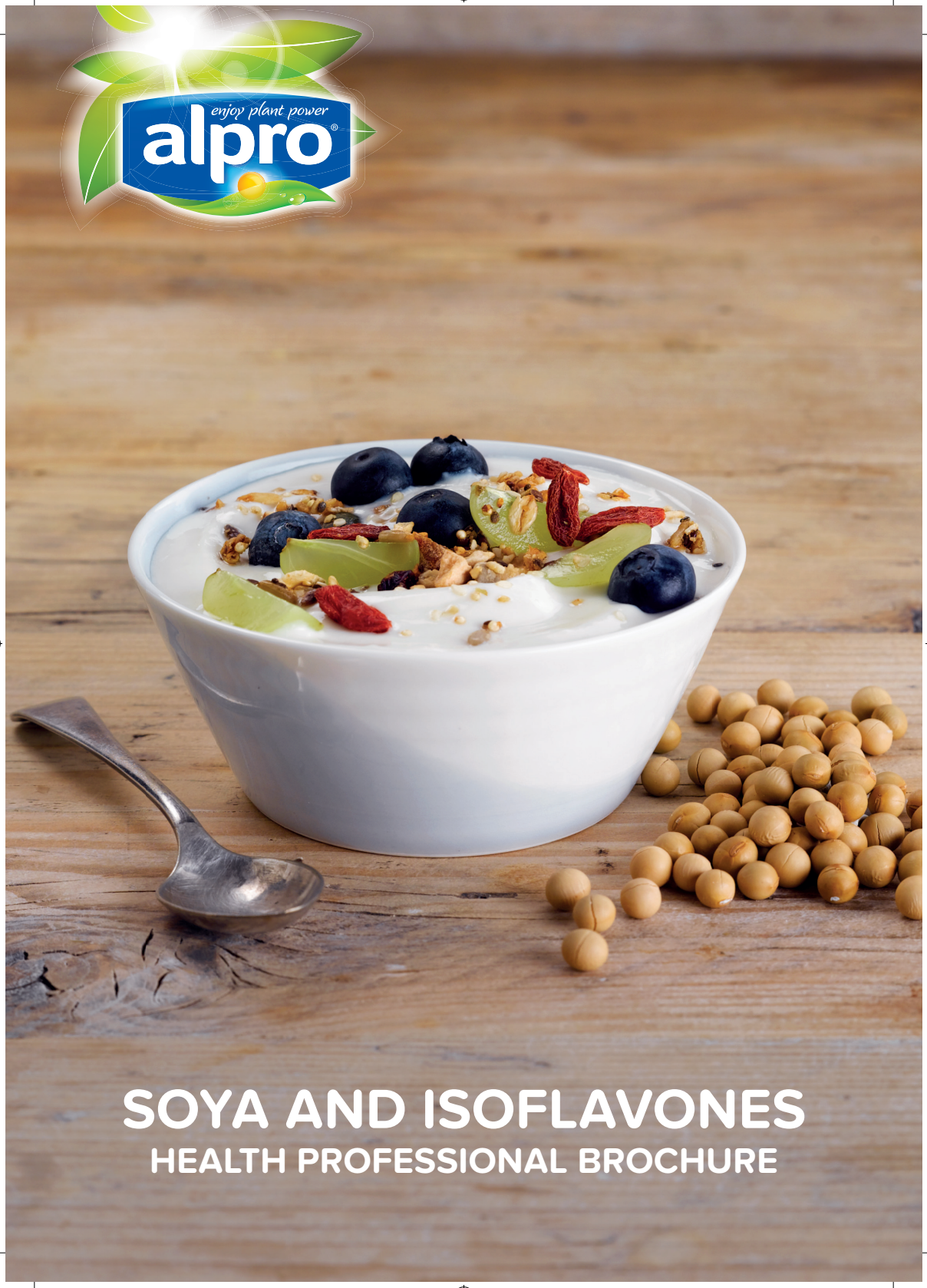


SOYA AND ISOFLAVONES

HEALTH PROFESSIONAL BROCHURE

ISOFLAVONES – A TYPE OF POLYPHENOL

Isoflavones, particularly found in soya, are the subject of much discussion. Some say they are good for our health, yet others claim they could be harmful.

To put an end to this confusion, we have reviewed the evidence and here we present the facts on soya and isoflavones.

