remain challenges for remote locations and poor communities with limited access to expensive technology. We propose a closed-loop biorefinery strategy to simultaneously mitigate environmental impacts and valorize whey resources. Anaerobic digestion utilizes whey to produce biogas and/or carboxylates. Alternative processes combining anaerobic digestion and low-cost open photobioprocesses can valorize whey and capture organic, nitrogenous, and phosphorous nutrients into microalgal biomass that can be used as food and crop supply or processed into biofuels, pigments, and antioxidants, among other value-added products. The complete valorization of cheese whey also depends on facilitating access to relevant information on whey production, identifying stakeholders, reducing technology gaps among countries, enforcing legislation and compliance, and creating subsidies and fostering partnerships with industries and between countries.

Keywords: cheese whey; food waste; anaerobic processes; microalgae; circular economy

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1. Introduction

Milk has been a part our daily lives for millennia. Unlike other mammals, humans continue to make use of this food past the lactation period. Although lactose tolerance is not inherent to most humans [1], the availability of dairy products continues to increase. Yogurts, cheese, and spreads, among other products, fill our shelves.

Despite the increasing consumption of plant-based dairy substitutes for milk, it is estimated that world milk production will grow at 1.6% per annum due to improved production systems and livestock husbandry [2]. According to Kim et al. (2022), cheese production is expected to increase by up to 14% by 2029 [3], leading to a rise in whey volume.

While environmental restrictions and limited domestic demand growth contribute to slower milk and cheese production in the European Union, India, Pakistan, and Africa are increasing their dairy consumption due to economic and population growth. It is estimated that in the coming decade, world per capita consumption of dairy products such as cheese will increase by 1.0% per annum [2].

In the dairy industry, liquid whey is what remains from milk after cheese or casein production [4], presenting a yellowish color with a bluish tinge depending on the type and quality of the milk used [5]. Sweet whey results from the manufacturing of hard cheeses such as cheddar or Swiss cheese, achieved by using rennet enzymes for coagulation. Acid whey results from milk acidification, either through the action of Lactobacillus bacteria or the addition of mineral acids (HCl or H_2SO_4) during cheese-making. Salty whey accounts for 2 to 5% of salted cheese production [6,7].

Generally, whey consists of water (90%), proteins (6.0 g L^{-1}), lactose (46–52 g L^{-1}), dissolved salts, lactic acid, lipids, minor components (e.g., citric acid, urea, and uric acid), and B-complex vitamins [8]. Its characteristics depend on its type (acid, sweet or salty), source of milk (e.g., bovine, caprine, sheep, and camel), animal feed, livestock stage of lactation, time of the year, and cheese-making processes. Variations in milk casein and fat ratio can lead to cheese yield and quality fluctuation between seasons and locations, influencing the quality of cheese whey produced [7]. This work focuses on bovine cheese whey.

Every 100 L of milk used in cheese production yields about 12 kg of cheese or 3 kg of casein [9]. This corresponds to the production of 87 L of whey per 100 L of milk. Large cheese-making plants can generate over a million liters of whey per day [4]. Cheese production is projected to increase by up to 14% by 2029 [3], leading to a corresponding increase in whey.

Amidst the COVID-19 pandemic, the dairy industry underwent major market adaptations in order to survive [10,11], as dairy products are highly perishable and reliant on complex distribution logistics that are time-critical [12]. The dairy sector suffered direct consequences from regulations that enforced the lockdown of education facilities and eating establishments for a certain period. Additionally, the fear that ruminants could carry the coronavirus contributed to a decrease in the demand for dairy products [2,13].

In many countries, milk had to be disposed of [11,14]. Some of the environmental, societal, and economic consequences of milk disposal can be translated into the contamination of soil and water bodies, eutrophication processes [15], farmer bankruptcies [16], and job losses [17]. Producing cheese as an alternative to disposing milk still generates a surplus of whey that must be considered.

Therefore, the complete valorization of cheese whey is necessary to guarantee the full transition of the dairy sector into the circular economy and to develop strategies to overcome unforeseen situations such as the coronavirus pandemic [18,19]. The circular economy (CE) aims to implement cascading processes that can further transform materials and their by-products into new value-added products [19–21] using renewable energy and moving toward zero waste production during processes [22].

The European Commission has introduced a purposeful agenda to foster the transition to the circular economy and sustainable development in all European Union (EU) member countries [19,23], with initiatives such as the Circular Economy Action Plan, which is part of the Green Deal [24]. Other countries investing in the CE include Japan (with the Circular Economy Vision), South Korea (with the Framework Act on Resource Circulation (FARC)), and China (with the Circular Economy Promotion Law of the People's Republic of China) [25–27].

In 2022, the cheese production forecast was approximately 160.1 million m^3 $year^{-1}$ [28]. However, in the first semester of the same year, this forecast was surpassed 700 thousand m^3 $year^{-1}$. This figure represents an excellent opportunity for fully valorizing cheese whey in the circular economy. Figure 1 depicts the global utilization of cheese whey for the year 2022 [7,9,28] and the growing world cheese production in tons from 1960 to 2020 [29]. Life cycle assessment can be used as an initial tool to address the cheese whey management issue.

Life cycle assessment (LCA) is a methodology used to identify factors and measure the impacts generated by a product or process from concept to end-use [30]. The implementation of LCAs in the dairy sector has only happened recently, with LCAs mostly being applied to cheese production [31]. Although some LCA studies consider the use of cheese whey in the production of polyhydroxyalkanoates (PHA) [23], lactic acid [32], and bioplastics [33], these studies still fail to address the complete environmental impacts of cheese whey from milk collection to final consumption or discharge [22,34]. The environmental impact assessment often depends on the chosen system boundaries (e.g., cradle-to-gate, gate-to-gate, cradle-to-grave) and the given allocations for the studies [31].

The valorization of cheese whey takes place after initial spray drying when both acid and sweet whey can be transformed into precursors for value-added products in the food, nutrition, and pharmaceutical industries [35] and as a substrate for the cultivation of microalgae biomass [36,37]. Salty whey has limited use in the industry due to its high salinity [38]. Additionally, whey cannot be used as the sole source of animal feed due to ruminants' dietary needs [39]. The same is valid for liquid whey, which is temperature-dependent, becoming unsafe for consumption once warm [40]. Soil application of whey or its direct discharge into water bodies is also not the best option as they result in severe environmental burdens. When used as a fertilizer, whey drastically acidifies the soil pH, and stabilization reaches as low as 2 units on the pH scale [41]. Its discharge into water bodies can unfavorably lead to eutrophication processes [7].

