

Soy Information Network

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SIN Newsletter # 2

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EDITORIAL

By Dave Woodhams, editor

The main action since the issue of the first SIN Newsletter in early November last year was the holding of the Third International Conference on Phytoestrogens in Little Rock, Arkansas, in the first week of December. In this issue we bring you information on the conference and some of the issues raised plus comments from one of the scientists who was there. [See "THE LITTLE ROCK CONFERENCE"]. Prof Cliff Irvine, who presented the NZ information and concerns at the Conference, also provides some background on the recent upsurge of interest in phytoestrogens. [See "PHYTOESTROGENS AND HUMANS"]

We also outline some of the extraordinary actions of soy industry people in their attempts to prevent the New Zealand information from reaching the Conference, and thereby the scientific community. [See "GAG THE MESSENGER"]

A number of the soy industry's more persistent lies and misleading statements are now being exposed. For instance, the issue of the relative strengths of the soy phytoestrogen, genistein, and the natural human estrogen, estradiol, has been resolved. [See "HOW WEAK IS WEAK?"]. Another issue laid to rest is the phytoestrogen content of human breast milk from mothers who are high soy consumers. [See "SOY BOYS GET IT WRONG AGAIN"]

HOW WEAK IS WEAK?

by Dave Woodhams

Soy industry representatives have for many months been trying to convince the Ministry of Health, the public and others that soy phytoestrogens are safe because they are so weak and have stated on numerous occasions that genistein is 10,000 times weaker than the normal human estrogen estradiol. The Ministry of Health's latest official statement [Prescriber Update, October 1995] says that the relative estrogenicity of the soy isoflavones relative to estradiol is disputed but is generally accepted as being somewhere between 1/1000 and 1/10,000 times as potent. The figure we have used consistently is 1/1200, derived from the estrogenic effects reported in 1993 by

Markiewicz and others. This is consistent with the findings in a number of research reports.

The first time the figure of 1/10,000 appeared was in an assessment of the Fitzpatrick report made by a Mr Anthony Hugget, a scientist at Nestlé's Research Centre in Lausanne, Switzerland. In this report he made reference to the same 1993 scientific report by Markiewicz as Dr Fitzpatrick did. Hugget had made a calculation error, misplacing the decimal point. Dr Fitzpatrick pointed this out to him during a visit to the Centre in September 1994 and even went through the calculation with him on a calculator to demonstrate the point.

However, the same 1/10,000 figure appeared in soy industry communications several times over the next few months, the most significant being in a report dated 14 December 1994 sent to the Ministry of Health by the World Health Organisation in Geneva. In a covering letter WHO explained that as they didn't have any information of direct relevance to the Ministry's specific questions, they had referred the query to the Nestlé Research Centre which, they understood, had specialist knowledge in this regard. Mr Anthony Hugget was kind enough to provide four pages of information which the WHO was pleased to share with the Ministry.

As the date of this report is well after Mike Fitzpatrick's September visit, the retention of the 1/10,000 figure would appear to be either a deliberate attempt to deceive or else gross negligence. It is interesting to note that neither Nestlé's nor WHO drew the Ministry's attention to the fact that Nestlé's, as a manufacturer of soy infant formula which they sell in a number of third world countries, had a vested interest.

More was to come, however. In their statement of 7 December 1994, prepared for the Ministry of Health, Wyeth-Ayerst, manufacturers of Infasoy, state that the soy phytoestrogens "exhibit very weak biological activity; 1/1000 - 1/100,000 that of estradiol". Unfortunately they did not provide the Ministry with the page that contained the references to the two papers cited in support of these figures.

In a press statement dated 22 December 1994, Sanitarium's nutritionist, K. Lindbeck, says that "...isoflavones have a potency of about 1/100,000 that of estrogen hormones", without defining which "estrogen hormones" he was referring to. The figure is correct for a comparison with the synthetic estrogen diethylstilbestrol, DES, but incorrect for a comparison with the natural estrogen estradiol. As infant formula is supposed to simulate human milk, a comparison with estradiol would have been more honest.

