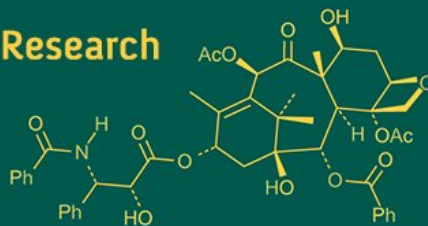


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Sheep milk proteins and peptides: Nutritional value and health implications: A review

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Abstract

Sheep milk, although a relatively small component of the global dairy sector, is gaining increasing attention due to its superior nutritional value and functional properties compared with bovine, caprine, and buffalo milk. It is rich in high-quality proteins, including casein and whey fractions, essential amino acids, bioactive lipids, vitamins, and minerals, making it an important source of bioactive peptides with significant health-promoting potential. These peptides are released through enzymatic hydrolysis, gastrointestinal digestion, or microbial fermentation and exhibit diverse biological activities such as antihypertensive, antioxidant, antimicrobial, anti-inflammatory, antidiabetic, immunomodulatory, and opioid-like effects that support metabolic health, immunity, gut function, and cognitive performance. In addition, the high solids content and favorable protein composition of sheep milk improve cheese yield, curd formation, and the development of functional foods, fermented dairy products, nutraceuticals, and medical nutrition formulations. Advances in peptidomics, fermentation technology, and process optimization have facilitated the identification and application of bioactive peptide sequences, while *in silico* and *ex vivo* studies have enhanced understanding of their stability and bioavailability. Despite these advancements, challenges related to peptide standardization, gastrointestinal stability, regulatory approval, and clinical validation persist. Future research integrating omics technologies, machine learning, personalized nutrition, and sustainable sheep farming practices is expected to expand the therapeutic and industrial applications of sheep milk-derived peptides, establishing sheep milk as a promising ingredient for next-generation functional foods and health-promoting biomaterials.

Keywords: *Ovis aries* milk, sheep milk proteins, bioactive peptides, casein, whey proteins, functional foods, nutraceuticals, antihypertensive activity, antioxidant activity, antimicrobial peptides, immunomodulatory effects, dairy biotechnology, peptide bioavailability, fermented dairy products, health-promoting foods

1. Introduction

Sheep milk, although representing a relatively small share of the global dairy industry, holds significant importance in regional food systems, particularly in the Mediterranean and Middle Eastern regions, where it has traditionally been used in the production of premium specialty cheeses such as feta, Roquefort, Manchego, and pecorino (Mioč *et al.*, 2024). Global sheep milk production is currently estimated at nearly 10 million metric tons annually (Singh and Sahoo, 2024) ^[60]. Nutritionally, sheep milk possesses a richer composition than bovine, caprine, and buffalo milk due to its higher levels of proteins, lipids, and total solids. It contains approximately 5.4-5.5% protein, compared with about 3.2-3.3% in cow milk, 3.1-4.6% in goat milk, and around 4.5% in buffalo milk (Park *et al.*, 2007). In addition, sheep milk is particularly rich in both casein and whey protein fractions, with concentrations ranging from 41.8-52.6 g/L and 10.2-16.1 g/L, respectively, which are generally higher than those found in milk from other dairy species (Roy *et al.*, 2020). Beyond its protein content, sheep milk is also an excellent source of vitamins A, B1, and B2, essential minerals such as calcium, and bioactive lipids including omega-3 fatty acids and conjugated linoleic acid (CLA). These components contribute to its enhanced nutritional quality and functional benefits, making sheep milk a valuable dairy resource with promising health-promoting properties compared with bovine and caprine milk (Yang *et al.*, 2024).

