

COWS' MILK A1 & A2 TYPE BETA-CASEIN PROTEIN DIGESTION

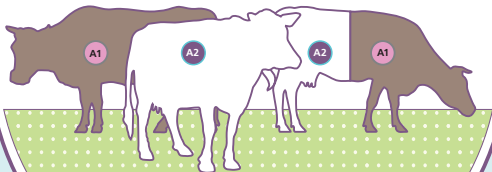


Investigate
Communicate
Collaborate

A2 beta-casein is the original beta-casein protein gene. A mutation caused the A1 protein to appear a few thousand years ago.

1

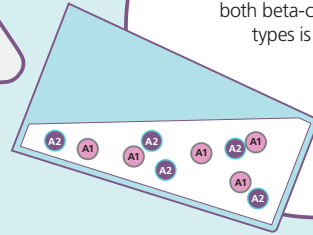
Milk herd carrying genes for both beta-casein protein types



Milk content	
250ml	
30-38g Solids	
9-15g Fat	
10-12g Lactose	
7-10g Protein	
5.5-8g Casein	
2-3g A1 & A2 type beta-casein proteins	

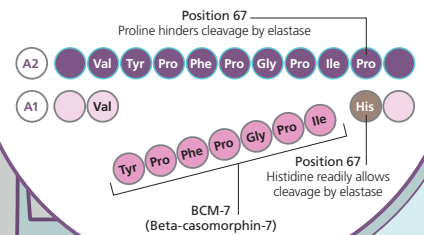
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Regular milk containing both beta-casein protein types is ingested



3

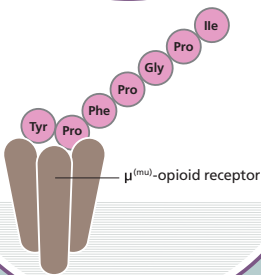
Digestion of A1 beta-casein in the small intestine releases BCM-7. The structure of A2 beta-casein limits the release of BCM-7 on digestion.



Milk digestion starts here

BCM-7 binds to opioid receptors present throughout the body. In the gut, BCM-7 can trigger inflammation and intestinal transit time delay, and consequently gastrointestinal symptoms in some people.

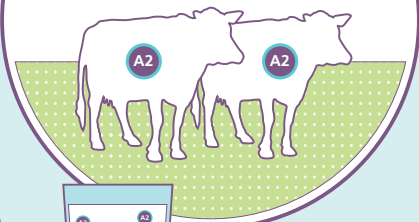
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In some patients with gastrointestinal discomfort following commercial milk intake, avoiding the A1 protein may make the difference

5

a2 Milk™ from purely A2 type beta-casein gene carrying herds



a2 Milk™ is free of A1 protein and naturally free of BCM-7 related issues

References:

