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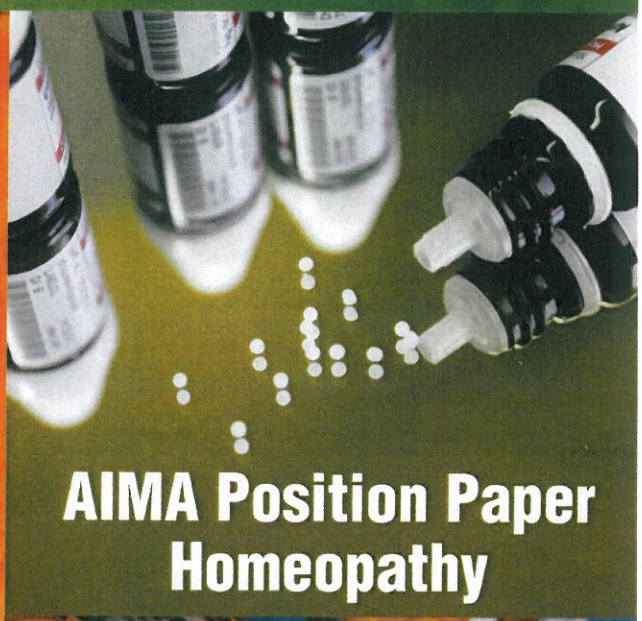
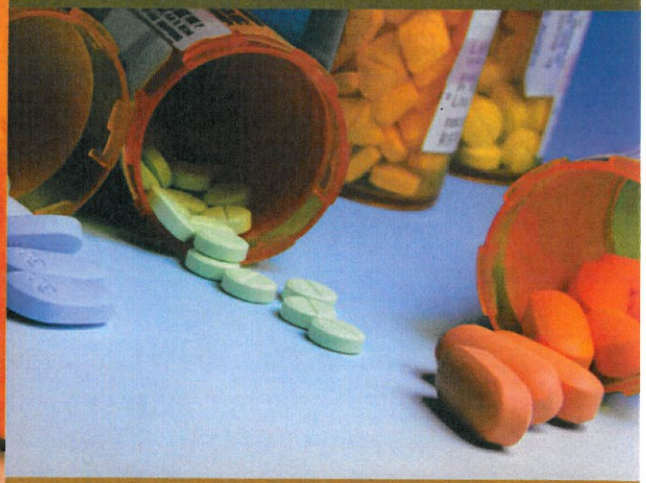
Mindful Art Therapy

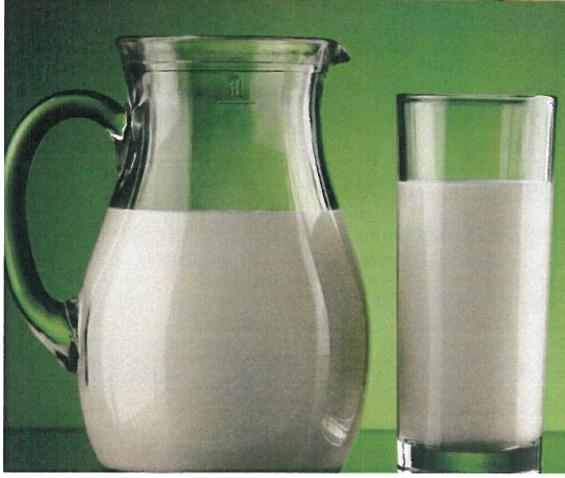


AIMA Position Paper Homeopathy



Integrative Pharmacology

***Hypericum perforatum* vs Fluoxetine Hydrochloride**



A1 Beta-Casein, BC-M7 & Human Health

Welcome to our July 2011 edition...

Once again, the ongoing debate between conventional and integrative medicine has reared its ugly head.

In response to the MJA's opinion piece as to whether it is "ethical" for medical practitioners to prescribe complementary or alternative therapies, Medical Observer recently conducted a snap poll regarding the same. With patients most definitely embracing CAM therapies, the results of this recent poll were also very encouraging, at least from an Integrative Medicine point of view, with 57% of responders stating that it was ethical compared with an archaic 43% who disagreed.

