***Review Article***

**Systematic Review on Exploration of Donkey Milk as a Safe Alternative for Alleviating Cow Milk Protein Allergy**

**Abstract**

Donkey milk has emerged as a potential alternative to cow milk for alleviating cow milk protein allergy (CMPA), a common food allergy affecting children worldwide. This systematic review explored the efficacy, nutritional benefits, and safety considerations of donkey milk in preventing CMPA. The unique composition of donkey milk, characterized by lower levels of allergenic proteins, high digestibility, and nutritional adequacy, contributes to its hypoallergenic properties. Several studies have demonstrated the tolerability of donkey milk in infants with CMPA, with a significant proportion exhibiting favorable responses to its consumption. The similarities in protein composition between donkey milk and human milk, including low casein content and whey-to-casein ratio, further enhance its suitability as a substitute for cow milk. Donkey milk is rich in essential vitamins, minerals, and bioactive compounds and offers a well-rounded nutritional profile. Its excellent digestibility and potential immunomodulatory effects make it a valuable resource for individuals with gastrointestinal disorders and allergies. However, the limited availability and higher cost of donkey milk compared to cow milk may pose challenges for its widespread adoption. Cultural preferences and social factors also influence the acceptance of donkey milk within communities. Ensuring safety, regulatory compliance, and consumer awareness is crucial to maximize the potential benefits of donkey milk while minimizing the associated risks. Further research is needed to elucidate the long-term effects and safety of incorporating donkey milk into the diet of children with CMPA. Nonetheless, donkey milk is a promising alternative for managing CMPA and offers a unique combination of hypoallergenicity, nutritional value, and therapeutic potential.

**Keywords**

Donkey milk, Cow milk protein allergy, Hypoallergenicity, Nutritional composition, Immunomodulatory effects, adult milk

**1. INTRODUCTION**

Food allergy is one of the most prevalent chronic disorders in infants and children and has surfaced as an epidemic in recent decades (Sicherer & Sampson, 2018). The cow milk protein allergy (CMPA) is prevalent in infants and children. This allergic reaction is associated with an abnormal immune response by the body to a protein present in cow's milk; in this condition, injury occurs in the stomach and intestines (Abrams & Sicherer, 2021; Edwards & Younus, 2024). Cow's milk allergy is the most common food allergy in developed countries like the US and Europe, where about 2-3% of infants and young children are affected (Høst, 2002) and rising rapidly in Asia as well (Lee et al., 2022). The CMPA has risen as a major public health concern among physicians and parents because of its high prevalence, risk of serious consequences, and influence on the quality of life for families (Vandenplas et al., 2015). The CMPA presents diverse symptoms, including gastrointestinal disturbances, skin rashes, and respiratory issues. Diagnosis typically involves an elimination diet, followed by an oral challenge to confirm the condition. Depending on the severity, CMPA can be categorized as IgE-mediated (immediate allergic reaction) or non-IgE-mediated (delayed immune response) (Al-Beltagi et al., 2022). The Management strategies include extensively milk protein hydrolyzed formulas as the first-line treatment, while severe cases the amino acid formulas are recommended (D’auria et al., 2021). Despite their higher cost, amino acid formulas provide superior symptom control in complex cases, but few research tried to developed the low-cost hydrolyzed formula using rice (Fiocchi et al., 2022), soy (Kipfer & Goldman, 2021). Moreover, there is need of further advancements in hypoallergenic formula development are critical to improving clinical outcomes and enhancing tolerance in affected infants (Wilsey et al., 2023). The other suitable strategies to dealing CPMA may include administration of probiotic-supplemented formulas that improved the gut health and enhance immune tolerance (Tan et al., 2021); baked milk that altered the structure of milk allergen and decreased the allergenicity by decreasing the binding of IgE (Giannetti et al., 2021).

The donkey milk (DM) has emerged as a potential alternative due to its unique nutritional composition and hypoallergenic properties. Compared to cow milk, donkey milk boasts a lower casein content, the main allergen in cow milk, and a whey-to-casein ratio similar to that of human breast milk (Polidori et al., 2015). Additionally, specific whey proteins in it may be less allergenic than those in cow milk (Souroullas et al., 2018). It has a rich nutritional profile similar to human milk, with low fat, high lactose, and a favorable casein-to-whey protein ratio (Singh et al., 2024). It contains abundant antibacterial components and protective elements (Meghwal et al., 2023; Singhal et al., 2023). With lower levels of β-lactoglobulin compared to cow milk, it is suitable for newborns with cow milk protein allergy and lactose intolerance.

