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Invited review: Camel milk and gut health—Understanding digestibility and the effect on gut microbiota

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ABSTRACT

Camel milk (CM), known for its immune-regulatory, anti-inflammatory, antiapoptotic, and antidiabetic properties, is a natural healthy food. It is easily digestible due to the high levels of β-casein and diverse secreted antibodies, exhibiting superior antibacterial and antiviral activities compared with bovine milk. β-casein is less allergic and more digestible because it is more susceptible to digestive hydrolysis in the gut; therefore, higher levels of β-casein make CM advantageous for human health. Furthermore, antibodies help the digestive system by destroying the antigens, which are then overwhelmed and digested by macrophages. The connection between the gut microbiota and human health has gained substantial research attention, as it offers potential benefits and supports disease treatment. The gut microbiota has a vital role in regulating the host's health because it helps in several biological functions, such as protection against pathogens, immune function regulation, energy harvesting from digested foods, and reinforcement of digestive tract biochemical barriers. These functions could be affected by the changes in the gut microbiota profile, and gut microbiota differences are associated with several diseases, such as inflammatory bowel disease, colon cancer, irritable bowel disorder, mental illness, allergy, and obesity. This review focuses on the digestibility of CM components, particularly protein and fat, and their influence on gut microbiota modulation. Notably, the hypoallergenic properties and small fat globules of CM contribute to its enhanced digestibility. Considering the rapid digestion of its proteins under conditions simulating infant gastrointestinal digestion, CM exhibits promise as a potential alternative for infant formula preparation due to the high β-/α_s-casein ratio and protective proteins, in addition to the absence of β-lactoglobulin.

Key words: camel milk, in vitro digestion, gut microbiome, casein, milk fat

INTRODUCTION

The health benefits of camel milk (**CM**) may partially arise from its beneficial effects on the hosts' gut microbiota (Aljutaily et al., 2020). Camel milk is characterized by its heat stability and high nutritional value (Seifu, 2023). The unique composition of CM makes it a favorable substitute for bovine milk in several purposes, such as the manufacture of infant formula. Compared with other milk species, CM is primarily valued for its better digestibility in the gastrointestinal system because of its hypoallergenic properties and the small size of fat globules (Rahmeh et al., 2022). Similar to human milk, CM lacks β-lactoglobulins. In addition, α-lactalbumin, the major whey protein in CM and human milk, represents only 25% of the total whey proteins in bovine milk (Lajnaf et al., 2023). Among all mammalian milk species, CM fat globules are the smallest, and they do not physically gather due to the lack of agglutinin substrate (Seifu, 2023). Furthermore, CM has interesting antimicrobial activities involving antibacterial activity against both gram-positive and gram-negative bacteria, as well as antiviral and antifungal properties (He et al., 2022). These beneficial effects are mainly due to the higher levels of protective proteins in CM.

More investigation is needed into the specific roles of CM in improving the diversity of the gut microbial community in humans (Solanki and Hati, 2018). The effect of CM on the growth of *Anaerostipes* and *Clos-*

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tridiales, in addition to its relationship with enhanced production of short-chain fatty acids in the gut and immune system response, is recently under consideration (Aljutaily, 2022). The presence of lactoferrin, immunoglobulins, lysozyme, and lactoperoxidase gives CM antimicrobial properties (Mohamed et al., 2022b). Due to its antimicrobial peptide content, CM can inhibit a wide range of microorganisms, including species and strains from the genera *Candida*, *Bacillus*, *Diplococcus*, *Listeria*, *Klebsiella*, *Salmonella*, *Pseudomonas*, *Streptococcus*, and *Staphylococcus* (Algboory and Muhialdin, 2021).

The human body is inhabited by large numbers of microorganisms (Woźniak et al., 2021). Most of these microorganisms colonize the digestive tract, founding the purported gut microbiota and comprising bacteria, fungi, viruses, eukaryotes, archaea, and phages. Complex cooperative relationships of coadaptation, coevolution, and interdependence exist between humans and microbiota. The digestive system is the most inhabited section, but the colonization degree is not identical. The diversity in gut microbiota composition is attributed to the environmental variations in the digestive tract parts (Hou et al., 2022). In addition, the gut microbiota has a valuable role in preserving health, principally contributing to the enhancement of immunity, and controlling numerous basic metabolic routes (Ceballos et al., 2021).

Changes in the gut microbiota impair homeostasis, causing gut microbiota-related diseases, such as gastrointestinal tract functional diseases, inflammatory bowel diseases, infectious intestine diseases, gastrointestinal cancers, liver diseases, metabolic and obesity syndromes, autism, allergies, and diabetes (Gupta et al., 2022). The gut microbiota community can be affected by multiple factors, including, diet, age, host species, and gastrointestinal tract parts (Lozupone et al., 2012; Anders et al., 2021). Nevertheless, diets and host species are the key factors contributing to gut microbiota composition (Ghosh and Pramanik, 2021). The microbiota repairs the plasma lipids profile of the host via modifications in metabolic gene expression. Moreover, microbiota health has been demonstrated to be correlated with lean and nonobese populations (Nicholson et al., 2012; Iwaki et al., 2021). Several reviews have examined the biofunctional properties and industrial processes of CM (Al haj and Al Kanhal, 2010; Lozupone et al., 2012; Nicholson et al., 2012; Baig et al., 2022; Liu et al., 2023; Salvo et al., 2023). Camel milk is well known for its nutritional benefits and therapeutic aspects (Alhaj, 2020). Due to its greater nutritional value, hypoallergenic properties, and superior digestibility in the gastrointestinal system of human body, CM is considered a favorable substitute to bovine milk. To the best of our knowledge, this is the first review that specifically focuses on the digestibility of CM and its effect on gut microbiota.