This review presents the problematic nature of cheese whey and how its management is fundamental to mitigate eutrophication and recover resources via bio-based processes while addressing the historical significance and contemporary challenges associated with whey utilization. The aim of this work is to present a closed-loop biorefinery scenario combining coupled processes such as acidogenic fermentation and photoheterotrophic processes in microalgal mixotrophic mixed-cultures. Acidogenic fermentation is discussed as a technology to solubilize cheese whey and microalgae for their ability to use the carbon, nitrogen, and phosphorus sources in whey and its derivatives (e.g., permeate, second cheese whey, and volatile fatty acids resulting from fermentation processes), leading to a biomass that is rich in these elements.

Additionally, we draw attention to the need to bridge stakeholders together to tackle cheese whey management, address the importance of improving the availability and affordability of technology to alleviate technology gaps among countries, and discuss the necessity of legislation enforcement and fostering partnerships between countries and industries to help in the full valorization of cheese whey. By addressing the environmental challenges posed by cheese whey and its potential to produce value-added products we aim to contribute to the realization of a circular economy in the dairy industry. 'Got Whey?'.

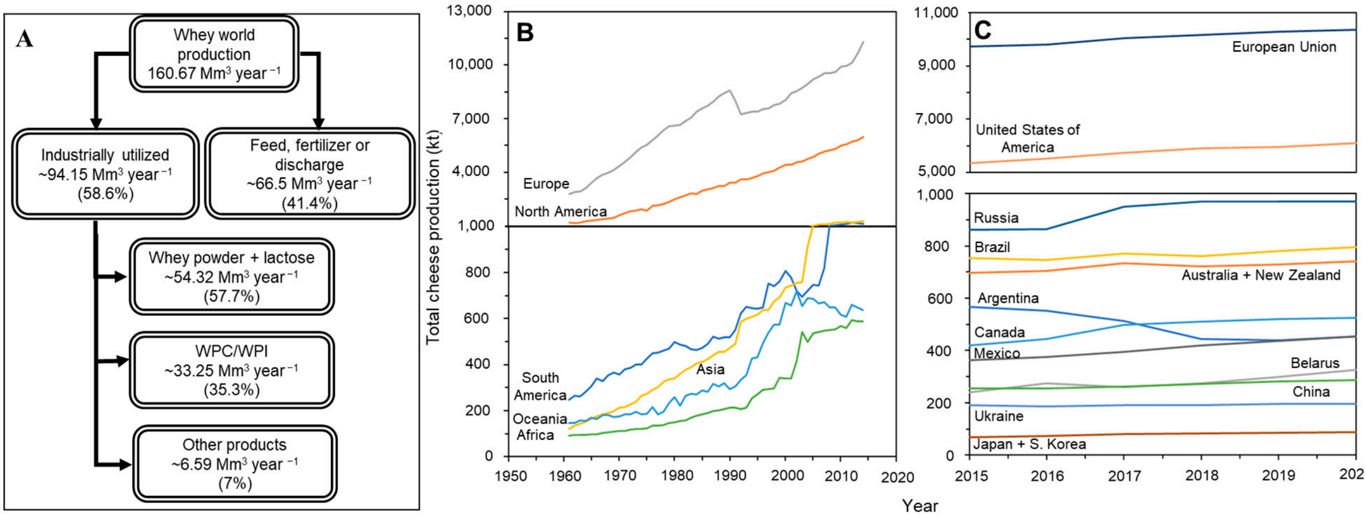

Figure 1. (**A**) Global utilization of cheese whey for the year 2022. Estimates were based on the amount of whey generated per kilogram of cheese, the percentages of whey repurposed by industry and their

remaining usage, and the forecast of cheese production for 2022 [7,9,28]. (**B**) Cheese production from 1960 to 2014 by continents. Geo-political changes were accounted for throughout the decades [29]. (**C**) Cheese production among the world's biggest producers from 2015 to 2020 (according to the authors of [42]). Values for the year 2020 were forecasted. Given recent changes in the main world cheese producers, the years 2021–2022 are not accounted for in the graph.

2. The Historical Significance and Contemporary Challenges of Dairying and Whey

2.1. From Dairy Discovery to the Role of Cheese and Whey

The Neolithic era, about 12,000 years before the present (BP), marked a significant shift from hunting and gathering to agriculture and livestock in the Near East and Anatolia, shaping human civilization [43,44]. Dairying emerged as a key practice, linked to animal domestication around 10,500 BP in Southeastern and Near East Anatolia, demonstrating the value of livestock. Strategies like culling the animals and harvesting them for meat production evolved during the early Neolithic period [43,45,46].

Lactose intolerance, resulting from decreased lactase production in mammals after weaning, was addressed in the Neolithic period by processing milk into cheese, yogurt, butter, and other dairy products [47]. These products released most lactose with whey, offering an option for lactose-intolerant individuals [43,48]. Genetic mutations around 7000 to 8000 BP in Europe and North Africa facilitated the digestion of lactose by adults, reducing lactose intolerance and expanding dairy consumption in these regions [49].

2.2. The Utilization and Environmental Impact of Whey

Dairying played a significant role in human settlements during the Neolithic period, when the discovery of cheese, yogurt, and derivatives resulted in the generation of whey as a by-product. Although the early uses of whey during the Neolithic period are not well documented, it found various applications over the following centuries.

Therapeutic uses: Whey's therapeutic potential dates back to 2410 BP, with Hippocrates continuing through the Middle Ages [50]. In Ancient Greece, whey was used as a skin balm or as a medicine [51]. Whey baths gained interest from the nineteenth century until World War II [50]. In 1760, Switzerland opened the first clinic to use cheese whey as medicine; cheese whey was used in this way primarily due to its diuretic and laxative properties. Central European spas served about 1.5 kg of whey per day to patients with various ailments, from gout to arthritis and liver diseases [52].

Food and beverages use: Whey became a fashionable drink in the mid-seventeenth century, with various preparations like whey borse (a broth), whey butter, whey porridge, and whey whig, a drink made with herbs [53]. In medieval Scandinavia, sour whey was used to pickle meats and produce a type of whey cheese with a high lactose content (30–35%) [54].