1. He M, et al., (2017). Effects of cow's milk beta-casein variants on symptoms of milk intolerance in Chinese adults: a multicentre, randomised controlled study. *Nutr J.* 16:72.
2. Jianqin S, et al., (2016). Effects of milk containing only A2 beta casein versus milk containing both A1 and A2 beta casein proteins on gastrointestinal physiology, symptoms of discomfort, and cognitive behavior of people with self-reported intolerance to traditional cows' milk. *Nutr J.* 15:35.
3. Deth R, et al., (2016). Clinical evaluation of glutathione concentrations after consumption of milk containing different subtypes of β -casein: results from a randomized, cross-over clinical trial. *Nutr J.* 15(1):82.
4. Trivedi MS, et al., (2014). Food-derived opioid peptides inhibit cysteine uptake with redox and epigenetic consequences. *J Nutr Biochem.* 25(10):1011-8.
5. Pelto L, et al., (1999). Milk hypersensitivity in young adults. *Eur J Clin Nutr.* 53(8), 620-4.
6. Phelan M, et al., (2009). Casein-derived bioactive peptides: Biological effects, industrial uses, safety aspects and regulatory status. *International Dairy Journal.* 19(11), 643-54.
7. Formaggioni P, et al., (1999). Milk protein polymorphism: Detection and diffusion of the genetic variants in *Bos* genus. *Ann. Fac. Med. Vet. Univ. Parma.* XIX: 127-165.
8. Ng-Kwai-Hang K.F & Grosclaude F, (2002). Genetic polymorphism of milk proteins. In: Fox PFA, P.L.H editor. *Advanced Dairy Chemistry: Volume 1: Proteins, Parts A&B.* New York: Kluwer Academic/Plenum Publishers. p. 739-816.
9. Kaminski S, et al., (2007). Polymorphism of bovine beta-casein and its potential effect on human health. *J Appl Genet.* 48(3), 189-98.
10. Scientific Report of EFSA prepared by a DATEX Working Group on the potential health impact of β -casomorphins and related peptides. EFSA Scientific Report (2009). 231, 1-107 [cited Dec. 2014].
11. De Noni I, (2008). Release of β -casomorphins 5 and 7 during simulated gastro-intestinal digestion of bovine β -casein variants and milk-based infant formulas. *Food Chemistry.* 110(4), 897-903.
12. Jinsmaa Y & Yoshikawa M, (1999). Enzymatic release of neocasomorphin and beta-casomorphin from bovine beta-casein. *Peptides.* 20(8), 957-62.
13. Ul Haq M.R, et al., (2015). Release of beta-casomorphin-7/5 during simulated gastrointestinal digestion of milk beta-casein variants from Indian crossbred cattle (Karan Fries). *Food chemistry.* 168, 70-9. Epub 2014/08/31.
14. Hartwig, A., et al., (1997). Influence of genetic polymorphisms in bovine milk on the occurrence of bioactive peptides. Seminar on milk protein polymorphism (pp. 459-460). IDF Special Issue no. 9702. Brussels: International Dairy Federation.
15. Brantl V, et al., (1979). Novel opioid peptides derived from casein (beta-casomorphins). I. Isolation from bovine casein peptone. *Hoppe Seylers Z Physiol Chem.* 360(9), 1211-6.
16. Henschen A, et al., (1979). Novel opioid peptides derived from casein (beta-casomorphins). II. Structure of active components from bovine casein peptone. *Hoppe Seylers Z Physiol Chem.* 360(9), 1217-24.
17. Lottspeich F, et al., (1980). Novel opioid peptides derived from casein (beta-casomorphins). III. Synthetic peptides corresponding to components from bovine casein peptone. *Hoppe Seylers Z Physiol Chem.* 361(12), 1835-9.
18. Brantl V, et al., (1981). Opioid activities of beta-casomorphins. *Life Sci.* 28(17), 1903-9.
19. Pleuvry B.J, (1991). Opioid receptors and their ligands: natural and unnatural. *Br J Anaesth.* 66(3), 370-80.
20. De Noni I & Cattaneo S, (2010). Occurrence of beta-casomorphins 5 and 7 in commercial dairy products and in their digests following *in vitro* simulated gastro-intestinal digestion. *Food chemistry.* 119(2), 560-6.
21. Boutrou R, et al., (2013). Sequential release of milk protein-derived bioactive peptides in the jejunum in healthy humans. *Am J Clin Nutr.* 97(6), 1314-23.
22. Svedberg J, et al., (1985). Demonstration of beta-casomorphin immunoreactive materials in *in vitro* digests of bovine milk and in small intestine contents after bovine milk ingestion in adult humans. *Peptides.* 6(5), 825-30.
23. Barnett M.P, et al., (2014). Dietary A1 beta-casein affects gastrointestinal transit time, dipeptidyl peptidase-4 activity, and inflammatory status relative to A2 beta-casein in Wistar rats. *Int J Food Sci Nutr.* 65(6), 720-7.
24. Ul Haq M.R, et al., (2014). Comparative evaluation of cow β -casein variants (A1/A2) consumption on Th2-mediated inflammatory response in mouse gut. *Eur J Nutr.* 53(4), 1039-1049.
25. De Ponti F, et al., (1989). Effect of beta-casomorphins on intestinal propulsion in the guinea-pig colon. *J Pharm Pharmacol.* 41(5), 302-5.
26. Daniel H, et al., (1990). Effect of casein and beta-casomorphins on gastrointestinal motility in rats. *J Nutr.* 120(3), 252-7.
27. Schulte-Frohlinde E, et al., (1994). Effect of bovine beta-casomorphin-4-amide on gastrointestinal transit and pancreatic endocrine function in man In: Brantl V, Teschemacher H, eds. *Beta-Casomorphins and related peptides: recent developments.* New York VCH Weinheim; 155-60.
28. Kromer W, et al., (1980). Opioids modulate periodicity rather than efficacy of peristaltic waves in the guinea pig ileum *in vitro*. *Life Sci.* 26(22), 1857-65.
29. Ward S.J & Takemori A.E, (1983). Relative involvement of receptor subtypes in opioid-induced inhibition of gastrointestinal transit in mice. *J Pharmacol Exp Ther.* 224(2), 359-63.
30. Zoghbi S, et al., (2006). Beta-Casomorphin-7 regulates the secretion and expression of gastrointestinal mucins through a mu-opioid pathway. *Am J Physiol Gastrointest Liver Physiol.* 290(6), G1105-13.
31. Kost N.V, et al., (2009). Beta-casomorphins-7 in infants on different type of feeding and different levels of psychomotor development. *Peptides.* 30(10), 1854-60.
32. Wasilewska J, et al., (2011). The exogenous opioid peptides and DPPIV serum activity in infants with apnoea expressed as apparent life threatening events (ALTE). *Neuropeptides.* 45(3), 189-95.
33. Claustre J, et al., (2002). Effects of peptides derived from dietary proteins on mucus secretion in rat jejunum. *Am J Physiol Gastrointest Liver Physiol.* 283(3), G521-8.
34. Trompette A, et al., (2003). Milk bioactive peptides and betacasomorphins induce mucus release in rat jejunum. *J Nutr.* 133(11), 3499-503.

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