

## АЛЛЕРГЕННОСТЬ БЕЛКОВ МОЛОКА И ПУТИ ЕЕ СНИЖЕНИЯ

Т.Н. Головач\*\*\*, В.П. Курченко\*\*

\*РУП «Институт мясо-молочной промышленности», Минск, Республика Беларусь

\*\*Белорусский государственный университет, Минск, Республика Беларусь

### Введение

1. Иммунные механизмы пищевой аллергии
- 2 Структура, функции и аллергенные свойства основных белков молока
- 3 Пути снижения аллергенности белков молока
  - 3.1 Термическая обработка белков молока
  - 3.2 Обработка белков молока высоким гидростатическим давлением
  - 3.3 Ультразвуковая обработка белков молока
  - 3.4 Химическая модификация белков молока в реакции Майара
  - 3.5 Ферментативный гидролиз белков молока
- 4 Применение белковых гидролизатов в специализированном питании

### Сокращения

IgE, IgG – иммуноглобулин класса Е и G;  
IL – интерлейкин;  
INF – интерферон;  
mr – молекулярная масса, кДа;  
α-ла – α-лактальбумин;  
β-лг – β-лактоглобулин;  
ААК – ароматические аминокислоты;  
АКМ – аллергия на коровье молоко;  
АКРЦ – аминокислоты с разветвленной цепью;  
Ат – антитело;  
БСА – бычий сывороточный альбумин;  
БКМ – белки коровьего молока;  
ВЭЖХ – высокоэффективная жидкостная хроматография;  
ДСК – дифференциальная сканирующая калориметрия;  
ДСН – додецил сульфат натрия;  
ИФА – иммуноферментный анализ;  
КД – круговой дихроизм;  
ПА – пищевая аллергия;

### Введение

Современное представление о развитии аллергических заболеваний придает определяющее значение иммунологическим нарушениям, которые вызваны аллергенами, в том числе пищевыми. Клиническим проявлением пищевой аллергии чаще всего выступает атопический дерматит – хроническое аллергическое воспаление кожи. Основной причиной заболевания являются нарушения функционирования иммунной системы [1]. Атопический дерматит встречается повсеместно, у людей разного возраста, но с большей частотой выявляется у женщин. В настоящее время рост заболеваемости атопическим дерматитом связывают с загрязнением окружающей среды, продуктами питания, укорочением сроков грудного вскармливания, искусственным вскармливанием, токсикозами и погрешностью питания матери во время беременности и периода лактации [2–4].

По последним данным до 10% детей раннего возраста страдают пищевой аллергией. У 80% пациентов с проявлениями атопического дерматита установлена связь данного заболевания с пищевой аллергией [5]. Пищевая аллергия обусловлена развитием

сенсибилизации организма больного к пищевым аллергенам [6]. Наследственная отягощенность по аллергическим заболеваниям обнаружена у 65,4% больных и только у 20,6% здоровых детей. У 31,4% больных отмечена аллергическая патология по материнской линии; в 20,4% были больны оба родителя [7].

У детей раннего возраста с признаками ПА обнаружены аллергенспецифические IgG и IgE не только к белкам коровьего молока, но и к наиболее распространенным пищевым антигенам животного и растительного происхождения. У больных выявлена поливалентная пищевая сенсибилизация. При этом преобладающими являются аллергические реакции на белки коровьего молока [8]. Наряду со сниженной сенсибилизирующей активностью белков козьего молока выявлена иммунологическая перекрестная реактивность с основными антигенами коровьего молока. Высокая частота сенсибилизации также обусловлена белковым компонентом мяса птицы и рыбы, фруктами, кисломолочными и глютенсодержащими продуктами (рисунок 1, 2).

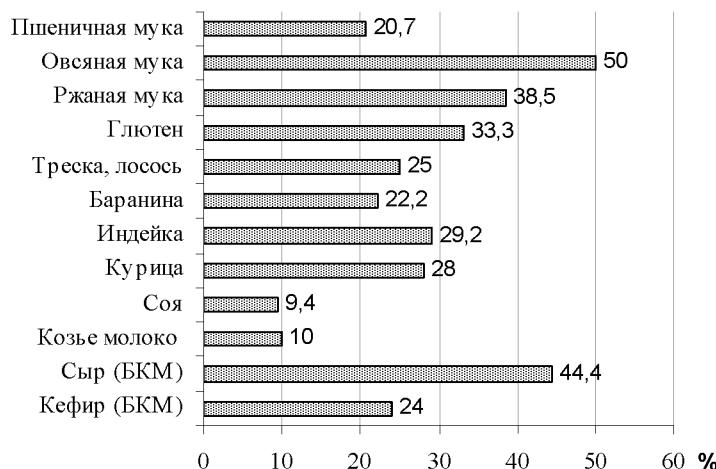


Рисунок 1 – Частота встречаемости специфических IgE к продуктам животного и растительного (содержащих глютен) происхождения у больных аллергией первых трех лет жизни [9]

Развитию ПА в раннем возрасте способствует повышенная проницаемость желудочно-кишечного тракта для белков пищи, которые проходят через слизистую в неизменном или частично переваренном виде. Кроме того, с молоком матери в пищеварительный тракт ребенка могут поступать пищевые антигены, способные вызывать развитие сенсибилизации к соответствующим продуктам [10].

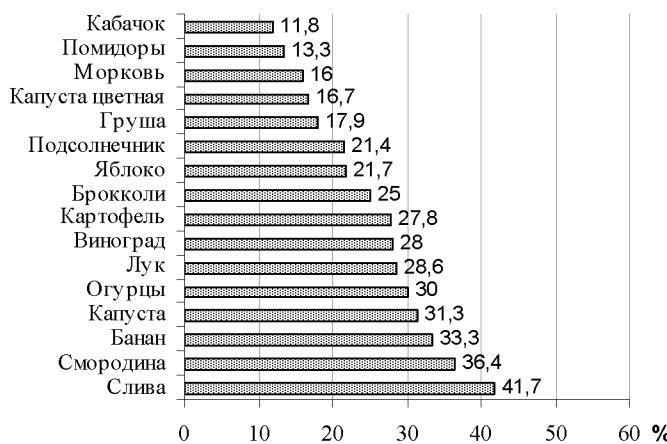


Рисунок 2 – Частота встречаемости специфических IgE к овощам и фруктам у больных аллергией первых трех лет жизни [9]

По результатам исследования детей с ПА установлена высокая частота обнаружения аллергенспецифических IgE к белкам коровьего молока (68,9%) и его фракциям: казеину (70,6%) и  $\beta$ -лактоглобулину (66,3%), а также к белку сои (68,9%). Частота обнаружения специфических IgE к козьему молоку в 2 раза ниже (35,9%) [9]. Таким образом, развитие атопического дерматита, главным образом, обусловлено аллергией к белкам коровьего молока.

Цель обзора – рассмотрение иммунных механизмов развития пищевой аллергии, характеристика основных белковых аллергенов молока и определение оптимальных способов снижения их иммунореактивности; анализ современных данных в области применения ферментативных гидролизатов в специализированном питании.

### **Выводы**

Большинство белков коровьего молока являются потенциальными аллергенами. Иммунореактивность белковых макромолекул определяется особенностями их структуры и физико-химическими свойствами.

В настоящее время для снижения аллергенности и повышения питательной ценности белков молока используют различные технологические приемы: ферментативный гидролиз, денатурацию под действием температуры и высокого гидростатического давления и др.

Физическое воздействие направлено на изменение конформации белковых молекул, что обеспечивает доступ к ранее скрытым сайтам протеолиза и разрушение областей антигенных детерминант. Уменьшение аллергенного потенциала гидролизатов обусловлено ферментативным расщеплением антигенных детерминант белков молока. Совместное применение физического воздействия, в частности термоденатурации, и протеолиза представляется наиболее приемлемым путем получения гипоаллергенного белкового компонента.