Animal feed: During the early centuries, surplus whey was mainly utilized as animal feed. Research on the nutritional aspects of whey began in the nineteenth century [50], and today, it continues to be a valuable animal feed source.

Agricultural uses: Excess whey can serve as a fertilizer, irrigation water, or be discarded into water bodies depending on location [4,5,7,50]. However, challenges such as its foul odor and high salinity limit its suitability as a fertilizer [55].

Environmental challenges: Whey disposal faces restrictions in many locations, with prohibitions regarding land disposal or municipal sewage systems. Small dairy farms can bear high costs for whey collection, treatment, and disposal, which sometimes leads to the illegal disposal in hydric bodies [55]. Such illegal disposal can lead to catastrophic consequences, including eutrophication processes that harm local ecosystems, water quality, and water resource availability.

Milk processing was a driving force for human settlements, allowing for the discovery of dairy and livestock management. However, despite its many uses throughout the centuries [56], whey production and handling still need to be addressed toward circular practices in the dairying sector.

3. Environmental Impacts and Management of Cheese Whey Residues

Whey is the most organic pollutant, as it is composed of the wastewater of the dairy industry. It presents an organic concentration as high as 50 to 80 g COD L^{-1} (in terms of chemical oxygen demand—COD) or 40 to 60 g BOD L^{-1} (expressed as biochemical oxygen demand—BOD) [57].

Once in the water stream, cheese whey can lead to eutrophication. In addition to organic matter, cheese whey is composed of organic nitrogen (0.2–1.8 kg N m^{-3}) and inorganic phosphorus (0.12–0.54 kg P m^{-3}), which drive algal blooms [58]. Whey treatment and recovery are paramount to valorize it and mitigate its environmental burden.

3.1. Environmental Burden and Elevated Costs of Treatment of Whey Residues

The treatment of surplus whey is fundamental to preventing adverse environmental impacts. As previously mentioned, the high organic and nutrient concentrations of whey render its utilization as fertilizer unfavorable. Whey acidifies and degrades quickly. When directly applied into the soil in large quantities, whey leads to soil acidification and increased salinity, which affects nutrient availability and microbial activity, consequently impacting plant growth and soil quality [59].

Additionally, whey has little microbial stability, and lactose has low water solubility, crystallizing at low temperatures [60]. The transportation of whey must be performed in temperature-controlled vehicles, and the farther the distance from the production site to the final destination, the higher the transportation costs. Most often, cheese producers must bear the costs of whey transportation [61], making its use as a fertilizer economically unfeasible. Still, depending on the location, the use of whey as a fertilizer is common.

The difficulty in establishing costs for treating cheese whey and dairy wastewater is not a recent issue. Procedures depend on the plant size, quality of the whey, and geological and climatic factors [62]. Hughes et al. [63] stated that small cheese producers in the USA seemingly only ensure the proper treatment and disposal of whey when production exceeds 5000 kg per year, with an average cost of USD 105.00 per ton being disposed of, leading to a substantial decrease in their profit margins.

Another matter in question is that logistics and regulations can be decisive in how whey and dairy wastewater are treated. This is oftentimes related to the producers' location [64]. Regarding cheese whey disposal, treatment, and valorization, in most cases, big dairy cooperatives are responsible for further processing cheese whey into other products [7].

Whey must be collected by an industrial and/or municipal sewer system. In developed countries, due to strict environmental regulations (such as the EU Landfill Directive 1999/31/EC [65]) and great road networks, whey and dairy wastewater usually undergo centralized treatment at a wastewater treatment plant [5].

In developing countries and remote locations, whey and dairy wastewater treatment are mostly decentralized [5]. Micro, small, and medium producers have limitations due to the lack of infrastructure connecting them to the industry, including minimal sector research and development (R&D) investments, the high cost vs. benefits to process cheese whey into value-added products, and the few markets available to sell the recovered products. These factors are closely related to the location of production [66]. Additionally, if regulations are not enforced, small and medium dairy producers may be encouraged to discharge their whey residues directly into a water stream [5].

Small and medium-sized dairy farms can benefit from centralized treatment facilities, where alternatives to whey valorization are combined with existing whey processing technology (i.e., spray drying), significantly reducing the disposal of whey in water bodies [67]. The greatest obstacles to small-scale whey processing remain health and safety issues, especially due to whey's potential for contamination and low shelf life [68,69].

Brazil provides an example of the importance of efficient road networks and centralized whey treatment and how they can have an effect on increasing whey valorization. Modern and artisanal cheese producers are scattered around the country, and about 40% of produced cheese whey is not exploited [70]. Small dairy farms must deal with higher costs to process whey; therefore, they often use whey as animal feed or fertilizer or discharge it into the environment [7,70].

The COVID-19 pandemic affected the dairy supply chain unprecedentedly. It disrupted supply chains worldwide. Consequently, the environmental burdens caused by milk dumping will persist for many years. The relaxation of the rules and regulations on dumping milk was a measure many countries implemented to keep dairy producers afloat during the unanticipated COVID-19 pandemic. Nevertheless, environmental regulations are crucial to guarantee a smooth transition to a circular economy that considers the full valorization of cheese whey.

3.2. Paving the Way for an Ecologically Balanced, Circular, and Participative Dairying Economy

Successful change implementation stems from engaging different stakeholders involved in the whey problem towards a common goal for its sustainable use, treatment, and disposal [71]. In a circular economy, the full valorization of cheese whey can be achieved by implementing a closed-loop approach, with cascading processes aiming to recover high-added value compounds with industrial applications (e.g., nutraceuticals, biofuels, food formulas) while producing minimum to zero waste [58,72,73].

Environmental laws and policies started in the 1970s with the establishment of the US Environmental Protection Agency and the first European environmental policy [74]. Community pressure led to changes in legislation, either banning or restricting the disposal of untreated whey, improving its waste management [4,5,51].

The European Green Deal, an ambitious initiative that covers all the different aspects of the economy, aims to mitigate climate change by fully transitioning to a circular economy and making the best use of the resources available while minimizing pollution and biodiversity loss [24].

Among other legislation and frameworks, the Circular Economy Package (CEP) [75] comprises regulations regarding waste management and recycling. Such laws and regulations were paramount to the development of alternatives on how to deal with surplus cheese whey. Table 1 shows the legislation pertinent to hydric resources and agro-industrial residues among the world's biggest cheese producers, considering the authors' best knowledge.

