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Bioactive Peptides and Their Presence in Some Milk Species

Biyoaktif Peptitler ve Bazı Süt Türlerindeki Varlıkları

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Bioactive Peptides and Their Presence in Some Milk Species

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Abstract

Milk proteins not only contain essential amino acids in their structure, but also they are the main source of nutrient, functional and health beneficial biologically active peptides. Bioactive peptides are present in protein in inactive form and released active form by heat treatment, fermentation of milk by proteolytic starter culture, digestion of milk in the gastrointestinal tract or hydrolysis by proteolytic enzymes (pepsin, trypsin and chymotrypsin, plant-derived papain, microbial-derived subtilisin, thermolysin, proteinase K and others). Recently, interest in milk proteins, particularly bioactive peptides released from the parent proteins, has increased. In vivo studies have shown that these milk protein-derived peptides have activity affecting digestion, immunity, circulation, and the nervous system. In addition, it has been found to have Angiotensin converting enzyme-inhibitor, antihypertensive and antioxidative effects. Most studies have used cow milk protein to identify these peptides. However, some other studies have found that bioactive peptides are also found in milk samples taken from other species such as sheep, goat and buffalo. The basic structure of milk proteins may vary due to genetic variations between species. Therefore, the potential activities of the resulting bioactive peptides may also differ. In this study, some nutritional properties of bioactive peptides, least studied animals such as sheep, goat, camel, donkey, buffalo milk and some of their bioactive peptides and their comparison with cow's milk are discussed.

Biyoaktif Peptitler ve Bazı Süt Türlerindeki Varlıkları

Öz

Süt proteinleri esansiyel amino asitleri içermekle birlikte; besleyici, fonksiyonel ve sağlığa yararlı biyoaktif peptitlerin ana kaynağıdır. Biyoaktif peptitler, proteinde inaktif formda bulunur ve ısıl işlem, proteolitik starter kültür ile sütün fermantasyonu ve gastrointestinal sistemde sütün sindirimi veya proteolitik enzimler (pepsin, tripsin ve kimotripsin, bitkisel kaynaklı papain, mikrobiyal kaynaklı subtilisin, termolizin, proteinaz K ve diğerleri) tarafından hidroliz yoluyla aktif forma geçer. Son zamanlarda süt proteinlerine, özellikle ana proteinlerden salınan biyoaktif peptitlere olan ilgi artmıştır. İn vivo çalışmalar, bu süt proteininden elde edilen peptitlerin sindirimi, bağışıklığı, dolaşımı ve sinir sistemini etkileyen aktiviteye sahip olduğunu göstermiştir. Ayrıca Anjiyotensin dönüştürücü enzim-inhibitör, antihipertansif ve antioksidatif etkilere sahip olduğu da bulunmuştur. Pek çok çalışmada, bu peptitleri tanımlamak için inek sütü proteini kullanılmıştır. Buna karşın, bazı araştırmalarda da koyun, keçi ve manda gibi diğer türlerden alınan süt örneklerinde biyoaktif peptitlerin bulunduğunu gözlemlenmiştir. Süt proteinlerinin temel yapısı, türler arasındaki genetik farklılıklar nedeniyle değişebilir. Bu nedenle, ortaya çıkan biyoaktif peptitlerin potansiyel aktiviteleri de farklılık gösterebilir. Bu çalışmada, biyoaktif peptitlerin bazı besleyici özellikleri ile koyun,
keçi, deve, eşek, manda gibi en az çalışılan hayvanların sütlerindeki bazı biyoaktif peptitlerinin inek sütü ile karşılaştırılması tartışılmıştır.