Кроме протеолиза, для изготовления гидролизатов с заданными свойствами: определенным пептидным и аминокислотным профилем и низким антигенным потенциалом, – предполагается использование развитых пост-гидролитических процессов.

Применение ферментативных белковых гидролизатов актуально при создании гипоаллергенных детских молочных смесей, продуктов диетического питания при фенилкетонурии, хронических заболеваниях печени.

### **Список использованных источников**

1. Greenhawt, M. The role of food allergy in atopic dermatitis / M. Greenhawt // Allergy Asthma Proc. – 2010. – Vol. 31, № 5. – P. 392–397.
2. Sorva, R.  $\beta$ -lactoglobulin secretion in human milk varies widely after cow's milk ingestion in mothers of infants with cow's milk allergy / R. Sorva, S. Makinen-Kiljumen, K. Juntunen-Backman // J. Allergy Clin. Immunol. – 1994. – Vol. 93. – P. 787–792.
3. Atopic eczema or atopiform dermatitis / J.D. Bos [et al.] // Exp. Dermatol. – 2010. – Vol. 19, № 4. – P. 325–331.
4. Ring, J. Looking ahead in dermatology: skin and allergy / J. Ring, B. Belloni, H. Behrendt // Actas Dermosifiliogr. – 2009. – Vol. 100, № 2. – P. 32–39.
5. Ревякина, В.А. Иммунологические основы развития атопического дерматита и новая стратегия терапии / В.А. Ревякина // Педиатрия. Приложение к журналу «Консилиум Медикум». – 2004. – № 3. – С. 3–7.
6. Natural course of sensitization to food and inhalant allergens during the first six years of life / M. Kulig [et al.] // J. Allergy Clin. Immunol. – 1999. – Vol. 103. – P. 1173–1179.
7. Частота обнаружения кишечных инфекций и дисбактериозов у детей с атопическим дерматитом / С.Н. Вахрамеева [и др.] // Int. J. of Immunorehabilitation. – 1999. – № 4. – P. 3.
8. Wal, J.M. Bovine milk allergenicity / J.M. Wal // Ann. Allergy Asthma Immunol. – 2004. – Vol. 93, № 3. – С. 2–11.
9. Денисова, С.Н. Клинико-иммунологическое обоснование дифференциальных подходов к лечению и профилактике пищевой аллергии у детей раннего возраста: автореф.

дис. на соискание ученой степени д-ра мед. наук: 14.00.09; 14.00.36 / С.Н. Денисова; НИИ педиатрии ГУ Научного центра здоровья детей РАМН. – М., 2008. – 48 с.

10. T cell «priming» against environmental allergens in human neonates: sequential deletion of food antigen specificities during infancy with concomitant expansion of responses to ubiquitous inhalant allergens / P.G. Holt [et al.] // Pediatr. Allergy Immunol. – 1995. – Vol. 6. – P. 85–90.

11. Digestion of bovine milk proteins in patients with a high jejunostomy / S. Mahe [et al.] // American Journal of Clinical Nutrition. – 1991. – Vol. 54. – P. 534–538.

12. Protein transport and processing by human HT29–19A intestinal cells: effect of interferon gamma / K. Terpend [et al.] // Gut. – 1998. – Vol. 42. – P. 538–545.

13. Heyman, M. Antigen handling by intestinal epithelial cells / M. Heyman, J. Desjeux // In Antigen Presentation by Intestinal Epithelial Cells. [D Kaiserlian, editor], Heidelberg: Springer Verlag. – 1997. – P. 1–16

14. Maternal fish oil supplementation in pregnancy reduces interleukin-13 levels in cord blood of infants at high risk of atopy / J.A. Dunstan [et al.] // Clin. Exp. Allergy. – 2003. – Vol. 33, № 4. – P. 442–448.

15. Regulation of the immune response to peptide antigens: differential induction of immediate-type hypersensitivity and T cell proliferation due to changes in either peptide structure or major histocompatibility complex haplotype / P. Soloway [et al.] // J. of Exp. Med. – 1991. – Vol. 174. – P. 847–858.

16. Allergy to cow's milk proteins in childhood: the author's personal experience and new diagnostic and therapeutic proposals / G. Cavagni [et al.] // Pediatr. Med. Chir. – 1994. – Vol. 16, № 5. – P. 413–419.

17. El-Agamy, E.I. The challenge of cow milk protein allergy / E.I. El-Agamy // Small Ruminant Research. – 2007. – Vol. 68. – P. 64–72.

18. Taylor, S.L. Immunologic and allergic properties of cow's milk proteins in humans / S.L. Taylor // J. Food Prot. – 1986. – Vol. 49, № 3. – P. 239–250.

19. Особенности козьего молока как сырья для продуктов детского питания / С.В. Симоненко [и др.] // Вестник РАСХН. – 2010. – № 1. – С. 84–87.

20. El-Agamy, E.I. Nutritive and immunological values of camel milk: a comparative study with milk of other species / E.I. El-Agamy, M.A. Nawar // In: Second International Camelid Conference: Agroeconomics of Camelid Farming, Almaty, Kazakhstan. – 8–12 September, 2000. – P. 33–45.

21. Milk allergy. I. Oral challenge with milk and isolated milk proteins in allergic children / A.S. Goldman [et al.] // Pediatrics. – 1963. – Vol. 32. – P. 425–443.

22. Mutational analysis of major, sequential IgE-binding epitopes in alpha s1-casein, a major cow's milk allergen / R.R. Cocco [et al.] // J. Allergy Clin. Immunol. – 2003. – Vol. 112, № 2. – P. 433–437.

23. Wal, J.M. Cow's milk proteins/allergens / J.M. Wal // Ann. Allergy Asthma Immunol. – 2002. – Vol. 89, № 1. – P. 3–10.

24. Enzyme immunoassay of specific human IgE to purified cow's milk allergens / J.M. Wal [et al.] // Food Agric. Immunol. – 1995a. – Vol. 7. – P. 175–187.

25. Cow's milk allergy: the humoral immune response to eight purified allergens / J.M. Wal [et al.] // Adv. Exp. Med. Biol. – 1995b. – Vol. 371B. – P. 879–881.

26. Walstra, P. On the stability of casein micelles / P. Walstra // J. Dairy Sci. – 1990. – № 73. – P. 1965–1979.

27. Horne, D.S. Casein micelle structure: models and muddles / D. S. Horne // Curr. Opin. Coll. Interf. Sci. – 2006. – Vol. 11. – P. 148–153.

28. Sawyer, L. The core lipocalin, bovine beta-lactoglobulin / L. Sawyer, G. Kontopidis // Biochim. Biophys. Acta. – 2000. – Vol. 1482, № 1–2. – P. 136–148.

29. Bovine β-lactoglobulin at 18A resolution - still an enigmatic lipocalin / S. Brownlow [et al.] // Structure. – 1997. – Vol. 5. – P. 481–495.