CAMEL MILK DIGESTIBILITY

Due to its high nutritional value and prospective therapeutic aspects, CM has attracted increasing interest in recent years. Compared with bovine milk, CM is characterized by its lower casein/whey proteins ratio and higher β-casein/α_{S1}-casein ratio (Roy et al., 2020). Table 1 shows a comparison between CM and other milk species. The definite profile of CM casein fractions and the large size of its casein micelles are the key players in the formation of a weak curd upon acidification during the manufacture of fermented CM products (Kamal et al., 2017). The authors' interest has focused on whether the soft curdling behavior of CM during cheese production would translate into enhancement in the infant digestive tract (Zou et al., 2022). The content of total protein in CM represents about 33.5 g/L of whole milk, with inconsistency influenced by the animals' geographic location (Konuspayeva et al., 2009). Caseins represent ~80% of the total CM protein content, and whey comprises various soluble proteins in addition to different indigenous peptides engendered by proteases existing in CM, such as cathepsin D and chymotrypsin A (Alhaider et al., 2013).

Whey proteins are the second major constituent of CM protein fraction representing 20–25% of total proteins. β-Lactoglobulin, the major whey protein and one of the main allergens in bovine milk, is absent in CM (Table 1). β-Lactoglobulin is the main constituent in bovine whey proteins making up 50%, followed by 25% of α-lactalbumin (Lajnaf et al., 2022). The average level of α-lactalbumin in CM represents 2.2 g/L, compared with 2.45 g/L in human milk and 0.5 g/L in bovine milk (El-Hatmi et al., 2007; Sabikhi, 2007). Camel milk α-lactalbumin contains slightly higher levels of essential amino acids than bovine milk α-lactalbumin (Beg et al., 1985). Due to the absence of β-lactoglobulin, CM α-lactalbumin presents high homology with human milk α-lactalbumin (Merin et al., 2001). α-Lactalbumin is present in high levels in CM and can be feasibly isolated. In vitro digestibility of α-lactalbumin by using trypsin and chymotrypsin revealed that CM α-lactalbumin had a greater degree of hydrolysis than that of bovine milk protein in both the native state and molten globule state. It was suggested that CM α-lactalbumin is a better substrate for intestinal enzymes than bovine milk protein (Salami et al., 2009). Compared with bovine and human milk, CM is rich in immune-associated proteins such as peptidoglycan recognition protein 1 and whey acidic protein

Table 1. Chemical composition of camel milk compared with other milk species[1]

Milk species	Water (%)	Fat (%)	Lactose (%)	Ash (%)	Protein fraction (g/L)					
					α_{s1}-CN	α_{s2}-CN	β-CN	κ-CN	β-LG	α-LA
Camel	88.1	3.5	4.4	0.79	5.3	2.3	15.6	0.8	—	2.3
	88.1	2–6	3.5–5.1	0.7–0.9	4.9–5.7	2.1–2.5	14.4–16.9	0.8–0.9	—	0.8–3.5
	88.69	3.47	4.28	0.78	—	—	—	—	—	—
	89.0	5.49	4.8	0.86	—	—	—	—	—	—
Human	87.8	3.8	7.0	0.2	0.43	—	2.4	0.87	—	3.2
	87.8	3.5	6.4	0.2	0.77	—	3.8	0.14	—	1.9–3.4
Bovine	87.3	3.7	4.8	0.7	9.5	2.5	9.8	3.3	3.1	1.1
	88.1	3.8	5.1	0.7	8–10.7	2.8–3.4	8.6–9.3	2.3–3.3	3.2–3.3	1.2–1.3
Buffalo	84.3	5.3	4.9	0.8	8.9	5.1	12.6–20.9	4.1–5.4	3.9	1.4
Goat	87.7	4.5	4.1	0.8	0–13	2.3–11.6	0–6.3	2.8–13.4	1.5–5.0	0.7–2.3
Sheep	80.7	7.4	7.0	1.0	2.4–22.1	6.0	15.6–39.6	3.2–12.2	6.5–13.5	1.0–1.9

[1]Data adapted from Hailu et al. (2016), Roy et al. (2020), Alhaj et al. (2022), and Seifu (2022).

(Han et al., 2023). Such proteins have the possibility of granting health advantages when ingested by infants, although in vivo and in vitro studies are necessary for a better confirmation (Zou et al., 2022).

β-Casein has a functional role in the formation and stabilization CM foams. The interfacial characteristics of the CM proteins β-casein, α-lactalbumin, and β-lactoglobulin, alone or in binary combinations at the air/water interface, have been investigated (Lajnaf et al., 2022). A high association was shown between foaming properties and surface tension progression as a function of time. In addition, CM and bovine milk β-casein displayed higher efficiency in decreasing the interfacial tension as compared with the globular proteins from CM and bovine milk. This performance was attributed to the molecular structure variations of globular proteins and caseins. The interfacial properties of CM and bovine milk protein mixture attitudes showed the ability of both CM and bovine milk β-caseins to regulate the rheological profiles and adsorption phenomena of the mixtures. This was attributed to the ability of β-casein to adsorb more quickly at the air/water interface and to easily modify its construction (Seta et al., 2014).