The several clinical studies investigating donkey milk's efficacy in preventing CMPA (Monti et al., 2007; Sarti et al., 2019; Vincenzetti et al., 2014). However, the evidence supporting DM's effectiveness comes primarily from observational studies, necessitating further well-designed clinical trials to establish its role in CMPA management definitively. Despite its potential, practical challenges, such as the high cost and limited availability of donkey milk, must be addressed to facilitate its widespread use as a dietary alternative for CMPA sufferers. Nonetheless, donkey milk presents itself as a promising hypoallergenic substitute for infants with CMPA due to its unique protein composition and reported high tolerability. Despite its numerous benefits, a key limitation of DM as an infant food is its low energy value due to its lower fat content than human and cow milk. Coscia et al., (2018) and Bertino et al., (2019) highlighted that although DM-derived fortifiers improve feeding tolerance and have comparable auxological outcomes to cow milk-derived fortifiers in preterm infants, the lower fat content necessitates additional supplementation to meet the energy requirements of infants. Martini et al., (2021) also emphasized that while DM is suitable for children with cow milk protein allergy, it should be fortified with fats to ensure adequate energy intake. Therefore, while DM is beneficial for allergic infants, its use requires nutritional adjustments to address the low caloric density. In conclusion, donkey milk holds promise as an effective strategy for preventing CMPA in infants. Its compositionally distinct nature and demonstrated tolerability make it an appealing option for those with CMPA. However, further research, including rigorous clinical trials, is essential to validate its efficacy and address practical barriers to access. By doing so, donkey milk can solidify its position as a valuable asset in the management of CMPA.

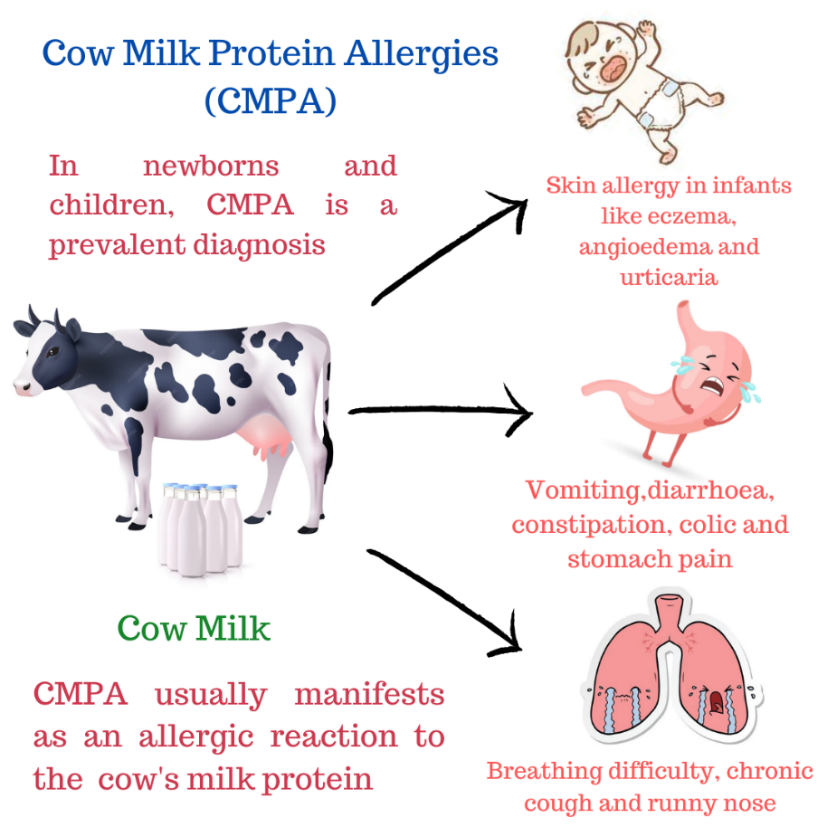
The present review highlights the importance of donkey milk in alleviating cow milk protein allergy, nutritional properties, therapeutic and technological applications, microbial diversity, potential risks, and safety considerations, with a special focus on enhanced health benefits to infants and elderly people.