30. Sakurai, K. Manipulating monomer-dimer equilibrium of bovine beta-lactoglobulin by amino acid substitution / K. Sakurai, Y. Goto // *J. Biol. Chem.* – 2002. – Vol. 277, № 28. – P. 25735–25740.
31. MM/PBSA analysis of molecular dynamics simulations of bovine  $\beta$ -lactoglobulin: free energy gradients in conformational transitions / F. Fogolari [et al.] // *PROTEINS: Structure, Function, and Bioinformatics*. – 2005. – Vol. 59, № 91. – P. 103.
32. Shimada, K. Sulfhydryl group/disulfide de bond interchange reactions during heatinduced gelation of whey protein isolate / K. Shimada, J.C. Cheftel // *J. Agricul. and Food Chemistry*. – 1989. – Vol. 34. – P. 161–168.
33. Characterization of intermediates formed during heat induced aggregation of  $\beta$ -lactoglobulin AB at neutral pH / E.P. Schokker [et al.] // *Int. Dairy J.* – 1999. – Vol. 9. – P. 791–800.
34. Relkin, P. Heat- and cold-setting gels of  $\beta$ -lactoglobulin solutions. A DSC and TEM study / P. Relkin, B. Launay, T.-X. Liu // *Thermochimica Acta*. – 1998. – Vol. 308. – P. 69–74.
35. Uptake and passage of beta-lactoglobulin, palmitic acid and retinol across the Caco-2 monolayer / P. Puyol // *Biochim. Biophys. Acta*. – 1995. – Vol. 1236, № 1. – P. 149–154.
36. Chrysina, E.D. Crystal structure of apo- and holo-bovine  $\alpha$ -lactalbumin at 2.2-A resolution reveal an effect of calcium on inter-lobe interactions / E.D. Chrysina, K. Brew, K. R. Acharya // *J. Biol. Chem.* – 2000. – Vol. 275. – P. 37021–37029.
37. Permyakov, E.A.  $\alpha$ -Lactalbumin: structure and function / E.A. Permyakov // *FEBS Letters*. – 2000. – Vol. 473. – P. 269–274.
38. Nomenclature of the proteins of cows milk-sixth revision / H.M. Farrell [et al.] // *J. Dairy Sci.* – 2004. – Vol. 87. – P. 1614–1674.
39. Structural basis for difference in heat capacity increments for  $\text{Ca}^{2+}$  binding to two  $\alpha$ -lactalbumins / A. Vanhooren [et al.] // *Biophysical Journal*. – 2002. – Vol. 82. – P. 407–417.
40. Kronman, M.J. Metal-ion binding and the molecular conformational properties of  $\alpha$ -lactalbumin / M.J. Kronman // *Crit. Rev. Biochem. Mol. Biol.* – 1989. – Vol. 24. – P. 565–667.
41. Brew, A.  $\alpha$ -Laclalbumin / A. Brew, J.A. Gobler // In *Adv. Dairy Chem.*, Vol. I, Proteins, Fox. P. R, Ed., Elsevier Applied Science, New York, 1992. – P. 191.
42. Bramaud, C. Thermal Isoelectric Precipitation of  $\alpha$ -Lactalbumin from a Whey Protein Concentrate: Influence of Protein-Calcium Complexation / C. Bramaud, G. Daufin // *Biotechnology and Bioengineering*. – 1995. – Vol. 47. – P. 121–130.
43. Carter, D.C. Structure of Serum Albumin / D.C. Carter, J.X. Ho // *Adv. Protein Chem.* – 1994. – Vol. 45. – P. 153–203.
44. He, X.M. Atomic structure and chemistry of human serum albumin / X.M. He, D.C. Carter // *Nature*. – 1992. – Vol. 358. – P. 209–214.
45. Peters, T. Serum Albumin / T. Peters // *Adv. Prot. Chem.* – 1985. – Vol. 37. – P. 161–245.
46. Foster, J.F. In *Albumin Structure Function and Uses* / J.F. Foster // V.M. Rosenoer, M. Oratz, M.A. Rolhchild Eds. Pergamon. Oxford, 1977. – P. 53.
47. Quantitative aspects of the interaction of bile acids with human serum albumin / A. Roda [et al]. // *J. Lipid Res.* – 1982. – Vol. 23, № 2. – P. 490–495.
48. Emerson, T.E. Unique features of albumin: A brief review / T.E. Emerson // *CRC Crit. Care Med.* – 1989. – Vol. 17. – P. 690–694.
49. IgE and IgG binding epitopes on alpha-lactalbumin and betalactoglobulin in cow's milk allergy / K.M. Jarvinen [et al.] // *Int. Arch. Allergy Immunol.* – 2001. – Vol. 126, № 2. – P. 111–118.
50. Cow's milk allergens identification by two-dimensional immunoblotting and mass spectrometry / M. Natale [et al.] // *Mol. Nutr. Food.* – 2004. – Vol. 48, № 5. – P. 363–369.
51. Anti-allergen antibodies can be neutralized by antibodies obtained against a peptide complementary to the allergen: towards a new peptide therapy for allergy / I. Selo [et al.] // *Immunol. Lett.* – 2002. – Vol. 80. – P. 133–138.

52. Structure and function of proteins involved in milk allergies / S. Sharma [et al.] // J. Chromatogr. B Biomed. Sci. Appl. – 2001. – Vol. 756, № 1. – P. 183–187.
53. Lara-Villoslada, F. The balance between caseins and whey proteins in cow's milk determines its allergenicity / F. Lara-Villoslada, M. Olivares, J. Xaus // J. Dairy Sci. – 2005. – Vol. 88, № 5. – P. 1654–1660.
54. Orlando, J.P. Anaphylactoid reaction to goat's milk / J.P. Orlando, A. Breton-Bouveyron // Allergy Immunol. – 2000. – Vol. 32, № 6. – P. 231–232.
55. Specificity of the human IgE response to the different purified caseins in allergy to cow's milk proteins / H. Bernard [et al.] // Int. Arch. Allergy Immunol. – 1998. – Vol. 115. – P. 235–244.
56. Phosphorylation is a post translational event which affects IgE binding capacity of caseins / H. Bernard [et al.] // FEBS Lett. – 2000. – Vol. 467. – P. 239–244.
57. Identification of IgE- and IgG-binding epitopes on  $\alpha$ S1-casein: differences in patients with persistent and transient cow's milk allergy / P. Chatchatee [et al.] // J. Allergy. Clin. Immunol. – 2001. – Vol. 107. – P. 379–383.
58. B-cell epitopes as a screening instrument for persistent cow's milk allergy / K.M. Jarvinen [et al.] // J. Allergy Clin. Immunol. – 2002. – Vol. 110, № 2. – P. 293–297.
59. Goat's milk of defective alpha (s1)-casein genotype decreases intestinal and systemic sensitization to beta-lactoglobulin in guinea pigs / C. Bevilacqua [et al.] // J. Dairy Res. – 2001. – Vol. 68, № 2. – P. 217–227.
60. Allergy to bovine beta-lactoglobulin: specificity of human IgE to tryptic peptides / I. Selo [et al.] // Clin. Exp. Allergy. – 1999. – Vol. 29, № 8. – P. 1055–1063.
61. The recognition pattern of sequential B cell epitopes of  $\beta$ -lactoglobulin does not vary with the clinical manifestations of cow's milk allergy / A. Heinzmann [et al.] // Int. Arch. Allergy Immunol. – 1999. – Vol. 120. – P. 280–286.
62. IgE-mediated rat mast cell triggering with tryptic and synthetic peptides of bovine beta-lactoglobulin / R. Fritzsche [et al.] // Int. Arch. Allergy Immunol. – 2005. – Vol. 138, № 4. – P. 291–297.
63. Interaction among human leucocyte antigen-peptide-T cell receptor complexes in cow's milk allergy: the significance of human leucocyte antigen and T cell receptor-complementarity determining region 3 loops / H. Sakaguchi [et al.] // Clin. Exp. Allergy. – 2002. – Vol. 32. – P. 762–770.
64. Epitopic characterization of native bovine beta-lactoglobulin / G. Clement [et al.] // J. Immunol. Methods. – 2002. – Vol. 266. – P. 67–78.
65. Antigenic determinants of bovine serum albumin / B. Beretta [et al.] // Int. Arch. Allergy Immunol. – 2001. – Vol. 126. – P. 188–195.
66. Cross-reactivity between mammalian proteins / P. Restani [et al.] // Ann. Allergy Asthma Immunol. – 2002. – Vol. 89. – P. 11–15.
67. Ribadeau-Dumas, B. Structure and variability of milk proteins / B. Ribadeau-Dumas // In: Barth CA, Schlimme E, editors. Milk Proteins: Nutritional, Clinical, Functional and Technological Aspects. Darmstadt, Germany: Steinkopff. – 1989. – P. 112–113.
68. Allergenicity of alpha-caseins from cow, sheep and goat / P. Spuergin [et al.] // Allergy. – 1997. – Vol. 52, № 3. – P. 293–298.
69. Crossreactivity between milk proteins from different animal species / P. Restani [et al.] // Clin. Exp. Allergy. – 1999. – Vol. 29. – P. 997–1004.
70. L'allergie au lait de chèvre ou de brebis sans allergie au lait de vache / E. Bidat [et al.] // Rev. Fr. Allergol. – 2003. – Vol. 43. – P. 273–277.
71. Allergy to goat and sheep cheese with good tolerance to cow cheese / A. Umpierrez [et al.] // Clin. Exp. Allergy. – 1999. – Vol. 29, № 8. – P. 1064–1068.
72. Immunological cross-reactions of alpha-lactalbumin from different species / J.P. Prieels [et al.] // Eur. J. Biochem. – 2006. – Vol. 50, № 3. P. 523–527.