Even more interesting is the "Technical Brief" sent to the Ministry by Columbit [New Zealand] Ltd, the leading supplier of soy protein isolate [the product used in infant

formula] in New Zealand on 26 January 1995. This technical brief was provided originally by Protein Technologies International of St Louis, Missouri, who supply the product sold by Columbit. In this document PTI state that the soy phytoestrogens "exhibit very weak biological activity; 1/1000 to 1/1,000,000 of the activity of estradiol", referring to two scientific papers in support of these figures. One of these two papers was written by a Dr Farmakalidis. When I checked on this work I found that Dr Farmakalidis had compared genistein [the soy phytoestrogen] not with estradiol, as claimed by PTI, but with the synthetic estrogen diethylstilbestrol, DES, which is known to be 100,000 times stronger than genistein. The second paper referred to was a review written by Dr Mark Messina, the soy expert brought to New Zealand by Wyeth-Ayerst last August to bury those of us who dared to question the safety of soy infant formula. In his review Messina says that genistein exerts "an estrogenic effect ranging from approximately 1×10^{-3} to 1×10^{-5} that of diethylstilbestrol [DES] or estradiol". He refers to a number of reports, including that of Farmakalidis, to support this statement. Now " 1×10^{-3} to 1×10^{-5} " is the same as saying "1/1000 to 1/100,000". But comparing the strength of something to two substances that themselves differ in strength by a factor of 100 is nonsense. As I wrote to the Assistant Director General of Health last June, Dr Messina's statement is the same as saying that "a rat is 1/1000 to 1/100,000 times the size of an elephant or a man". How PTI managed to turn Messina's already nonsensical 1/100,000 into 1/1,000,000 is not clear but it is not supported by either of the referenced reports.

At the Little Rock Conference the matter was resolved without argument. It was universally accepted that the strength ratio was about 1/1000 to 1/1200, as we have consistently maintained. Even strong soy supporters, like Dr Steve Barnes [Univ of Alabama at Birmingham], accepted that figure.

But the story doesn't quite end there. Work at the University of Missouri-Columbia, reported to the Conference by Dr Wade Welshons, indicated that the effective strength of natural estradiol in the body is influenced by the degree to which it is bound by "serum binding proteins". In the pregnant female rat and in the foetus more than 99% of the natural estradiol may be bound by these substances, thus protecting the foetus from the sea of estrogens it is swimming in. Welshons produced evidence that some phytoestrogens may not be bound in the same way and developed an assay that showed that the strength of genistein relative to estradiol was enhanced approximately 10-fold when it was in the presence of adult male serum. He went on to suggest that this enhanced strength could be 100- to 1000-fold in foetal serum. This suggests that in the body during pregnancy the relative strength of genistein could be between 1 and 1/10 that of estradiol, a very far cry indeed from the 1/10,000, 1/100,000 and

1/1,000,000 figures variously advised by soy interests. Until this latest research is replicated elsewhere, however, we will be happy to use 1/1200.

Because our argument relies on the measured effects of the soy phytoestrogens in humans, [see Newsletter #1] the relative strengths of genistein and estradiol are of only minor concern to us. However, because soy interests have tried to use them to discredit us, we have had to take an interest. We have found that soy supporters have been very keen to give people their interpretation of the relative strength of the soy phytoestrogens, as illustrated above, but fail completely to discuss the relative quantities in soy foods. As an example, they have made much of the fact that breast milk contains natural estrogens and have extrapolated from that to assume that soy phytoestrogens are safe, because they are so weak. However, we have been able to show, and have advised the Ministry of Health, that the effective strength of the estradiol in human breast milk, one week after birth, is about 1% of that of the genistein in soy formula, in spite of the estradiol being 1200 times stronger than genistein. Why should this be? Because there is about 130,000 times more of the soy isoflavones in soy infant formula than there is estradiol in human breast milk.

SOY BOYS GET IT WRONG AGAIN

by Dave Woodhams

“Japanese women eat a lot of soy products. Obviously, they must have a lot of soy phytoestrogens in their breast milk. Thus, if there were any problems arising from soy phytoestrogens in infants, we would see it in Japanese babies. Because we don’t see any problems in Japanese children there are no problems with soy formula.”

So runs one of the main arguments used by soy advocates to ridicule the concerns we took to the Ministry of Health in November 1994. Dr Mark Messina, US Co-editor of “Soy Connection” and co-author of the book “The Simple Soybean and Your Health”, used this argument three times in the course of an interview with Kim Hill on National Radio, on 21 Dec 94. It has been used many times since.

However, as I pointed out to the Ministry on 31 December 1994, nobody had reported any measurements of the soy isoflavones in breast milk from women on high soy diets although the levels of genistein in the blood serum of such women has been measured and reported. We calculated that the concentration of soy isoflavones in soy infant formula is about 35 times higher than the concentration in the blood serum of women on a high soy diet. We argued theoretically that the level in breast milk would be no higher than that in the blood serum.

This was one of the issues that did not get an airing during discussion at the NZ Nutrition Society's Phytoestrogen Symposium. However, when I presented it privately to Dr Ken Setchell, the keynote speaker at the Symposium, he suggested that it might be possible for the concentration in breast milk to be higher than in the blood serum and said that he would be measuring it before the Little Rock Conference.