However, the Environment Rule of Law of the United Nations [76] divulged that, although most countries have environmental conservation regulations, only a few comply with them. This is often due to incomplete, irregular, or ineffective enforcement. In countries that embrace the polluter pays principle/model, industries often fail to comply with effective mitigation solutions beyond 'polluter pays'. Non-compliance can also originate from the difficulty in interpreting regulations due to an overload of information, jargon, and amendments. It also results from the misconception that environmental regulations hinder economic growth and competitiveness [77].

Oftentimes, the implementation of environmental management and resource recovery plans by companies mostly relies on economic viability and/or business opportunities. The management of cheese whey residues is an excellent illustration of this. Economical support programs should be implemented for small producers to collect, dispose of, treat, and possibly valorize cheese whey. On a larger scale, market niches should be identified for the recovered products; if not, they should be directly re-used as resources or energy on industrial sites.

In the Basque region of Spain, an action plan has been implemented for recovering whey over territory, in close connection to the industry [78]. This has resulted in the development of whey processing plants and the production of 15 different value-added products for food and fodder. Another successful example is AgriChemWhey (ACW) in Lisheen, Ireland. ACW is an integrating biorefinery that produces lactic acid and other added-value chemicals from whey permeate (WP) and de-lactose whey permeate (DlWP). This project counts on a consortium of 11 partners across five different countries (Austria, Belgium, Germany, Ireland, and The Netherlands). The project was also funded by the Bio-Based Industries Joint Undertaking under the EU's Horizon 2020 Framework [79].

Industries are already processing cheese whey into added-value products. Glanbia (Kilkenny, Ireland), Fonterra (Auckland, New Zealand), and its joint ventures, Friesland-Campina Ingredients (Amersfoort, Netherlands), Saputo (Montreal, Canada), Carbery (Cork, Ireland), Milk Specialties Global (Eden Prairie, Minnesota, USA), Arla (Viby, Denmark), and Lactalis Global (Choisy-le-Roi, France), are some of the companies that are already repurposing their cheese whey into added-value products such as whey powder concentrate (WPC), isolate (WPI), and hydrolysate (WPH); galactooligosaccharides (GOS), caseins, and caseinates; probiotics; and prebiotics, which are employed in pharmaceutical, nutraceutical, food, and animal feed industries [80–87].

Governance, regulations, and law enforcement are of the utmost importance to implement environmental changes and boost the circular economy. Policymakers, industry stakeholders, and dairy producers must align their interests to implement regulations and R&D for integrating cheese whey valorization into a bio-based economy. This can be achieved by the implementation of progressive policies favoring renewable energies and material resource recovery from used streams rather than focusing only on prices and the understanding that low-income countries' transition can only be effective with financial and technological investments from high-income countries [88].

Table 1. Available legislation on (waste)water management in countries with higher cheese whey production.

Country	Legislation	General Provisions	Reference
AR	National constitution ART 121 civil code	Establishes that the provinces hold power that is not assigned to the Federal Government.	[89]
	National constitution ART 124 civil code, 1994	States that each province is the owner of the existing natural resources in their territory.	[90]
	Regime of Environmental Management of Waters (Law 25.6888), 2002	Establishes the requirements for the preservation and use of water resources.	[91]
AU	Environmental Protection Act, 1993	Regulatory framework for land, air, and water protection.	[92]
	The National Waste Policy, 2009	National framework for waste and resource recovery in Australia.	[93]
BY	Water Code of the Republic of Belarus, 2014	Governs the public relations regarding the ownership, use, and order of waters and water objects in Belarus.	[94]
BR	Water code, 1934	Allows the free use of any water for basic life necessities while complying with administrative regulations.	[95]
	National Policy of Hydric Resources (Federal Law 9433), 1997	Defines the objectives, principles, and instruments of the National Water Resources Policy and the National Water Resources Management System.	[96]
	National Solid Waste Policy, PNRS, 2010	Sets the guideline to integrated management and solid waste management, generator's responsibilities, and economic instruments.	[97]
CA	Canada Water Act, 1985	Framework for the conservation, development, and use of Canada's water resources.	[98]
	Wastewater Systems Effluent Regulations 2015	Establishes a national baseline effluent quality standard in Canada.	[99]
CN	The Water Law of the People's Republic of China, 1988	Allows for the development, use, and protection of water resources, as well as the prevention and control of water hazards.	[100]

Table 1. *Cont.*

Country	Legislation	General Provisions	Reference
EU	Waste Framework Directive (2006/12/EC)	Framework regarding waste management, waste disposal, and waste recovery.	[101]
	Urban Wastewater Directive (91/271/EEC)	Framework regarding the collection, treatment, and discharge of urban waste water and the treatment and discharge of industrial waste water.	[102]
JP	The Water pollution control law, 1970	Framework for water pollution prevention (i.e., public waters and groundwater) by regulating effluent discharged by factories, businesses, and households.	[103]
KR	Water Quality and Ecosystem Conservation Act, 2009	Establishes the regulation of the total water quality pollutants in an area.	[104]
MX	National Water Law	Regulates the use and exploitation of waters and their distribution, control, and preservation.	[105]
NZ	National Policy Statement for Freshwater Management under the Resource Management Act 1991	Framework on the management of freshwater under the Resource Management Act 1991.	[106]
RU	Water Code of the Russian Federation, 2006	Framework for water resources in the Russian Federation addressing the issues in the energy-water nexus.	[107]
UA	The Water Code of Ukraine, 1995	Framework for the use of waters, pollution, contamination, and exhaustion prevention.	[108]
US	Clean Water Act, 1972	Establishes the structure for regulating the discharges of pollutants in water bodies and the quality standards for surface waters.	[109]

4. Clearing the Whey: Product, Resource, and Energy Recovery

About 66.5 million m^3 $year^{-1}$ of whey is not currently absorbed by the industry [7]. The potential of valorization, which can facilitate the manufacturing of value-added products, could improve the sustainability of cheese processing [3]. Until recently, whey by-products were seen as low-value products. The lack of understanding of whey characteristics and functionality, together with its inconsistent performance in food systems (i.e., water and flavor binding, solubility, and emulsification properties) and the consolidated soy protein market, limited the use of whey, regardless of the available processing technology. This scenario has changed considerably since the initial development of lactose downstreaming and its related value-added products [5,110].