Sheep milk, containing approximately 5.8% protein, is primarily composed of casein (76-83%) and whey proteins (17-24%), making it an excellent source for investigating protein digestibility, metabolism, and the generation of bioactive compounds (Dalabasmaz *et al.*, 2023) ^[17]. It is particularly recognized for its rich content of bioactive peptides that exhibit antioxidant, antihypertensive, antimicrobial, anti-inflammatory, and antidiabetic activities, highlighting its significant nutraceutical potential (Pipaliya *et al.*, 2024; Flis *et al.*, 2025) ^[26]. In addition to its health-promoting properties, the high levels of protein, fat, and minerals in sheep milk contribute to improved cheese yield, better curd formation, and the development of innovative functional dairy products (Rako *et al.*, 2019; Kayihura, 2023; Lai *et al.*, 2024) ^[37]. Owing to its superior nutrient density and distinctive peptide composition compared with milk from other dairy species, sheep milk is increasingly considered a valuable resource for functional food research and product development (Wang *et al.*, 2025) ^[63]. This review summarizes recent advances in the study of sheep milk proteins and peptides, highlighting their nutritional, functional, and industrial significance. Sheep milk contains approximately 5.8% protein, mainly consisting of casein (76-83%), including α s1-, α s2-, β -, and κ -caseins, along with 17-24% whey proteins, which together provide a well-balanced amino acid profile and may exhibit lower allergenicity because of reduced α s1-casein content (Zenk *et al.*, 2024; Mohapatra *et al.*, 2019) ^[65]. Bioactive peptides produced through enzymatic hydrolysis and fermentation demonstrate several health-promoting activities, including antioxidant, antihypertensive, antidiabetic, antimicrobial, and immunomodulatory effects. For example, the peptide HPHPHLSF derived from κ -casein has shown antioxidant activity comparable to BHT, while other peptides exhibit ACE-inhibitory activity for blood pressure regulation and DPP-IV inhibition for glycemic control. Peptidomic studies of fermented products such as kefir have also identified numerous bioactive peptide sequences (Taibo Li *et al.*, 2017; Singh & Gaur, 2024; Nielsen *et al.*, 2024) ^[51, 60]. In addition, the high total solids content of sheep milk improves cheese yield and curd quality, supporting its use in the development of functional

dairy products, including sheep milk-based ice cream enriched with whey proteins, inulin, omega-3 fatty acids, and probiotics (Kayihura, 2023; Kowalczyk *et al.*, 2021) ^[37, 41]. Despite these promising findings, further research is required to better understand peptide stability, bioavailability, and clinical efficacy, as well as to expand their applications in functional foods and biomedical fields such as wound healing and controlled-release delivery systems (Albenzio *et al.*, 2017; Nizam *et al.*, 2025; Al Shaer *et al.*, 2024) ^[3, 4, 52].

2. Composition of sheep milk proteins

Sheep milk possesses a significantly richer macronutrient profile than milk from most other dairy species, particularly in terms of protein content. It contains approximately 5.5-6.36% protein, which is considerably higher than the levels reported in cow, goat, buffalo, and camel milk (Arrichiello *et al.*, 2022; Felice *et al.*, 2021) ^[11, 24]. Around 80% of the protein fraction in sheep milk consists of caseins, a proportion similar to bovine milk but higher than that found in human or mare milk (Flis *et al.*, 2025) ^[26]. All major casein fractions, including α s1-, α s2-, β -, and κ -casein, are present, with total casein content ranging from 63-85% of total protein depending on breed variations. Among these fractions, α -caseins constitute about 23-35%, β -casein 6-12%, and κ -casein 7-9% (Alibekov *et al.*, 2025) ^[6]. The remaining protein fraction is composed of whey proteins, primarily β -lactoglobulin, which accounts for nearly 22-24% of total protein and is important for binding hydrophobic compounds. α -lactalbumin contributes around 7-15% and provides essential amino acids along with immunomodulatory properties. Other whey proteins, such as serum albumin, lactoferrin, and immunoglobulins, are present in smaller quantities but play important antimicrobial and immune-supportive roles (Pillai *et al.*, 2024; Figueroa Pires *et al.*, 2021) ^[25, 53]. This balanced composition of casein and whey proteins, together with the overall higher protein concentration, enhances the nutritional quality, cheese-making efficiency, and functional potential of sheep milk, making it a valuable dairy source for both nutritional and industrial applications (Salhi *et al.*, 2025) ^[57].