73. Aalberse, R.C. Structure of food allergens in relation to allergenicity / R.C. Aalberse, S.O. Stapel, // Pediatr. Allergy Immunol. – 2001. – Vol. 12, № 14. – P. 10–14.
74. Evidence for a common epitope between bovine alpha-lactalbumin and beta-lactoglobulin / C. Baroglio [et al.] // Biol. Chem. – 1998. – Vol. 379, № 12. – P. 1453–1456.
75. Detection and identification of a soy bean component that cross reacts with caseins from cow's milk / P. Rozenfeld [et al.] // Clin. Exp. Immunol. – 2002. – Vol. 130. – P. 49–58.
76. Besler, M. Stability of food allergens and allergenicity of processed foods / M. Besler, H. Steinhart, A. Paschke // J. Chromatogr. B Biomed. Sci. Appl. – 2001. – Vol. 756. – P. 207–228.
77. Головач, Т.Н. Протеолиз и антигенные свойства нативного и термизированного β-лактоглобулина / Т.Н. Головач, Е.М. Червяковский, В.П. Курченко // Доклады НАН Беларуси. – 2010. – Т. 54, № 4. – С. 78–83.
78. Bahna, S.L. Milk hypersensitivity. II. Practical aspects of diagnosis, treatment and prevention / S.L. Bahna, M.D. Gandhi // Ann. Allergy. – 1983. – Vol. 50. – P. 295–301.
79. Allergenicity of individual cow milk proteins in DBPCFC-positive milk allergic adults / A. Norgaard [et al.] // J. Allergy Clin. Immunol. – 1996. – Vol. 97. – P. 237.
80. Milk-responsive atopic dermatitis is associated with a casein-specific lymphocyte response in adolescent and adult patients / T. Werfel [et al.] // J. Allergy Clin. Immunol. – 1997. – Vol. 99. – P. 124–133.
81. Allergen-specific IgE antibodies against antigenic components in cow milk and milk substitutes / B. Gjesing [et al.] // Allergy. – 1986. – Vol. 41, № 1. – P. 51–56.
82. Host, A. Allergic Reactions to Raw, Pasteurized and Homogenized/Pasteurized Cow Milk: A Comparison. A Double-Blind Placebo-Controlled Study in Milk Allergy Children / A. Host, E.G. Samuelsson // Allergy. – 1998. – Vol. 43. – P. 113–118.
83. Hanson, L.A. Immune electrophoretic studies of bovine milk and milk products / L.A. Hanson, I. Mansson // Acta Pediatr. – 1961. – Vol. 50. – P. 480–484.
84. Denaturation of beta-actoglobulin and native enzymes in the plate exchanger and holding tube section during continuous flow pasteurization of milk / M. Villamiel [et al.] // Food Chem. – 1997. – Vol. 58, № 1–2. – P. 49–52.
85. Kitabatake, N. Digestibility of bovine milk whey protein and β-lactoglobulin in vitro and in vivo / N. Kitabatake, Y. Kinekawa // J. Agric. Food Chem. – 1998. – Vol. 46, № 12. – P. 4917–4923.
86. Epitope mapping of a monoclonal antibody specific to bovine dry milk: involvement of residues 66–76 of strand D in thermal denatured beta-lactoglobulin / Song C.Y. [et al.] // J. Biol. Chem. – 2005. – Vol. 280, № 5. – P. 3574–3582.
87. Sawyer, L. β-lactoglobulin / L. Sawyer // P.F. Fox and P.L.H. McSweeney (eds) Advanced dairy chemistry, Vol. 1, 3rd Edn, Kluwer Academic/Plenum Publishers, 2003. – P. 319–386.
88. Crystal structures of bovine beta-lactoglobulin in the orthorhombic space group C222(1). Structural differences between genetic variants A and B and features of the Tanford transition / K.M. Oliveira [et al.] // Eur. J. Biochem. – 2001. – Vol. 268, № 2. – P. 477–483.
89. Effect of temperature on the secondary structure of b-lactoglobulin at pH 6,7, as determined by CD and IR spectroscopy: a test of the molten globule hypothesis / X.L. Qi [et al.] // Biochem. J. – 1997. – Vol. 324. – P. 341–346.
90. Casal, H.L. Structural and conformational changes of beta-lactoglobulin B: an infrared spectroscopic study of the effect of pH and temperature / H.L. Casal, U. Kohler, H.H. Mantsch // Biochim. Biophys. Acta. – 1988. – Vol. 957, № 1. – P. 11–20.
91. Prabakaran, S. Thermal unfolding of β-lactoglobulin: Characterization of initial unfolding events responsible for heat-induced aggregation / S. Prabakaran, S. Damodaran // J. Agric. Food Chem. – 1997. – Vol. 45. – P. 4303–4308.
92. Heat-resistant structural features of bovine β-lactoglobulin A revealed by NMR H/D exchange observations / P.J.B. Edwards [et al.] // Int. Dairy J. – 2002. – Vol. 12. – P. 331–344.

