

SUPPLEMENTARY MATERIALS

Fedchenko V.I., Veselovsky A.V., Kopylov A.T, Medvedev A.E. (2023) The search for potential hypotensive peptides in the amino acid sequence of human renalase and their identification in proteolytic fragments of this protein. Biomeditsinskaya Khimiya, 69(6), 403-408. <http://dx.doi.org/10.18097/PBMC20236906403>

Table S1. Peptide inhibitors of Angiotensin 1 converting enzyme (ACE) from the AHTPDB: Database of Antihypertensive Peptides, containing tetrapeptide fragments equivalent to the renalase tetrapeptide sequences

RNLS peptide	ACE inhibitor	Peptide length	IC ₅₀ (μM)	Peptide source	Database ID	Reference
P ²¹⁵ TSN ²¹⁸	SAYPGQITSN	10	7.08	Not shown	2352	Sagardia I, Roa-Ureta RH, Bald C. A new QSAR model, for angiotensin I-converting enzyme inhibitory oligopeptides. Food Chem. 2013 Feb 15;136(3-4):1370-6. doi: 10.1016/j.foodchem.2012.09.092.
	SAYPGQITSN	10	0	Milk	6396	Gobbetti M, Ferranti P, Smacchi E, Goffredi F, Addeo F. Production of angiotensin-I-converting-enzyme-inhibitory peptides in fermented milks started by <i>Lactobacillus delbrueckii</i> subsp. <i>bulgaricus</i> SS1 <i>Lactococcus lactis</i> subsp. <i>cremoris</i> FT4. Appl Environ Microbiol. 2000 Sep;66(9):3898-904. doi: 10.1128/AEM.66.9.3898-3904.2000.
P ²⁴⁹ FGV ²⁵²	VPPFGVG	6	336	Not shown	5395	in Tan, Feifei Tian, Yonggang Lv, Wanqian Liu, Li Zhong, Yongle Liu & Li Yang (2013) Integration of QSAR modelling and QM/MM analysis to investigate functional food peptides with antihypertensive activity, Molecular Simulation, 39:12, 1000-1006, DOI: 10.1080/08927022.2013.788247
	VPPFGVG	6	336	Wheat (<i>Triticum sp sour dough</i>)	6284	Nakamura T, Yoshida A, Komatsuzaki N, Kawasumi T, Shima J. Isolation and characterization of a low molecular weight peptide contained in sourdough. J Agric Food Chem. 2007 Jun 13;55(12):4871-6. doi: 10.1021/jf070069r.

RNLS peptide	ACE inhibitor	Peptide length	IC ₅₀ (μM)	Peptide source	Database ID	Reference
P ²⁷⁵ GLP ²⁷⁸	GFPGTPGLPGF	11	436	hen (<i>Gallus gallus domesticus</i>)	<u>5713</u>	Saiga A, Okumura T, Makihara T, Katsuta S, Shimizu T, Yamada R, Nishimura T. Angiotensin I-converting enzyme inhibitory peptides in a hydrolyzed chicken breast muscle extract. J Agric Food Chem. 2003 Mar 12;51(6):1741-5. doi: 10.1021/jf020604h.
	GAPGLPGP	8	29.4 μM	Hen (<i>Gallus gallus</i>)	<u>6950</u>	Saiga A, Iwai K, Hayakawa T, Takahata Y, Kitamura S, Nishimura T, Morimatsu F. Angiotensin I-converting enzyme-inhibitory peptides obtained from chicken collagen hydrolysate. J Agric Food Chem. 2008 Oct 22;56(20):9586-91. doi: 10.1021/jf072669w.
V ⁷ GAG ¹⁰	GVGAGY	6	4.07	Not shown	<u>2328</u>	Sagardia I, Roa-Ureta RH, Bald C. A new QSAR model, for angiotensin I-converting enzyme inhibitory oligopeptides. Food Chem. 2013 Feb 15;136(3-4):1370-6. doi: 10.1016/j.foodchem.2012.09.092.
V ⁸⁴ LRP ⁸⁷	FCVLRP	6	12.3	Shrimp	<u>1039</u>	He HL, Liu D, Ma CB. Review on the angiotensin-I-converting enzyme (ACE) inhibitor peptides from marine proteins. Appl Biochem Biotechnol. 2013 Feb;169(3):738-49. doi: 10.1007/s12010-012-0024-y
	FCVLRP	6	12.3	Not shown	<u>5352</u>	in Tan, Feifei Tian, Yonggang Lv, Wanqian Liu, Li Zhong, Yongle Liu & Li Yang (2013) Integration of QSAR modelling and QM/MM analysis to investigate functional food peptides with antihypertensive activity, Molecular Simulation, 39:12, 1000-1006, DOI: 10.1080/08927022.2013.788247
	FCVLRP	6	12.3	Shrimp (<i>Acetes chinensis</i>)	<u>6196</u>	Hai-Lun H, Xiu-Lan C, Cai-Yun S, Yu-Zhong Z, Bai-Cheng Z. Analysis of novel angiotensin-I-converting enzyme inhibitory peptides from protease-hydrolyzed marine shrimp <i>Acetes chinensis</i> . J Pept Sci. 2006 Nov;12(11):726-33. doi: 10.1002/psc.789.