Table 1: Comparison of protein content among different dairy species

Dairy Species	Total Protein Content (g/100 g)	Casein to Whey Protein Ratio
Sheep milk	Approximately 5-6% (average 5.5 g)	Nearly 80% casein and 20% whey proteins
Cow milk	Around 3.2-3.4 g	About 82% casein and 18% whey proteins
Goat milk	Approximately 3.1-3.7 g	Roughly 78% casein and 22% whey proteins
Buffalo milk	About 4.3 g	Comparable to cow milk

3. Bioactive peptides derived from sheep milk

Bioactive peptides are short chains of amino acids, typically containing 2-20 residues that are gaining considerable attention because of their health-promoting properties beyond basic nutrition. These peptides are naturally encrypted within milk proteins and become biologically active only after being released through enzymatic hydrolysis, gastrointestinal digestion, or microbial fermentation. Once liberated, they exhibit a wide range of physiological activities, including antihypertensive, antioxidant, anti-inflammatory, antimicrobial, immunomodulatory, anti-obesity, opioid-like, and antithrombotic effects, making them valuable for functional foods, nutraceuticals, and medical nutrition applications

(Mohanty *et al.*). Their release is commonly achieved through enzymatic action using proteases such as pepsin, trypsin, chymotrypsin, and microbial enzymes from *Bacillus* species, which effectively hydrolyze casein and whey proteins. Studies have shown that hydrolysis of sheep milk casein can generate peptides with strong ACE-inhibitory and antioxidant properties, including the κ -casein-derived peptide HPHPHLSF, which exhibits lipid peroxidation inhibitory activity comparable to the synthetic antioxidant butylated hydroxytoluene (BHT) (Corrêa *et al.*, 2014) ^[16]. In addition, microbial fermentation involving lactic acid bacteria such as *Lactobacillus plantarum* and *Limosilactobacillus fermentum* can produce multifunctional peptides with antioxidant, antimicrobial, antidiabetic, and

anti-inflammatory activities (Prete *et al.*, 2024) ^[54]. These findings demonstrate the important role of enzymatic and microbial processes in enhancing the therapeutic potential of sheep milk proteins through the production of bioactive peptides.

Bioactive peptides derived from sheep milk exhibit a broad range of biological functions that contribute significantly to human health. Among the most studied are antihypertensive peptides, particularly those with angiotensin-converting enzyme (ACE) inhibitory activity, which are important for blood pressure regulation. Hydrolysates obtained from κ -casein have shown strong ACE-inhibitory effects, and fermentation of sheep milk with *Lactocaseibacillus paracasei* M11 has demonstrated substantial ACE inhibition along with the production of peptides possessing antidiabetic potential (Pipaliya *et al.*, 2025). Antioxidant peptides are another important group, including the κ -casein-derived peptide HPHPHLSF produced through *Bacillus* protease hydrolysis, which displays lipid peroxidation inhibitory activity comparable to the synthetic antioxidant BHT due to the presence of amino acids such as histidine and leucine (Ashokbhai *et al.*, 2022) ^[12]. Sheep milk peptides also exhibit antimicrobial properties, with peptides derived from α s1-, α s2-, β -, and κ -caseins identified in fermented products such as sheep milk kefir. Well-known examples include isracidin and casocidin, which are effective against several foodborne pathogens (Dallas *et al.*, 2015; Park & Nam, 2015) ^[18]. In addition, immunomodulatory peptides generated during fermentation can support immune regulation, while lactoferrin-derived fragments such as lactoferroxins are known to stimulate natural killer cell activity and enhance humoral immune responses (Baars *et al.*, 2023; Kashung & Karuthapandian, 2025) ^[14, 36]. Certain peptides also possess opioid-like properties, including casomorphins from α - and β -caseins and whey-derived lactorphins and serorphins, which may influence gut motility and neural signaling (Trompette *et al.*, 2003) ^[61]. Overall, the multifunctional nature of sheep milk-derived peptides highlights their potential application in functional foods, nutraceuticals, and therapeutic products.

Sheep milk is recognized as an important source of multifunctional bioactive peptides, with both casein- and whey-derived peptides exhibiting a wide range of health-promoting activities. MALDI-TOF-MS analyses have identified numerous bioactive sequences from α -, β -, and κ -caseins, including peptides with antibacterial, antioxidant, anticancer, anticoagulant, immunomodulatory, opioid-like, and ACE-inhibitory properties (Balthazar *et al.*, 2024) ^[15]. Whey proteins also contribute valuable bioactive peptides, such as antibacterial and antidiabetic sequences. Processing techniques, particularly enzymatic hydrolysis and microbial fermentation, further enhance peptide production and biological activity. For instance, hydrolysis of sheep cheese whey generated β -lactoglobulin-derived peptides with significant ACE-inhibitory activity, while fermentation with *Lactocaseibacillus paracasei* M11 produced peptides exhibiting strong ACE inhibition along with α -amylase, α -glucosidase, and lipase inhibitory activities associated with antidiabetic potential (Das *et al.*, 2025; Mudgil *et al.*, 2024) ^[19, 48]. Similarly, fermentation using *Lactobacillus plantarum* yielded peptide fractions with pronounced antioxidant and antimicrobial effects (Yilmaz *et al.*, 2022) ^[64]. Peptidomic investigations of sheep milk kefir have identified a large number of peptide sequences, including