93. Manderson, G.A. Effect of Heat Treatment on the Circular Dichroism Spectra of Bovine  $\beta$ -Lactoglobulin A, B and C / G.A. Manderson, L.K. Creamer, M.J. Hardman // J. Agric. Food Chem. – 1999. – Vol. 47, № 11. – P. 4557–4567.
94. Donovan, M. Effects of chemical modification and sodium dodecyl sulphate binding on the thermostability of whey protein / M. Donovan, D.M. Mulvihill // Ir. J. Food Sci. Technol. – 1987. – Vol. 11. – P. 77.
95. Harwalker, V.R. Kinetic Study of Thermal Denaturation of Proteins in Whey / V.R. Harwalker // Milchwissenschaft. – 1986. – Vol. 41. – P. 206–210.
96. Wong, D.W.S. Structures and functionalities of milk proteins / D.W.S. Wong, W.M. Camirand, A.E. Paviath // Crit. Rev. Food Sci. Nutr. – 1996. – Vol. 36. – P. 807–844.
97. Monahan, F.J. Effect of pH and temperature on protein unfolding and thiol/disulfide interchange reactions during heat-induced gelation of whey proteins / F.J. Monahan, J.B. German, J.E. Kinsella // J. Agric. Food Chem. – 1995. – Vol. 43. – P. 46–52.
98. Otani, H. Antigenic reactivities of chemically modified  $\beta$ -lactoglobulins with antiserum to bovine  $\beta$ -lactoglobulins / H. Otani, T. Uchio, F. Tokita // Agric. Biol. Chem. – 1985. – Vol. 49. – P. 2531–2536.
99. Modifications occur at different structural levels during the heat denaturation of beta-lactoglobulin / S. Iametti [et al.] // Eur. J. Biochem. – 1996. – Vol. 237. – P. 106–112.
100. Yong, Y.H. Effects of Caseins on Thermal Stability of Bovine  $\beta$ -Lactoglobulin / Y.H. Yong, E.A. Foegeding // J. Agric. Food Chem. – 2008. – Vol. 56, № 21. – P. 10352–10358.
101. Monoclonal antibodies as probes for monitoring the denaturation process of bovine  $\beta$ -lactoglobulin / S. Kaminogawa [et al.] // Biochem. Biophys. Ada. – 1989. – Vol. 50. – P. 998.
102. The antigenic response of  $\beta$ -lactoglobulin is modulated by thermally induced aggregation / N. Kleber [et al.] // European Food Research and Technology. – 2004. – Vol. 219. – P. 105–110.
103. Effect of heat denaturation on beta-lactoglobulin-induced gastrointestinal sensitization in rats: denatured  $\beta$ -lg induces a more intensive local immunologic response than native  $\beta$ -lg / T.J. Karttunen [et al.] // Paediatric Allergy and Immunology. – 2002. – Vol. 13. – P. 269–277.
104. Elicitation of the allergic reaction in  $\beta$ -lactoglobulin-sensitized Balb/c mice: biochemical and clinical manifestations differ according to the structure of the allergen used for challenge / K. Adel-Patient [et al.] // Clin. Exp. Allergy. – 2003. – Vol. 33. – P. 376–385.
105. Differential scanning calorimetric study of different genetic variants of  $\beta$ -lactoglobulin / G.I. Imafidon [et al.] // J. Dairy Sci. – 1991. – Vol. 74. – P. 2416.
106. Comparative analysis of refolding of chemically denatured  $\beta$ -lactoglobulin types A and B using the dilution additive mode / A. Divsalar [et al.] // Int. J. of Biol. Macromolecules. – 2006. – Vol. 38. – P. 9–17.
107. Zhang, G. Effect of sulfated polysaccharides on heat-induced structural changes in  $\beta$ -lactoglobulin / G. Zhang, E. Allen Foegeding, C. Charles // J. Agric. Food Chem. – 2004. – Vol. 52, № 12. – P. 3975–3981.
108. Effect of heat treatment on denaturation of bovine  $\alpha$ -lactalbumin: determination of kinetic and thermodynamic parameters / Z. Wehbi [et al.] // J. Agric. Food Chem. – 2005. – Vol. 53, № 25. – P. 9730–9736.
109. Control of aggregational behaviour of  $\alpha$ -lactalbumin at acidic ph / J. B. Pedersen [et al.] // Journal of Fluorescence. – 2006. – Vol. 16, № 4. – P. 611–621.
110. Boye, J.I. Use of differential scanning calorimetry and infrared spectroscopy in the study of thermal and structural stability of  $\alpha$ -lactalbumin / J.I. Boye, I. Alli, A.A. Ismail // J. of Agric. Food Chem. – 1997. – Vol. 45. – P. 1116–1125.
111. Fang, Y. The conformation of  $\alpha$ -lactalbumin as a function of pH, heat treatment and adsorption at hydrophobic surfaces studied by FTIR / Y. Fang // Food Hydrocolloids. – 1998. – Vol. 12. – P. 121–126.
112. Hendrix, T.M. Energetics of structural domains in  $\alpha$ -lactalbumin / T.M. Hendrix, P. Privalov // Protein Science. – 1996. – Vol. 5. – P. 923–931.

113. Maynard, F. Immunological IgE crossreactions of bovine and human  $\alpha$ -lactalbumins in cow's milk allergic patients / F. Maynard, J.M. Chatel, J.-M. Wal // Food Agric. Immunol. – 1999. – Vol. 11. – P. 179–189.
114. Temperature Behaviour of Human Serum Albumin / R. Wetzel [et al.] // Eur. J. Biochem. – 1980. – Vol. 104. – P. 469–478.
115. Poole, S. Protein-Protein Interactions: Their Importance in Foaming of Heterogeneous Protein Systems / S. Poole, S.I. West, C.L. Walters // J. Sci. Food Agric. – 1984. – Vol. 35. – P. 701–711.
116. Ruegg, M. A calorimetric study of the thermal denaturation of whey proteins in simulated milk ultrafiltrate / M. Ruegg, U. Moor, B. Blanc // J. Dairy Res. – 1977. – Vol. 44. – P. 509–520.
117. Kinetic study of the pH influence on bsa thermal denaturation / V.E. Sahini [et al.] // Analele Universitatii Bucuresti: Chimie. – 2002. – Vol. 11. – P. 127–132.
118. Heppell, L.M.J. Reduction in the antigenicity of whey proteins by heat treatment: A possible strategy for producing a hypoallergenic infant formula / L.M.J. Heppell, A.J. Cant, P.J. Kilshaw // Br. J. Nutr. – 1984. – Vol. 51. – P. 29–36.
119. Habeeb, A.F.S.A. Effect of conformation of bovine serum albumin on reaction with its antibody / A.F.S.A. Habeeb, L. Borella // J. Immunol. – 1966. – Vol. 97. – P. 951–958.
120. Использование термической обработки белков коровьего и козьего молока для повышения их усвояемости и снижения аллергенных свойств / С.В. Симоненко [и др.] // Труд. Белорусск. гос. ун-та. Сер.: Инновационные технологии в XXI веке. – 2009. – Т. 4, ч. 2. – С. 261–276.
121. Chaplin, L. Irreversible heat denaturation of bovine  $\alpha$ -lactalbumin / L. Chaplin, R.L. Lyster // Dairy Res. – 1986. – Vol. 53. – P. 249.
122. Ju, Z.Y. Effects of preheating on properties of aggregates and of cold-set gels of whey protein isolate / Z.Y. Ju // J. of Agric. and Food Chem. – 1998. – Vol. 46. – P. 3604–3608.
123. Boye, J.I. Thermal denaturation of mixtures of  $\alpha$ -lactalbumin and  $\beta$ -lactoglobulin: a differential scanning calorimetric study / J.I. Boye, I. Alli // Food Res. Int. – 2000. – Vol 33. – P. 673–682.
124. Paulsson, M. Thermal Denaturation of Whey Proteins in Mixtures with Caseins Studied by Differential Scanning Calorimetry / M. Paulsson, P. Dejmek // J. of Dairy Sci. – 1990. – Vol. 73, № 3. – P. 590–600.
125. López-Fandiño, R. Functional Improvement of Milk Whey Proteins Induced by High Hydrostatic Pressure / R. López-Fandiño // Crit. Rev. Food Sci. Nut. – 2006. – Vol. 46. – P. 351–363.
126. Lullien-Pellerin, V. High pressure as a tool to study some proteins' properties: conformational modification, activity and oligomeric dissociation / V. Lullien-Pellerin, C. Balny // Innovative Food Science and Emerging Technologies. – 2002. – Vol. 3. – P. 209–221.
127. Jonas, J. High-resolution nuclear magnetic resonance studies of proteins / J. Jonas // Biochim. Biophys. Acta. – 2002. – Vol. 1595. – P. 145–159.
128. Effect of high hydrostatic pressure on the enzymic hydrolysis of  $\beta$ -lactoglobulin B by trypsin, thermolysin and pepsin / H. Stapelfeldt [et al.] // J. Dairy Res. – 1996. – Vol. 63. – P. 111–118.
129. Molecular modifications of  $\beta$ -lactoglobulin upon exposure to high pressure / S. Iametti [et al.] // J. Agric. Food Chem. – 1997. – Vol. 45. – P. 3–29.
130. Pressure-induced denaturation of monomer  $\beta$ -lactoglobulin is partially reversible: comparison of monomer form (highly acidic pH) with dimer form (neutral pH) / Y. Ikeuchi [et al.] // J. Agric. Food Chem. – 2001. – Vol. 49. – P. 4052–4059.
131. Interactive effects of pressure, temperature and time on the molecular structure of  $\beta$ -lactoglobulin / L.-A. Tedford [et al.] // J. Food Sci. – 1999. – Vol. 64. – P. 396–399.