Milk digestion by stomach enzymes (primarily pepsin and gastric lipases in the presence of hydrochloric acid) is the initial main stage, which is then followed by additional digestion in the small intestine by the actions of intestinal lipases and proteases (Mulet-Cabero et al., 2020a; Ye et al., 2020). Some infants might have chymosin-like enzymes together with pepsin, which vanish from the gastric fluid by d 11 after parturition. Pepsin and chymosin both belong to the same aspartic proteinase group and use aspartic acid residues in their active centers. These enzymes can favorably hydrolyze the phenylalanine-methionine bond of the κ-casein fraction, except that pepsin displays a general proteolytic action to the bonds with tyrosine, tryptophan, valine, or leucine residues, and accordingly, it has a higher proteolytic action in relation to its milk coagulation activity as compared with chymosin (Leite Júnior et al., 2015; Suwareh et al., 2021).

Because both pepsin and chymosin have the same active site, their mechanisms are expected to be comparable regarding milk coagulation. Chymosin is more stable at pH values in the range of 5.3 to 6.3 and rapidly loses its activity under higher pH values beyond 9.8, as well as under acidic conditions, specifically at pH values less than 3 to 4 (Yang et al., 2022). On the other hand, pepsin has a maximum proteolytic action at pH 2, with an ideal pH range of 2 to 5, and some activity in the pH range of 5.5 to 7.5. Pepsin is conclusively deactivated at pH values beyond 7.5 (Salelles et al., 2021). Compared with intestinal proteases, pepsin has different protein hydrolysis sites. It favorably acts on the

κ-casein fraction during early stages of gastric digestion of milk, resulting in the clotting of casein micelles at a fairly high pH about 6.0, while whey proteins remain soluble (Ye et al., 2016). Accordingly, the initial function played by the stomach in milk digestion is a crucial step in controlling milk proteins digestion rate in the gastrointestinal tract. In this context, understanding CM coagulation behavior and the digestive dynamics during gastric digestion is of great significance because milk coagulation can affect the delivery levels of proteins, fats, and other milk-related components (Roy et al., 2020).

Tagliazucchi et al. (2018) revealed that goat milk proteins were hydrolyzed more quickly and proficiently by gastric and duodenal enzymes than CM, bovine milk, and sheep milk proteins. By using human gastrointestinal proteolytic enzymes, Almaas et al. (2006) reported that goat milk proteins were degraded more quickly compared with bovine milk proteins. In contrast, the degree of hydrolysis of CM caseins with pancreatic enzymes was better than that of bovine milk caseins (Salami et al., 2008). Analysis of the digestion of CM, bovine milk, and goat milk demonstrated that goat milk had a higher degree of digestibility than CM and bovine milk (Tagliazucchi et al. 2016; Tagliazucchi et al., 2017).

Previous studies have evaluated CM protein digestibility (Maqsood et al., 2019; Zou et al., 2022; Mudgil et al., 2023). However, the conditions of gastrointestinal digestion applied using in vitro models have mimicked the digestion system of adults. In infants, the gastric pH is much higher, whereas pepsin output is much lower than in adults. Consequently, milk protein digestion kinetics might considerably differ between adults and infants (Ménard et al., 2018). Potential bioactive peptides have been detected in CM protein hydrolysates (Ali Redha et al., 2022); however, the research is still in its primary stage. Zou et al. (2022) evaluated the digestibility of CM, bovine milk, and human milk proteins by using an in vitro infant gastrointestinal digestion model. They reported that the lower level of pepsin and the higher pH of infant gastric digestion caused a minor degree of protein digestion during the gastric phase. Camel milk casein digestion slowed down due to the formation of a single clot during gastric digestion. During the intestinal phase, rapid and large protein hydrolysis was observed. The 3 milk digesta showed similar peptide levels at the end of the intestinal digestion stage, implying that they were similarly digestible, although the digestion rate was related to the type of milk. Various peptide profiles produced after in vitro digestion of milk species were attributed to the low sequence identity among milk proteins. Furthermore, substantial peptides were released after digestion, although the function of peptides in vivo is unclear.

Figure 1A shows the coagulation behavior of CM during gastric digestion by using confocal laser scanning microscopy. The lower level of pepsin and the high gastric pH of infant digesta caused a minor protein digestion extent throughout gastric stage. During digestion, a single clot was formed in CM, which reduced its casein digestion. An extensive and rapid hydrolysis of protein during intestinal stage was observed (Zou et al., 2022). At the end of intestinal digestion phase, the levels of peptides in the 3 milk digesta were comparable, suggesting that they were equivalently digestible, but the digestion rate was related to the type of milk. Because the content of protein in human milk is much lower than that of bovine milk and CM (1.2%, 3.9%, and 2.6%, respectively), bovine milk and CM were diluted to 1.2% total protein with water. The finding from the higher dilution of bovine milk with water to standardize the content of protein against human milk was attributed to the more extensively solubilized colloidal calcium phosphate, which is critical for milk gastric coagulation. (Huppertz and Lambers, 2020; Wang et al., 2023). Milk dilution might cause substantial solubilization of micellar calcium phosphate, leading to the disruption of the larger casein structure and, finally, reducing the coagulation of casein. Figure 1B displays the digestion of emulsified fat into small lipids and its absorption into intestinal cells. Fat is separated from other milk components in the stomach. While in the small intestine, fat is emulsified by bile and digested by enzymes. The intestinal cells absorb fatty acids released during digestion of milk fat (Drackley, 2007). A large lipoprotein structure, called a chylomicron, is formed by long-chain fatty acids, and plays an important role in fats transportation through the lymph system. Chylomicrons are formed in the intestinal cells and carry lipids from the digestive tract into circulation (Mansbach, 2004). Short- and medium-chain fatty acids can be absorbed immediately into the bloodstream from the intestinal microvilli because they are water-soluble (Lairon, 2009).