In the event, three different researchers measured soy isoflavones in the breast milk of humans on and off a soy diet and reported their results in Little Rock. Their findings? Dr Franke initially stated that the phytoestrogen levels in breast milk were equivalent to those in soy infant formula but his method of analysis was strongly criticised by Setchell and his extrapolation of the measured data was also suspect. Prof Cliff Irvine presented the results of the analyses of breast milk obtained by Dr Mike Fitzpatrick from a number of New Zealand women, including some on a soy diet. Mike had found that the levels of soy phytoestrogens in the breast milk of women on a soy diet were insignificant, bordering on the lower limit of the ability of his method [GC/MS] to detect. Setchell, reporting his results said, "My results concur with those of Dr Irvine. I have to agree with him. The levels of phytoestrogens in soy formula are many times higher than in the breast milk of high soy consumers."

THE LITTLE ROCK CONFERENCE

by Prof Cliff Irvine

My initial impression of the delegates at the "ice-breaker" was that they regarded the NZ position as extreme and irrational. When we gave them the evidence for our position the hostility decreased and we wound up having a reasonable dialogue. Mike Fitzpatrick did a great job on our image and my talk was an unbiased report on our experiments and their logical interpretation.

It seems certain that NZ has provided the impetus for research into soy in infants which, in my view, is certain to keep going until some of the issues are resolved. [Which is really all that we want.] Nothing that was said at the Conference caused me to be any happier about soy for infants but now we need the proof. Considering the difficulties of doing experiments on infants, this will be hard to get.

At the Conference the 80 delegates were addressed by speakers from USA, Sweden, Finland and New Zealand. Attendance at the three conferences to date were 1990: 9; 1993: 40; 1995: 80. The intensity of the debate and the quality of the research presented suggested that the delegates knew they were dealing with some serious and important issues.

At the conference there was a session on methods of measurement of phytoestrogens which brought out some differences between Dr Ken Setchell and Dr Adrian Franke. I don't know who won because I am not an expert in that area. *[Editor's note for the scientists: Franke was advocating HPLC because, without derivatisation, it allows the measurement of a variety of isoflavonoids, including aglycones and conjugated analytes in one run. Setchell uses GC/MS and, as I understand it, challenged Franke over the detection limits of his method, which he considered to be too high to be useful.]*

The second morning was a love affair with the bean, especially from Steve Barnes who believes it cures or prevents nearly all the serious diseases of mankind - heart disease by lowering cholesterol, kidney disease, autoimmune diseases by being an immunosuppressant, cancer of many types, inflammatory processes and so on. I do think that soy does have some very useful health properties in adults but that doesn't mean that it can't be harmful to infants - in fact quite the reverse. Anything that can have such effects on a mature adult is likely to have much stronger, and often deleterious, effects on the newborn who is much more susceptible. For instance, reining in a hyperimmune response in an adult can be very advantageous because so many diseases are caused by autoimmunity or hyperimmunity. However, suppressing an immune response in a neonate can suppress its defences against important invaders, with serious consequences.

[MORE TO COME ON LATER STAGES OF THE CONFERENCE]

PHYTOESTROGENS AND HUMANS

by Prof Cliff Irvine

What is the reason for the upsurge in interest in phytoestrogens?

Firstly, what are phytoestrogens? Phytoestrogens are defined as substances of plant origin [hence the 'phyto-'] which cause effects like those of the body's natural oestrogens. Oestrogens are sex steroid hormones produced by the ovary which cause the female of many mammalian species [although not the higher primates, including women] to become sexually receptive during a fairly brief period known as 'oestrus'. Also, in all species, oestrogens cause marked changes in the mammary gland, cervix and uterus.

The primary reason for the upsurge of interest in phytoestrogens is the observation that people living in countries in which the consumption of soy products is high, Japan, for instance, have a reduced incidence of hormone-dependent cancers. These include cancers of the prostate, cervix and mammary gland or breast. Experiments with rats

show that a high intake of soy phytoestrogens, especially the isoflavone, genistein, increases their resistance to several cancer-producing substances. The evidence for a beneficial response to tumor development is increasing rapidly. As well, there is increased enthusiasm for the use of soy phytoestrogens as an alternative to hormone replacement therapy [HRT] in post-menopausal women.