The high concentrations of organic matter (2500 mg L^{-1} sCOD), nitrogen (250 mg L^{-1}), and phosphorus (40 mg L^{-1}) in whey [111] make this residue an interesting feedstock for resource and energy recovery. Alternatives for valorization include the production of health and other industrial value-added products [4,5], phosphorus and nitrogen recovery [112], carbon capture [113], transformation via anaerobic digestion and fermentation processes [114], and other biotechnological processes for the valorization of biomass, biofuel, and biomaterials [115]. The following sections discuss these alternatives as well as our proposal to couple the anaerobic digestion or acidogenic fermentation of cheese whey with photobioprocesses to biorecover energy and resources and safeguard the natural environment. These different scenarios are presented in Figure 2.

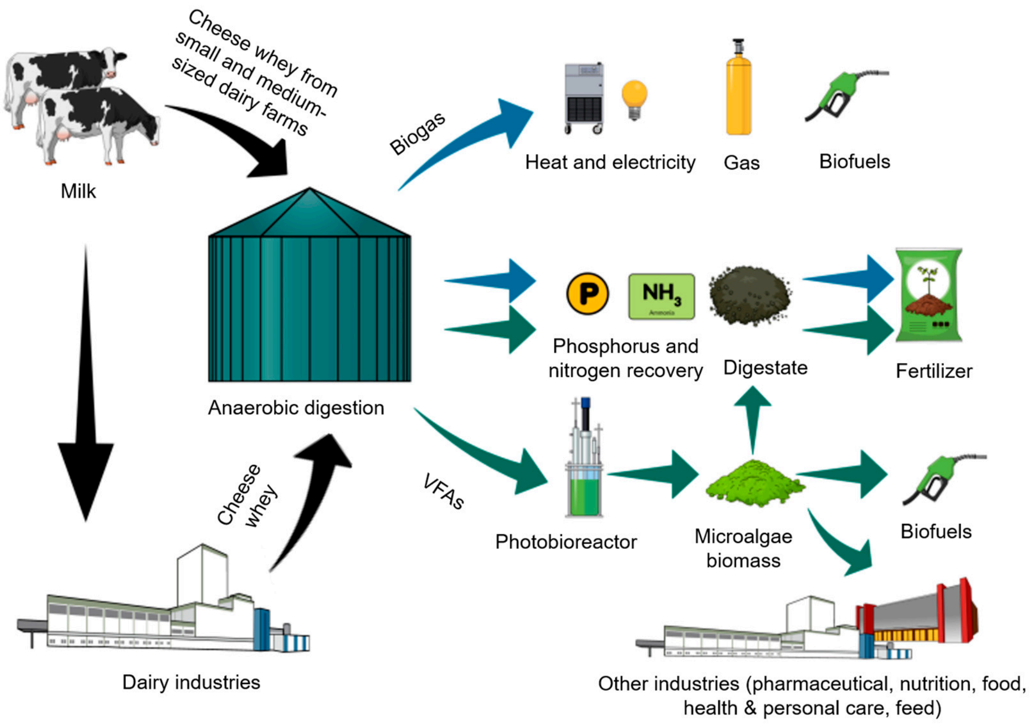

Figure 2. Scenarios for the full valorization of cheese whey. Surplus whey can undergo biogas production, generating heat, electricity, gas, and biofuels, and VFAs production, which would serve as a carbon source for photoorganoheterotrophic processes. Microalgae biomass could serve as raw material to produce biofuels or be absorbed by the industry to produce high-added-value products. Struvite precipitation is possible regardless of the chosen pathway. Anaerobic digestion and microalgal biomass-harvesting digestates, along with phosphorus and nitrogen recovery, can facilitate the processing of whey into fertilizers.

4.1. Advancements in Whey Processing Technologies and Valued-Added Products

Lactose is highly hygroscopic [59], and most small- and medium-sized cheese producers do not have the equipment and facilities to process cheese whey [39]. Despite this, the hot drum drying process is still one of the most used processes for whey powder production [50]. Table 2 depicts the different techniques currently used in whey processing and its added-value products, and applications.

Table 2. Cheese whey downstream processes, available technologies, and product spectra.

Process	Technique	Description	Products Obtained	References
Physical Separation	Membrane Separation	Broadly used in milk and whey processing to separate concentrated whey proteins and whole milk after the production of cheese so whey proteins can be fractionated into specific components. This process has evolved and can be subdivided into particulate filtration (PF), microfiltration (MF), ultrafiltration (UF), reverse osmosis (RO), and nanofiltration (NF).	Whey powder Dry whey powder (DWP) Whey powder concentrate (WPC) 35% Whey permeate α-, β-lactoalbumin Lactose Casein	[116–121]

Table 2. *Cont.*

Process	Technique	Description	Products Obtained	References
Physical Separation	High Hydrostatic Pressure	High pressure processing (HPP) was used to induce changes in milk proteins, and it does not influence the hydrolysis, the nutritional characteristics of milk, or the stability of vitamins significantly. However, it does affect the proteins, casein micelles, and whey proteins.	Whey powder Dry whey powder (DWP) Whey powder concentrate (WPC) 35% Whey permeate α-, β-lactoalbumin Lactose Casein	[116–121]
	Pulsed Electric Field	Pulsed electric field (PEF) is a nonthermal process where pulsed electric fields of alternating currents (10–100 kV) are applied in circa 20 µs, creating high-voltage fields (up to 50 kV/cm), thus killing microorganisms and rupturing spores in the medium in the process. It is speculated that whey proteins that have undergone PEF are less denaturated, meaning that they could offer better immunological benefits.		
	Ultrasound	The applications of ultrasound and sonication in milk processing are diverse. The whey product depends on the effects of sonication on the proteins, and this process can be combined with high temperatures to produce products with new properties.		
	Microwave	The main issue of microwave processing for pasteurized milk products is inconsistent heating, which can be sorted through improving the tubular design and using focused microwave heaters. Microwave-processed milk or whey may present whey products with superior functionality and improved flavor.		
Protein Modification	Enzymatic Modification	Whey proteins' functions and values can be enhanced by enzymatic hydrolysis, generating hydrolysates with low-molecular-weight peptides.	Lactic acid, lactulose Bovine serum albumin (BSA) D-Tagatose Galactooligosacchatides (GOS) Other bioactive compounds (immunoglobulins, lactoferrins, glycomacropeptides, transferrins, lactoperoxidase, lysozymes, albutensin A, lactorphin, β-lactotensin, β-lactorphin, serorphin)	[116,122–124]
	Chemical Modification	Milk can be modified chemically either via rennet–enzyme action or direct acidification. Primary structures are significantly changed in milk proteins through reactions involving the sulfide residues of the amino acids.		
Protein separation	Extrusion Texturization	Short-time shear processing that modifies food structure, imparting texture.	Whey powder concentrate 80% Lactose pharma grade Whey protein blends (WPI + WPC) Pure whey isolate Minerals	[116,125]
	Spray Drying	Conversion of liquid or slurry materials into dried powders or granules by atomizing the solution into fine droplets and drying them with hot air or gas, resulting in dried particles that can be easily stored, transported, and reconstituted when needed.		