Bioactive peptides derived from CM proteins showed obvious structural similarities with previously recognized antibacterial, antihypertensive, anti-inflammatory, immunomodulatory, and antioxidant peptides and are therefore potentially beneficial bioactive peptides. Research on these peptides is expected to be a challenging task in the coming years. To evaluate the biological influence of the peptides of interest, in vivo and clinical studies are required (Mati et al., 2017). An in vitro digestion approach simulating the physicochemical conditions of the gastrointestinal system to process skimmed CM has been applied (Tagliazucchi

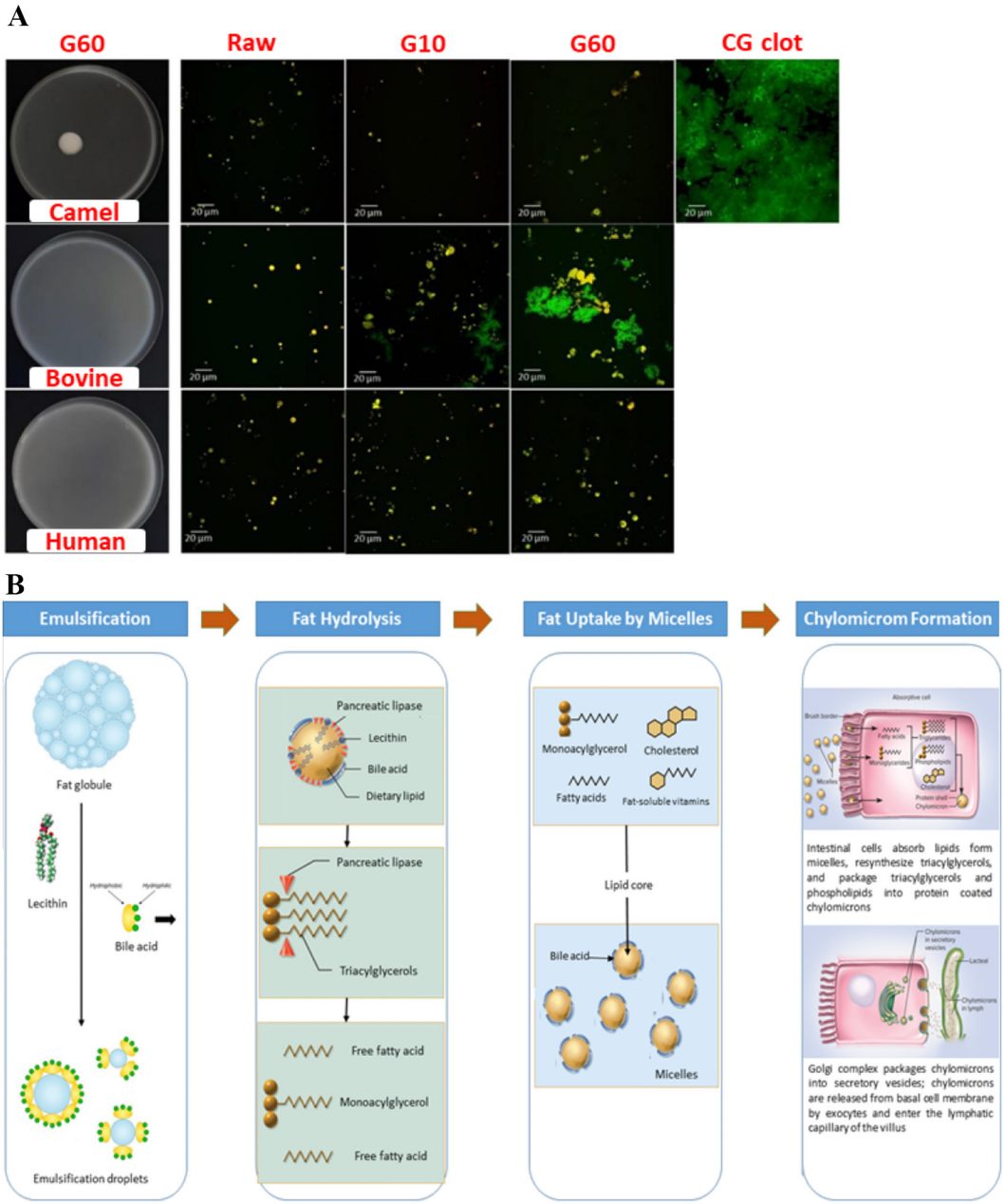

Figure 1. (A) Photos and confocal laser scanning microscopy images of milk samples during in vitro gastric digestion. Green = protein stained with rhodamine B; yellow = fat stained with both rhodamine B and Nile red; G10 = after 10 min of gastric digestion; G60 = after 60 min of gastric digestion; CG = camel milk gastric digesta; Zou, 2022. (B) Digestion of emulsified fat into small lipids and absorption into intestinal cells.

et al., 2016). The digested samples were evaluated for angiotensin-converting enzyme inhibitory activity and separated using high-performance liquid chromatography, and the different fractions were characterized for their angiotensin-converting enzyme inhibitory activity. The results demonstrated the presence of angiotensin-converting enzyme inhibitory peptides in the low molecular mass (less than 3 kDa) fraction of digested CM. Some of the detected peptides displayed noticeable structural resemblances to previously reported angiotensin-converting enzyme inhibitors (Salami et al., 2011; Bidasolo et al., 2012).