132. Bull, L.A. Interactive effects of pressure, temperature and time on the molecular structure of ovalbumin, lysozyme and  $\beta$ -lactoglobulin / L.A. Bull, C.J. Schaschke // High Pressure Res. – 2002. – Vol. 22. – P. 689–691.
133. Tedford, L.-A. Induced structural change to  $\beta$ -Lactoglobulin by combined temperature and pressure / L.-A. Tedford, C.J. Schaschke // Biochem. Eng. J. – 2000. – Vol. 5. – P. 73–76.
134. Tanaka, N. Effect of pressure on the denaturation exchange reaction of  $\alpha$ -lactalbumin and  $\beta$ -lactoglobulin / N. Tanaka, S. Kunugi // Int. J. Biol. Macromol. – 1996. – Vol. 18. – P. 33–39.
135. Hosseini-nia, T. Effect of high hydrostatic pressure on the secondary structures of BSA and Apo- and holo- $\alpha$ -lactalbumin employing fourier transform infrared spectroscopy / T. Hosseini-nia, A.A. Ismail, S. Kubow // J. Food Sci. – 2002. – Vol. 67. – P. 1341–1347.
136. Thiol-induced oligomerisation of  $\alpha$ -lactalbumin at high pressure / M. Jegouic [et al.] // J. Protein Chem. – 1996. – Vol. 15. – P. 501–509.
137. Grinberg, V.Y. Reducer driven baric denaturation and oligomerisation of whey proteins / V.Y. Grinberg, T. Heartle // J. Biochem. – 2000. – Vol. 79. – P. 205–209.
138. Influence of high pressure on bovine serum albumin and its complex with dextran sulfate / V.B. Galazka [et al.] // J. Agric. Food Chem. – 1997. – Vol. 45. – P. 3465–3471.
139. Modification of food ingredients by ultrasound to improve functionality: a preliminary study on a model system / M. Ashokumar [et al.] // Inn. Food Sci. and Emer. Tech. – 2008. – Vol. 9. – P. 155–160.
140. Meltretter, J. Application of mass spectrometry for the detection of glycation and oxidation products in milk proteins / J. Meltretter, M. Pischetsrieder // Ann. N. Y. Acad. Sci. – 2008. – Vol. 1126. – P. 134–140.
141. Characterization of heat-induced lactosylation products in caseins by immunoenzymatic and mass spectrometric methodologies / A. Scaloni [et al.] // Biochim. Biophys. Acta. – 2002. – Vol. 1598, № 1–2. – P. 30–39.
142. Taheri-Kafrani, A. Effects of heating and glycation of  $\beta$ -lactoglobulin on its recognition by IgE of sera from cow milk allergy patients / A. Taheri-Kafrani [et al.] // J. Agric. Food Chem. – 2009. – Vol. 57, № 11. – P. 4974–4982.
143. Reduced immunogenicity of  $\beta$ -lactoglobulin by conjugation with acidic oligosaccharides / M. Hattori [et al.] // J. Agric. Food Chem. – 2004. – Vol. 52, № 14. – P. 4546–4553.
144. Adler-Nissen, J. Proteases / J. Adler-Nissen // In Enzymes in food processing; T. Nagodawithana, G. Reed, Eds.; Academic Press: San Diego. – 1993. – P. 159–203.
145. Adler-Nissen, J. Enzymatic Hydrolysis of Food Proteins / J. Adler-Nissen // Elsevier Applied Science Publishers: London. – 1986. – P. 263–313.
146. Lahl, W.J. Spices and seasonings: hydrolyzed proteins / W.J. Lahl, D.A Grindstaff // Proceedings of the 6th SIFST Symposium on Food Ingredients – Applications, Status and Safety, Singapore, 27–29 April 1989, Singapore institute of Food Science and Technology. – 1989. – P. 51–65.
147. Clemente, A. Vegetable protein hydrolysates / A. Clemente, J. Vioque, F. Miiian // Nutricion y Obesidad. – 1999. – Vol. 2. – P. 289–296.
148. Fox, P.F. Chemical and enzymatic modification of food proteins / P.F. Fox, P.A. Morrisey, D.M. Muivihill // Developments in Food Proteins–1 (Hudson, B.J., ed.), Appl. Sci. Pub. Inc, New Jersey. – 1982. – P. 1–60.
149. Molecular mass distribution, immunological properties and nutritive value of whey protein hydrolysates / E.C. Van Beresteijn [et al.] // J. Food Prot. – 1994. – Vol. 57. – P. 619–625.
150. Hydrolysed cow's milk formulae allergenicity and use in treatment and prevention / L. Businco [et al.] // An ESPACI Position Paper' in Pediatr. Allergy Immunol. – 1993. – Vol. 4. – P. 101–111.
151. Clemente, A. Enzymatic protein hydrolysates in human nutrition / A. Clemente // Trends in Food Science and Technology. – 2000. – Vol. 11. – P. 254–262.

152. Recent advances in enzymatic modifications of food proteins for improving their functional properties / J.M. Chobert [et al.] // Nahrung. – 1996. – Vol. 40. – P. 177–182.
153. Influence of Enzymatic Treatment on the Nutritional And Functional Properties of Pea Flour / M.J. Periago [et al.] // Food Chem. – 1998. – Vol. 63. – P. 71–78.
154. Gueguen, J. Pea and fababean proteins developments / J. Gueguen // Food Proteins-7 (Hudon, B.J.F., ed.), Elsevier Applied Sci, New Jersey. – 1991. – P. 35–78.
155. Peptide Characteristics of Sunflower Protein Hydrolysates / A. Villanueva [et al.] // J. Am. Oil Chem. Soc. – 1999. – Vol. 76. – P. 1455–1460.
156. Partially Hydrolyzed Rapeseed Protein Isolates with Improved Functional Properties / J. Vioque [et al.] // J. Am. Oil Chem. Soc. – 2000. – Vol. 77. – P. 447–450.
157. Swaisgood, H.E. Chemistry of the caseins / H.E. Swaisgood // Advanced Dairy Chemistry. Fox, P.F., Ed.; Elsevier Science Publishers: Essex. – 1992. – Vol. 1. – P. 63–110.
158. Susceptibility of beta-lactoglobulin and sodium caseinate to proteolysis by pepsin and trypsin / M.R. Guo [et al.] // J. Dairy Sci. – 1995. – Vol. 78. – № 11. – P. 2336–2344.
159. Dixon, M. Enzymes / M. Dixon, E.C. Webb // 31ed. London: Longman, 1979. – P. 1–6.
160. Rolle, R.S. Review: Enzyme applications for agro-processing in developing countries: an inventory of current and potential applications / R.S. Rolle // World J. Microbiol. Biotechnol. – 1998. – Vol. 14. – P. 611–619.
161. Molecular and biotechnological aspects of microbial proteases / M.B. Rao [et al.] // Microbiol. Mol. Biol. Rev. – 1998. – Vol. 62. – P. 597–635.
162. Barrett, A.J. Handbook of proteolytic enzymes / A.J. Barrett, N.D. Rawlings, J.F. Woessner // Academic Press: San Diego. – 1998. – P. 164–166.
163. Whitaker, J.R. Classification and nomenclature of enzymes / J.R. Whitaker // In Principles of Enzymology for the Food Sciences, 2 ed. Marcel Dekker, New York. – 1994. – P. 367–385.
164. Uhlig, H. Industrial enzymes and their applications / Uhlig, H. // Wiley: New York. – 1998. – P. 146–178.
165. Clemente, A. Production of extensive chickpea (*Cicer arietinum* L.) protein hydrolysates with reduced antigenic activity / A. Clemente // Agric. Food Chem. – 1999. – Vol. 47. – P. 3776–3781.
166. Alting, A.C. Selective hydrolysis of milk proteins to facilitate the elimination of the ABBOS epitopes of bovine serum albumin and other immunoreactive epitopes / A.C. Alting, R.J. Meijer, E.C. van Beresteijn // J. Food Prot. – 1998. – Vol. 61, № 8. – P. 1007–1012.
167. Rutherford-Markwick, K.J. Bioactive peptides derived from food / K.J. Rutherford-Markwick, P.J. Moughan // J. AOAC Int. – 2005. – Vol. 88, № 3. – P. 955–966.
168. Partial hydrolysis of cow's milk proteins by human trypsins and elastases *in vitro* / I. Jakobsson [et al.] // J. Pediatr. Gastroenterol. Nutr. November. – 1983. – Vol. 2, № 4. – P. 613–616.
169. Raising the pH of the pepsin-catalysed hydrolysis of bovine whey proteins increases the antigenicity of the hydrolysates / D.G. Schmidt [et al.] // Clin. Exp. Allergy. – Vol. 25. – 1995. – P. 1007–1017.
170. Astwood, J.D. Stability of food allergens to digestion *in vitro* / J.D. Astwood, J.N. Leach, R.L. Fuchs // Nat. Biotechnol. – 1996. – Vol. 14, № 10. – P. 1269–1273.
171. Enzymatic hydrolysis of whey protein concentrates: peptide HPLC profiles / M.V.T. Mota [et al.] // J. Liq. Chrom. & Related Tech. – 2004. – Vol. 27, № 16. – P. 2625–2639.
172. Головач, Т.Н. Перспективные биокатализаторы для получения ферментативных гидролизатов сывороточных белков / Т.Н. Головач, Н.К. Жабанос, В.П. Курченко // Перспективные биокатализаторы для перерабатывающих отраслей АПК: сб. науч. трудов V Международного научно-практического симпозиума, 26–27 мая 2010 г., Москва / Под ред. В.А. Полякова и Л.В. Римаревой, ГНУ ВНИИПБТ Россельхозакадемии. – М.: ВНИИПБТ, 2010. – С. 171–176.