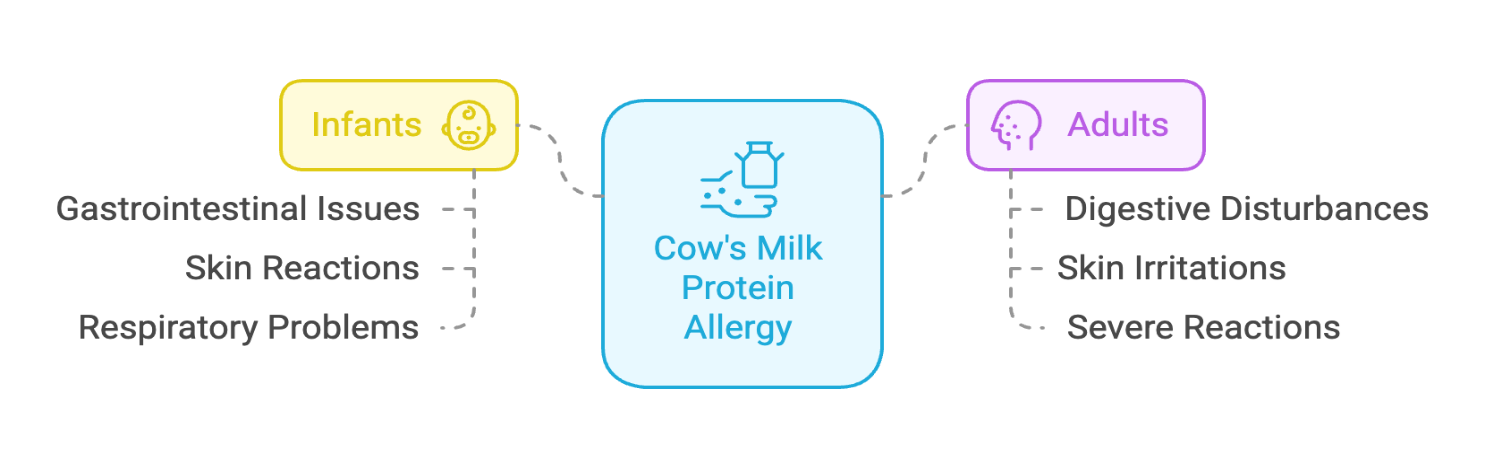
**2. PREVALENCE OF COW MILK PROTEIN ALLERGY**

The CMPA is a prevalent food allergy affecting children globally, characterized by immune reactions to proteins present in cow milk, such as casein and whey proteins. The CMPA can cause mild symptoms, such as eczema and gastrointestinal discomfort, and even severe reactions, including asthma exacerbations. The CMPA management typically involves avoiding cow milk and its derivatives, necessitating exploring alternative sources of nutrition. Donkey milk has emerged as a potential substitute for cow milk due to its hypoallergenic properties and nutritional composition resembling human milk (Lajnaf et al., 2023; Yang et al., 2021). The CMPA is the most common food allergy in infants of up to 1 year, associated with ingestion of milk protein fraction, i.e., immunoglobulin E (IgE) (Sackesen et al., 2019). The prevalence of CMPA was higher in the developed countries, about 0.5 to 3% in infants aged 1 year (Flom & Sicherer, 2019). Several researchers conducted a systemic study to assess the prevalence of CMPA across the globe. The Warren et al., (2022) conducted a prevalence study of CMPA in different population segments in the US. They reported that the prevalence of cow milk allergy is 1.3 – 4.4% among the different variables, i.e., race and ethnicity, origin, sex, age, and income groups. The estimated prevalence of CMPA in the other countries of the Middle East is in the range of 1 – 5% with 86.7% of agreement level (El-Hodhod et al., 2021). As per the Meta study by Laha et al., (2022) of 229 articles on CMPA for a period of 1967 to 2001, and findings revealed that the incidence of CMPA in infancy was about 2 – 3% in developed countries. In developing countries like India, no study has been performed on the prevalence of CMPA, but very few studies have been conducted on the prediction model of milk allergy. Laha et al., (2022) assessed milk allergies among the Indian age group 0 – 19 years using a food allergy predictive model with 98 patients, and the model predicted milk allergy with a 0.94 correlation coefficient and 98% accuracy. Similarly, Prasad et al., (2018) also developed a predictive tool for cow's milk allergy (CMA) in Indian infants (age 0 – 24 months) using Cow's Milk-related Symptom Score (CoMiSS).

**2.1 Causes and Symptoms of Cow Milk Protein Allergy**

The CMPA arises from an immune response to cow milk proteins, triggered by the immune system's recognition of these proteins as foreign invaders. Genetic predispositions play a role in predisposing individuals to allergic reactions to cow milk proteins (Sicherer & Sampson, 2014). It is characterized by an aberrant immune response to proteins found in cow's milk. This immune-mediated reaction gives rise to a diverse range of symptoms spanning various bodily systems, delineating a broad clinical spectrum. Eczema, a chronic inflammatory skin disorder typified by pruritus, erythema, and cutaneous lesions, stands as a cardinal manifestation of CMPA, particularly prevalent in pediatric populations. Notably, the persistence of eczematous symptoms underscores the imperative of diligent allergy management from infancy into adulthood. Respiratory manifestations, mirroring asthma-like symptoms, including wheezing, coughing, and dyspnea, emerge as another salient feature of CMPA pathology (Giovanna et al., 2012). These symptoms stem from the intricate interplay of cow's milk protein exposure and subsequent airway inflammation and constriction, emphasizing the multisystemic impact of the allergy. The gastrointestinal disturbances constitute a hallmark feature of CMPA, embracing a gamut of clinical presentations from mild to severe.