Table 2. *Cont.*

Process	Technique	Description	Products Obtained	References
Protein separation	Carbon Dioxide Precipitation	Pressurized CO_2 (27–55 bar, 54–64 °C) is used as an acid source, lowering whey's protein pH, thus precipitating α-LA. Afterwards, solubilized CO_2 is then released during the extraction and depressurization of the protein fractions, resulting in 55% α-La and 78% β-Lg. These ratios can be selectively enriched depending on the applications and functionality desired.	Whey powder concentrate 80% Lactose pharma grade Whey protein blends (WPI + WPC) Pure whey isolate Minerals	[116,125]

Whey by-products (e.g., whey powder concentrate or isolate) have become commodities of interest for the nutritional, pharmaceutical, and medical industries because their protein and peptide components present nutritional value and antimicrobial, anti-viral, anticarcinogenic, and antioxidant properties [5,7,110].

D-tagatose, a low-calorie sweetener, can be produced from whey. It presents prebiotic properties and antihyperglycemic activities [126]. It is also used in the food, cosmetic, and pharmaceutical industries as a bulking agent and acts as an additive in detergents or as an intermediate component for the synthesis of other substances [124].

Galactooligosaccharides (GOS) are a by-product of cheese whey known for their prebiotic functions and high market value. GOS are usually present in infant formulas but are also used as sweeteners and bulking agents; they are present in beverages, meal replacers, and sweets. Lactulose, another prebiotic derived from lactose, is mainly used in food formulas for medical purposes [57].

The evolution of the technology needed to facilitate protein separation and modification has enabled the discovery of new uses for whey (such as isolates and other bioactive compounds [110]). Therefore, the current technologies used for cheese whey processing notably involve physical separations and bioengineering for protein recovery and modification.

4.2. Anaerobic Digestion and Acidogenic Fermentation of Cheese Whey

The anaerobic digestion of cheese whey has been widely studied despite its tendency for acidification [127]. The high biodegradability (~99%) of cheese whey, pH reduction (below 5), and low bicarbonate alkalinity (50 meq L^{-1}) can lead to operational difficulties [128,129]. However, the high organic content of cheese whey makes it suitable for energy recovery via biogas production by anaerobic digestion [130].

The anaerobic digestion of cheese whey offers significant advantages in terms of biogas production [131]. Biomethane production depends on factors such as the feedstock used (e.g., cheese whey), temperature, and microbial activity. The efficiency of the bioprocess can be adjusted by addressing parameters like the substrate feed, temperature, pH (around 6.5 to 7.5), alkalinity enhancement (to buffer the system and regulate the pH), and hydraulic retention time and employing different microbial consortia to enhance resilience during the fluctuations of the parameters [132].

Methane-rich biogas has various applications; for example, it can be used as fuel to generate electricity, heat, and combined heat and power (CHP) systems and as an alternative fuel for vehicles. Biohydrogen can be an alternative to methane during the anaerobic digestion of cheese whey, as it produces water vapor as a by-product. It can also be used in fuel cells to produce electricity and heat. Currently, some anaerobic digestion plants use cheese whey or whey permeate as the substrate for their processes (e.g., Iona-Lemming Biogas) [133]. The anaerobic digestion of cheese whey seems a sound bet for repurposing surplus whey.

The acidogenic fermentation of cheese whey is an interesting alternative to anaerobic digestion [134]. Methanogenesis can be stopped after the conversion of whey by fermentative microorganisms to accumulate hydrogen and volatile fatty acids (VFAs) [135].

Anaerobic digestion without the production of biogas is an opportunity for the valorization of VFAs via the carboxylate platform [136–138].

The acidogenic fermentation of cheese whey can be driven by inoculum pre-treatment (e.g., physical, biological) [139,140], lowering hydraulic retention times (i.e., between 2 and 5 days) [141], and controlling pH (i.e., below 7.0 to 3.3) [142], thus selecting acidogens to outcompete methanogens. Other fermentation processes can also valorize cheese whey. These processes can be performed either in axenic pure culture systems or via mixed-culture fermentation in non-sterile open systems [143,144].

Some of the products obtained from cheese whey valorization include short-, mid-, and long-chain organic acids [145–147], intracellular storage products (i.e., polyhydroxyalkanoates, PHAs) [148–150], bioplastics [22,151], biohydrogen [152], bioethanol [153,154], and biobutanol [155,156]. Other innovative bioprocesses involve the conversion of VFAs into electricity or other value-added products using bioelectrochemical systems (i.e., microbial fuel cells and microbial electrosynthesis cells) [157].

4.3. Co-Digestion of Whey

Anaerobic co-digestion is a process where different substrates from agricultural farming, manure, municipal, food, and industrial wastes are combined in anaerobic digestion to optimize parameters such as temperature (30–50 °C), pH (5–7), organic matter concentration, nutrient availability, alkalinity, and carbon/nitrogen (25 to 35:1) ratio. Consequently, the overall biogas yield is increased and resource recovery is facilitated, diverging from waste disposal in landfills and leading to environmental and financial benefits [158,159].