RNLS peptide	ACE inhibitor	Peptide length	IC ₅₀ (μM)	Peptide source	Database ID	Reference
F ¹⁰⁴ VAP ¹⁰⁷	FFVAPFPEVFGK	12	Not shown	Beta-CN	<u>1347</u>	Hernandez-Ledesma B (ed.) (2013) Bioactive Food Peptides in Health and Disease. InTech. Available at: http://dx.doi.org/10.5772/3318 .
	FFVAPFPEVFGK	12	77	Casein	<u>1656</u>	Wakai T and Yamamoto N (2012) Antihypertensive Peptides Specific to Lactobacillus helveticus Fermented Milk. Biotechnology - Molecular Studies and Novel Applications for Improved Quality of Human Life. InTech. Available at: http://dx.doi.org/10.5772/28695
	FFVAPFPGVFGK	12	77	Tryptic hydrolysis	<u>1716</u>	Hernández-Ledesma B, del Mar Contreras M, Recio I. Antihypertensive peptides: production, bioavailability and incorporation into foods. Adv Colloid Interface Sci. 2011 Jun 9;165(1):23-35. doi: 10.1016/j.cis.2010.11.001
	FVAPFPEV	8	475.89 ± 41.73	Casein	<u>1771</u>	María del Mar Contreras, Rosalía Carrón, María José Montero, Mercedes Ramos, Isidra Recio. Novel casein-derived peptides with antihypertensive activity. International Dairy Journal, 19(10), 2009, 566-573, https://doi.org/10.1016/j.idairyj.2009.05.004 .
	FVAPFPEVFGKEKVNE	16	Not shown	Casein	<u>1798</u>	María del Mar Contreras, Rosalía Carrón, María José Montero, Mercedes Ramos, Isidra Recio. Novel casein-derived peptides with antihypertensive activity. International Dairy Journal, 19(10), 2009, 566-573, https://doi.org/10.1016/j.idairyj.2009.05.004 .
	FVAPFPEV	8	475.89	Not shown	<u>2499</u>	Sagardia I, Roa-Ureta RH, Bald C. A new QSAR model, for angiotensin I-converting enzyme inhibitory oligopeptides. Food Chem. 2013 Feb 15;136(3-4):1370-6. doi: 10.1016/j.foodchem.2012.09.092.
	FFVAP	5	503.51	Not shown	<u>2505</u>	Sagardia I, Roa-Ureta RH, Bald C. A new QSAR model, for angiotensin I-converting enzyme inhibitory oligopeptides. Food Chem. 2013 Feb 15;136(3-4):1370-6. doi: 10.1016/j.foodchem.2012.09.092.