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**Figure 1**: **Cow milk protein allergy symptoms in infant and adult**

Diarrhea, vomiting, abdominal discomfort, bloating, and flatulence represent common gastrointestinal manifestations mediated by inflammatory responses within the gastrointestinal milieu elicited by cow's milk protein ingestion (Lozinsky et al., 2015). Furthermore, CMPA extends beyond conventional gastrointestinal symptoms to encompass broader food intolerance or sensitivity manifestations. General malaise, fatigue, irritability, and cognitive impairments post-consumption of cow's milk protein-containing foods underscore the systemic repercussions of this immune-mediated disorder. Thus, CMPA embodies a complex interplay between immune dysregulation and systemic manifestations, necessitating meticulous diagnostic scrutiny and comprehensive management strategies to mitigate symptomatology and forestall long-term sequelae (Vandenplas et al., 2015; Yang et al., 2021).

**2.2 Management of Cow Milk Protein Allergy**

Proper management of CMPA is paramount in alleviating symptoms and ensuring optimal nutrition for affected individuals. A cornerstone of CMPA management involves the complete elimination of cow's milk and its derivatives from the diet. This necessitates the substitution of cow's milk with alternative sources of nutrition, such as plant-based milk (e.g., soy, almond, oat, rice) or hypoallergenic infant formulas designed explicitly for CMPA management. Maintaining nutritional adequacy is essential during CMPA management. Calcium, a vital nutrient abundant in cow's milk, must be supplemented through alternative sources to prevent deficiencies. Additionally, calcium supplementation may be recommended, especially in infants and young children, under the guidance of healthcare professionals. Thus, the proper management of CMPA necessitates the elimination of cow's milk and its derivatives from the diet, substitution with alternative sources of nutrition, maintenance of nutritional adequacy through calcium-rich foods and supplementation, and comprehensive education and support for affected individuals and caregivers (Venter et al., 2013).

The UK guideline on the diagnosis and management of non-IgE-mediated cow's milk allergy in infancy, known as the Milk Allergy in Primary Care (MAP) guideline, was published in 2013 and has had a significant impact on healthcare, particularly in primary care settings. The MAP guideline's influence transcends national boundaries, as its adoption internationally underscores its relevance and applicability in various healthcare contexts. An international interpretation of the MAP guideline has been developed to recognize the global need for practical guidance in managing cow's milk allergy (Venter et al., 2017).

(Venter et al., 2018) studied the realm of non-IgE-mediated cow’s milk allergy (CMA) in infancy, shedding light on its significant impact on pediatric healthcare. The research illuminated the multifaceted clinical presentations of non-IgE-mediated CMA, from gastrointestinal symptoms to cutaneous manifestations, advocating for a comprehensive diagnostic approach. Diagnostic hurdles, notably the absence of standardized testing protocols and overreliance on elimination diets, were pinpointed, prompting exploration into novel diagnostic avenues such as oral food challenges and component-resolved diagnostics. Moreover, the study emphasized evidence-based dietary interventions as the cornerstone of managing non-IgE-mediated CMA, advocating for the utilization of extensively hydrolyzed formulas and amino acid-based formulas, alongside nutritional support, to ensure optimal growth and development in affected infants. Overall, the findings underscored the evolving understanding of non-IgE-mediated CMA and underscored the necessity for optimized diagnostic and management strategies in infancy, accentuating the pressing need for further research and clinical innovation in this domain.

**3. EFFICACY OF DONKEY MILK IN PREVENTING COW MILK PROTEIN ALLERGY**

Donkey milk has garnered attention as a potential alternative to cow milk for individuals with CMPA due to its hypoallergenic properties and nutritional composition resembling human milk. Studies have demonstrated the tolerability of donkey milk in infants with CMPA, with a significant proportion exhibiting favorable responses to its consumption (Monti et al., 2007). Donkey milk's similarity to human milk in terms of whey-to-casein ratio and protein composition makes it a promising substitute for cow milk in CMPA management. Donkey milk stands out for its clinical tolerance, palatability, and nutritional completeness, making it an excellent choice for children with cow's milk protein allergy (CMPA). Its low levels of caseins and other highly immunogenic proteins further enhance its suitability for these children (Bertino et al., 2022). The mode of action of donkey milk in preventing cow's milk protein allergy (CMPA) is supported by several factors, as evidenced by scientific research. Compared to cow milk, donkey milk boasts a lower casein content, the main allergen in cow milk, and a whey-to-casein ratio similar to that of human breast milk (Polidori et al., 2015). Additionally, specific whey proteins in it may be less allergenic than those in cow milk (Souroullas et al., 2018). Despite its potential practical challenges, such as the high cost and limited availability of donkey milk, there is a need to be addressed to facilitate its widespread use as a dietary alternative for CMPA sufferers.