It appears contradictory that increasing the consumption of soy phytoestrogens increases oestrogen availability for post-menopausal women, yet decreases oestrogen availability for pre-menopausal women, thus reducing the development of tumours that require oestrogen. The explanation may be that both phytoestrogens and the body's own oestrogens bind to a molecule found in many body tissues called an 'oestrogen receptor'. Binding to the receptor initiates all the actions induced by oestrogens. However, although phytoestrogens occupy the receptor adequately, they are much less potent in stimulating the receptor's activity. If there is no natural oestrogen available, as in post-menopausal women, phytoestrogen can partly make up for the deficiency and relieve the symptoms. On the other hand, if levels of natural estrogen are high, as in oestrogen-dependent cancers, large doses of phytoestrogens can displace the more potent natural oestrogens from the receptors, thus reducing their effectiveness. Thus phytoestrogens can act as either oestrogens or anti-oestrogens.

Now, although a reduction of sex steroid levels induced by phytoestrogens may have some beneficial aspects for mature women, in infant monkeys a decline in the level of sex steroids causes some very undesirable effects at and after puberty. Normally there is a burst of secretion of sex steroids in the first few months after birth. If this does not occur, physical and mental deficits occur at puberty. Investigations in which sex steroids are lowered experimentally cannot be done ethically in humans; however conditions in which there is a natural deficiency of male sex hormones in baby boys are associated with physical and mental deficits at puberty, just as in monkeys. Also, if the sex hormone deficiency is corrected for a brief period in the young infant, post-pubertal development is normal. There is a critical period during which sex steroids have to be high, at least in the male, otherwise the pubertal surge of growth and development is reduced. There are many experiments in animals which show that soy phytoestrogens in the newborn can inhibit sex hormone production and eventual post-pubertal development.

It is only in the last year or two that these very important actions of phytoestrogens have become established by experiments on several species. However there are still large gaps in our knowledge of the relevance of this to human health. This was reflected in the vigorous debate which occurred during question time and at meal breaks at the Little Rock Conference.

Apart from its actions on the reproductive hormones, genistein, which is in high concentration in soy, has a wide range of actions from immunosuppression to slowing down the breakdown of acetaldehyde [and thus increasing both the duration and the intensity of a hangover!] Speaker after speaker at Little Rock dealt with various aspects of the benefits and the drawbacks of soy. It emerged that, provided soy is properly processed, the benefits may outweigh the drawbacks for adults. Genistein does have the capability of inhibiting many important processes in young infants but whether it exerts that capability, at what age, and how it may be circumvented are important subjects for future research.

At present I have ceased, or at least suspended, my research programme in reproductive endocrinology which has been my major interest for many years. I would not have done that unless I thought that the soy infant formula subject was of major importance. After hearing both sides of the story from experts I have no regrets that all my spare time has been taken over by soy.

GAG THE MESSENGER

by Dave Woodhams

Pressure by the soy industry has resulted in Dr Mike Fitzpatrick's being forbidden to speak or write publicly in the soy debate on pain of instant dismissal from his job with Grayson Laboratories. He was prevented from presenting the invited scientific paper "The Phytoestrogen Content of Soy-based Infant Foods" at the Little Rock Conference and strenuous [but unsuccessful] attempts were made to prevent him from even attending the Conference. He was not permitted to ask questions in the open sessions. He was forbidden to speak to the press on his return.

The news that Dr Mike Fitzpatrick had been invited to present a paper on phytoestrogens in soy infant formula at the Third International Conference on Phytoestrogens at Little Rock, Arkansas, broke in mid-August last year, with the publication of the proposed programme. This announcement, together with the publicity generated by the NZ Nutrition Society's Symposium a week or so later, initiated a series of actions designed to prevent him from attending the conference.

In the United States, a staff member of the United Soybean Board in Washington DC phoned the Conference Chairman in Jefferson, Arkansas. She advised that the industry was concerned about who he had invited to speak at the Conference. They were concerned that Dr Fitzpatrick was going to speak. They wanted the invitation withdrawn or else they wanted an invited slot to rebut his arguments. She was informed that the soy industry could not dictate who should speak and who should not speak at a

USFDA -sponsored international conference. This phone call was repeated virtually every day, sometimes twice a day, throughout September, October and November.