This reflects the results of a National Prescribing Survey (NPS) in late 2008 which indicated that approximately 30% of GPs in Australia describe themselves as actually practising IM, by combining orthodox with complementary medicine.

Indeed, it is great to see that Integrative Medicine in Australia is truly aligning with our international counterparts. AIMA has recently been invited to be a participating organisation in the 2012 International Research Congress on Integrative Medicine and Health to be held in Portland Oregon USA in May 2012.

AIMA has also recently endorsed letters to the Federal Government regarding the United Nations Mercury Treaty which is calling for a global phase-out of all mercury products including dental amalgams and mercury-based medical devices from the health care sectors around the world. Australia is unfortunately the only nation to request an exemption from the United Nations regarding mercury amalgams, despite a wealth of evidence demonstrating the toxic effects of mercury to the health of both humans and the environment alike. Please see AIMA's Position Statement on Mercury Amalgams on our website (www.aima.net.au) for more information.

As members of AIMA (and, indeed, the human race), we have a critical responsibility to protect the health of future generations. I invite all of you to stand tall and take pride in the work that you do, for together we *can* be the change we wish to see in the world.

Lily Tomas
Editor JIM
Vice President AIMA

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The Australasian Integrative Medicine Association (AIMA) is a national, voluntary non-profit organisation and is the peak medical body that promotes the safe integration of evidence based holistic and complementary medicine with current mainstream medical practice, in pursuit of complete whole person care.

See AIMA Membership form on page 32.

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A1 Beta-Casein, BCM7 and Human Health:

the state of evidence in 2011

by **Professor Keith Woodford**

Early papers implicating A1 beta-casein in human health, and specifically to Type 1 diabetes, were published in the late 1990s.[1,2] Well before that, there was widespread evidence that the peptide beta-casomorphin7 (BCM7) was an opioid of considerable strength[3-6] and of neurological significance.[7,8] It has also been known to animal geneticists for more than 20 years that the A1 variant of beta-casein is the consequence of a mutation some thousands of years ago.[9] Another group of scientists knew that, under the pH and enzymatic conditions of the human digestive system, BCM7 was released from A1 beta-casein but not A2 beta-casein.[10-12] However, these scientific groups did not in general read each others' literature, and so there were considerable delays in integrating the findings of the various groups. By 2006, when I was attempting to bring the existing knowledge together, I found more than 100 relevant peer-reviewed scientific and medical papers.[13] However, the literature is so diverse that in 2011 I now have a database approaching 500 papers of relevance.

A Systemic Approach

A systemic approach is fundamental to understanding health issues associated with A1 beta-casein and BCM7. The starting point is recognition that BCM7 is an opioid with a strong affinity for mu opioid receptors.[14-16] These receptors are found throughout the digestive system and internal organs including the brain.[16-19] This is because mu-opioid pathways are fundamental to many hormonal messaging systems. Accordingly, there should be nothing controversial about the notion that BCM7 will, like other opioids, act to slow peristaltic movement of food through the digestive tract, and that it will induce behavioural responses and respiratory depression if it can get through to the brain. Indeed casein has been associated with constipation for many years.[20-23] Similarly, there is ample evidence from animal studies that when animals are injected with BCM7 that this passes through to the brain and causes dramatic behavioural responses.[24-26]

The second fundamental point to understanding health issues associated with A1 beta-casein and BCM7 is the recognition that some of these health conditions are auto-immune. Consequently, individual susceptibility will be determined by genetic haplotypes and associated antibody and other immune mechanisms. Accordingly, specific auto-immune conditions usually affect only a small proportion of the population. In addition, for auto-immune conditions there are typically major delays between the time of exposure and the development of symptoms. Given these factors, human trials for auto-immune conditions are particularly challenging.

Absorption of BCM7

A key constraint to wider acceptance of the need to eliminate A1 beta-casein from milk has been the difficulty in demonstrating quantitatively that BCM7, once formed, does pass through into the circulatory system, and from there enters susceptible organs. It has been this difficulty that underpinned the finding of the European Food Safety Authority (EFSA) in January 2009 that there was no 'cause and effect' proof at that time that A1 beta-casein was a food safety issue.[27] In doing so, EFSA chose to place minimal weighting on extensive human epidemiological evidence and animal trials.

