

# **Dietary Supplementation with Fermented Soy Nutraceutical, Haelan 951: Tumor Regression and Improved Treatment Responses in Patients Diagnosed with Breast Cancer.**

**Vijaya Nair, MD, FAMS, MS**

## **Introduction**

Soy and soy products have been a staple in the standard diet in China, Japan, Indonesia and other Asian countries for centuries. Epidemiological studies have shown that the incidences of breast and prostate cancers are much higher in the US and in European countries than in these Asian countries where the consumption of traditional soy based foods such as tofu, tempe, natto, shoyu, soy sauce, miso, is higher. It is believed that the inclusion of a moderate amount of these fermented soy products in the traditional diet of Asian populations play an important role in overall disease prevention and enhancement of well being.

Soy based diets are safe and provide powerful health benefits. The isoflavones in soy based diets have been studied extensively and shown to have many therapeutic and preventive properties against different types of cancers.

Typically soyfoods are divided into two categories: non-fermented and fermented soy products. Traditional nonfermented soyfoods include fresh green soybeans, whole dry soybeans, soy nuts, soy sprouts, whole-fat soy flour, soymilk and soymilk products, tofu, okara and yuba. Traditional fermented soyfoods include tempe, miso, soy sauces, natto and fermented tofu and soymilk products. In Asia, the traditional fermented soy foods are considered to have more health promoting benefits when consumed in moderate amounts than the super-processed soy products that are consumed in the West . It has been suggested that the fermentation process increases the bioavailability of isoflavones in soy. A recent Korean study concluded that tofu was one of the foods that decreased the rates of certain cancers such as stomach cancer while heavy salt consumption and

cooking methods increased the rates . The limited epidemiological evidence so far from these cultures with diets that are high in soy products indicates that such diets may reduce the risk of breast, colon, lung and stomach cancers, as well as offer some protection from cardiovascular diseases, osteoporosis and menopausal symptoms. But the clinical data to date is often flawed with poor design and other methodological issues.

In 1989 the National Cancer Institute funded a \$20 million, five year program aimed at examining the potential role of common foods, including soybeans, in preventing cancer. In 1990, the NCI added a \$2.9 million on research to focus just on the role of soy.

Research has now isolated a number of nutrients and micro nutrients in soybeans that have anti-cancer properties. The latest research has focused on the micronutrient isoflavones, protease inhibitors, saponins, phytosterols and phytic acid compounds in soybeans. The NCI published a copy of its report in the April, 1991 issue of the National Journal of Cancer, titled: Commentary: The Role of Soy Products in Reducing Cancer Risks. Some of the issues raised in the NCI report will be discussed in this paper in later sections.

Haelan 951, a novel fermented soy supplement that has been sold as a food beverage in the US for past 12 years. The patented fermentation process involved in the manufacture of Haelan951 hydrolyzes many of the soybean proteins into amino acids and compounds that are rich in nitrogen, polysaccharides, and fermentation metabolites of the naturally occurring isoflavones, protease inhibitors, saponins, phytosterols and inositol hexaphosphate compounds in soybeans. The unique process uses the autogenic antiammonia azotobacter mutant strain, induced from *Azotobacter vinelandii* as inoculum in an industrial fermentation. They are specific bacterial strains belonging to the species *Stenotrophomonas maltophilia* Q-can. The soy beverage is a concentrated nutritional supplement that is rich in soybean proteins, selenium, zinc, beta-carotene (vitamin A) riboflavin (vitamin B1), thiamine (vitamin B2), cyanocobalamin (vitamin B12), ascorbate (vitamin C), cholecalciferol (vitamin D3), alpha tocopherol (vitamin E), and phylloquinone (vitamin K1). It also contains additional micronutrients such as daidzein,

genistein, protease inhibitors, saponins, phytosterols, and inositol hexaphosphate, and essential fatty acids such as linolenic and linolic acids, polysaccharide peptide, and twenty of the twenty-two amino acids including ornithine. It takes over 25 pounds of soybeans to make one concentrated eight ounce bottle of the Haelan951 beverage. Of these naturally occurring nutritional items in the Haelan951 formula, more than 20 of them are known individually for their ability to enhance the nutritional profiles of individuals with cancers. The fermented soy and its metabolites have also been shown to have different biological properties, such as anti-viral, anti-bacterial, anti-inflammatory, anti-mutagenic and anti-carcinogenic activities.