several unique bioactive candidates specific to sheep milk fermentation products (Izquierdo-González *et al.*, 2019) ^[33]. In silico studies further support the potential of sheep milk proteins as precursors of ACE- and DPP-IV-inhibitory peptides with antihypertensive and antidiabetic activities (Iram *et al.*, 2022) ^[32]. Overall, these findings demonstrate that sheep milk represents a valuable reservoir of bioactive peptides with promising applications in functional foods, nutraceuticals, and therapeutic products.

4. Nutritional value of sheep milk proteins

Sheep milk is recognized for its high protein concentration and superior amino acid composition, providing important nutritional advantages over other dairy milks. It contains up to 6.62 g of protein per 100 g, which is significantly higher than the protein levels commonly reported in cow and goat milk (Landi *et al.*, 2021). In addition to its elevated protein content, sheep milk proteins exhibit improved digestibility and bioavailability. Animal studies have shown greater ileal absorption of essential amino acids such as leucine, lysine, and methionine when compared with cow milk (Shrestha *et al.*, 2021) ^[59]. Human studies also indicate that consumption of sheep milk leads to a stronger postprandial increase in circulating branched-chain amino acids, including leucine, isoleucine, and valine, as well as other essential amino acids like lysine, methionine, and proline, relative to cow milk (Milan *et al.*, 2020). These characteristics highlight the nutritional value of sheep milk as a rich and highly digestible protein source.

The superior digestibility and balanced amino acid profile of sheep milk contribute significantly to muscle growth, recovery, and satiety. A randomized controlled trial involving physically active individuals showed that sheep milk effectively supported recovery after exercise-induced muscle damage, producing results comparable to cow milk and highlighting its potential in tissue repair and regeneration (Ravenwood *et al.*, 2024). In particular, the high leucine content of sheep milk plays an important role in stimulating muscle protein synthesis through activation of the mTOR signaling pathway, making sheep milk especially relevant for sports nutrition and post-exercise recovery applications (Drummond & Rasmussen, 2008) ^[21].

Quantitative amino acid analyses further demonstrate the nutritional richness of sheep milk, particularly in essential and sulphur-containing amino acids. Studies on Alto Casertano sheep milk have shown that essential amino acids constitute nearly 41% of the total amino acid content, while methionine and cysteine together contribute about 4% (Rafiq *et al.*, 2015) ^[55]. In addition, the free amino acid fraction is notably rich in proline and leucine, which are important for anabolic functions, muscle metabolism, and overall metabolic regulation (Kulzhanova *et al.*, 2024) ^[42]. These characteristics highlight the nutritional and functional importance of sheep milk proteins in supporting metabolic health, muscle maintenance, and improved dietary quality.

5. Health implications of sheep milk proteins and peptides:

Sheep milk and its bioactive compounds have gained attention for their potential role in promoting human health through metabolic regulation, immune support, and inflammation control. Bioactive proteins and peptides derived from sheep milk may assist in weight management and obesity prevention by influencing satiety and energy