Li et al. (2023) recently conducted a dynamic in vitro gastric digestion study of CM. Unlike bovine milk, CM did not form a coagulum during digestion, and no coagulum remained in the stomach. Instead, CM formed

small particles composed of caseins that were rapidly emptied from the stomach. The particle structure became more spherical and compact over time, with αS1-casein being more highly digested than β-casein. This structural shift was attributed to the neutralization of protein negative charges and colloidal calcium phosphate dissolution as the pH decreased, as well as to changes in peptide and protein profiles. The association of fat globules with protein particles also increased as the pH decreased. After 60 to 120 min, the particle size of the drained digesta decreased and stabilized, with no intact proteins remaining. This indicates a high overall rate of gastric digestion and emptying.

The SDS-PAGE profiles of CM digesta emptied at different stages of gastric digestion are presented in Figures 2B and 2C. It was shown that the digesta emptied after 20 min exhibited an identical protein profile to that of the undigested CM, excluding small peptide bands, which implied insignificant proteolytic pepsin activity. Furthermore, the digesta emptied after 60 min was primarily composed of α-lactalbumin, with slight traces of other peptides, caseins, and whey proteins. At 120 to 240 min of digestion, no whole proteins stayed in the digesta, with only a small number of peptides (<5 kDa) being noticeable. The persistence of α-lactalbumin after 60 min of digestion and its vanishing after 120 min in CM agrees with other studies of ruminant milks. That is, the susceptibility of α-lactalbumin to pepsin hydrolysis depends on the pH value and is evidently higher at pH values lower than 3.5 to 4 (Roy et al., 2020; Li et al., 2022).

It is well established that during gastric digestion of whole milk, fat globules undergo physical entrapment within the formed protein coagulum. Consequently, the structure and properties of this protein matrix exert an influence on the rate of fat release and digestion by gastrointestinal lipases (Mulet-Cabero et al., 2019; Ye et al., 2019). The protein composition, including the proportion of casein and whey protein, the ratio of protein to fat, and various production conditions, contributes to the formation and characteristics of the protein network (Ye et al., 2020). In a study conducted by Mulet-Cabero et al. (2020b), an in vitro investigation was performed using model milk systems to simulate the stomach digestion process. Different levels of casein and whey protein were employed. The researchers observed that as the ratio of casein to whey protein increased in the model protein system, the resulting curd exhibited heightened firmness and viscosity. Consequently, this led to a deceleration in gastric emptying and a slower rate of digestion and absorption of nutrients. Furthermore, they noted that the incorporation of higher amounts of fat into protein-rich models resulted in a more fragmented coagulum with a significant decrease in firmness. This observation suggests that the presence of fat delayed protein aggregation, potentially influencing the rates at which nutrients in whole milk are digested.

Limited data are available on the gastric digestion of CM fat. Lipolysis throughout the gastric digestion phase was less significant during the general process of digestion, as gastric lipolysis only represents 10% to 25% of the whole lipid digestion in adults (Mulet-Cabero et al., 2020b). Thus, several studies on milk fat digestion have principally focused on intestinal digestion. Nevertheless, it is extensively recommended that gastric lipases should be included in the in vitro digestion analyses, as their initial role might assist further breakdown of lipids by the intestinal lipases (Ménard et al., 2018). In addition, the role of gastric lipases in infants is significant due to their elevated postprandial gastric pH in comparison to adults. It is hypothesized that the smaller size of fat globules in CM could enhance fat digestibility. This is attributed to the larger surface area of smaller fat globules, which facilitates rapid digestion by gastrointestinal lipases (Bourlieu et al., 2015). The smaller size of CM fat globules plays a crucial functional role in promoting higher fat digestibility (Ho et al., 2022; Vincenzetti et al., 2022; Muthukumaran et al., 2023). Camel milk fat is present in the form of milk fat globules dispersed in water, with an average size ranging from 1.1 to 2.1 mm. This size is smaller than buffalo (3.9–7.7 mm), bovine (1.6–4.9 mm), and goat milk (1.1–3.9 mm), indicating a faster digestion rate for CM relative to other milk species (Bakry et al., 2021). The fatty acid composition of CM is characterized by elevated levels of saturated fatty acids, particularly myristic and palmitic acids, as well as long-chain fatty acids, odd-numbered fatty acids, and unsaturated fatty acids. Furthermore, CM exhibits lower levels of short-chain fatty acids (Benmeziane-Derradji, 2021).