The objective of this paper is to highlight case reports and studies that pertain to the current controversy among health care professionals over the use of soy in breast cancer patients and survivors of the disease. Case reports are presented to focus the discussion around the role of Haelan951, a novel fermented soy nutraceutical, within the context of chemoprevention and in therapeutics both as sole mainstay treatment and as adjuvant nutrition to successfully treat 2 patients presenting with the diagnosis of breast cancer. The 2 case reports presented below were submitted together with other case reports on patients diagnosed with different forms of terminal cancers as part of the National Cancer Institute's Best Case Series Program. The Best Case Series focuses on documented case reports of patients diagnosed with cancers who showed significant improvements in their clinical conditions after using complementary and alternative supplements as mainstay therapies for their conditions. A total of 7 out of 12 of these case reports were accepted by the NCI to meet criteria set by the Best Case Series Program, Office of Cancer, Complementary and Alternative Medicine, National Cancer Institute, Bethesda, Maryland.

#### **CASE REPORT #1: Tumor Type: Infiltrating Ductal Carcinoma of the Breast.**

PS, a 67 year old married great grandmother, retired nurse and wife of a physician, first noticed a lump in her right breast in August 1997. Ultra-sound breast report in August '97

revealed ‘..... a solid lesion, mildly lobular, well circumscribed .....’ Mammogram report in October 1997 stated “..... irregular lobular very dense lesion containing several tiny calcifications and coarse calcifications in the right breast , barely upper outer quadrant, roughly measuring 15x 15 x 20 mm, and very suspicious for carcinoma ... no nodes seen.” There was no metastasis noted at that time but a breast biopsy in October 1997 revealed a moderately differentiated infiltrating ductal carcinoma of the right breast. A total mastectomy or lumpectomy with removal of the auxiliary lymph nodes and followed by aggressive radiation was recommended but she refused all standard therapy. She was offered mastectomy or lumpectomy with removal of axillary lymph nodes followed by aggressive radiation therapy and hormonal treatment regime. She was given a prognosis of 6months to live without treatment.

PS began taking the fermented soy beverage, Haelan951 as of November 1997 and was followed radiologically via mammograms until the present time. Per her report and confirmed by serial mammograms, she has residual disease that has gradually decreased in size since diagnosis. In January 2001, the area of density measures 7x5x6mm as compared to the 15x15x20mm at the time of her diagnosis. Her most recent mammogram in February 2004 showed a low density oval mass with circumscribed margins measuring 4mm in the upper outer quadrant. This was thought to be most likely benign in nature. An ultra sound reading done in the same period revealed a 1mm calcification in the same area of the right breast. No mass was detected.

When PS started Haelan951 she initially took one bottle or 8ozs daily in two divided doses for 7 months. This dose was cut down to 4 ozs a day for a further 7 months and then to 2 ozs a day for several months. She is currently on 1 oz a day. PS is clinically well and continues to lead an active life.

**CASE REPORT #2: Tumor Type: Infiltrating ductal carcinoma with history of lymphangitic spread, metastases to skin, lungs, bronchi, pericardium and bones.**

JH, a 50 year old woman, was first diagnosed to have infiltrating ductal carcinoma of left breast in 1986 when she underwent mastectomy and reconstruction of breast tissue with no adjuvant therapy at that time. She was noted to be estrogen receptor positive. Her tumor was staged at T1N0M0.

She remained clinically well and was followed up as an out patient for the period between 1986 till September 2000. During that visit she presented with a history of gradual weight loss, persistent cough, shortness of breath or dyspnea on exertion and developed a skin nodule in her peri-xiphoid area. She was treated with steroids without significant relief. Her CT scan showed lymphangitic infiltrate and a very large pericardial effusion. There was also a 4 cm mass posterior to the left hilum; additional mass versus consolidation right lung base posteriorly . Infiltrates in the right middle lobe and lingular segment of the left upper lobe. A large pericardial effusion and a smaller right pleural effusion were also noted. JH underwent a 2-D echocardiogram of her heart which showed no evidence of a pericardial tamponade. She underwent bronchoscopy, which showed the presence of a small tumor nodule that was subsequently diagnosed as an adenocarcinoma. She also had a skin biopsy which also showed metastatic adenocarcinoma . The tumor architecture was described as “ non specific but could suggest primary breast ductal carcinoma”. She also had small lymph nodes and a lymph node on her anterior abdomen.