1. INTRODUCTION

Protein is the most important component of milk with about 27% of the dry matter. Not only milk protein is a single and homogeneous protein, but also it consists of a mixture of proteins of different qualities and

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contains a large number of fractions. 80% of this protein is casein (α-, β- and κ-casein) and 20% is serum proteins (albumin, β-lactoglobulin, α-lactalbumin, IgG, lactoperoxidase, lysozyme, lactoferrin). These proteins have specific biological properties [1]. There are a large number of peptides of animal or plant origin with bioactive potential, and a substantial proportion of these peptides are produced from milk proteins. Milk proteins are a rich source of bioactive peptides (BAPs) with many antihypertensive, antioxidative, opioid, antimicrobial and immunoregulatory biological activities in the body [2]. The proportions of BAPs in milk proteins are as follows; 36% (338) β-casein, 13% (119) αs1-casein, 11% (105) β-lactoglobulin, 10% (98) κ-casein, 8% (77) αs2-casein, and 5% (43) α-lactalbumin, lactoferrin 15% (141) and less than 1% is serum albumin [3,4].

2. BIOACTIVE PEPTIDES

BAPs, also known as functional peptides; are defined as amino acid chains that are inactive in the structural protein but have important physiological roles with specific properties when released by enzymatic activity [5,6]. BAPs are encoded into amino acid chains of natural protein structure and they are short peptides, usually containing from 3 to 20 amino acid residues in each molecule. However, caseinomacropeptide (CMP) contains 64 amino acids is an exception. Its basic activities also result from this amino acid composition and sequence. These peptides are inactive in the protein sequence and can be activated in three ways [7,8].

(a) Digestion in the gastrointestinal tract (in vivo)

BAPs may be released by digestive enzymes such as pepsin, trypsin, or chymotrypsin. Nutritional proteins are denatured in the presence of hydrochloric acid (HCl) secreted by the parietal cells of the stomach. This acid stimulates pepsinogen and turns into its active form which is pepsin. Thus, it allows the activity of enzymes such as pepsin, trypsin or chymotrypsin in the small intestine which are responsible for gastrointestinal digestion protein hydrolysis [9].

b) Fermentation of some lactic acid bacteria (Lactococcus lactis, Lactobacillus helveticus etc.) (in vivo)

The system consists of a number of different intracellular peptidases, including endo-peptidases, amino-peptidases, di-peptidases and tripeptidases by hydrolysis by proteolytic microorganisms. Thus, BAPs are released [9,10].

(c) Hydrolysis by enzymes released from plants or microorganisms (in vitro)

It is the most common way to obtain BAP from milk. A combination of digestive enzymes and different proteinases (alkalosis, chymotrypsin, pepsin and thermolysin) and digestive enzymes of bacterial or fungal origin are used [7]. One of the main proteins responsible for BAP formation is casein. However, αs1-, β- and κ-casein have little or no bioactivity in their natural state (except α-lactalbumin and lactoferrin). This generally shows the complexity of bioactivity in milk. Because it has different biological activities in its natural form and after hydrolysis to peptides [11].

In general, BAPs classified according to the mechanism of action; antimicrobial peptides (casecidin, casocidin-I, Isracidin, lactoferricin B), antihypertensive peptides (αs1-casokinin-5, β-casokinin-7, α-lactorphin, β-lactorphin, β-casokinin-10, β-lactorphin), antithrombotic peptides (casoplatelin thrombin inhibitory peptide), immunomodulatory peptides (as1-immunosacokinin, β-casokinin-10, lactoferricin B, immunopeptides), opioid milk peptides (casomorphins, α-lactorphine, β-lactorphine, serorphin, lactoferoxins and casokinin) and various peptides (phosphopeptides, caseinophosphopeptides) [12-14].

Numerous peptides exhibiting diversified physiological activities such as mineral binding, opioid, ACE inhibiting, immunomodulator, antibacterial and antioxidant activities are isolated and characterized from hydrolyses of different milk proteins using various proteolytic enzymes and fermented milk products [17]. Detection of BAPs; specific, it has been difficult because of the large number and quantity. However, some online databases are used to process the sequences of the BAPs obtained; BioPep (includes proteins, BAPs, as well as allergenic proteins, epitopes including single amino acid residues and sensory peptides, and means for evaluating proteins as BAPs by proteolytic processing), PepBank (based on sequence data mining) identifies 20 amino acid or shorter sequences), EROP-Moscow (includes identification of structures, sources and functions of oligopeptides containing 2-50 amino acid residues, etc.), PeptideDB (related to peptides of animal origin), APD (includes antimicrobial peptides) [18].