Table 1 illustrates that the lactose content CM is comparable to that of bovine milk. Initial measurements indicate lower lactose levels in CM at birth (2.8%, wt/vol), followed by an increase to 3.8% within the first day of lactation (Ho et al., 2022). With unrestricted access to water, the average lactose content in camels reaches approximately 5%. Conversely, in dehydrated camels, the lactose content decreases to around 2.9%. Notably, CM presents itself as a preferable and safer option for individuals with lactose intolerance (Cardoso et al., 2010). This preference may be attributed to the diminished casomorphin levels in CM, resulting in reduced intestinal motility. Consequently, lactose remains exposed to the action of lactase for an extended period. Additionally, the higher concentration of L-lactate in CM, which exceeds that of bovine milk by a factor of

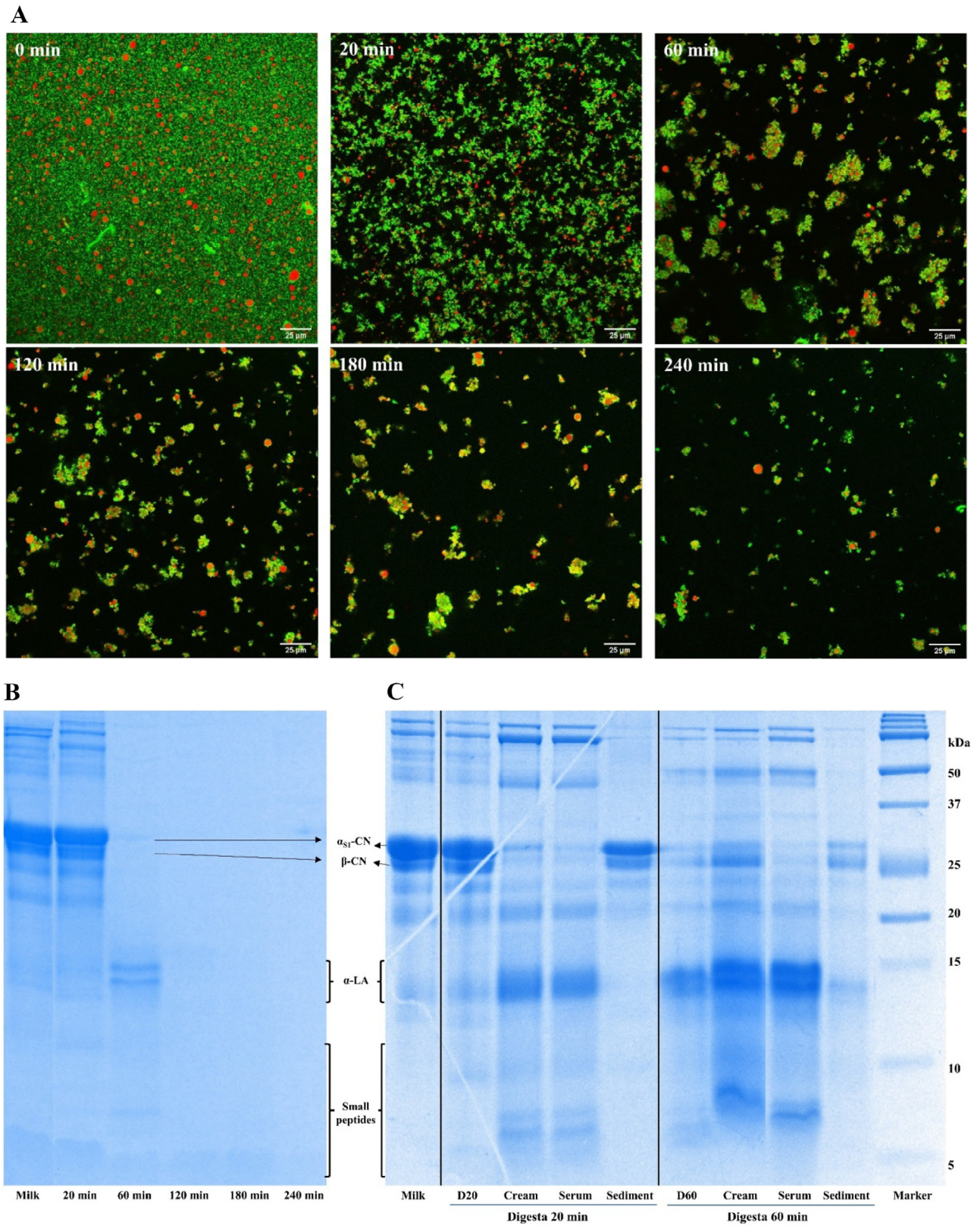

Figure 2. (A) Confocal laser scanning microscopy micrographs of the digesta emptied at diverse stages of dynamic gastric digestion of reconstituted camel milk (CM). The SDS-PAGE profiles of (B) the digesta emptied at different stages of the gastric digestion of CM and (C) diverse fractions (separated by centrifugation) of the digesta collected at 20 (D20) and 60 min (D60) of digestion (Li et al., 2023).

100, may contribute to its lower lactose intolerance compared with bovine milk (Konuspayeva et al., 2019; Oselu et al., 2022). The possibility of whether CM could be ingested by individuals intolerant to lactose deprived of adverse reactions was studied. It was concluded that CM could be a potential alternative for patients intolerant to lactose who present symptoms when consuming bovine milk (Cardoso et al., 2010). The effect of CM intake on the glycemic status of diabetic individuals and in vitro models was investigated (Ayoub et al., 2018; Khakhariya et al., 2023). The studies demonstrated blood glucose and glycosylated hemoglobin reduction. An assumption of the high levels of natural insulin in CM was suggested, but the reported levels could not fully elucidate the valuable effect of CM intake. It was stated that the deficiency of coagulum development of CM in the stomach may be an active vehicle for taking unaffected milk insulin through the digestive system and being absorbed in the intestine (Aqib et al., 2019). Other proteins that existed in higher levels in CM than in other milk species could interact with the insulin receptors and contribute by way of their anti-inflammatory and antioxidant activities to regenerate β-cells in the pancreas (Agrawal et al., 2020).