RNLS peptide	ACE inhibitor	Peptide length	IC ₅₀ (μM)	Peptide source	Database ID	Reference
	FFVAPFPQVFGF	12	Not shown	Casein	<u>2948</u>	Norris R (2013) Antihypertensive Peptides from Food Proteins. Bioactive Food Peptides in Health Disease. InTech. Available at: http://dx.doi.org/10.5772/51710 .
	EFVAPFPEVFGK	12	Not shown	Not shown	<u>3609</u>	Iwaniak A., Dziuba B. (2009). Motifs with potential physiological activity in food proteins – BIOPEP database. Acta Sci.Pol. Technol. Aliment. 8 (3), 59-85
	FFVAP	5	Not shown	Not shown	<u>3610</u>	Phelan M, Kerins D. The potential role of milk-derived peptides in cardiovascular disease. Food Funct. 2011 Apr;2(3-4):153-67. doi: 10.1039/c1fo10017c.
	FVAPFPEVFGK	11	Not shown	Cheese (Cheddar (with probiotics))	<u>3626</u>	Pihlanto A (2013) Lactic Fermentation and Bioactive Peptides. Lactic Acid Bacteria - R & D for Food, Health Livestock Purposes. InTech. Available at: http://dx.doi.org/10.5772/51692.dair
	FVAPFPEVFGK	11	Not shown	Cheese (Fresco)	<u>3634</u>	Pihlanto A (2013) Lactic Fermentation and Bioactive Peptides. Lactic Acid Bacteria - R & D for Food, Health Livestock Purposes. InTech. http://dx.doi.org/10.5772/51692 .
	FFVAPFEVFGK	11	Not shown	Not shown	<u>3660</u>	Phelan M, Kerins D. The potential role of milk-derived peptides in cardiovascular disease. Food Funct. 2011 Apr;2(3-4):153-67. doi: 10.1039/c1fo10017c.
	FFVAPFPEVFGK	12	Not shown	Not shown	<u>3669</u>	Phelan M, Kerins D. The potential role of milk-derived peptides in cardiovascular disease. Food Funct. 2011 Apr;2(3-4):153-67. doi: 10.1039/c1fo10017c.
	FFVAP	5	Not shown	Not shown	<u>3670</u>	Phelan M, Kerins D. The potential role of milk-derived peptides in cardiovascular disease. Food Funct. 2011 Apr;2(3-4):153-67. doi: 10.1039/c1fo10017c.

RNLS peptide	ACE inhibitor	Peptide length	IC ₅₀ (μM)	Peptide source	Database ID	Reference
	FFVAPFPEVFGK	12	Not shown	Milk	3748	Fekete AA, Givens DI, Lovegrove JA. The impact of milk proteins and peptides on blood pressure and vascular function: a review of evidence from human intervention studies. <i>Nutr Res Rev.</i> 2013 Dec;26(2):177-90. doi: 10.1017/S0954422413000139.
	FFVAPFPGVFGK	12	Not shown	Milk	4142	Martínez-Maqueda D, Miralles B, Recio I, Hernández-Ledesma B. Antihypertensive peptides from food proteins: a review. <i>Food Funct.</i> 2012 Apr;3(4):350-61. doi: 10.1039/c2fo10192k.
	FFVAPFPEVFGK	12	Not shown	Cow casein	4272	Nagpal R, Behare P, Rana R, Kumar A, Kumar M, Arora S, Morotta F, Jain S, Yadav H. Bioactive peptides derived from milk proteins and their health beneficial potentials: an update. <i>Food Funct.</i> 2011 Jan;2(1):18-27. doi: 10.1039/c0fo00016g.
	FFVAP	5	Not shown	Cow casein	4273	Nagpal R, Behare P, Rana R, Kumar A, Kumar M, Arora S, Morotta F, Jain S, Yadav H. Bioactive peptides derived from milk proteins and their health beneficial potentials: an update. <i>Food Funct.</i> 2011 Jan;2(1):18-27. doi: 10.1039/c0fo00016g.
	FVAPFP	6	Not shown	Cow milk	4369	Gútiéz L, Gómez-Sala B, Recio I, del Campo R, Cintas LM, Herranz C, Hernández PE. Enterococcus faecalis strains from food, environmental, and clinical origin produce ACE-inhibitory peptides and other bioactive peptides during growth in bovine skim milk. <i>Int J Food Microbiol.</i> 2013 Aug 16;166(1):93-101. doi: 10.1016/j.ijfoodmicro.2013.06.019.
	FVAP	4	Not shown	Milk	4380	Katrin A. Kopf-Bolanz, Flurina Schwaer, Martin Gijs, Guy Vergères, Reto Portmann, Lotti Egger. Impact of milk processing on the generation of peptides during digestion. <i>International Dairy Journal,</i> 35(2), 2014, 130-138, https://doi.org/10.1016/j.idairyj.2013.10.012 .