173. Effect of genetic variation on the tryptic hydrolysis of bovine-lactoglobulin A, B and C / L.K. Creamer [et al.] // *J. Dairy Sci.* – 2004. – Vol. 87. – P. 4023–4032.
174. Пути снижения аллергенности белков молока и повышения их усвояемости / Т.Н. Головач [et al.] // Научные стремления – 2010: сборник материалов Республиканской научно-практической молодежной конференции с международным участием, г. Минск, 1–3 ноября 2010 г. – Минск: Беларус. наука. – 2010. – Ч. 2. – С. 420–422.
175. Whey protein antigenicity reduction by fungal proteinases and a pepsin/pancreatic combination / J.M. Ena [et al.] // *Journal of Food Science.* – 1995. – Vol. 60. – P. 104–116.
176. Maynard, F. Human IgE binding capacity of tryptic peptides from bovine  $\alpha$ -lactalbumin / F. Maynard, R. Jost, J.-M. Wal // *Int. Arch. Allergy Immunol.* – 1997. – Vol. 113. – P. 478–488.
177. Ragno, V. Allergenicity of milk protein hydrolysates formulae in children with cow's milk substitutes / V. Ragno // *Eur. J. Pecliatr.* – 1993. – Vol. 152. – P. 760–762.
178. de Boissieu, D. Allergy to extensively hydrolyzed cow milk proteins in infants: identification and treatment with an acid-based formula / D. de Boissieu, P. Matarazzo, C. DuPont // *J. Pediatr.* – 1997. – Vol. 131. – P. 744–747.
179. Reddy, I.M. Structural and conformational basis of the resistance of  $\beta$ -lactoglobulin to peptic and chymotryptic digestion / I.M. Reddy, N.K. Kella, J.E. Kinsella // *J. Agric. Food Chem.* – 1988. – Vol. 36. – P. 737–741.
180. Thermal modifications of structure and co-denaturation of  $\alpha$ -lactalbumin and  $\beta$ -lactoglobulin induce changes of solubility and susceptibility to proteases / C. Bertrand-Harb [et al.] // *Nahrung Food.* – 2002. – Vol. 46, № 4. – P. 283–289.
181. Peptic and Tryptic Hydrolysis of Native and Heated Whey Protein to Reduce Its Antigenicity / S.B. Kim [et al.] // *J. Dairy Sci.* – 2007. – Vol. 90. – P. 4043–4050.
182. Heremans, K. Protein structure and dynamics at high pressure / K. Heremans, L. Smeller // *Biochim. Biophys. Acta.* – 1998. – Vol. 1386. – P. 353–370.
183. Reduction of immunoreactivity of bovine  $\beta$ -lactoglobulin upon combined physical and proteolytic treatment / F. Bonomi [et al.] // *J. Dairy Res.* – 2003. – Vol. 70. – P. 51–59.
184. Kudryashova, E.V. Catalytic activity of thermolysin under extremes of pressure and temperature: Modulation by metal ions / E.V. Kudryashova, V.V. Mozhaev, C. Balny // *Biochim. Biophys. Acta.* – 1998. – Vol. 1386. – P. 199–210.
185. Application of high hydrostatic pressure for increasing activity and stability of enzymes / V.V. Mozhaev [et al.] // *Biotechnol. Bioeng.* – 1996. – Vol. 52. – P. 320–331.
186. The effect of high pressure on themolysin / S. Kunugi [et al.] // *Eur. J. Biochem.* – 1997. – Vol. 248. – P. 567–574.
187. Dufour, E. Hydrolysis of  $\beta$ -lactoglobulin by thermolysin and pepsin under high hydrostatic pressure / E. Dufour, G. Herve, T. Haertle // *Biopolym.* – 1995. – Vol. 35. – P. 475–483.
188. Effect of high hydrostatic pressure on the conformation of  $\beta$ -lactoglobulin A as assessed by proteolytic peptide profiling / J.C. Knudsen [et al.] // *Int. Dairy J.* – 2002. – Vol. 12. – P. 791–803.
189. Proteolytic pattern, antigenicity, and serum immunoglobulin E binding of beta-lactoglobulin hydrolysates obtained by pepsin and high-pressure treatments / R. Chicón [et al.] // *J. Dairy Sci.* – 2008. – Vol. 91, № 3. – P. 928–938.
190. Evaluation of the residual antigenicity of dairy whey hydrolysates obtained by combination of enzymatic hydrolysis and high-pressure treatment / E. Peñas [et al.] // *J. Food Prot.* – 2006. – Vol. 69, № 7. – P. 1707–1712.
191. Effects of combined microwave and enzymatic treatments on the hydrolysis and immunoreactivity of dairy whey proteins / F.J. Izquierdo [et al.] // *Int. Dairy J.* – 2008. – Vol. 18. – P. 918–922.
192. Gmoshinskii, I.V. Effect of Maillard protein modification on protein resistance to hydrolysis by digestive proteinases / I.V. Gmoshinskii, V.K. Mazo, N.F. Samenkova // *Vopr Pitan.* – 1981. – Vol. 6. – P. 19–24.