Isoflavones are natural plant compounds belonging to the polyphenol family.

Plants develop these polyphenols to protect themselves from UV radiation, bacteria, fungi and other damaging micro-organisms. Research is suggesting these plant compounds may also be beneficial for our health. For example, polyphenols have been shown to have antioxidant properties which help protect cells against free radical damage. Chronic inflammation and a number of age-related diseases have been linked with free radical damage.

Isoflavones: natural plant compounds

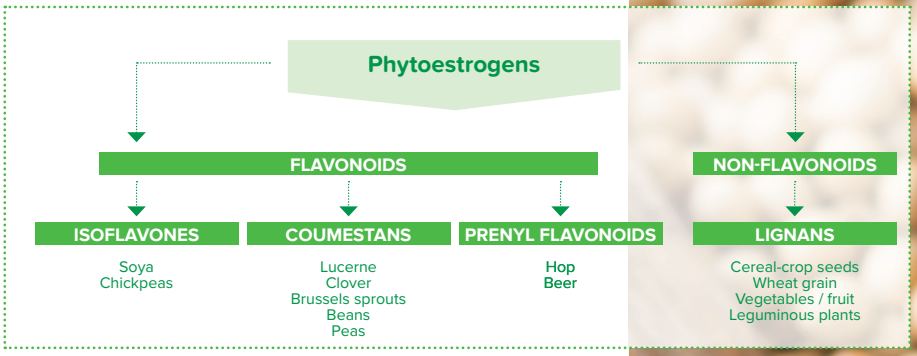
Isoflavones belong to a group of plant compounds called phytoestrogens. As well as in soya, isoflavones are also found in legumes such as chick peas and lentils. The other main types of dietary phytoestrogens are lignans and coumestans. Lignans are found in whole-grain cereals including flaxseed, fruits and vegetables (including celery, asparagus and broccoli). Coumestans are found in very small quantities in many vegetables, such as Brussel sprouts & mungbean sprouts.

Soya is recognised as the major source of isoflavones in our diets. The two main isoflavones found in soya are genistein and daidzein. Glycitein is also present in soya, but in much smaller quantities.

Isoflavones: the difference between phytoestrogens and oestrogen

Isoflavones are often described as phytoestrogens because their chemical structure show similarities to the human hormone oestrogen. The term ‘phyto’ refers to the fact they are of plant origin. Although classified as phytoestrogens, they behave differently to oestrogen. Two types of estrogen

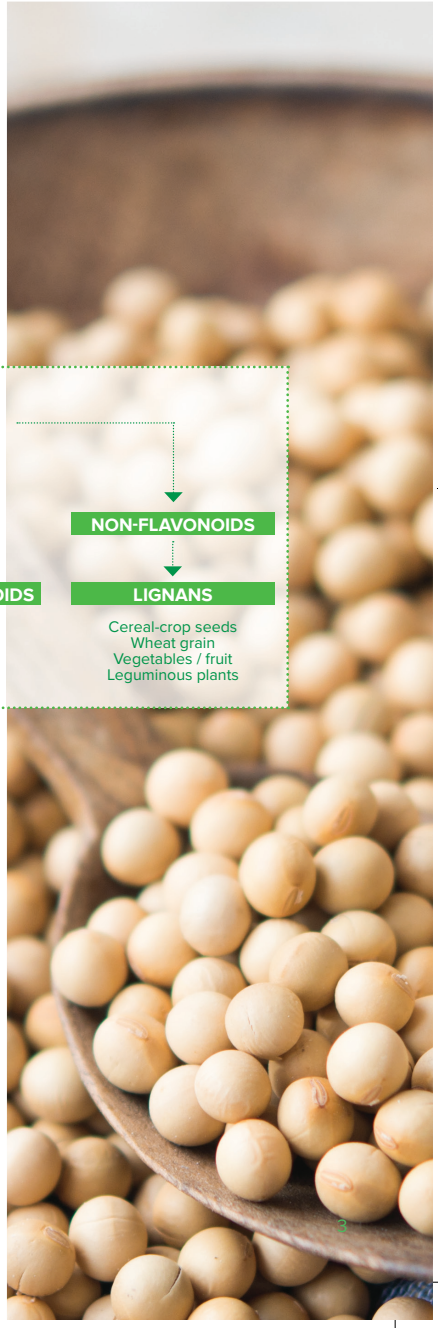
receptors (ER) exist in human body, alpha (ERα) and beta (ERβ). Isoflavones differ from oestrogen in that isoflavones preferentially bind to and activate the ERβ, whereas oestrogen binds to and activates each receptor equally *(Kuiper et al., 1998)*. This difference is important because when activated these two receptors can have different and sometimes opposite physiological effects. In addition to being phytoestrogens, isoflavones are classified as natural selective oestrogen receptor modulators (SERMs). SERMs exert oestrogenic effects in some tissues, anti-estrogenic effects in others and in some tissues affected by oestrogen they have no effect at all.