**3.1****Lower Levels of Allergenic Proteins**

Donkey milk contains lower caseins and other proteins known to trigger allergic reactions compared to cow's milk. This reduced immunogenicity contributes to minimizing the risk of allergic responses in susceptible individuals (Guo et al., 2007; Luo et al., 2019). Casein-derived bioactive peptides possess notable immunomodulatory and antimicrobial properties. Peptides produced during the digestion of bovine and human milk, such as the hexapeptide fragment Val-Glu-Pro-Ile-Pro-Tyr from β-casein, have demonstrated immunostimulatory effects. Due to its protein composition resembling that of human milk, donkey milk holds promise as an alternative to cow's milk for children with CMPA, offering both clinical tolerability and nutritional advantages. It is rich in functional proteins like α-lactalbumin, lactoferrin, and lysozyme, which exhibit antimicrobial, anti-inflammatory, and anticancer activities. Nonetheless, its low-fat content reduces its caloric value, highlighting the need for further clinical research to assess its nutritional efficacy. Additionally, small peptides derived from donkey milk β-casein may play beneficial roles in cardiovascular, digestive, and immune health, though further exploration is necessary (Vincenzetti et al., 2017).

**3.2 High Digestibility and Tolerance**

Donkey milk is known for its high digestibility and compatibility with the human digestive system. Its composition closely resembles that of human milk. It contains lower casein protein levels than cow's milk, reducing the likelihood of provoking adverse reactions in individuals with CMPA. Additionally, the protein profile of donkey milk is more similar to human milk, further enhancing its tolerability. These factors contribute to donkey milk's reputation as a hypoallergenic option for those with CMPA (Salimei & Fantuz, 2012).

**3.3 Nutritional Adequac**y

While ensuring minimal risk of exacerbating allergic symptoms, its nutritional composition closely mirrors that of human milk, offering a well-rounded mix of proteins, fats, carbohydrates, vitamins, and minerals vital for maintaining optimal health. Furthermore, the hypoallergenic properties of donkey milk, stemming from its low casein content and similarity to human milk, contribute to its reduced allergenicity and decreased likelihood of eliciting adverse reactions in individuals with CMPA (Singh et al., 2024). This distinctive nutritional profile promotes overall well-being and effectively addresses specific dietary needs, rendering donkey milk a suitable alternative for children grappling with CMPA-related nutritional challenges. By furnishing a safe and enriching option devoid of cow's milk proteins, donkey milk fosters ideal growth and development while mitigating the potential for allergic manifestations, thus fostering the health and comfort of CMPA-affected children.Thus,by considering these factors, donkey milk emerges as a promising alternative for managing CMPA in children, offering both nutritional support and reduced allergenicity (Anusha Siddiqui et al., 2024; Salimei et al., 2004; Salimei & Fantuz, 2012).

Several studies have investigated the efficacy of donkey milk in preventing cow milk protein allergy. According to (Monti et al., 2007), donkey milk can be a valid alternative to cow's milk for individuals with cow's milk protein allergy. The study found that donkey milk is well-tolerated in 82.6-98.5% of infants with cow's milk protein allergies. The similarities in the composition of donkey milk and human milk, including the low casein content and total whey protein content, make it an attractive alternative for these children (Inglingstad et al., 2010).

Sarti et al., (2019) conducted another study that reported the well-accepted and tolerated nature of donkey milk among infants with cow's milk food enterocolitis syndrome. The study also suggested that donkey milk could be a suitable substitute for human milk, especially for infants with cow's milk protein allergy, due to its nutritional similarities and excellent palatability.

The similarities in chemical composition between donkey milk and human milk may contribute to its potential benefits. Donkey milk possesses a unique protein composition, featuring levels of α-lactoglobulin similar to those found in human milk. Furthermore, it contains a substantial amount of β-lactoglobulin, a prominent allergen in cow's milk that is absent in human milk. These characteristic highlights donkey milk's potential as a hypoallergenic substitute for individuals with cow milk protein allergy (CMPA), as it lacks the allergenic proteins abundant in cow's milk. Additionally, donkey milk is distinguished by its heightened lysozyme content compared to cow milk, a trait it shares with human milk. Lysozyme's antimicrobial properties contribute to donkey milk's immune-boosting capabilities, further solidifying its suitability as a nourishing and allergen-reduced option for infants with CMPA (Derdak et al., 2020; Lajnaf et al., 2023).

**4. NUTRITIONAL BENEFITS OF DONKEY MILK**

DM contains a balanced composition of macronutrients, including proteins, carbohydrates, and fats. While the precise composition may vary, on average, donkey milk contains about 1.5-2.5% protein, 6-7% lactose, and 1.5-1.8% fat. The protein fraction primarily consists of whey proteins, which are easily digestible and well-tolerated, making donkey milk suitable for individuals with lactose intolerance or CMPA (Monti et al., 2007).