Table 1. BAPs from milk proteins, their sources and bioactivities [15, 16]

BAP	Source of Protein	Bioactivity
Casomorfins	α-, β-casein	Opioid effect
α-lactorfin	α-Lactalbumin	Opioid effect
β-Lactorfin	β-Lactoglobulin	Opioid effect
Lactoferoxins	Lactoferrin	Opioid effect
Casocins	k-casein	Opioid effect
Casokinins, Lactokinins	α-, β-casein	ACE* inhibitor
Immunopeptides	α-, β-casein	Immunomodulatory
Lactoferricin	Lactoferrin	Antimicrobial effect
Casoplatelins	κ-casein, transferrin	Antithrombotic effect
Fosfopeptides	α-β-casein	Mineral binding
(*:Angiotensin I-converting enzyme (ACE) inhibitor: ACE is an exopeptidase that breaks down various peptide substrates from the end carbon atom to release dipeptides and has important effects in regulating body blood pressure and water balance. Milk-derived antihypertensive peptides (kazokinin and lactokinin) inhibit ACE and regulate these catalytic reactions)		

3. VARIOUS MILK AND BIOACTIVE PEPTIDES

The bioactivity of BAPs due to genetic diversity between milk species and differences in the primary structure of milk proteins may vary [19].

The formation of specific bioactivities encoded in proteins of milk BAPs depends on where the proteolysis takes place (mammary gland or gastrointestinal tract) and the synergistic effects of BAPs and other agents (lipids, sphingolipids, oligosaccharides, etc.). Cow milk proteins as the source of BAPs have been one of the first and extensively studied proteins. Most studies also use cow's milk protein to identify these peptides (11). However, some studies have found that BAPs are also found in milk samples taken from other species such as sheep, goats and camels [20,21].

3.1. Milk of Sheep

In some parts of the world (especially arid and semi-arid regions) there is greater interest in sheep milk. Composition of sheep milk is more valuable in terms of nutritional value and consumer health as it contains higher dry matter and essential components than goat and cow's milk [22].

In recent years, some milk components have been found to have biological properties (as an ingredient for nutraceuticals or functional foods) beyond their nutritional significance [23]. Sheep milk has a high protein content (average 5.8%). Similar to cow's milk, sheep's proteins were distributed between caseins (76-83% of the total) and whey proteins (17-24% of the total). However, there may be some differences between sheep milk proteins and other ruminants. These differences are due to genetic polymorphism, post-transitional modification and the presence of proteins of different chain lengths [17]. In general, β-lactoglobulin (β-Ig) and α-lactalbumin (α-la) are the source of BAP in sheep milk [24]. In particular, β-lactoglobulin hydrolysates produced by microbial digestive enzymes have higher ACE inhibitory effect. The first antimicrobial effect of sheep milk, although existence in cow's milk is low, was the f (17-41) fragment of the BAP lactoferrin [25]. Likewise, αs2-casein in sheep's milk is a source of antimicrobial peptide (fragments f(165–170), f(165–181), f(184–208) and f(203–208)). κ-CMP from sheep's milk is also a good source of antithrombotic peptide [26].

3.2. Milk of Goat

Goat milk bioactive protein is less allergenic and better digestible than cow's milk [27]. Antioxidant capacity of goat milk is higher than other milk (cow, sheep, donkey and buffalo) [28]. Bioactive components in goat milk include conjugated linoleic acid, gangliocytes, glycolipids, glycosphingolipids and cerebrocytes, alkylglycerol, phospholipids, growth factors, hormones, immunoglobulins, oligosaccharides, lactose derivatives, lactoferrin, lysozyme, nucleosides, nucleosides, nucleosides [29]. Gangliocytes, a BAP, are found in goat and buffalo milk [30].