Isoflavones: 1000 times weaker than oestrogen

In foods, isoflavones are mainly present as inactive 'glycosides' (i.e. bound to a sugar molecule). To be absorbed into the body, this sugar has to be removed, through a process called deglycosylation, carried out by a specific intestinal enzyme. The 'aglycon' isoflavones (freed of their sugar) are then absorbed by the body.

After absorption, the majority of aglycon isoflavones are further metabolised in the liver: the aglycons are glucuronidated or sulphuronidated and most are inactivated again. Overall isoflavones have very weak estrogenic activity *(Setchell KD, et al. 2011)*.



Some of the aglycon forms can be further metabolised in the gut by our gut bacteria and these metabolites are also absorbed. For example, daidzein can be converted into equol, which is more active than its parent compound. However, only about 30% of men and women are able to carry out this conversion as it depends on an individual's characteristic gut bacteria. The activity of aglycon isoflavones has been shown under laboratory conditions to be 1000 times lower than that of endogenous oestrogens *(Matsumura et al., 2005; Zhu et al., 2008).*

Isoflavones: a traditional component of Asian diets

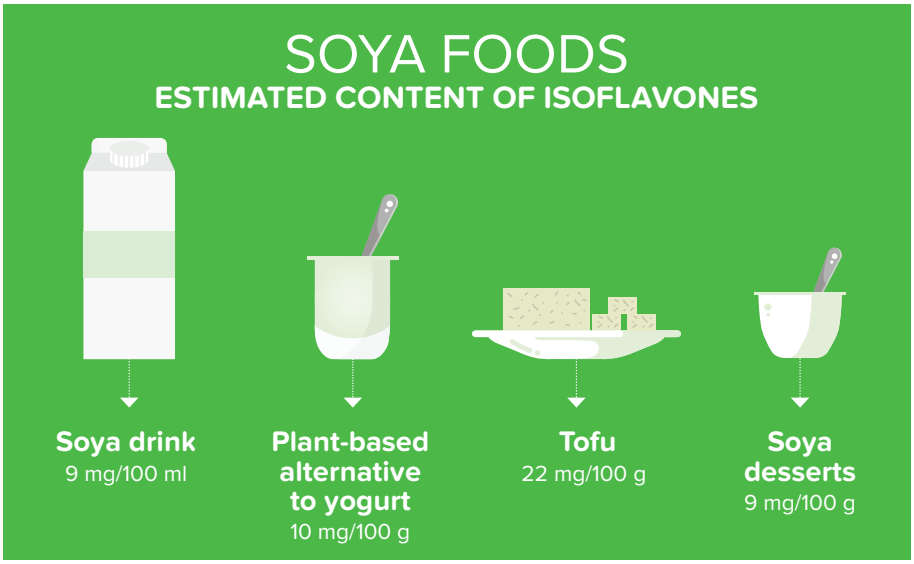
In Asia, where soya foods are a traditional part of the diet, isoflavones are consumed in significant quantities. This has been the case for over 4000 years!

In countries traditionally consuming soya, average intake of isoflavones range from between 11 to 50 mg a day and can reach up to 100 mg *(Yang et al., 2005; Messina et al., 2006; Lee et al., 2007).* In Japan, where consumption of soya-based foods varies less between regions than it does in China, isoflavone intake averages 50 mg/day, but can exceed 100 mg/day *(Otaki et al., 2009).*

The types of soya foods consumed in Asia vary from country to country. In China, Hong Kong and Singapore, hardly any of the foods consumed are fermented, whereas in Korea, Indonesia and Japan, between 30% and 60% of the soya eaten is in a fermented form *(ENSA, 2016).*

In Western countries, where soya consumption is very low, dietary intake of isoflavones is much lower: around 1-2 mg per day *(de Kleijn et al., 2001;; Zamora-Ros et al., 2012).*

The figure below summarises the isoflavone content of different soya foods.