It has several nutritional benefits compared to cow milk. It contains a lower level of linolenic acid, cholesterol, and total whey proteins. The low linolenic acid content in donkey milk may be beneficial for infants with cow's milk protein allergy, as it is known to have anti-inflammatory properties (Živkov Baloš et al., 2023). Furthermore, donkey milk has a lower cholesterol content, which can be advantageous for children with a family history of cardiovascular disease. To date, the advantageous qualities of donkey milk have primarily been associated with its whey proteins, with β-lactoglobulin being the most prevalent at 6.06 g/L, lysozyme at 1.07 g/L, and α-lactalbumin at approximately 2 g/L (Martini et al., 2021).

**Table 1: Physico-chemical properties of donkey milk**

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| **S. No.** | **Composition** | **Average value** |
|  | Total solids | 8.24–9.96% |
|  | Solid not fat | 8.70–8.96% |
|  | Fat | 0.30-1.41% |
|  | Protein | 1.00-2.11% |
|  | Lactose | 5.38–7.21% |
|  | Ash | 0.32-0.47% |
|  | Casein | 0.83–0.85% |
|  | Lysozyme | 1.0 g/kg |
|  | Energy | 40 kcal/100 ml |
|  | pH | 7.0 – 7.2 |
|  | Titrable acidity | 0.03 - 0.04% lactic acid |
|  | Water activity | 0.973 - 0.985 |

Modified from(Garhwal et al., 2023; Meena et al., 2024; Nayak et al., 2020; Singh et al., 2024)

**4.1 Micronutrient Profile**

DM is rich in essential vitamins and minerals crucial for overall health. It contains significant amounts of vitamins A, B1, B2, B6, C, D, and E, as well as minerals such as calcium, phosphorus, magnesium, and zinc (Vincenzetti et al., 2020, 2021). These micronutrients play vital roles in various physiological functions, including bone health, immune function, and antioxidant defense (Cimmino et al., 2023).

**4.2 Bioactive Compounds**

DM is also abundant in bioactive compounds with potential health benefits. It contains lysozyme, lactoferrin, and immunoglobulins, which possess antimicrobial and immunomodulatory properties. These bioactive compounds contribute to the protective effect of donkey milk against infections and support immune function (Martini et al., 2018; Salari et al., 2019). It has garnered attention as a potential functional food with various health benefits. The anti-proliferative properties of whey proteins from donkey milk suggest potential for lung cancer treatment. Alpha-lactalbumin, a protein type, demonstrates antiviral, anticancer, and anti-stress properties (Aspri et al., 2018; Deepa et al., 2023). Additionally, positive outcomes in children's growth metrics further underscore the potential health advantages of incorporating donkey milk into their diet (Meena et al., 2024; Vandenplas et al., 2015)

One prominent benefit of donkey milk is its ability to enhance immunological responses. This effect has been observed across various studies, including in vitro experiments, animal models, and clinical research involving older individuals (Monti et al., 2007). Donkey milk has demonstrated potential in boosting antioxidant and detoxifying enzyme activity in rodent models. Moreover, lysozyme derived from donkey milk has exhibited direct inhibitory effects on tumor cell line development, suggesting its potential in cancer prevention (Martini et al., 2018; Monti et al., 2007). Animal studies have provided further insights into the health-promoting properties of donkey milk. Research on rodents has highlighted its ability to improve energy metabolism, induce hypolipidemic effects, and modulate body composition by increasing body protein content relative to body fat (Cimmino et al., 2023; Vincenzetti et al., 2021). Additionally, donkey milk has shown promise in weight control, indicating its potential utility in managing obesity-related conditions

Despite the promising findings regarding the health benefits of donkey milk, further exploration and validation are required to fully understand its potential for human health. While existing research supports its efficacy in managing specific health conditions, such as CMPA and atopic dermatitis, a comprehensive understanding of its mechanisms of action and long-term effects is essential (Lajnaf et al., 2023). Additionally, practical considerations such as the scalability and sustainability of donkey milk production must be addressed to ensure its accessibility to a broader population (Salimei & Fantuz, 2012).

Thus, donkey milk emerges as a valuable resource with multifaceted health benefits, including enhancing immune function and exerting antioxidant and anticancer properties. However, rigorous research efforts are necessary to fully elucidate its therapeutic potential and address practical challenges associated with its production and accessibility. By harnessing the nutritional and functional properties of donkey milk, we can pave the way for its integration into dietary strategies aimed at enhancing human health and preventing disease.

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**Figure 2**: **Health benefits of donkey milk**

**4.3 Digestibility and Tolerance**

One of the key nutritional benefits of donkey milk is its excellent digestibility and tolerance, particularly in individuals with gastrointestinal disorders or allergies. The unique composition of donkey milk, characterized by smaller fat globules and higher levels of whey proteins, facilitates easier digestion and absorption compared to other types of milk. This property makes donkey milk a suitable alternative for infants, the elderly, and those with digestive issues (Meena et al., 2024).