Goat milk BAPs have been reported to exhibit high ACE-inhibitor properties. (In particular, Tyr-Gln-Glu-Pro linked to β-casein, Val-Pro-Lys-Val-Lys, and Tyr-Gln-Glu-Pro-Val-Leu-Gly-Pro, Arg-Pro-Lys linked to αs1-casein and Arg-Pro-Lys-His-Pro-Ile-Lys-His, fragment of β-lactoglobulin (113-122) [31]. Another study has shown that goat milk proteins and hydrolysates can be excellent BA sources that can be used as ingredients in functional foods [32].

3.3. Milk of Camel

Camel milk is thought to not only to have medicinal properties but also may help in the treatment of some traditional disease. Numerous studies have shown that camel milk has different therapeutic benefits, such as antihypertensive, anti-inflammatory, anti-diabetic, antioxidant, antiviral, antimicrobial, and anti-rheumatoid arthritis [33, 34, 35, 36].

Milk-derived antihypertensive peptides (casokinin and lactokinin) are found in camel milk as well as in cow, sheep, and goat milk [37]. The composition and relative distribution of milk proteins in camel milk is quite different from that of cow milk proteins. Camel milk casein contains four main fractions similar to that of cow milk (αs1-CN, β-CN, αs2-CN and κ-CN). However, there are significant differences between the casein of these two milks. The β-CN is found in 65% camel and 34% in cow; αs1-CN is found in 22% in camel and 45% in cow; κ-CN is found in 3% in camel and 10-12% in cow. This shows that the potential number, type and concentration of BAPs obtained from camel milk caseins may be different from those obtained from cow milk proteins.

Cow's milk β-CN contains several ACE-inhibiting peptide sequences, but not in camel β-CN [38]. Camel milk is characterized by the absence of β-lactoglobulin, which forms the majority of serum proteins in cow's milk [39]. Therefore, β- lactoglobulin derived BAPs are not found in fermented camel milk. Peptidoglycan recognition protein (PGRP) was isolated from camel milk and was not found in cow's milk. PGRP belongs to a new family of proteins that can bind pathogens to peptidoglycan structures in the cell wall. In addition, PGRP is found in higher amounts in camel milk than other antibacterial proteins such as lactoferrin, lactoperoxidase or lysozyme [17].

3.4. Milk of Donkey

In recent years, there has been an increasing popularity in donkey milk due to its close composition and functional properties. Especially, a good balance between casein and serum proteins makes donkey milk an alternative food source for babies with cow's milk protein allergy [28]. In addition to hypoallergenic, it has antimicrobial, antiviral, anti-inflammatory and immune modulating properties. These features; immunoglobulins, lysozyme, lactoferrin, ω-3 fatty acids, BAPs and an appropriate casein / whey protein ratio is caused by a significant amount of milk components [40]. It is a very important source especially for BAPs.

In some studies conducted on this subject, it was found that donkey milk has anti-tumor, anti-proliferative and very strong angiotensin converting enzyme (ACE) activity and some fragments of β-casein (184-210,199-226) have antimicrobial and antihypertensive properties [41, 42, 43, 44]. In another study, it is stated that donkey milk ranks second after goat milk in terms of total antioxidant capacity [28].

3.5. Milk of Buffalo

Buffalo milk contains almost all bioactive compounds (proteins, peptides, fatty acids, vitamins and other bioactive compounds) found in cow's milk. Buffalo milk has higher total protein, medium chain fatty acids, CLA, retinol and tocopherol content than cow's milk. Gangliocytes, a BAP in goat milk, are found only in buffalo milk [30].