ESSENTIAL TAKE-HOME MESSAGES

1. Isoflavones are natural compounds found in many plants, belonging to the large family of polyphenols.
2. Isoflavones are also referred to as phytoestrogens as their chemical structure show similarities to the human hormone oestrogen. However, their effects in the body are clearly different.
3. Isoflavones have weak oestrogenic activity: 1000 times lower than endogenous oestrogens. Isoflavones first need to be converted in the gut to aglycones before they can be absorbed.
4. Isoflavones are present in soya - a nutritious, high quality food.

SOYA – A PLANT OF GREAT VALUE, AND GROWN IN EUROPE

Soya: from beans to soya foods

In ancient China, soya was one of five sacred grains, along with wheat, barley, rice and millet. Originally the beans were used to enrich the soil. Later, fermentation methods made it suitable for humans to eat. Soya foods then became a traditional part of the diet in countries of the Far East, particularly China, Japan and Indonesia, where it is found in various forms, such as beverages, tofu and miso.

The soya bean used to produce these foods comes from the leguminous plant, Glycine max. These beans are sometimes referred to as “yellow soya”. The various ways used to process the beans will produce different soya products, all of which fit into a healthy balanced diet.

The soya plant should not be confused with what is sometimes called “green soya” (Vigna radiata) also called mungbeans, from which we get “beansprouts”. This is another leguminous plant that has very different characteristics to soya beans.

World production of soya is estimated to have been 350 million tonnes in 2016/17 (source: Terres Univia), with the United States, Brazil and Argentina alone producing over 80%, mainly used for animal feed.

Europe also produces soya (2.5 million tonnes in 2016). Here it is mainly grown in Italy, France, Romania, Croatia, Hungary and Austria (source: Terres Univia).

In France (342,000 tonnes produced in 2016), soya is grown mainly in the south-west (Occitania and New-Aquitaine) and the centre-east (Burgundy-Franche-Comté and Auvergne-Rhône-Alpes) (source: Terres Univia).

Soya is also grown in the Netherlands (800 tonnes produced in 2017) and Belgium (around 100 tonnes in 2017).

Soya: an environmentally friendly plant

Soya is able to pull nitrogen from the air and ‘fix’ it into the plant and so does not require any additional nitrogen fertiliser.

Soya requires very little treatment to protect it against plant diseases and parasites.

It is an autogamous plant, meaning that it can reproduce without needing another of the same species to pollinate (self-fertilisation). This avoids cross-contamination that could occur, for example from GMO crops.

Soya: local production and traceable history

As voluntary members of the ENSA (European Plant-based Foods Association), companies are committed to using only whole soya beans for soya foods production. They also pledge to using only traditional production processes (water and mechanical procedures – notably grinding and filtering). Finally, they guarantee their products to be GMO-free. Each member has set-up close monitoring programs to ensure traceability and non-contamination (whether by GMOs or otherwise) all the way from the field to the plate. Supplies that come directly from the growers and/or warehousing organisations are favoured by member companies. ENSA supports the rational and environmentally friendly cultivation of soya, which does not involve deforestation.

SOYA – A PARTICULARLY NUTRITIOUS BEAN

The benefits of soya can be attributed to its various nutritional components (a source of high quality protein, a healthy balance of fats, presence of isoflavones, etc), together with the plant matrix in which these are found.

A healthy fat profile

Being 100% plant origin, soya and its products are cholesterol free.

Soya beans also have a healthy balance of fats: they contain lower amounts of saturated fat (15% of the total fat content) and are predominately made up of unsaturated fat (85% of the total fat, including 7% omega-3 polyunsaturated fat). For these reasons, soya foods are useful in diets requiring a healthy fat profile.

High-quality protein

Soya comes from the legume family and has excellent nutritional qualities. Firstly, the bean is the richest source of protein in the plant world.
Secondly, it contains all the nine essential amino acids and its digestibility is high, on average 90% that of reference proteins (WHO/FAO/UNO, 2007), and so its protein quality is comparable to animal proteins.