**4.4 Immunomodulatory Effects**

Emerging evidence suggests that donkey milk may exert immunomodulatory effects, contributing to its potential health-promoting properties. Several studies have reported the presence of bioactive peptides in donkey milk that can modulate immune responses and inflammatory processes. These immunomodulatory effects may have implications for the prevention and management of certain immune-related disorders (Guha et al., 2021; Salvo et al., 2023).

**4.5 Clinical Applications**

Donkey milk, known for its rich nutritional profile and therapeutic potential, has been investigated for a range of clinical applications. Research indicates its efficacy in managing gastrointestinal disorders such as irritable bowel syndrome (IBS) and inflammatory bowel disease (IBD) due to its anti-inflammatory and gut-soothing properties. The presence of bioactive compounds like lysozyme and lactoferrin in donkey milk plays a significant role in promoting gut health and reducing inflammation (Tidona et al., 2014). Additionally, donkey milk has demonstrated benefits for dermatological conditions like atopic dermatitis. Its high vitamin D content, essential fatty acids, and other nutrients help maintain skin integrity and reduce allergic reactions. Clinical studies have shown that topical application of donkey milk can improve skin hydration and alleviate eczema symptoms (A.J. et al., 2015). Moreover, donkey milk-based formulas have been found beneficial for the growth and development of preterm infants. The unique composition of donkey milk, which includes lower levels of casein and higher levels of whey proteins, closely resembles human milk, making it an ideal alternative for infants’ intolerance to cow's milk. Studies have highlighted the positive impact of donkey milk on the growth parameters and nutritional status of preterm infants, leading to better health outcomes (Salimei & Fantuz, 2012). Thus, donkey milk's therapeutic potential spans various clinical applications, making it a valuable alternative for managing various health conditions.

**4.6 Yield of Donkey Milk**

The production of donkey milk (DM) is influenced by genetic, environmental, and physiological factors, as well as herd management and milking practices. Donkey mammary glands have a low capacity (less than 2.5 liters), resulting in significantly lower yields (100–150 kg per 300-day lactation period) compared to cow milk (CM) (8724 ± 163 kg per 305-day lactation period) (Martini et al., 2021; Meena et al., 2024). This low yield poses challenges for commercial production. Studies have shown that DM yield varies with season, milking frequency, and lactation stage. For example, Ragusana breed donkeys produced 489 kg of milk over a 295-day lactation when milked twice daily, with higher yields in winter and summer compared to spring and autumn (Giosuè et al., 2008). Protein, casein, lactose, and ash content varied significantly with lactation stages, with some studies reporting decreased protein and fat but increased lactose content over time. Diet, breed, and parity also affect milk yield and quality (Meena et al., 2024).

**5. COMPARING DONKEY MILK WITH HUMAN AND COW MILK**

Several factors come into play when comparing donkey milk with human and cow milk. Human milk stands out as the optimal source of nutrition for infants, rich in diverse bioactive molecules crucial for growth and development. While cow milk is widely available, its allergenicity and high saturated fatty acid content raise concerns, particularly for infants with cow milk protein allergies and cardiovascular health (Derdak et al., 2020). Donkey milk presents a promising alternative, with a composition closer to human milk, making it suitable for infants with allergies. It contains bioactive molecules that are beneficial for health, although its limited availability and lower energy content compared to human milk may pose challenges for widespread use. Despite these differences, all these milk offer valuable nutrients, with human milk remaining the preferred choice for infants when possible (Cimmino et al., 2023). Human milk (HM) stands as the gold standard for infant nutrition due to its complex biological composition, providing essential nutrients and bioactive molecules crucial for optimal growth and development. It contains a variety of bioactive molecules, including immunoglobulins, cytokines, growth factors, and enzymes, which contribute to various positive effects such as protection against infections, maturation of the gut microbiota, and neurodevelopment (Christian et al., 2021; Meng et al., 2021; Okburan & Kızıler, 2023).

On the other hand, cow milk, while widely available and often used as a substitute for HM, contains β-lactoglobulin (β-LG), a primary allergen responsible for allergic reactions in infants with cow milk protein allergies (Lajnaf et al., 2023; Matthai et al., 2020). Moreover, concerns have been raised regarding the high content of saturated fatty acids (SFA) in milk and dairy products, which are implicated in increasing low-density lipoprotein cholesterol levels, a risk factor for cardiovascular disease (CVD) (Benbrook et al., 2018; Vanderhout et al., 2020, 2021).