RNLS peptide	ACE inhibitor	Peptide length	IC ₅₀ (μM)	Peptide source	Database ID	Reference
	FVAP	4	Not shown	Not shown	<u>4888</u>	Zhou P, Yang C, Ren Y, Wang C, Tian F. What are the ideal properties for functional food peptides with antihypertensive effect? A computational peptidology approach. Food Chem. 2013 Dec 1;141(3):2967-73. doi: 10.1016/j.foodchem.2013.05.140.
	FFVAPFPEVFGK	12	77	Casein (As1-casein)	<u>5052</u>	Jian-Hui Wang, Yong-Le Liu, Jing-Heng Ning, Jian Yu, Xiang-Hong Li, Fa-Xiang Wang. Is the structural diversity of tripeptides sufficient for developing functional food additives with satisfactory multiple bioactivities? Journal of Molecular Structure, 1040, 2013, 164-170, https://doi.org/10.1016/j.molstruc.2013.03.004 .
	FVAP	4	10	Not shown	<u>5279</u>	in Tan, Feifei Tian, Yonggang Lv, Wanqian Liu, Li Zhong, Yongle Liu & Li Yang (2013) Integration of QSAR modelling and QM/MM analysis to investigate functional food peptides with antihypertensive activity, Molecular Simulation, 39:12, 1000-1006, DOI: 10.1080/08927022.2013.788247
	FFVAP	5	6	Not shown	<u>5313</u>	in Tan, Feifei Tian, Yonggang Lv, Wanqian Liu, Li Zhong, Yongle Liu & Li Yang (2013) Integration of QSAR modelling QM/MM analysis to investigate functional food peptides with antihypertensive activity, Molecular Simulation, 39:12, 1000-1006, DOI: 10.1080/08927022.2013.788247
	FFVAPFPEVFGK	12	Not shown	Milk	<u>5534</u>	F. Javier Espejo-Carpio, Cristian De Gobba, Antonio Guadix, Emilia M. Guadix, Jeanette Otte, Angiotensin I-converting enzyme inhibitory activity of enzymatic hydrolysates of goat milk protein fractions. International Dairy Journal, 32(2), 2013, 175-183. https://doi.org/10.1016/j.idairyj.2013.04.002 .
	FVAPFPEVF	9	Not shown	Cheese (Cheddar)	<u>5535</u>	Lydia Ong, Anders Henriksson, Nagendra P. Shah Angiotensin converting enzyme-inhibitory activity in Cheddar cheeses made with the addition of