The quality of food proteins is determined by two criteria: the protein's digestibility and the amino acids present. The Protein Digestibility Corrected Amino Acid Score, or PDCAAS, is a value that has been used for many years to express the quality of a protein. It compares the protein's content of essential amino acids with our requirement for those amino acids, while taking into account the ease with which the protein is digested. Food proteins are categorised according to these criteria, with a maximum score of 1 corresponding to the highest quality protein.

Examples of PDCAAS values for various foods, for adults

	PDCAAS	LIMITING AMINO ACID(S)
ANIMAL SOURCES		
Egg	1.0	-
Milk & cheese	1.0	-
Meat & fish	1.0	-
PLANT SOURCES		
Soya	~ 0.95	-
Dried beans	~ 0.7 - 0.75	Met + Cys
Rice	~ 0.65	Lys
Wheat	~ 0.5	Lys
Maize	~ 0.5	Lys

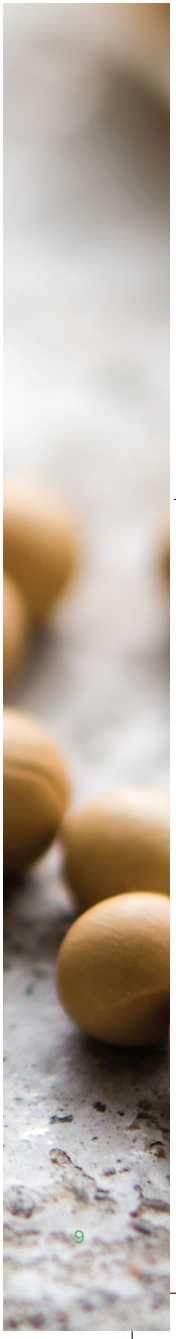
(modified from AFSSA-ANSES 2007; Michaelson et al., 2009; WHO/FAO/UNO, 2007)

In 2014 the FAO proposed to abandon the PDCAAS index, in favour of another method, the Digestible Indispensable Amino Acid Score (DIAAS). The DIAAS, determined by a different method, is considered to be more accurate for measuring the real digestibility of individual amino acids (FAO, 2014).

While the DIAAS value for soya protein may be slightly lower than its PDCAAS score, the former still has a value of around 0.9, which means soya can still be considered a high-quality protein.

Soya provides variety into the diet

The wide range of soya foods available, along with soya's excellent nutritional properties, makes them ideal to include into a varied, healthy and balanced diet.
Soya drinks and fermented soya alternatives to yoghurt, soya desserts and soya alternatives to cream bring opportunities to experience new taste sensations and widen our culinary repertoire. While soya burgers and cooked dishes including protein rich soya and vegetables are great alternatives to traditional, familiar meals.



A varied diet, incorporating soya foods, at the expense of animal-derived foods, can help reduce fat intake, particularly saturated fat, and increase unsaturated fat, helping to achieve a healthy fat profile while also providing fibre.
Soya-cream alternatives can be very useful. They can be used in the same way as conventional single cream, with the added bonus of being cholesterol free, low in saturated fat and containing valuable essential fats.

Soya foods : clever alternatives

Soya foods have the added benefit of being naturally lactose free and do not contain cows' milk proteins. This makes them suitable for people with lactose intolerance and/or who have allergies to cows' milk proteins. In most cases they are fortified with calcium, vit D, B2 and B12 helping people meet their requirements for these valuable nutrients.

Fortified soya drinks and soya -based alternatives to yoghurt are considered nutritionally comparable to dairy foods. This is recognised by their inclusion within the dairy section of several countries food based dietary guidelines.

Food Triangle (2017) from The Flemish Institute for Healthy Living

The Food Triangle not only focuses on health but also includes sustainability messages. The main recommendation is to eat proportionally more plant-based foods than animal foods. Calcium fortified soya products are part of the new dietary model, both soya drinks and soya-based alternatives to yoghurt.

Eatwell Guide (2016, UK)

The names of the food group segments have been updated to place emphasis on certain food products within a food group that can be considered more environmentally sustainable. The 'Milk and Dairy' section has been changed to 'Dairy and Alternatives' and includes calcium fortified soya foods (drinks and alternative to yoghurt) highlighting their nutritional equivalence to dairy. The protein segment is named "Beans, pulses, fish, eggs, meat and other proteins" to highlight the relevant contribution of non-meat sources to protein intake.