The introduction of milk and dairy products into the human diet has been questioned due to these concerns. However, conflicting research results exist regarding the relationship between SFA content in dairy and adverse cardiovascular effects. Some studies suggest an inverse correlation between SFA content and negative cardiovascular outcomes, while others highlight the beneficial effects of bioactive molecules such as ω-3 and ω-6 fatty acids(Dehghan et al., 2017; Pereira, 2014). Donkey milk emerges as a potential alternative to human milk and cow milk, with a composition more akin to human milk. Donkey milk is particularly suitable for children with cow milk protein allergies due to its low allergenicity and palatability (Vincenzetti et al., 2021). It contains various bioactive molecules with important functions, including antimicrobial activity, anti-inflammatory actions, and support for gut microbiota growth (Barlowska et al., 2011).

**6**. **POTENTIAL RISKS AND CONSIDERATIONS**

While donkey milk has been found to be an effective alternative to cow milk for preventing cow milk protein allergy, there are some potential risks and considerations associated with its use. Donkey milk is not readily available in most countries, and its price may be higher than that of cow milk. Additionally, there may be cultural preferences and social aspects to consider when introducing donkey milk into a family's diet (Salimei et al., 2004). Moreover, ensuring safety, regulatory compliance, and consumer awareness are imperative to maximize the potential benefits of donkey milk while minimizing associated risks.

One significant consideration when contemplating the use of donkey milk is its availability. Unlike cow milk, which is widely accessible in most regions, donkey milk may not be readily available in many countries. The production of donkey milk is limited, primarily due to the small population of lactating donkeys and the lower milk yield compared to cows (Salimei et al., 2004; Salimei & Fantuz, 2012). Consequently, accessing donkey milk can be challenging for consumers residing outside regions where its production is prevalent. The cost of donkey milk is another factor that may deter its widespread adoption as a substitute for cow milk. Donkey milk tends to be more expensive than cow milk due to various factors, including limited supply, higher production costs, and lower milk yield per animal. In regions where donkey milk is available, its price may be prohibitive for some families, making it financially inaccessible as a daily dietary option (Messias et al., 2022). The elevated cost of donkey milk may pose a barrier, particularly for individuals from lower socioeconomic backgrounds.

Cultural preferences and attitudes toward donkey milk may influence its acceptance and utilization within communities. In some cultures, donkey milk may be perceived as unconventional or unfamiliar, leading to resistance or reluctance to incorporate it into the diet. Cultural beliefs, traditions, and dietary habits play a significant role in shaping food choices, and introducing a novel food item such as donkey milk may encounter resistance due to cultural conservatism or stigma associated with unconventional foods (Anusha Siddiqui et al., 2024; Meena et al., 2024; Monti et al., 2007). Therefore, understanding cultural perceptions and sensitivities is essential when promoting the use of donkey milk as a dietary alternative. Social factors also play a pivotal role in determining the acceptability and adoption of donkey milk. Social norms, peer influence, and social networks can influence individuals' decisions regarding food choices and consumption patterns. The social acceptability of donkey milk within a community may impact its uptake, with factors such as peer recommendations, social media influence, and community attitudes shaping individuals' attitudes toward this alternative milk option (Vandenplas et al., 2015). Additionally, social support networks and access to information and resources may influence individuals' ability to procure and incorporate donkey milk into their diet effectively.

**7. SAFETY AND REGULATORY CONSIDERATIONS**

Ensuring donkey milk's safety and regulatory compliance is paramount to its utilization as a food product. Quality control measures, hygiene practices, and adherence to regulatory standards are essential to mitigate health risks associated with donkey milk consumption. Additionally, addressing concerns related to contamination, adulteration, and microbial safety is critical to safeguard consumer health and confidence in the product (Martini et al., 2021; Martini et al., 2018; Meena et al., 2025) Regulatory frameworks governing the production, processing, and distribution of donkey milk vary across regions, highlighting the importance of robust regulatory oversight and enforcement to uphold safety standards.

**8. CONCLUSION**

In summary, the effectiveness of donkey milk in mitigating cow milk protein allergy has been substantiated through diverse studies. Its nutritional resemblance to human milk and its potential advantages presents it as a compelling option for children afflicted with cow milk protein allergy. Nonetheless, factors such as availability, cost, and cultural inclinations should be weighed when considering its substitution for cow milk. Additional investigation is imperative to delve into the prolonged repercussions and safety of integrating donkey milk into children's diets with cow milk protein allergies. In essence, donkey milk emerges as a valuable nutritional resource, offering a distinctive amalgamation of essential nutrients, micronutrients, and bioactive elements. Its notable digestibility, capacity for immune modulation, and clinical utility underscore its promise as a functional food with potential health-enhancing properties for individuals across different age groups. Substantial further exploration is warranted to comprehensively unravel the therapeutic attributes of donkey milk and its role in fostering human well-being.

Disclaimer (Artificial intelligence)

Author(s) hereby declare that NO generative AI technologies such as Large Language Models (ChatGPT, COPILOT, etc.) and text-to-image generators have been used during the writing or editing of this manuscript.

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