Meanwhile, back in Auckland, the local soy cavalry was also getting into action. One of the first things to happen was that Mike was advised by Mr Bruce Kirk, the manager of Columbit [New Zealand] Ltd, an importer of soy protein isolate, that if he was intending to go to the Conference he should be sure to wear body armour. Now no doubt this comment was made tongue-in-cheek, but there was no doubt in Mike's mind that it was said with the intent to dissuade him from going there. Then Mr Trevor Johnston, owner and marketing manager of Bean Supreme, a local manufacturer of largely traditional soy products, made a complaint to Mr Bill Grayson, managing director of Grayson Laboratories, about Mike's appearance on Jenny Anderson's Radio Pacific talkback show on 31 August and specifically the linking of Grayson's name with Mike's involvement in the soy debate. His complaint was accompanied by a transcript of the show with various comments highlighted. [The points highlighted seemed mostly to be those where, being honest with the audience, we were pointing out our assumptions or where we were drawing a parallel that was not necessarily scientifically proven.] The transcript of Mike's comments show that, as a result of the work he had done for the James as an independent consultant, he had reached personal conclusions. Because there are no actual data on human infants, one way or the other, Mike made it clear that he assessed the risks as a father of small children, not specifically as a scientist. As a result of that assessment he said he would not feed soy infant formula to his own child.

During September Nestlé's must have become involved in bringing pressure to bear on Bill Grayson because on 4 October Mike was formally instructed, in person and in writing, to cease all communication with the media on soy matters.

"As this matter has now escalated to involve one of our most prestigious clients, Nestlé's, I must warn you that should you choose to disobey this instruction I would have little choice but to dismiss you over such misconduct."

The content of the letter makes it clear that the Company feared being sued for libel or slander. However, in a later letter to the James Bill Grayson says:

"You assume that Nestlé's have applied pressure to us over this matter. Nothing could be further from the truth. We have had no communication of any kind from Nestlé's on this subject." [13 Oct 95]

It was made clear to Mike that the prohibition included the actual presentation of the paper in Little Rock or his being named as an author. However, he still had leave of

absence for the period of the Conference. At that time the decision was taken that Prof Cliff Irvine would write and present the paper at the Conference.

It is clear that the two “anti-Mike Fitzpatrick campaigns in US and NZ were related because, almost immediately after Mike was forbidden to present the paper, back in the U.S.A. the Conference Chairman received a slightly different phone call from the United Soybean Board. They were so disappointed that Dr Fitzpatrick would not be coming to the conference. They were really heartbroken. What a shame he would not be there.

“Well hold on a minute. Who said he was not coming to the Conference? He’s coming but he isn’t actually presenting the paper.”

“What do you mean he’s still coming to the Conference. That is very disconcerting. We don’t think he should be able to attend” [or words to that effect].

Meanwhile, down under in NZ the pressure continued. On the Wednesday before his Saturday departure for Little Rock, Mike was called into Bill Grayson’s office and told he was not permitted to attend the Conference, on pain of dismissal. After getting legal advice Mike decided to go anyway. He wasn’t fired! It is interesting, however, that the announcement in the NZ Herald that Cliff and Mike were leaving to attend the Little Rock Conference initiated another spate of phone calls to Bill Grayson complaining that this fact was reported!

Such behaviour by the soy proponents is somewhat familiar. After being advised by the Ministry of Health that the Northern Advocate was planning to print an article in December 1994, a prominent soy importer made 11 phone calls to the reporters and the editor in the course of two days. While it was never said, the staff were convinced the paper would be sued if they published the story. It wasn’t.

The editor of the NZ Herald has come under increasing pressure from Mr Trevor Johnston of Bean Supreme to stop publication of further articles by Camille Guy.

As of 1 February Mike Fitzpatrick’s situation has changed. He has resigned from Grayson’s and will take up a position in the Chemistry Department of Auckland University in time for the new Term.

SOY-FREE, LACTOSE-FREE INFANT FORMULA ALTERNATIVE:

Bristol-Myers Company announced in November the release in NZ of a soy-free, lactose-free, dairy-based infant formula, O-Lac, for babies with lactose intolerance. In a press release they quite properly advised that if infants are being fed soy formula under medical advice then the child's doctor should be consulted before changing formula as O-Lac is not suitable for infants with an allergy to cows milk protein. However, where infants are being "fed soy because of personal preference of their parents [they] can be switched from soy formulas without increased risk".

We also suggest that mothers read again the comments on lactose intolerance in SIN Newsletter #1, page 6. Primary [ie permanent] lactose intolerance is very rare in infants and secondary lactose intolerance, after a gastric infection, tends to revert to normal tolerance after a few days.

SUPPORT GROUPS:

If mothers of children who may have been adversely affected by soy formula or other soy products would like to contact other mothers in their area who have similar problems, please write to the Soy Information Network and we will provide your name and phone number to a group near you if one exists.

DONATIONS:

If you would like to support the work of the Soy Information Network you may send cheques to us at SIN, C/- Dr DJ Woodhams, Whatarangi Road, R D 2, Featherston 5952, New Zealand.

ENCLOSURES:

We are enclosing a copy of the most recent article from the NZ Herald, written by Camille Guy, which covers the Little Rock Conference and current research directions.

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