Wheel of Five (2016, The Netherlands)

The Wheel of Five also seeks to limit the environmental footprint of food consumption and therefore suggests keeping the intake of dairy within recommended limits. Calcium fortified soya drinks, desserts and yoghurt alternatives (< 6g sugars) are included in the dairy segment.

ESSENTIAL TAKE-HOME MESSAGES

Soya has been consumed in Asia for thousands of years and is still a mainstay of the continent's culinary culture. It is now being increasingly appreciated in Europe's cuisine.

It has gone past the stage of being an "alternative" dietary ingredient and is now an integral part of a varied and balanced diet.

Soya makes it possible to increase plant protein intake and reduce saturated fat and cholesterol intakes.

FREQUENTLY ASKED QUESTIONS

1 SOYA AND BREAST CANCER

Does eating soya increase the risk of developing breast cancer?

Given that lifelong exposure to oestrogens is associated with an increased risk of breast cancer, some people have been concerned that the isoflavones found in soya could be harmful and increase the likelihood of developing breast cancer. Is this fear justified? It doesn't appear so. The available data shows soya has a protective effect against breast cancer in Asian women. When these women move to Western countries and abandon their traditional soya-rich diet, they lose that protective effect of the diet, becoming more vulnerable to breast cancer *(Stanford et al, 1995).*

The most recent epidemiological studies show soya consumption helps reduce the risk of developing breast cancer, particularly if this is adopted early (before adolescence) and is maintained throughout life *(Shu et al, 2000; Yamamoto et al, 2003).*

Many studies now support the view that soya has a protective effect against breast cancer.

EFSA, the European Food Safety Authority, published an expert's report in 2015 which concluded there was no increased risk of breast cancer and no effect on either the uterus or the concentrations of thyroid hormones in menopausal women when consuming a supplement of 150 mg of isoflavones a day. Such a dose well exceeds the intake from foods, as it is equivalent to more than 10 soya-based alternatives to yoghurt a day!

What about women with a personal or family history of breast cancer?

Animal studies have suggested that exposure to isoflavones could favour the proliferation and growth of tumours in menopausal women who have a history of breast cancer. However, animal studies are of limited value because rodents metabolise soya isoflavones very differently to humans.

There is now impressive human data from epidemiologic studies indicating that soya foods do not worsen the prognosis of breast cancer patients but may actually improve it. A meta-analysis of five prospective studies *(two in the United States: Caan, 2011 and Guha, 2009; and three in China: Kang, 2010, Shu, 2009 and Zhang, 2012),* which included over 11,000 women who had had breast cancer, and who were followed up for periods ranging from four years to over seven years, found that consuming soya after their disease had been diagnosed, was associated with a significant reduction in cancer recurrence risk and mortality *(Chi, 2013).* In the study carried out in Shanghai, with over 5,000 patients followed up for nearly four years, women consuming the most soya protein (< 15.3 g/day), had a 30% lower mortality rate and incidence of recurrence of the disease than those with smaller intakes (≤ 5.3 g/day) *(Shu, 2009).* In that study, consuming soya had a protective effect for both pre- and post-menopausal women. Nechuta's meta-analysis *(2012)* established isoflavone consumption, in excess of 10 mg per day, following a diagnosis of breast cancer, was associated with a 25% reduced risk of the breast cancer recurring.

It is important to note that the protective effect of soya consumption is observed in both Asian women and non-Asian women *(Nechuta, 2012).* Two studies were carried out in the United States, mainly with Caucasian women: the WHEL study (*Women's Healthy Eating and Living study, Caan, 2011),* including nearly 3,000 patients, and the LACE study, involving nearly 2,000 patients *(Guha, 2009).* In these two studies, a high intake of soya was associated with a better prognosis.

Also, whereas animal studies suggested an unfavourable effect of soya isoflavones on the effectiveness of anti-cancer medication such as tamoxifen, the recent epidemiological data suggest an improved outcome with such medication *(Guha, 2009; Nechuta, 2012; Kang, 2010).*

Furthermore, unlike the animal studies, human intervention studies suggest that isoflavones do not pose a risk for breast cancer patients. Soya products do not increase the proliferation of breast cells in women who have undergone biopsies both before and after being exposed to isoflavones *(Messina and Wood, 2008; Khan et al., 2012).*

This recent data has led the American Cancer Society (Rock et al., 2012) and the American Institute for Cancer Research (2012) to update their positions on soya and breast cancer risk. Both these institutions now state that soya foods can be consumed as part of a varied, balanced diet by women who have breast cancer.