RNLS peptide	ACE inhibitor	Peptide length	IC ₅₀ (μM)	Peptide source	Database ID	Reference
						probiotic <i>Lactobacillus casei</i> sp. Lait, 87 2 (2007) 149-165 DOI: https://doi.org/10.1051/lait:2007004
	FVAPFPEVF	9	Not shown	Cheese (Cheddar)	5536	Lydia Ong, Anders Henriksson, Nagendra P. Shah Angiotensin converting enzyme-inhibitory activity in Cheddar cheeses made with the addition of probiotic <i>Lactobacillus casei</i> sp. Lait, 87 2 (2007) 149-165 DOI: https://doi.org/10.1051/lait:2007004
	FFVAPFPEVFGK	12	Not shown	Casein	5550	Baum F, Fedorova M, Ebner J, Hoffmann R, Pischetsrieder M. Analysis of the endogenous peptide profile of milk: identification of 248 mainly casein-derived peptides. J Proteome Res. 2013 Dec 6;12(12):5447-62. doi: 10.1021/pr4003273.
	FVAPFPEVFG	10	Not shown	Casein	5556	Baum F, Fedorova M, Ebner J, Hoffmann R, Pischetsrieder M. Analysis of the endogenous peptide profile of milk: identification of 248 mainly casein-derived peptides. J Proteome Res. 2013 Dec 6;12(12):5447-62. doi: 10.1021/pr4003273.
	FFVAPFPEVFGK	12	77	Casein	5557	Yamamoto, N. (2010). Functional Food Products with Antihypertensive Effects. In Bioactive Proteins and Peptides as Functional Foods Nutraceuticals (eds Y. Mine, E. Li-Chan and B. Jiang). https://doi.org/10.1002/9780813811048.ch12
	FFVAPFPEVFGK	12	18	Cow casein	5834	Jérôme Tauzin, Laurent Miclo, Jean-Luc Gaillard. Angiotensin-I-converting enzyme inhibitory peptides from tryptic hydrolysate of bovine αS2-casein. FEBS Letters, 531(2), 2002, 369-374. https://doi.org/10.1016/S0014-5793(02)03576-7 .
	FFVAP	5	6	Cow casein	5845	Susumu MARUYAMA, Kazuya NAKAGOMI, Noboru TOMIZUKA, Hideo SUZUKI, Angiotensin I-Converting Enzyme Inhibitor Derived from an Enzymatic Hydrolysate of Casein. II.

RNLS peptide	ACE inhibitor	Peptide length	IC ₅₀ (μM)	Peptide source	Database ID	Reference
						Isolation and Bradykinin-potentiating Activity on the Uterus and the Ileum of Rats, Agricultural and Biological Chemistry, 1985, 49(5), 1405-1409. https://doi.org/10.1271/bbb1961.49.1405 ,
	FFVAPFPEVFGK	12	77	Cow casein	<u>5846</u>	Susumu MARUYAMA, Hideo SUZUKI, A Peptide Inhibitor of Angiotensin I Converting Enzyme in the Tryptic Hydrolysate of Casein, Agricultural Biological Chemistry, 1982, 46(5), 1393-1394. https://doi.org/10.1271/bbb1961.46.1393
	FVAP	4	10	Cow casein	<u>5848</u>	Susumu MARUYAMA, Hajime MITACHI, Hideoki TANAKA, Noboru TOMIZUKA, Hideo SUZUKI, Studies on the Active Site and Antihypertensive Activity of Angiotensin I-Converting Enzyme Inhibitors Derived from Casein, Agricultural Biological Chemistry, 1987, 51(6), 1581-1586. https://doi.org/10.1271/bbb1961.51.1581
	FVAPFPEVFGKEKVNEL SKDIGS	23	Not shown	Casein	<u>6073</u>	Robert MC, Razaname A, Mutter M, Juillerat MA. Identification of angiotensin-I-converting enzyme inhibitory peptides derived from sodium caseinate hydrolysates produced by Lactobacillus helveticus NCC 2765. J Agric Food Chem. 2004 Nov 17;52(23):6923-31. doi: 10.1021/jf049510t.
	NENLLRFFVAPFPE	14	Not shown	Casein	<u>6074</u>	Robert MC, Razaname A, Mutter M, Juillerat MA. Identification of angiotensin-I-converting enzyme inhibitory peptides derived from sodium caseinate hydrolysates produced by Lactobacillus helveticus NCC 2765. J Agric Food Chem. 2004 Nov 17;52(23):6923-31. doi: 10.1021/jf049510t.
	FVAPFPEVFGKEKVNEL SKDIGSE	24	Not shown	Casein	<u>6079</u>	Minervini F, Algaron F, Rizzello CG, Fox PF, Monnet V, Gobbetti M. Angiotensin I-converting-enzyme-inhibitory and antibacterial peptides from Lactobacillus helveticus PR4 proteinase-hydrolyzed