Buffalo milk proteins show high homology to cow's milk (higher than 92%). αs1-casein, as2-casein and β-casein have phosphoserine clusters similar to cow's milk. Thus, proteolysis of buffalo milk casein fractions yields phosphopeptides similar to those obtained from cows. The β-CN f (165-209) region in buffalo and cow's milk has the same amino acid sequence (a region with immunomodulator, opioid and ACE-inhibitory activity). Thus, the similarity of the buffalo and cow amino acid sequences suggests that a similar BAP can be obtained from both sources. Similarly, because of the similarity of the amino sequence of α-lactalbumin and β-lactoglobulin in cow and buffalo milk, similar BAPs can be produced [45].

4. CONCLUSION

BAPs derived from sheep, goat, camel, donkey and buffalo milk proteins have been studied less than cow milk proteins. Limited studies of non-cow's milk have also yielded new and unique BAPs. Therefore, the production and characterization of BAPs from non-cow's proteins is essential for any developmental study. Future studies suggest that these peptides can be purified and used in food formulations [33]. However, although the legal regulations have not yet been fully clarified, a number of functional foods have been produced in some countries using BAPs.

In the United States, the United Kingdom, Japan, the Netherlands, Sweden, Finland, and France, these components are used in dairy products and beverages [46]. Milk-derived BAPs will be produced more extensively in the near future and may be used in the content of food or pharmaceutical products or directly as supplement products.

CONFLICT OF INTEREST

The authors contributed equally to the preparation of the article.

REFERENCES

[1] S. Semen, A. Altıntaş, Sütte Biyoaktif Peptitler ve Biyolojik Önemi. Türk Veteriner Hekimleri Birliği Dergisi 2015; 3 – 4.

[2] H. Korhonen, Milk-Derived Bioactive Peptides: From Science to Applications. Journal of Functional Foods 2009; I: 177-187.

[3] S.D. Nielsen, R.L. Beverly, Y. Qu, D.C. Dallas, Milk bioactive peptide database: A comprehensive database of milk protein-derived bioactive peptides and novel visualization. Food Chemistry 2017; 232: 673–682.

[4] F.B. Otağ, M. Hayta, GIDA 2013; 38: 307-314.

[5] L. Egger, O. Ménard Update on bioactive peptides after milk and cheese digestion. Current Opinion in Food Science 2017; 14: 116-121.

[6] Ö. Kınık, O. Gürsoy, Süt Proteinleri Kaynaklı Biyoaktif Peptitler. Mühendislik Bilimleri Dergisi 2002; 8: 195-203.

[7] H. Korhonen, A. Pihlanto-Leppälä, Bioactive Peptides: Production and Functionality. International Dairy Journal 2006; 16: 945-960.

[8] H. Korhonen, A. Pihlanto-Leppälä, Milk protein-derived bioactive peptides-novel opportunities for health promotion. IDF Bulletin 2001; 363: 17–26.

[9] D.P. Mohanty, S. Mohapatra, S. Misra, P.S. Sahu, Milk derived bioactive peptides and their impact on human health – A review. Saudi Journal of Biological Sciences, 2016; 23: 577–583.

[10] J.E. Christensen, E.G. Dudley, J.A. Pederson, J.L. Steele, Peptidases and amino acid catabolism in lactic acid bacteria. Antonie Van Leeuwenhoek 1999; 76: 217–246.

[11] S. Piovesana, A.L. Capriotti, C. Cavaliere, G. La Barbera, R. Samperi, R.Z. Chiozzi, A. Lagana, Peptidome characterization and bioactivity analysis of donkey milk Journal of Proteomics 2015; 119: 21 – 29.

[12] H. Meisel, Overview on Milk ProteinDerived Peptides. Int. Dairy Journal 1998; 8: 363-373.

[13] D.A. Clare, H.E. Swaisgood, Bioactive Milk Peptides: A Prospectus. J Dairy Sci 2000; 83:1187–1195.