This has just been reconfirmed by the World Cancer Research Fund International (2018) who concluded there may be an association between consuming soya-based foods and a better prognosis following breast cancer.

2 SOYA AND CALCIUM

Will I get enough calcium from soya drinks and plant-based alternatives to yoghurt?

Most soya foods are enriched with calcium and contain 120 mg of calcium per 100g, the same as in dairy products. A study published in the Journal of Nutrition *(Zhao et al., 2005)* showed that the absorption of calcium from soyfoods is comparable to that of dairy products, but with reduced calcium losses, providing better overall calcium bioavailability. *(Macdonald, 2005; Matsuzaki, 2006; Kitchin, 2007).*

3 SOYA AND CHILDREN

Should young children avoid soya foods?

In the Far East children have been eating soya foods for thousands of years.

When considering soya foods in infancy, it's important to take into account two different stages:

- The period when the infant is exclusively fed on mother's milk or infant-formula (ideally the best food for a baby or young infant is mother's milk)
- The period when foods are introduced into the diet

In Asian countries, foods, including tofu, are gradually introduced from 4 months.
This is generally later in Europe, starting around 6 months old or when the first teeth appear.

The advice for introducing soya foods into the diet is the same as other foods; introduce gradually, in moderate amounts, as part of a varied and balanced diet.

Between 1 and 3 years old, conventional soya foods can be enjoyed as part of a healthy, balanced diet.

Can children's sexual development be affected by eating soya?

As isoflavones have structural chemical similarities to the hormone oestrogen, questions have been raised as to

whether soya isoflavones can influence children's growth, the onset of puberty and fertility in adulthood.

Firstly, it's important to remember that while soya isoflavones and oestrogens show structural chemical similarities, in reality they are quite different, and have very different effects in our bodies. For example, the oestrogenic activity of isoflavones is 1000 times lower than that of oestrogen.

Furthermore, human studies have not shown any adverse effects on children's sexual maturation. A study published in 2001 compared adults who had been fed either cow's milk infant formula or soya infant formula from birth to 4 months old. *(Strom, 2001).* The results showed no significant difference in terms of age of puberty, regularity of periods, hormone-related diseases, etc. As a result, the authors concluded that soya infant formulas were safe.

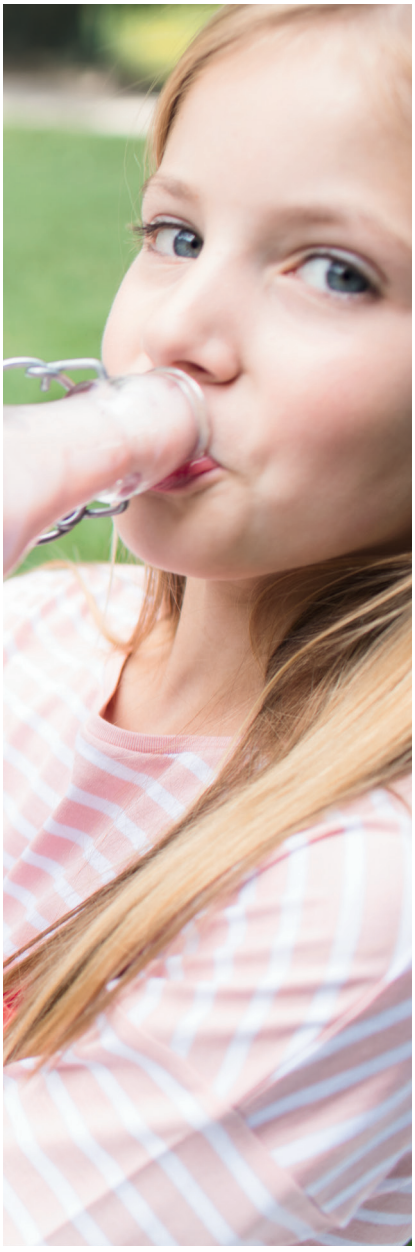
A more recent US study, which included 339 girls from the Seventh-Day Adventist community (who are mainly vegetarian and regularly consume soya foods), aged between 12 and 18, showed that soya consumption was not connected to the age when puberty starts (on average 12.5 years). The average amount of soya foods consumed in these adolescents was 12.9 portions per week *(Segovia, 2014).*

Does soya influence children's growth and development?