193. Dalsgaard, T.K. Proteolysis of milk proteins lactosylated in model systems / T.K. Dalsgaard, J.H. Nielsen, L.B. Larsen // Mol. Nutr. Food Res. – 2007. – Vol. 51, № 4. – P. 404–414.
194. Villamiel, M. Influence of high-intensity ultrasound and heat treatment in continuous flow on fat, proteins, and native enzymes of milk / M. Villamiel, P. de Jong // J. Agric. Food Chem. – 2000. – Vol. 48. – P. 472–478.
195. Effects of high pressure and microwave on Pronase and α-chymotrypsin hydrolysis of β-lactoglobulin / F.J. Izquierdo [et al.] // Food Chemistry. – 2005. – Vol. 92. – P. 713–719.
196. Nielsen, P.M. Functionality of protein hydrolysates / P.M. Nielsen // Food proteins and their applications; Damadoran, S., Paraf, A., Eds.; Marcel Dekker: New York. – 1997. – P. 443–472.
197. β-Lactoglobulin hydrolysis. II. Peptide identification, SH/SS exchange, and functional properties of hydrolysate fractions formed by the action of plasmin / P.W.J.R. Caessens [et al.] // J. Agric. Food Chem. – 1999. – Vol. 47. – P. 2980–2990.
198. Mahmoud, M.I. Physicochemical and functional properties of protein hydrolysates in nutritional products / M.I. Mahmoud // Food Technol. – 1994. – Vol. 48. – P. 89–95.
199. Iwaniak, A. Proteins as the source of physiologically and functionally active peptides / A. Iwaniak, P. Minkiewicz // Acta Sci. Pol. Technol. Aliment. – 2007. – Vol. 6, №3. – P. 5–15.
200. López-Expósito, I. Protective effect of milk peptides: antibacterial and antitumor properties / I. López-Expósito, I. Recio // Adv. Exp. Med. Biol. – 2008. – Vol. 606. – P. 271–293.
201. Ebringer, L. Beneficial health effects of milk and fermented dairy products – Review / L. Ebringer, M. Ferenčík, J. Krajčovič // Folia Microbiol. – 2008. – Vol. 53, № 5. – P. 378–394.
202. Isolation and characterization of a novel antibacterial peptide from bovine αS1-casein / K.B. McCann [et al.] // Int. Dairy J. – 2006. – Vol. 16. – P. 316–323.
203. Increased remineralization of tooth enamel by milk containing added casein phosphopeptide-amorphous calcium phosphate / G. Walker [et al.] // J. Dairy Res. – 2006. – Vol. 73. – P. 74–78.
204. Hartmann, R. Food-derived peptides with biological activity: from research to food applications / R. Hartmann, H. Meisel // Curr. Opin. Biotechnol. – 2007. – Vol. 18. – P. 163–169.
205. Jost, R. Whey Protein Aller-genicity and its Reduction by Technological Means / R. Jost, J.C. Monti, J.J. Pahud // Food Technol. – 1987. – Vol. 41. – P. 118–121.
206. Gorthler, I. Characterization of antigens and allergens in hypoallergenic formulae / I. Gorthler, R. Urbank, J. Forster // Eur. J. Pediatrics. – 1995. – Vol. 154. – P. 289–294.
207. Nakamura, T. Antigenicity of whey protein hydrolysates fractionated with ultrafiltration membrane / T. Nakamura, H. Sado, Y. Syukunobe // J. Japan. Soc. Food Sci. Technol. – 1992. – Vol. 39. – P. 113–116.
208. Knights, R.J. Processing and Evaluation of Protein Hydrolysates / R.J. Knights // Nutrition for Special Needs (Lifshitz, F., ed.), Marcel Dekker, New York. – 1985. – P. 105–115.
209. Allergenic and antigenic activity of peptide fragments in a whey hydrolysate formula / E.M. Van Hoeyveld [et al.] // Clin. exp. Allergy. – 1998. – Vol. 28. – P. 131–137.
210. Siemersma, A.D. The importance of peptide lengths in hypoallergenic infant formulae / A.D. Siemersma, W.J. Weijer, H.J. Bak // Trends Food Sci. Technol. – 1993. – Vol. 4. – P. 16–21.
211. Pedersen, B. Removing Bitterness from Protein Hydrolysates / B. Pedersen // Food Technol. – 1994. – Vol. 48. – P. 96–98.
212. Smith, I. Treatment of phenylalanine hydroxylase deficiency / I. Smith // Acta Paediatr. – 1994. – Vol. 407. – P. 60–65.
213. Brenner, H.J. Amino acid composition of food products used in the treatment of patients with disorders of the amino acid and protein metabolism / H.J. Brenner, A. Aninnos, B. Schulz // Eur. J. Pediatr. – 1996. – Vol. 155. – P. 108–114.
214. Manufacture of phenylalanine-free protein hydrolysates / M. Heindorff [et al.] // East German Patent DD 262. – 1988. – P. 674.

215. Cogan, U. Debittering and nutritional upgrading of enzymic casein hydrolysates / U. Cogan, M. Moshe, S. Mokady // *Sci. Food Agric.* – 1981. – Vol. 32. – P. 459–466.
216. Enzymatic production of a low-phenylalanine product skim milk powder and casemate / L.J. Lopez-Bajonero [et al.] // *J. Food Sci.* – 1991. – Vol. 56. – P. 938–942.
217. Ambrus, C.M. Phenylalanine depletion for the management of phenylketonuria: use of enzyme reactors with immobilized enzymes / C.M. Ambrus // *Science.* – 1978. – Vol. 201. – P. 837–839.
218. Use of hydrolysates in the treatment of cow's milk allergy / L. Terracciano [et al.] // *Ann. Allergy Asthma Immunol.* – 2002. – Vol. 89, № 1. – P. 86–90.
219. Dean, T. Cow's milk allergy: therapeutic options and Immunological aspects / T. Dean // *Eur. J. Clin. Nutr.* – 1995. – Vol. 49, № 1. – P. 19–25.
220. The natural history of intolerance to soy and extensively hydrolyzed formula in infants with multiple food protein intolerance (MFPI) / D.J. Hill [et al.] // *J. Pediatr.* – 1999. – Vol. 135. – P. 118–121.
221. Evaluation of an extensively hydrolyzed casein-whey protein formula in immediate cow's milk protein hypersensitivity / M. Martin-Esteban [et al.] // *J. Pediatr. Gastroenterol. Nutr.* – 1998. – Vol. 26, № 4. – P. 398–401.
222. Fischer, J.E. Nutrition In Liver Disease / J.E. Fischer, T.D. Kane // Present Knowledge in Nutrition (Ziegler, E.E., Filer, L.J., eds), ILSI Press, Washington, DC. – 1996. – P. 472–481.
223. Schenker, S. Nutrients in the pathogenesis and treatment of hepatic encephalopathy / S. Schenker, J.E. Fische, T.D. Kane // Nutrition and the Origins of Disease (Halsted, C.H., Rucker, R.B., eds), Academic Press, London. – 1989. – P. 285–307.
224. The role of plasma amino acids in hepatic encephalopathy / J.E. Fischer [et al.] // *Surgery.* – 1975. – Vol. 78. – P. 276–290.
225. Okita, M. Treatment of Liver Cirrhosis by branched-chain amino acids enriched nutrient mixture / M. Okita, A. Watanabe, H. Nagashima // *Nutr. Sci. Vitaminol.* – 1985. – Vol. 31. – P. 291–230.
226. Campolio, O. The BCAA/AAA ratio of plasma amino acids in three different groups of cirrhotics / O. Campolio, D. Sprengers, N. McIntyre // *Rev. Invest. Clin.* – 1992. – Vol. 44. – P. 513–518.
227. Use of branched amino acids for treating hepatic encephalopathy: clinical experiences / R.F. Fanelli [et al.] // *Gut.* – 1986. – Vol. 27. – P. 111–115.
228. Enzymatic modification of zein to produce an non-bitter peptide fraction with a very high fisher ratio for patients with hepatic encephalopathy / S. Tanimoto [et al.] // *Agric. Biol. Chem.* – 1991. – Vol. 55. – P. 1119–1123.
229. Low Molecular weight sunflower protein hydrolysate with low concentration in aromatic amino acids / J. Bautista [et al.] // *J. Agric. Food Chem.* – 1991. – Vol. 44. – P. 967–971.
230. Sunflower protein hydrolysates for dietary treatment of patients with liver failure / J. Bautista [et al.] // *J. Am. Oil Chem. Soc.* – 2000. – Vol. 77. – P. 121–126.

## ALLERGENICITY OF MILK PROTEINS AND WAYS OF ITS DECREASE

T.N. Halavach \*\*\*, V.P. Kurchenko \*\*

\*RUF «Institute of Meat and Dairy Industry», Minsk, Belarus

\*\*Belarusian State University, Minsk, Belarus

Review has been devoted to the problem of milk proteins allergenicity and the methods that allows to receive a hypoallergenic protein component for products of baby and specialised food. Current information about the immune mechanism of food allergy formation, physical and chemical properties and antigenic determinants of casein and whey proteins has been presented. As the basic approaches of decrease in milk proteins allergenicity have been defined heating, processing by a high pressure, chemical modification (Maillard reaction), enzymatic hydrolysis. The combination of

physical influence, in particular thermodenaturation, and proteolysis have been represented in the capacity of the most accessible and effective way of hypoallergenic protein component making. Importance of post-hydrlisis processes for enzymatic hydrolysates manufacture with the desired properties has been shown. The main categories of products of specialised food on the basis of protein hydrolysates have been characterised.