RNLS peptide	ACE inhibitor	Peptide length	IC ₅₀ (μM)	Peptide source	Database ID	Reference
						caseins of milk from six species. Appl Environ Microbiol. 2003 Sep;69(9):5297-305. doi: 10.1128/AEM.69.9.5297-5305.2003.
	FFVAPFPFEVFGK	13	77	Casein	<u>6415</u>	Susumu MARUYAMA, Kazuya NAKAGOMI, Noboru TOMIZUKA, Hideo SUZUKI, Angiotensin I-Converting Enzyme Inhibitor Derived from an Enzymatic Hydrolysate of Casein. II. Isolation and Bradykinin-potentiating Activity on the Uterus and the Ileum of Rats, Agricultural and Biological Chemistry, 1985, 49(5), 1405-1409. https://doi.org/10.1271/bbb1961.49.1405 ,
	FFVAPFPEVFGK	12	18	Cow alpha s2-casein	<u>6704</u>	Tauzin J, Miclo L, Gaillard JL. Angiotensin-I-converting enzyme inhibitory peptides from tryptic hydrolysate of bovine alphaS2-casein. FEBS Lett. 2002 Nov 6;531(2):369-74. doi: 10.1016/s0014-5793(02)03576-7.
	FFVAP	5	6	Human beta casein	<u>6856</u>	Masanori KOHMURA, Noriki NIO, Kazuki KUBO, Yumi MINOSHIMA, Eisuke MUNEKATA, Yasuo ARIYOSHI, Inhibition of Angiotensin-converting Enzyme by Synthetic Peptides of Human β-Casein, Agricultural and Biological Chemistry, 1989, 53(8), 2107-2114 https://doi.org/10.1271/bbb1961.53.2107
	LNENLLRFFVAPFPEVFG	18	280 μM	Cow casein	<u>6940</u>	Robert MC, Razaname A, Mutter M, Juillerat MA. Identification of angiotensin-I-converting enzyme inhibitory peptides derived from sodium caseinate hydrolysates produced by Lactobacillus helveticus NCC 2765. J Agric Food Chem. 2004 Nov 17;52(23):6923-31. doi: 10.1021/jf049510t.
	NENLLRFFVAPFPEVFG	17	55 μM	Cow casein	<u>6941</u>	Robert MC, Razaname A, Mutter M, Juillerat MA. Identification of angiotensin-I-converting enzyme inhibitory peptides derived from sodium caseinate

RNLS peptide	ACE inhibitor	Peptide length	IC ₅₀ (μM)	Peptide source	Database ID	Reference
						hydrolysates produced by <i>Lactobacillus helveticus</i> NCC 2765. <i>J Agric Food Chem.</i> 2004 Nov 17;52(23):6923-31. doi: 10.1021/jf049510t.
	ENLLRFFVAPFPEVFG	16	250 μM	Cow casein	<u>6942</u>	Robert MC, Razaname A, Mutter M, Juillerat MA. Identification of angiotensin-I-converting enzyme inhibitory peptides derived from sodium caseinate hydrolysates produced by <i>Lactobacillus helveticus</i> NCC 2765. <i>J Agric Food Chem.</i> 2004 Nov 17;52(23):6923-31. doi: 10.1021/jf049510t.