CAMEL MILK AND GUT MICROBIOTA

The gut microbiota has a critical function in improving the health and disease resistance of the host. Host health significantly depends on gastrointestinal tract microbiota, and an imbalanced microbiota composition might cause several diseases (Sheikh et al., 2022). Gut microorganisms differ in nature and have numerous functions that affect the physiological functions of the host, such as energy balance, immunity, and metabolic activities (Ghosh and Pramanik, 2021). Gut microbiota investigations depend on feces and include the noninvasive collection of fecal samples because feces reveal the DNA profile of the hindgut microbiota (Mo et al., 2021). The presence of several beneficial microorganisms, such as those from the genera *Lactobacillus*, *Bifidobacterium*, *Akkermansia*, and *Allobaculum*, in the gastrointestinal tract has been reported due to the consumption of CM (Kadri et al., 2021). These bacteria offer immunity and have a significant role in fighting cancer and other metabolic diseases (He et al., 2018).

Due to its noteworthy antioxidant, anti-inflammatory, immune-regulatory, antiapoptotic, and antidiabetic properties, CM is considered as a natural healthful product (Aqib et al., 2019). Camel milk comprises higher amounts of lactoferrin, immunoglobulin, and calcium, but lower amounts of fat. It also contains a mixture of secreted antibodies, such as IgA and IgM, which have functional roles in enhancing its antibacterial and antiviral activities compared with bovine milk. Likewise, CM contains a diversity of biologically active proteins possessing immunomodulatory features, such as lysozyme, lactoperoxidase, lactoferrin, and *N*-acetylglucosaminidase (He et al., 2022). Camel milk oligosaccharides are essential to improving the proliferation of intestinal bifidobacteria, in addition to effectively inhibiting the adhesion of pathogenic microorganisms to the colonic mucosa (Urashima et al., 2014). Cui et al. (2020) stated that CM effectively alleviated colonic mucosa damage and immune cell inequality in mice. Recently, He et al. (2022) reported that CM could inhibit the inflammatory response by defeating the overexpression of inflammatory cytokines in the colon. Camel milk intensified the expression of Zonula Occludens-1, Occludin, and Claudin-1 to maintain the intestinal barrier functions. It also adjusted the intestinal microbiota of mice with colitis by improving the diversity of gut microbiota, modifying the gut microbiota abundance, and improving the levels of short-chain fatty acids.

He et al. (2020) reported that feeding mice an UHT or HTST CM diet increased the levels of short-chain fatty acids in feces, signifying that the influence of UHT CM on gut microbiota was to endorse the proliferation of short-chain fatty acids-producing bacteria. It was concluded that the variations in the physicochemical properties of CM were caused by diverse heat treatments, and these variations were suggested to be the main causes of the variety in the gut microbiota of mice fed on different treatments of CM. The alteration in gut microbiota provoked the production of short-chain fatty acids. The nutritional value of CM is affected by diverse heat treatments (Mohamed et al., 2022a). The treatment of CM with UHT can break down some constituents that could induce differences in gut microbiota with adverse consequences on the growth of gut probiotics. The low-temperature, long-time treatment of CM preserved certain nutrients and did not cause variations in the composition or diversity of gut microbiota (He et al., 2020).

Figure 3A displays the relative abundance of several bacterial genera in the gut microbiota of mice fed on CM compared with another group fed on distilled water (Wang et al., 2018). It was shown that *Firmicutes*, *Verrucomicrobia*, *Bacteroidetes*, *Actinobacteria*, *Saccharibacteria*, and *Proteobacteria* were the major phyla present in gut microbiota and among them, *Bacteroidetes* and *Firmicutes* accounted for more than 80% of the bacteria that existed and were consequently the main phyla. In addition, *Allobaculum*, *Desulfovibrio*, *Akkermansia*, *Romboutsia*, *Lactobacillus*, *Bifidobacterium*, and *Turicibacter* were the predominant genera found in gut microbiota. *Allobaculum* and *Akkermansia* were the main genera, respectively denoting 40.4% and 7.8% of