Cheese whey co-digestion can help balance the carbon/nitrogen (C:N) ratio of the substrate mix since it is rich in nitrogen and organic matter. A balanced C:N ratio can promote the growth of specific microorganisms and improve the overall efficiency and stability of the process [131]. Additionally, the co-digestion of cheese whey mitigates the inhibitory effects of excess ammonia during AD processes and increases biogas yield. However, this synergy is yet to be proved in full-scale reactors [160]. The co-digestion of cheese whey and other organic wastes, such as food waste [161], agricultural residues [162], and animal manure [163], not only promotes resource recovery but also allows for the selection of substrates based on local availability. Some studies have explored the co-digestion of cheese whey with microalgae [164]. Microalgae are known for their high lipid content, and when combined with cheese whey, they can offer a complementary nutrient profile for enhanced biogas and bioenergy production.

Cheese whey co-digestion promotes a more sustainable approach to waste management and resource utilization and is aligned with the principles of circular economy. Ongoing research continues to investigate the optimal combinations of cheese whey with other substrates and the scaling of co-digestion processes in real-world applications. Innovations in co-digestion technology aim to maximize biogas production efficiency.

4.4. Light-Based Valorization of Cheese Whey Using Photobioprocesses: Harnessing Eutrophication in Bioprocess Boundaries

We advocate for new biorecovery process alternatives that couple the acidogenic fermentation of cheese whey into short- and mid-chain VFA production before feeding into algal ponds, photo-activated sludge systems, or photobiotechnologies to produce a photoorganoheterotrophic microalgal biomass. This biomass can be processed into a variety of products of industrial interest (e.g., pigments, antioxidants, vitamins, anticancer drugs) and products with a higher value compared to biogas.

Although the majority of hydrogen production results from “dark fermentation” processes performed by chemoheterotrophic bacteria and microalgae [165], it can also occur in the presence of light. This process is known as biophotolysis, which involves direct and indirect biophotolysis and photofermentation [166]. In direct biophotolysis, water is oxidized into hydrogen and oxygen in the presence of light during photosynthesis by photoautotrophic microalgae. In indirect photolysis, hydrogen is the product of the reduction of organic compounds by photosynthetic bacteria, cyanobacteria, and microalgae [167].

Photofermentation is a process where anoxygenic photosynthetic bacteria (i.e., green sulfur bacteria, purple sulfur, and purple non-sulfur bacteria) use alternative reduced compounds as electron donors (e.g., hydrogen sulfide, organic acids, and carbon sources) nitrogenase and light as an energy source to synthesize hydrogen [168]. The biological water–gas shift is performed by hydrogenogenic carboxydotrophic bacteria that oxidize carbon monoxide while catalyzing the water–gas shift reaction [168,169], producing hydrogen. The biological water–gas shift can be an alternative to the current chemical shift used for syngas production [169].

Cheese whey has been used both in dark fermentation [147] and photofermentation [170] processes. It has also served as a substrate for microalgae cultivation. Given microalgae's photosynthetic and lipid production efficiency, photofermentation processes using VFAs as carbon sources for biomass production can provide more profitable use cases for the 66.5 million m^3 $year^{-1}$ of cheese whey currently used as animal feed or fertilizer or discharged in water streams.

4.5. Synergetic Interactions between Microalgal and Bacterial Processes to Valorize Whey

Compared to other feedstocks for biofuel production, microalgae are advantageous as they can be cultivated in arid land [171] and brackish or high-strength waters [171]. They can remove nitrogen and phosphorus from wastewater simultaneously [172] and mitigate carbon dioxide due to their photosynthetic efficiency [173]. Zeng et al. [174], Behera et al. [175], Mutanda et al. [176], and Patel et al. [177] serve as excellent starting points for comprehending the bioprocesses in microalgal cultivation. Table 3 shows the value-added products that can be obtained from microalgae and their uses in industrial applications.

The carbon metabolism of microalgae can be photolithoautotrophic, photoorganoheterotrophic, and mixotrophic [178]. Heterotrophic microalgae are attractive for light-based processes designed to treat and capture organic matter and nutrients from municipal and agro-industrial wastewater [179,180]. Mixotrophic microalgae can display a combination of photolithoautotrophic and/or chemoorganoheterotrophic regimes. Hence, they are able to grow through using both the carbon dioxide produced via photosynthesis and organic carbon sources (e.g., cheese whey, permeate, second cheese whey, and volatile fatty acids resulting from cheese whey acidogenic fermentation) [36,37,181].

Due to respiratory metabolic propensities, mixotrophic microalgae exhibit lower photoinhibition, improved growth rates, and reduced losses of biomass by night [182]. The contemporary industrial applications involve the production of unsaturated fatty acids (e.g., omega-3 fatty acids or arachidonic acid), antibiotics, and pigments such as carotenoids [183]. However, the carbon assimilation and growth mechanisms of mixotrophic microalgae are yet to be elucidated [184].

Microalgal mixed-culture bioprocesses have gained significant attention, particularly in conjunction with anaerobic bacterial processes, for various applications, such as the digestion and methanization of microalgal biomass, nutrient polishing from anaerobic digester supernatants with microalgae, the production of biomass from used water streams, or the production of lipid-based biofuels and biopolymeric materials [185–187]. Beyond their technological applications, microalgal–bacterial assemblies drive scientific interest in ecological relationships [188,189] and can foster mixed-culture photobiotechnologies.

On a cellular level, the symbiotic relationships between microalgae and bacteria are important with respect to the exchange of substrates, such as the CO_2–O_2 exchange between bacteria and microalgae, as well as the supply of bacterial cobalamin to auxotrophic microalgae. These interactions also encompass signaling transduction (e.g., quorum sensing, growth inhibition, or stimulation via exudate release) or horizontal gene transfer [190]. Microbial ecology still presents various knowledge gaps regarding the study and comprehension of microalgal–bacterial symbiosis [191]. The knowledge of bacto-microalgal chemical interactions is still scarce. The advent of 'multi-omics' (e.g., metagenomics, transcriptomics, proteomics, lipidomics, metabolomics) is now providing key analytical tools to unravel these complex relationships.

Even though there has been substantial research into utilizing cheese whey in microalgal growth and co-digestion processes (e.g., biomass, biofuel, and value-added product production; CO_2 mitigation; or wastewater treatment), the potential of tailored microalgal–bacterial mixed-culture biotechnologies for cheese whey bio-valorization remains relatively unexplored. The challenges associated with integrating mixed cultures include the costs and energy requirement associated with harvesting microalgae biomass, the complex dynamics of micro-ecosystems that can rapidly shift, and the absorption of light across mixed liquors and biofilms beyond the photic zone [36,181,192].

Table 3. Microalgae biomass applications considering different uses and product spectra.