[14] A. Pihlanto, Bioactive Peptides. In: Milk Proteins Products, Fuquay, J.W Encyclopaedia of Dairy Science 2011, 2nd ed. Academic Press: 879-886.

[15] C. Ay, T. Şanlı, Süt Ürünlerinde Biyoaktif Peptitlerin Oluşumu ve Fonksiyonel Özellikleri. ADÜ Ziraat Derg. 2018; 15 (1):115-120.

[16] R. López-Fandiño, J. Otte, J. Van Camp, Physiological, chemical and technological aspects of milk-protein-derived peptides with antihypertensive and ACE-inhibitory activity. International Dairy Journal 2006; 16: 1277–1293.

[17] M.H. Abd El-Salam, S. El Shibiny, Bioactive Peptides of Buffalo, Camel, Goat, Sheep, Mare, and Yak Milks and Milk Products. Food Reviews International 2013; 29 (1): 1-23.

[18] J. Giacometti, A. Buretić-Tomljanović, Peptidomics as a tool for characterizing bioactive milk peptides. Food Chemistry 2017; 230: 91–98.

[19] M. Abdel-Hamid, J. Otte, C. De Gobba, A. Osman, E. Hamad, Angiotensin I-converting enzyme inhibitory activity and antioxidant capacity of bioactive peptides derived from enzymatic hydrolysis of buffalo milk proteins. International Dairy Journal 2017; 66: 91-98.

[20] D. Tagliazucchi, S. Martini, S. Shamsia, A. Helal, A. Conte, Biological activities and peptidomic profile of in vitro-digested cow, camel, goat and sheep milk. International Dairy Journal 2018; 81: 19-27.

[21] E. Vargas-Bello-Pérez, R.I. Márquez-Hernández, L.E. Hernández Castellano, Bioactive peptides from milk: animal determinants and their implications in human health. Journal of Dairy Research 2019; 86: 136–144.

[22] J.E. Dalziel, G.A. Smolenskic, C.M. McKenzied, S.R. Hainese, L. Day, Differential effects of sheep and cow skim milk before and after fermentation on gastrointestinal transit of solids in a rat model. Journal of Functional Foods 2018; 47: 116–126.

[23] M. Juarez, Dairy Foods Symposium: Bioactive Components in Milk and Dairy Products: Recent international perspectives and progresses in different dairy species. J. Anim. Sci. 2012; 90: Suppl. 3/J.

[24] G. Moatsou, L. Sakkas, Sheep milk components: focus on nutritional advantages and biofunctional potential. In press, 2019.

[25] L.H. Vorland, H. Ulvatne, J. Andersen, H.H. Haukland, Ø. Rekdal, J.S. Svendsen, T.J. Gutteberg, Lactoferricin of bovine origin is more active than lactoferricins of human, murine and caprine origin. Scandinavian J. Infect. Dis.1998; 30: 513–517.

[26] Y.W. Park, M. Juarez, M. Ramos, G.F.W. Haenlein, Physico-chemical characteristics of goat and sheep milk Small Ruminant Research 2007; 68: 88–113.

[27] S. Verruck, A. Dantas, E.S. Prudencio, Functionality of the components from goat's milk, recent advances for functional dairy products development and its implications on human health. Journal of Functional Foods 2019; 52: 243–257.

[28] Ş. Öztürkoğlu-Budak, A. Gürsel, Alternatif Bir Süt: Eşek Sütü. GIDA 2012; 37 (4): 243-250.

[29] Y.W. Park, Dairy Foods Symposium: Bioactive Components in Milk and Dairy Products: Recent international perspectives and progresses in different dairy species. J. Anim. Sci. 2012; 95: Suppl. 2.

[30] M. Guo, Dairy Foods Symposium: Bioactive Components in Milk and Dairy Products: Recent international perspectives and progresses in different dairy species. J. Anim. Sci. 2012; 90: Suppl. 3/J.