metabolism. Fermented sheep milk products enriched with these peptides have been reported to stimulate gut hormones such as GLP-1 and PYY, which enhance feelings of fullness and may contribute to body-weight regulation (Tingirikari *et al.*, 2024). In addition, these peptides exhibit inhibitory effects against enzymes including DPP-IV, α -glucosidase, and α -amylase, thereby slowing carbohydrate digestion and improving postprandial blood glucose responses. Fermented products such as kefir have also demonstrated insulinotropic effects, although their efficacy depends on the starter cultures and fermentation conditions used (Kumawat *et al.*, 2025) ^[40]. Sheep milk is further enriched with conjugated linoleic acid (CLA) and angiotensin-converting enzyme (ACE)-inhibitory peptides that may support lipid metabolism, reduce inflammation, and promote cardiovascular health, although additional clinical evidence is needed (Alhaj & Kanekanian, 2014) ^[5]. Beyond metabolic functions, sheep milk contains important immune-related components such as immunoglobulins and lactoferrin, a multifunctional protein known for its antibacterial, antiviral, iron-binding, and immunomodulatory activities. Lactoferrin and its derived fragments help strengthen host defense by preventing pathogen adhesion and regulating cytokine activity, thereby enhancing innate immunity (Eker *et al.*, 2024) ^[22]. Peptidomic analyses of sheep milk and fermented products have also identified peptides with anti-inflammatory and immunomodulatory properties, including the ability to suppress pro-inflammatory cytokines in experimental studies (Joshi *et al.*, 2025) ^[34]. Collectively, these findings suggest that sheep milk may serve as a valuable natural source of dietary immunomodulators and functional bioactive compounds, although further human studies are necessary to confirm their clinical benefits (Azizi *et al.*, 2021) ^[13].

Sheep milk and its fermented products provide several advantages for gut and digestive health due to their effects on microbiota balance, digestibility, and lactose metabolism. Fermented products such as kefir and yogurt contain probiotic microorganisms and bioactive peptides that can positively influence gut microbiota composition, promote the formation of beneficial metabolites, and stimulate incretin release, thereby supporting digestive and metabolic health (Ahmad, Zhu, Chu, Danni, *et al.*, 2025) ^[1]. Sheep milk also possesses distinct proteolytic and peptide characteristics compared with cow milk, which may contribute to improved digestibility and fewer intolerance-related symptoms in some individuals who avoid cow milk. However, it still contains lactose and may trigger reactions in people with true bovine milk protein allergy (Nguyen *et al.*, 2020) ^[50]. Fermentation further enhances tolerability by reducing lactose content and producing metabolites that support digestion, making fermented sheep milk beverages potentially suitable for lactose-sensitive consumers (Meena *et al.*, 2025) ^[46]. The effectiveness of these benefits is influenced by factors such as the starter cultures used and the processing and storage conditions applied during production (Alm, 1982) ^[7].

Sheep milk and its bioactive compounds may also support cognitive, neurological, antimicrobial, and antioxidant functions. Proline-rich polypeptides (PRPs) and lactoferrin-derived fragments obtained from sheep colostrum have demonstrated neuroprotective, anti-amyloidogenic, and antioxidant activities in preclinical studies, while some human studies have reported improvements in short-term

memory and attention in older adults. However, larger and well-controlled clinical trials are still required to confirm these effects (Hong *et al.*, 2024) ^[30]. Mechanistic evidence suggests that the antioxidative and immunomodulatory properties of these compounds may contribute to brain development and cognitive health, although further research is needed to establish their safe and effective dietary use (Nagai *et al.*, 2019) ^[49]. Sheep milk also contains antimicrobial peptides effective against several foodborne pathogens, including *E. coli*, *Salmonella typhimurium*, *Bacillus cereus*, and *Enterococcus faecalis*, indicating their potential applications in food preservation and therapeutic interventions (Ván *et al.*, 2006). In addition, antioxidant peptides derived from κ -casein have shown strong free radical-scavenging and lipid peroxidation inhibitory activities, in some cases comparable to synthetic antioxidants, highlighting their potential for reducing oxidative stress when incorporated into functional foods or stable bioactive formulations (Gómez-Ruiz *et al.*, 2008) ^[28].

6. Technological and industrial applications

Sheep milk-based products such as yogurt, cheese, and kefir are considered effective carriers of bioactive peptides generated during fermentation and storage (Kumawat *et al.*, 2026) ^[37]. Peptidomic studies of sheep milk kefir have identified a large number of peptide sequences, including several with potential bioactive properties unique to sheep milk, with peptide concentration increasing as fermentation progresses, highlighting kefir as a rich source of functional peptides (Amorim *et al.*, 2019) ^[9]. Specific starter cultures can further enhance these functional properties (Meena *et al.*, 2022) ^[47]. For example, fermentation with *Lactocaseibacillus paracasei* M11 has been associated with strong ACE-inhibitory and antidiabetic activities through inhibition of α -amylase, α -glucosidase, and lipase enzymes, while *Limosilactobacillus fermentum* KGL4 has demonstrated similar metabolic enzyme inhibitory effects, with peak bioactivity observed after approximately 48 hours of fermentation (Deveci *et al.*, 2023) ^[20]. These findings emphasize the importance of selecting suitable starter cultures and fermentation conditions for industrial applications.