However, the EFSA report did acknowledge (p3) that BCM7 is released upon digestion of all bovine milk products containing A1 beta-casein. Subsequent research has confirmed that this includes fresh milk, cheese, ice-cream, yoghurt and infant formula.[11] At the time I wrote *Devil in the Milk*,[13] I left open the possibility that the release of BCM7 might be considerably less from cheese and other fermented products than from non-fermented products. However, this now seems less likely.[11]

Back in 2007 there was still considerable uncertainty as to whether some heat treatments of milk increased the release of BCM7. De Noni (2008) has produced theoretical evidence as to why this is unlikely, and has reinforced this

with empirical data[10,11] Nevertheless, there remains a strong health lobby for unpasteurised milk in some countries, and there are unanswered questions as to whether some heat treatments may impact on BCM7 glycation.

A key area where research has advanced since the EFSA review is in relation to absorption of BCM7 from the alimentary to the circulatory systems. The theoretical logic against this had been based on the supposed inability of BCM7 (and other peptides) to pass through the tight junctions within the epithelial layer lining the gut. This ignored the evidence that in some adults, tight junctions may be dysfunctional for a range of reasons, both genetic and environmental, and hence they have a 'leaky gut'.[28-31] Although evidence for leaky gut is overwhelming, awareness remains limited amongst many health professionals. The argument against BCM7 absorption also ignored that all babies have permeable intestines up to at least one year of age as a normal physiological condition.

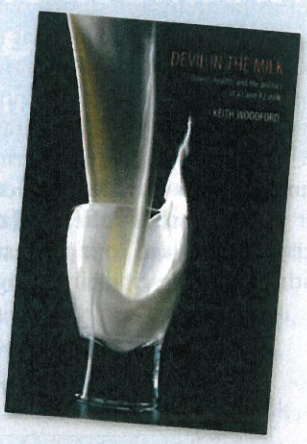
The second pillar of the EFSA argument was that BCM7, if it does enter the circulatory system, will have only a short half life on account of the presence within the circulatory system and many organs of the enzyme dipeptidyl peptidase IV (DPP IV; EC 3.4.14.5; CD26). DPPIV is the only known enzyme that degrades proline-rich peptides such as BCM7.[32,33] However, there is now evidence showing that some babies and children may be naturally low in DPP4.[34,35] In addition, the gliptin drugs which are increasingly being used to treat Type 2 diabetes do so specifically by DPP4 inhibition.[36,37] Both of these new pieces of evidence reinforce the notion that susceptibility to BCM7 will vary between individuals.

The reason the debate about BCM7 absorption has lasted so long relates to the complexity of measuring BCM7 within the blood. However, there are now both commercial ELISA kits and complementary HPLC/MS methods that are available as research tools. At least three research groups have identified BCM7 immuno-reactive materials in babies fed formula, and in each case have linked this to paediatric health issues. However, the fact that this new research has come out of Russia, Poland and the Czech Republic has allowed Western health organisations to remain sceptical. Confirmatory evidence from North America, Britain or Australia is now needed to remove that scepticism. There is also a need to extend the testing of BCM7 to adults, for which there are no published results. Absorption in adults is most likely to be found in people with specific haplopypes that predispose to leaky guts (i.e. those of particular susceptibility to auto-immune conditions), or in people who have environmentally induced or disease mediated inflammation of the intestines.

Paediatric issues

Within the last four years it is in the field of paediatrics that most progress in relation to A1 and BCM7 has occurred. Russian researchers have shown not only that babies fed >>

Devil in the Milk: Illness, Health and the Politics of A1 and A2 Milk [Paperback] Keith Woodford (Author), Tom Cowan (Foreword)



"Highly recommended, this book is academic yet conversational and gossipy at the same time. It's subjective writing on objective facts. It's timely and definitely connected to contemporary issues such as health care, pharmaceutical dishonesty, and the guiling and beguiling use of media sound bytes. For academic reading, *Devil in the Milk* is pretty accessible. It's an informational look into the puzzling nature of studies. The author's successful attempt to bare all – about himself and about the industry he's involved in – is quirky at times but definitely believable. And the book leaves one feeling angry, informed and empowered, which is always a good thing – and which a good health book should always do."