[31] H.R. Ibrahim, A.S. Ahmed, T. Miyata, Novel angiotensin-converting enzyme inhibitory peptides from caseins and whey proteins of goat milk Journal of Advanced Research 2017; 8: 63–71.

[32] S. Rani, K. Pooja, G.K. Pal, Exploration of potential angiotensin converting enzyme inhibitory peptides generated from enzymatic hydrolysis of goat milk proteins Biocatalysis and Agricultural Biotechnology 2017; 11: 83-88.

[33] P. Mudgil, B. Baby, Y.Y. Ngoh, H. Kamal, R. Vijayan, Molecular binding mechanism and identification of novel anti-hypertensive and anti-inflammatory bioactive peptides from camel milk protein hydrolysates. LWT - Food Science and Technology 2019; 112: 108193.

[34] H.R. Ibrahim, H. Isono, T. Miyata, Potential antioxidant bioactive peptides from camel milk proteins. Animal Nutrition 2018; 4: 273-280.

[35] P. Mudgil, H. Kamal, G.C. Yuen, S. Maqsood, Characterization and identification of novel antidiabetic and anti-obesity peptides from camel milk protein hydrolysates. Food Chemistry 2018; 259: 46–54.

[36] D. Tagliazucchi, S. Shamsia, A. Conte, Release of angiotensin converting enzyme-inhibitory peptides during in vitro gastro-intestinal digestion of camel milk. International Dairy Journal 2016; 56: 119–128.

[37] O. Yerlikaya, D. Saygılı, C. Karagözlü, Deve Sütü: Bileşimi, Sağlık Üzerine Etkileri, Deve Sütü Ürünleri. I.Uluslararası Devecilik Kültürü ve Deve Güreşleri Sempozyumu 2016; Selçuk, İzmir.

[38] Food and Agriculture Organization. www.fao.org/3/i3396e/i3396e.pdf, 2013.

[39] E.I. El-Agamy, Bioactive components in camel milk. In Bioactive Components in Milk and Dairy Products; Park, Y.W., Ed.; Wiley-Blackwell: Ames, IA, pp 159–194, 2009.

[40] M. Aspri, G. Leni, G. Galaverna, P. Papademas, Bioactive properties of fermented donkey milk, before and after in vitro simulated gastrointestinal digestion. Food Chemistry 2018; 268: 476–484.

[41] F. Minervini, F. Algaron, C.G. Rizzello, P.F. Fox, V. Monnet, M. Gobbetti, Angiotensin I-converting-enzymeinhibitory and antibacterial peptides from *Lactobacillus helveticus* PR4 proteinase-hydrolyzed caseins of milk from six species. Appl. Environ. Microbiol. 2003; 69: 5297–5305.

[42] V. Cunsolo, R. Saletti, V. Muccilli, S. Foti, Characterization of the protein profile of donkey's milk whey fraction. J. Mass Spectrom. 2007; 42: 1162–1174.

[43] A. Tafaro, T. Magrone, F. Jirillo, G. Martemucci, A.G. D'Alessandro, Immunological properties of donkey's milk: its potential use in the prevention of atherosclerosis. Curr Pharmaceut Design 2007; 13: 3711-3717.

[44] I.B. Bidasolo, M. Ramos, J.A. Gomez-Ruiz, In vitro simulated gastrointestinal digestion of donkeys' milk. Peptide characterization by high performance liquid chromatography-tandem mass spectrometry. Int Dairy J. 2012; 24: 146-152.

[45] M.H. Abd El-Salam, S. El Shibiny, A comprehensive review on the composition and properties of buffalo milk. Dairy Sci. & Technol. 2011; 91:663–699.

[46] N. Durmuş, M. Kılıç Akyılmaz, B. Özçelik, Süt Proteinlerinden Biyoaktif Peptid Eldesi. Gıda, Metabolizma ve Sağlık: Biyoaktif Bileşenler ve Doğal Katkılar Kongresi 2016; İstanbul.