Milk-derived peptides are increasingly recognized for their multifunctional properties, including antihypertensive, antidiabetic, antioxidant, antimicrobial, and mineral-binding activities, making them valuable ingredients for functional foods, nutraceutical formulations, and natural food preservatives. Their production can be optimized through techniques such as enzymatic hydrolysis, controlled fermentation, membrane separation, and mild processing methods that help preserve peptide bioactivity (Kashung & Karuthapandian, 2025) ^[36]. Studies have also shown that cardioprotective peptides derived from fermented milk can retain ACE-inhibitory activity after absorption, supporting their bioavailability and therapeutic potential (Zambrano-Cervantes *et al.*, 2025). In addition, advanced processing approaches such as ultrasound-assisted fermentation have been reported to enhance peptide release while simultaneously improving texture and sensory quality, thereby increasing the value of premium sheep milk products (Gholamhosseinpour *et al.*, 2025) ^[27].

Sheep milk possesses considerable potential for use in medical nutrition formulations because of its high protein content and good digestibility. Products enriched with sheep

milk-derived bioactive peptides may provide metabolic benefits through ACE-inhibitory, DPP-IV-inhibitory, and glucosidase-inhibitory activities, while fermented low-lactose formulations may support immune function and gut health. Preliminary translational studies have indicated opportunities for developing specialized products such as ready-to-drink clinical nutrition beverages, high-protein gels, and peptide-based modular supplements designed for

specific patient requirements. Nevertheless, successful application in the medical nutrition sector will require standardized methods for peptide analysis, improved understanding of gastrointestinal stability and bioavailability, and well-designed human clinical studies to validate efficacy and support health-related claims (Amigo & Hernández-Ledesma, 2020) ^[8].