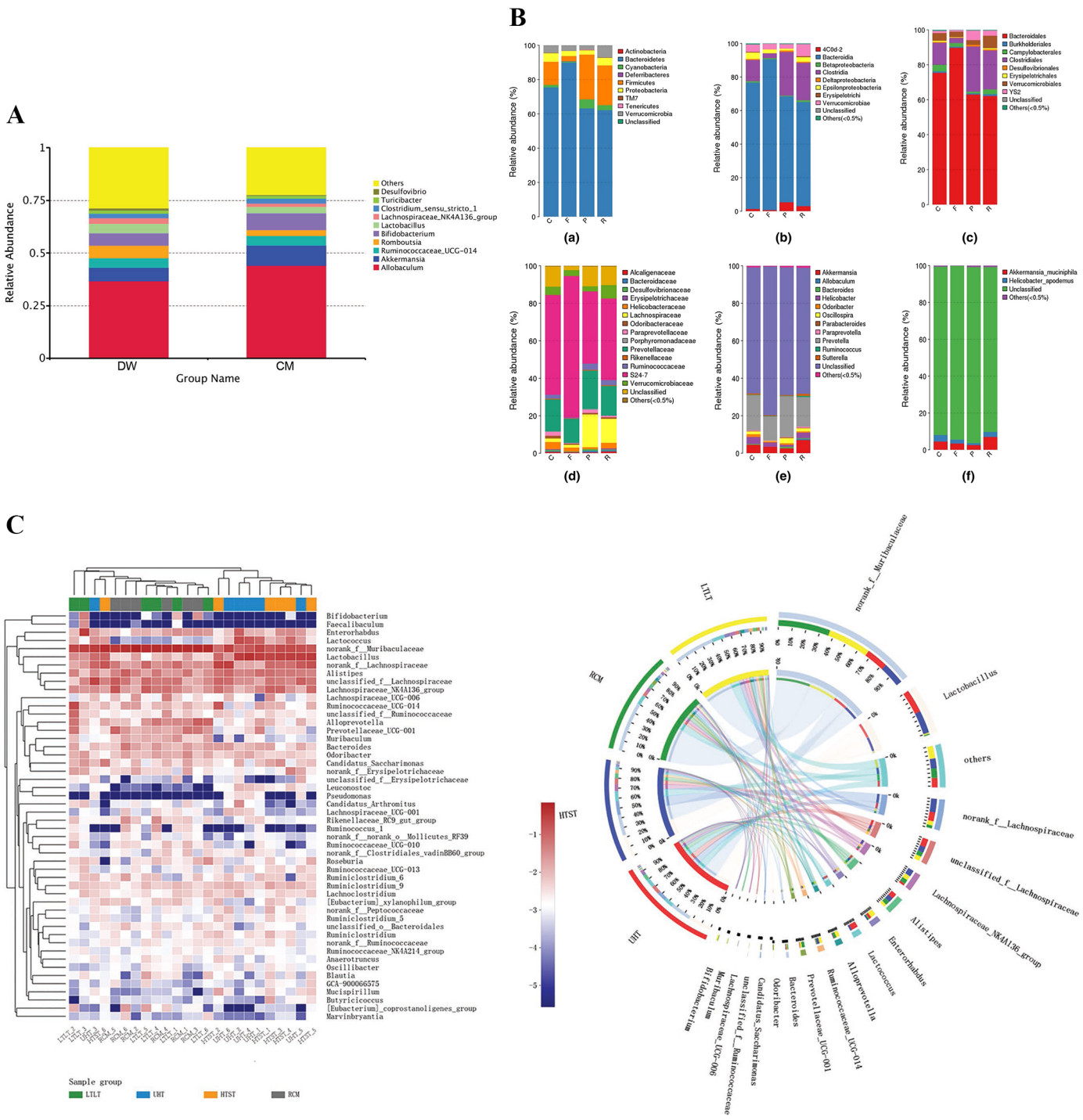

Figure 3. (A) Relative abundances of various bacterial genera in gut microbiota of mice group fed on camel milk (CM) and distilled water (DW) (Wang et al., 2018). (B) Taxonomic profile distribution chart at different levels (a, phylum; b, class; c, order; d, family; e, genus; f, species; Sheikh et al., 2022). (C) The composition of diverse genera in the gut microbiota. RCM = raw camel milk; LTLT = low-temperature long-time (He et al., 2020).

gut microbiota (Wang et al., 2018). In another study, Sheikh et al. (2022) assessed the effect of CM on the gut microbiota of mice by using 16S rRNA sequence analysis. It was reported that CM raised the beneficial bacteria, including *Allobaculum* and *Akkermansia*, and decreased the growth of harmful bacteria, such as *Erysipelotrichaceae*, *Proteobacteria*, and *Desulfovibrionaceae* (Figure 3B). The harmful bacterial levels were

presented to be lower in mice groups fed on fermented or pasteurized CM. Also, *Allobaculum* and *Akkermansia* were detected in the microbiota that was revealed from milk-treated mouse feces, which have a potential healthful effect against inflammatory and metabolic syndromes. Figure 3C summarizes the composition of different gut microbiota in mice fed on different types of CM. It was shown that the various heat treatments could prevent harmful bacteria in the gut microbiota of mice (He et al., 2020).

CONCLUSIONS AND FUTURE RESEARCH

Camel milk has garnered increasing attention as a nutritious food with protective properties for the gut microbiota along with immune-regulatory and anti-inflammatory properties. In addition to its commercialization, CM consumption has become more prevalent and is no longer limited to individuals in arid regions. Numerous studies have confirmed the beneficial functional aspects of CM on health. However, it is important to consider the substantial influence of the vast number of microorganisms in the gut when drawing functional conclusions about CM. The functional constituents of CM may interact with the gut microbiota, playing a positive role in health. The variations in the physicochemical properties of CM resulting from diverse heat treatments have been identified as crucial factors in the modulation of gut microbiota in mice. Further investigation is needed to explore the effects of CM on the gut microbiota, focusing on its functional properties and unidentified bacteria. Moreover, the applications of CM in infant formula and pharmaceutical industries represent a promising research area that warrants attention, particularly regarding the pretreatments of CM and its digestibility. Detailed studies are required to elucidate the mechanisms through which CM influences and modulates the gut microbiota.

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