Uses	Products	References
Fine chemicals	Fatty acids, carotenoids, antioxidants, vitamins, and other bioactive compounds	[193]
Industrial	Pharmaceutical, aquaculture, animal feed, biofertilizer	[194–197]
Drug screening	Antimicrobial agents, antiviral drugs, anticancer drugs	[194]
Environmental	Pollutants removal, wastewater co-digestion, CO_2 mitigation	[198,199]
Commercial	Nutraceuticals, nutrition, cosmetics, pigments, recombinant proteins, stable isotopes, biochemicals	[200–204]
Biofuels	Biodiesel, bioethanol, biobutanol, bio syngas, biogas electricity, heat	[205–207]

The bio-valorization of cheese whey has seldom been tailored by combining microalgal–bacterial mixed-culture biotechnologies [208]. This approach involves the integration of microalgae and specific bacterial strains within mixed cultures designed to optimize the utilization of cheese whey. The microalgae can efficiently capture and convert nutrients and organic compounds present in cheese whey into biomass, while the bacteria in the mixed culture can fulfill various functions, including enhancing nutrient cycling, improving overall system stability, and potentially producing valuable bioactive compounds. Tailored microalgal–bacterial systems have the potential to enhance process efficiency, reduce nutrient losses, and yield high-value bioproducts. However, further research is required to comprehensively grasp the synergistic interactions between microalgae and bacteria in the context of cheese whey bio-valorization.

While some studies have explored microalgal growth on cheese whey [209] and-related products such as dairy waste, digested cheese whey, second cheese whey, and permeate [210], as well as co-digestion processes [180], the full potential of combined microalgal–bacterial mixed culture biotechnologies for the bio-valorization of cheese remains largely untapped. This represents a significant step toward sustainability and resource recovery in the dairy sector.

4.6. Phosphorus and Nitrogen Removal and Recovery from Cheese Whey

Eutrophication prevention often involves the biological or chemical removal of phosphorus and nitrogen from wastewater [211]. Bioprocesses for nutrient removal from municipal and industrial wastewater have been widely studied and operated extensively worldwide [212]. Technologies using biofilms and granular sludge have enabled the intensification and integration of process units in wastewater treatment plants [213].

The combination of anaerobic digestion and digestate polishing for nutrient removal is a standard operation for the treatment of high-loaded agro-industrial streams, including cheese whey [214]. Over the last decade, a shift in the environmental engineering sector has occurred wherein the attention of those in the sector has turned towards transforming wastewater treatment plants into water resource recovery facilities [215–217]. The increasing demand for fertilizers highlights the need for recovering nitrogen and phosphorus, which are non-renewable resources [218,219]. Phosphorus can be removed and/or recovered from wastewater streams via sedimentation-enhanced biological phosphorus removal (i.e., by phosphorus-accumulating organisms) or chemical precipitation (i.e., precipitating aluminum or iron salts into insoluble phosphates compounds) [220]. Nitrogen recovery uses energy from ammonia production to produce atmospheric nitrogen, followed by the Haber–Bosch process, which reverses the previous reaction. Other methods for nitrogen recovery include struvite precipitation, adsorption, ammonia stripping, the combination of air stripping and absorption, membrane distillation, and membrane gas separation [221].

Struvite ($NH_4MgPO_4{\cdot}6H_2O$) production is a well-established process used to recover phosphorus and nitrogen via crystallization [218]. Most struvite recovery studies focus on municipal wastewater (le Corre et al., 2009) or source-separated urine [222], but the low water solubility of whey and its high N and P concentration is advantageous for struvite precipitation [130].

Numviyimana et al. [223] successfully recovered P (94%) and N (72%) from dairy wastewater by adding zeolite, making struvite precipitation more thermodynamically favorable, while Escalante et al. (2018) demonstrated the potential of struvite precipitation, obtaining 8.5–10.4 g struvite L^{-1} from the anaerobic digestion of cheese whey. Struvite precipitation reduces the overall costs of anaerobic digestion processes as well as the costs of sludge handling, disposal, and scaling [220].

Vivianite ($Fe_3(PO_4) \cdot 8H_2O$) recovery, although more thermodynamically favorable than struvite precipitation, is challenging due to the difficulty in separating it from the sludge. Given its high aggregate value, technologies for vivianite recovery are currently being studied via magnetic separation [224,225].

These active developments highlight the strong technological potential for the capture and recovery of organic matter and nutrients from used streams. The combination of biological and physical–chemical processes is efficient for capturing and recovering resources. The key will consist of developing economically affordable, scalable, and implementable processes to valorize resources across regions.

The photoorganoheterotrophic processes using microalgae or purple phototrophic bacteria form in concert with anaerobic fermentation processes, provide an efficient bio-based solution for capturing and concentrating organics and nutrients into valuable biomass and associated bioproducts [226–228] from waste feedstocks like cheese whey at a low cost; this biomass and the associated bioproducts can subsequently be used in agriculture and food supply.

5. Future Perspectives

Future research should focus on optimizing process strategies for selecting and interacting fermentative and photoorganoheterotrophic organisms while controlling metabolic routes to produce selected bioproducts (e.g., biogas, bioethanol, VFAs, biohydrogen).

Developing scalable solutions tailored to local geography, economy, and politics is essential. This can be achieved through LCA studies, stakeholder engagement, action plans, research and development (R&D) investments, legislative updates, and government incentives.

Raising awareness about global cheese whey production and its potential valorization is crucial for promoting sustainable practices and safeguarding the environment. By addressing the aforementioned challenges and harnessing opportunities in cheese whey management, we can facilitate the dairy sector's transition to a circular economy via the use of more sustainable and resource-efficient processes.

6. Conclusions

Cheese production and whey management are interdependent due to increasing cheese demand. Whey has historically found various uses as food, feed, medicine, and fertilizer. Technological advances have transformed whey into a sought after commodity. However, a significant portion (i.e., about 42%) of annual whey production is not fully absorbed by the industry.

To tackle this issue, several scenarios for the valorization of surplus cheese whey residues have been proposed, including anaerobic digestion for biogas production, acidogenic fermentation and photobioprocesses for biomass production, and phosphorus and nitrogen recovery through struvite precipitation. These integrated processes demonstrate the potential of closed-loop whey biorefineries for resource biorecovery and eutrophication mitigation.

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