All data from clinical studies show growth and development is completely normal in children fed soya infant formula when compared to those fed cow's milk infant formula. No differences in the timing of puberty or in fertility rates have been reported in humans who were fed soya formulas as infants.

An international group of paediatric experts have confirmed that babies fed soya infant formulae grow and develop completely normally.

Vandenplas et al *(2014)* reviewed 35 studies comparing the growth and development of infants and children fed either breast milk, cow's milk formula or soya formula.



There were no differences in any of the 31 growth and development parameters; such as immunity, growth, sexual and reproductive functions, mental and neurological development. The fear that soya infant formulae would have negative effects on infants is not confirmed in this extensive literature study. Compared with cow's milk formulae, there was no difference in sexual, reproductive or mental development, growth or nutritional status.

Can soya influence adult fertility?

In adult women, consuming soya foods does not have an impact on hormonal status, although menstrual cycle length may be slightly increased, but it does not prevent ovulation *(Hooper, 2009)*. Longer menstrual cycles are considered to be a protective factor in relation to breast cancer risk.

With regards to adult men, a review of the literature and a meta-analysis including 32 clinical studies found that soya and their isoflavones have no effect on male hormones including testosterone, SHBG (sex hormone binding globulin), free testosterone, or the FAI (free androgen index) *(Hamilton-Reeves, 2010)*.

Furthermore, following an initial pilot study suggesting there was a reduction in sperm count associated with soya consumption *(Chavarro, 2008),* the same research team recently published a cross-sectional study showing soya intake was not associated with fertilisation or implantation rates, nor with pregnancies or births *(Minguez, 2015)*. Two clinical studies have strengthened this observational data and show that soya isoflavones have no effect on male reproductive health *(Mitchell, 2001; Beaton, 2010)*.

GLOSSARY

SATURATED FATTY ACIDS
Saturated fatty acids are present in all fats, whether plant or animal, but in greater amounts in fats from animal origin (e.g. cheese, butter, meat, etc.). If eaten in excess they can increase LDL blood cholesterol and so increases the risk of cardiovascular disease. For this reason they are often referred to as the "bad" fats.

POLYUNSATURATED FATTY ACIDS
Polyunsaturated fatty acids are mainly found in plants and oily fish. Two types of polyunsaturated fatty acids are the omega-3 and omega-6 fatty acids, some of which are "essential". Both are present in soya. In contrast to the saturated fats, they are often referred to as the "good" fats.

BIOAVAILABILITY
Bioavailability refers to the quantity of a nutrient that can be absorbed and used by the body.

EQUOL
A metabolite of daidzein. Depending on the composition of the gut flora, daidzein may or may not be metabolised to equol, a compound that is more active than daidzein.

OESTROGENS
The oestrogens are female hormones which act on tissues in women's bodies. The main female hormone, before the menopause, is oestradiol, which is primarily produced by the ovaries. The oestrogens act on the urogenital system, mammary glands, skeleton, skin and mucous membranes, cardiovascular system, brain and digestive system.

OESTRADIOL
Oestradiol is the principal oestrogen hormone. It gradually increases in concentration during the first phase of the menstrual cycle, ultimately stimulating ovulation.

PROTEINS
Proteins are biological compounds that are often described as the body's "building blocks". They are the only dietary source of nitrogen, an element that is essential for life.
A protein (or polypeptide) is an assembly of amino acids. Generally speaking, we talk of a "protein" when there are over 100 amino-acid units linked in a chain. There are proteins of animal origin and of plant origin.

REFERENCE PROTEIN
To judge the biological value of dietary proteins, efforts have been made to define a "reference protein" to which all other proteins in the diet can be compared. In this reference protein, the quantities of each of the essential amino acids are those considered to be optimal for humans. The FAO and WHO have worked out a standardised method (PDCAAS – FAO/WHO, 1990) to evaluate protein quality. This method compares the essential amino acids in the protein to be analysed with that of the reference protein defined by the FAO, together with an assessment of its digestibility. An indicator of the quality of each protein is then calculated and compared with the maximum value of 1 for the reference protein.

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