Available from http://www.craigpotton.co.nz/products/published/books/bookwine/devilinthemilk

A1 Beta–Casein, BCM7 and Human Health: the state of evidence in 2011

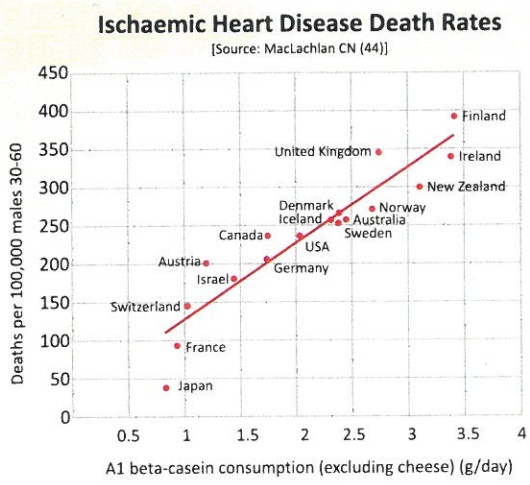
formula containing A1 beta-casein have measurable levels of BCM in the blood, but that there is a tail of slow psychomotor developers within this group which correlates with slow catabolism of BCM7 within the blood.[38]

Polish researchers have shown that babies who have near-death experiences from respiratory depression are characterised by high levels of BCM7 in the blood and correspondingly low levels of DPP4.[35] This group of researchers have also found that bovine BCM7 is in the blood of babies who are exclusively fed human milk, implying that bovine BCM7 from milk drunk by the mother passes into her own milk.

Other Polish research[39] has shown that BCM5, which is a derivative of BCM7 and apparently an even stronger opioid than BCM7,[3] is found in the blood of breast-fed babies in situations where the mother has been drinking bovine milk. A group from the Czech Republic has shown that babies fed formula but not breast-fed have high antibodies to oxidised LDL indicating oxidative stress and that these antibodies bind preferentially to A1 beta-casein and BCM7.[40,41]

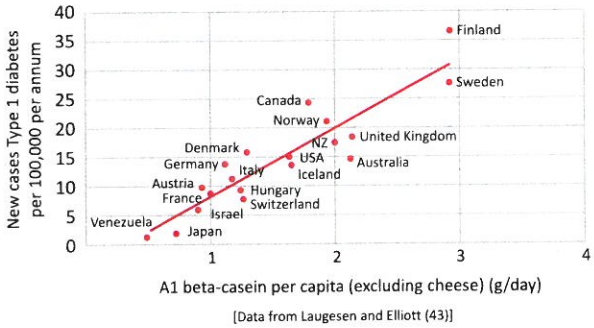
Heart disease

The major recent advance implicating A1 beta-casein and BCM7 in relation to heart disease has been evidence that formula-fed babies have high serum levels of antibodies to oxidised LDL and that these antibodies have high affinity to A1 beta-casein and BCM7 relative to A2 beta-casein and maternal milk.[40,41] Also, in piglets, a direct trial comparison has shown a statistically significant 'cause and effect' relationship between A1 beta-casein intake and oxidised LDL antibodies.[42] The importance of this is not necessarily to babies who may well outgrow the oxidative stress as tight junctions develop. Rather, it is important as a model of what might happen in adults with 'leaky gut' syndrome, and as an indicator of arterial plaque. This new evidence supports earlier evidence that the incidence of heart disease mortality in countries within the developed world correlates remarkably with A1 beta-casein intake.[43,44] Previous evidence includes a 'cause and effect' relationship in rabbits between A1 beta-casein intake and formation of arterial plaque.[45] In humans, it has long been recognised that high milk diets for stomach ulcer sufferers (a potential cause of stomach permeability) lead to high death rates from heart disease,[46] with A1 beta-casein being a logical causal candidate.