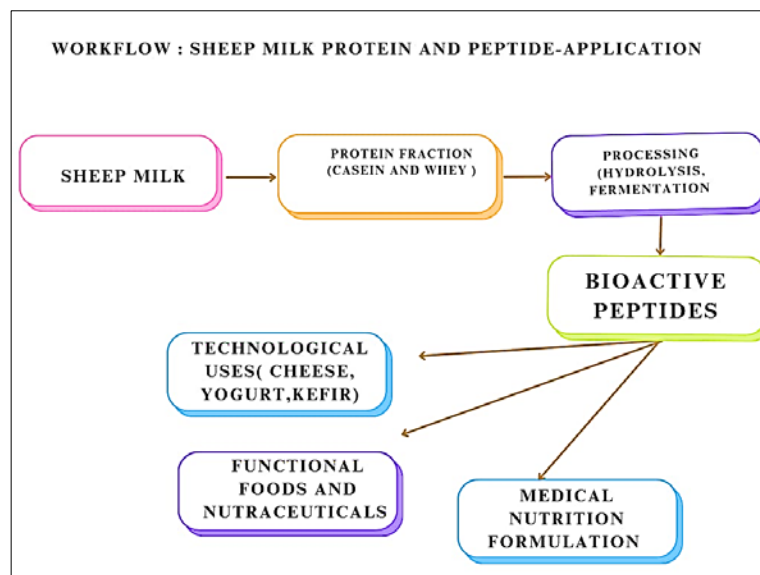


Fig. 1: Applications of Sheep Milk Proteins and Bioactive Peptides

7. Challenges and future perspectives

One of the major challenges in sheep milk peptide research is the absence of standardized methods for peptide isolation, characterization, and identification. Procedures used for peptide extraction, enzymatic hydrolysis, and analytical techniques such as mass spectrometry and chromatography differ considerably among laboratories, resulting in reproducibility problems and limited comparability between studies (Karamoutsios *et al.*, 2025) ^[35]. Although recent developments in proteomics, including integrated LC-MS/MS, MALDI-TOF, and chemometric approaches, have enhanced peptide detection and profiling, validation across different breeds, geographical regions, and sample types remains limited (Rysova *et al.*, 2022) ^[56]. Therefore, establishing standardized protocols for sample preparation, enzymatic digestion, and database utilization is essential to improve biomarker discovery, strengthen inter-study consistency, and support future regulatory acceptance of sheep milk-derived bioactive peptides (Punia *et al.*, 2020). The bioavailability and stability of sheep milk-derived peptides remain important challenges for their successful application in functional foods and therapeutic products. Many bioactive peptides are vulnerable to degradation during gastrointestinal digestion, which can reduce their biological effectiveness (Mudgil, Ajayi, *et al.*, 2024) ^[48]. However, *in silico* and *in vitro* digestion studies have shown that certain peptides, especially those containing high levels of proline residues, demonstrate greater resistance to enzymatic breakdown and are able to maintain their biological activity after digestion (Li *et al.*, 2025) ^[44]. To identify peptides with the highest functional potential, researchers increasingly employ ADME profiling and computational platforms such as BIOPEP-UWM to predict absorption, distribution, metabolism, excretion, and

nutraceutical properties. Despite these advances, further well-designed *in vivo* studies are necessary to validate the predicted stability, bioactivity, and clinical significance of these peptides (Kęska *et al.*, 2021) ^[38].

Regulatory approval of functional foods containing sheep milk-derived peptides requires clear evidence of safety, efficacy, and consistent quality in accordance with standards established by authorities such as the EFSA and FDA (Luparelli *et al.*). The approval of health claims depends on the availability of standardized analytical techniques and clinically validated results, which can slow the commercialization of new products (Lee *et al.*, 2025) ^[43]. Regulatory evaluation also includes requirements related to accurate labeling, allergenicity assessment, and dose-response validation, especially in the case of novel peptides and specialized functional formulations (Elsayed *et al.*, 2025) ^[23].

Future research on sheep milk-derived peptides is expected to focus on strengthening clinical evidence, developing personalized nutrition strategies, promoting sustainable production systems, and advancing innovative peptide discovery. Well-designed human clinical trials are required to better understand the effects of these peptides on cardiometabolic health, satiety, immune regulation, and allergy management (Ahmad *et al.*, 2025) ^[1]. Personalized nutrition approaches based on individual genetic, microbiome, and metabolic profiles may further enhance the targeted use of sheep milk peptides, although substantial foundational research is still needed in this area (Sarraz *et al.*, 2022) ^[58]. In parallel, sustainable sheep farming practices, including selective breeding for desirable milk protein characteristics and evaluation of environmental impacts, are essential for the ethical and large-scale production of functional sheep milk products (Sathika *et al.*).

Additionally, the integration of high-throughput peptidomics with machine learning technologies is accelerating the identification and design of bioactive peptides with specific health benefits and improved potential for regulatory approval (Madsen *et al.*, 2022) ^[45].

8. Conclusion

Sheep milk proteins and bioactive peptides constitute an important source of nutritional and functional compounds, offering advantages over many other dairy species due to their high protein content, bioactive properties, and technological applications. The rich casein and whey protein composition enhances digestibility and amino acid availability while serving as a precursor for peptides with multiple health-promoting activities, including antihypertensive, antioxidant, antimicrobial, antidiabetic, and immunomodulatory effects. Findings from *in vitro*, *in silico*, and animal studies, together with limited but encouraging human research, indicate that sheep milk-derived peptides may contribute to metabolic health, immune support, gut function, and cognitive well-being.

From an industrial perspective, the high solids content and favorable protein composition of sheep milk make it particularly suitable for the production of cheese, yogurt, kefir, and other functional dairy products. Ongoing advances in fermentation technology, enzymatic hydrolysis, and peptidomics are further expanding its applications in nutraceuticals, medical nutrition, and biomedical fields. Despite these developments, important challenges remain, including the need for standardized peptide extraction methods, improved understanding of gastrointestinal stability and bioavailability, and stronger clinical validation of health benefits. In addition, regulatory approval requires substantial evidence regarding safety and efficacy before health claims can be accepted. Future progress is expected through the integration of high-throughput omics technologies, machine learning, and precision nutrition approaches, which may accelerate the discovery and application of novel bioactive peptides. At the same time, sustainable sheep farming practices and environmentally efficient processing methods will be essential for long-term development. Together, these advancements position sheep milk as not only a traditional dairy product but also a valuable resource for next-generation functional foods and health-promoting biomaterials.

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