Type 1 diabetes

Evidence linking A1 beta-casein to Type 1 (insulin-dependent) diabetes has not advanced greatly in the last few years. The starting point is still the major differences in Type 1 diabetes (IDDM) incidence between individual countries within the developed world (i.e. countries with similar lifestyles). These differences correlate remarkably with A1 beta-casein intake of these populations[43] and alternative hypotheses are unable to explain this. Supportive evidence comes from animal trials,[2,47] evidence linking IDDM to milk exposure in general (47-49) and A1 beta-casein in particular[50,51] and high antibodies to A1 beta-casein relative to A2 beta-casein antibodies.[51] The increasing incidence of Type 1 diabetes over time is likely to be a function of issues affecting gut permeability or antigenic susceptibility (viruses, antibiotics, hygiene factor, Vitamin D etc.) rather than the quantity of A1 beta-casein *per se*. Pilot study results from the international double blind clinical TRIGR trial are providing supportive evidence for the implication of milk proteins in relation to Type 1 diabetes,[52] but results from the main trial will not be available until 2017. Even then, the trial design is not specific to A1 versus A2 beta-casein.



Type 2 diabetes

There is no direct trial evidence linking A1 beta-casein or BCM7 to Type 2 diabetes. However the gliptins that are increasingly being used to control insulin levels in sufferers of Type 2 diabetes act by inhibition of the enzyme DPPIV.[53] It is therefore logical to assume that the ability to catabolise BCM7 will similarly be inhibited, given that DPPIV is the only known enzyme which metabolises BCM7, with implications for heart disease for those with 'leaky gut' syndrome. However, the clinical trials of gliptins have not evaluated long term development of plaque (54).

Autism

There is increasing understanding of how BCM7 may lead not only to symptoms of autism but also to fundamental abnormal neurological development linked to the seratoninergic system.[38,55] There is also increasing evidence that many autistic children suffer from digestive complaints which may make them susceptible to BCM7 absorption.[56] However, the hypotheses linking autism with BCM7 remain controversial. Earlier trials with animals have shown that BCM7 crosses the blood-brain barrier and leads to autistic type behaviour.[26] Milk elimination trials in humans have produced positive results[57,58] but are often criticised for lack of double blind protocols.

Milk Intolerance Issues

Evidence for milk A1 beta-casein intolerance is observational and empirical, but still lacks rigorous scientific testing. Nevertheless, it is largely A1 beta-casein intolerance issues that have driven the Australian commercial success of the alternative a2 milk over the last four years. This might seem surprising given the conventional perspective that milk intolerance is generally caused by lactase deficiency. However, there are two likely explanations. The first is that the BCM7, in slowing down passage of food through the digestive system (as do pharmaceutical opioids[17,59]), is providing longer time for lactose fermentation to occur. Given that lactose fermentation is an exponential process, a modest slowing down could lead to major production of gas and other fermentation products. The second likely explanation is that some people are intolerant specifically to BCM7.[60-63] A simple test to investigate whether someone who is intolerant to 'ordinary' cows' milk will be able to drink 'a2 milk' is to ask them whether they can tolerate goats' milk. If the answer is 'yes' then my experience is that they can also tolerate a2 milk.

Mild Allergies

Anecdotal and observational evidence continues to build that some allergies presenting as asthma and eczema are linked to A1 beta-casein. Unlike intolerances, these allergies are immune conditions. BCM7 is also known to stimulate production of mucins which are the sticky proteins in mucus.[16,60,63]

The Path Ahead

There will always be difficulties in 'proving' with double blind clinical trials that A1 beta-casein causes illness. This is because of the complexity created by genetic susceptibility, long pre-clinical stages, and human ethics issues with clinical testing. However, if clinical trials were the only way forward, then we would still be debating whether smoking causes cancer and heart disease. The wide ranging evidence in relation to A1 beta-casein and BCM7 starts with fundamental science, is supported by animal trials, and is strongly reinforced by wide ranging epidemiology. The key requirement to reduce ongoing scepticism about BCM7 is the confirmatory evidence from North American, Western European or Australian research groups that BCM7 is indeed present in the circulatory system of various sub groups within the population. With that evidence available, the issue should be resolved. ●

Keith Woodford is Professor of Farm Management and Agribusiness at Lincoln University, NZ. His interest in the A2 milk issue spans the value chain from human nutrition and health to dairy production. His book 'Devil in the Milk', which presents the health and politics of A1 beta-casein, was published by Craig Potton Publishing in 2007, with an American edition published by Chelsea Green in 2009, and an updated NZ/Australian Edition in 2010.

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Integrating Complementary and Mainstream Medicine

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