An x-ray of her right humerus in September 2000 revealed on the antero-posterior and lateral views, destructive change in the glenoid process of the right scapula. The humeral head, neck, and shaft appeared normal. Her bone scan in October 2000 showed diffuse bony metastases, unchanged since September 2000, with focal metastatic disease in right parietal bone, right scapula, and bilateral ribs. There were also multiple foci of activity in the thoracic and lumbar spine, left iliac bone, sacrum, and left femoral neck.

In September 2000 she was started on a 3 month cycle of Cytosan and Adriamycin with a continuous infusion of 5-FU. She tolerated chemo well without significant side effects.

At time of discharge her Hb was 12.6, WBC 8.1, platelets 245. She developed a deep vein thrombosis that resolved with treatment regime of Lovenox and Coumadin.

On follow up visit in April 2002, her estradiol level was at 43 and FSH and LH levels were quite low at premenopausal levels. She was started on Lupron to render her menopausal together with Aredia. Her CT scan showed decreased in size of her hilar mass as well as disappearance of her right pleural effusions but most noticeably she had a very large pericardial effusion. Bone scan showed stable to improved metastatic disease. Pericardiocentesis was done in May 2002 and she underwent pericardial window with pericardial biopsy in June 2002. She refused another round of chemotherapy.

JH started taking Haelan951 in May 2002 just before her surgical procedure to drain the large malignant pericardial effusion. Her physicians at that time warned her of a rapid recurrence of her condition within a few months. Post-operatively, she did well with no difficulties in breathing or recurrence of her malignant pericardial effusion in subsequent follow up visits till last follow up visit in June of 2003. Her clinician noted that despite her malignant disease state she had done excellently. At present time, JH has no other significant problems. She does a lot of activities on her own and denies any complaints of shortness of breath, nausea, vomiting, diarrhea or constipation, lymphadenopathy or skin changes. Whole body PET scan in June 2003 showed a marked decrease in number of metastasis with no overt major activity.

JH attributes her improvement in her clinical condition, especially with regards to her breathing and general well being over the past one year as a result of her faith and consuming the fermented soy beverage, Haelan951. She currently plays blue-grass music with her children and does music tours around the country with them.

## **Discussion**

PS, a 65 year old female diagnosed with moderately differentiating infiltrating ductal carcinoma of the right breast 7years ago refused standard conventional therapy. She began taking Haelan951 soon after her diagnosis was made and was followed up radiologically via mammograms and ultrasounds until the present time. As per her medical reports and confirmed by serial mammograms, she had residual disease that has gradually decreased in size since diagnosis. As of February 2004 PS's latest mammogram and ultrasound readings do not show any evidence of malignant lesions.

In JH's case, she was already diagnosed to have Stage 4 or terminal breast cancer with multiple metastases to the lungs, heart, bones, heart, pericardial fluid, lymph nodes and lymphangitic system. She had one round of chemotherapy and was on hormonal therapy which resulted in some clinical improvement of her condition for a short while. In less than 2 years, there was marked deterioration in her clinical condition as she experienced respiratory difficulties due to the recurrence of a massive malignant pericardial effusion. Her condition stabilized over the next several months after she started taking Haelan951, the fermented soy beverage just before the surgical drainage of her pericardial fluid. Her clinical condition has markedly improved over the past 2 years without any further conventional treatment for her cancer except for the fermented soy beverage.

The clinical progress noted in the above 2 case reports are remarkable given their initial diagnosis and prognosis.

The study by Morrison et al is often cited as support of recommendations for breast cancer patients to consume soy as even after controlling for many other possible confounding variables including stage at diagnosis, Japanese breast cancer patients exhibit better survival than do the other ethnic groups.

### **An Overview of The Anti-Carcinogenic Action of Soy.**

Soy contains a number of putative anticarcinogens especially the isoflavone,

The evidence for the anti-carcinogenic action of Soya based traditional foods in breast, prostate and other cancers comes from population based studies, the recognition of the “weak estrogenic effects” of soy isoflavones, genistein and daidzein and the antiandrogenic effects of genistein. Additionally, the primary isoflavone in soybeans, genistein has also studied for its antiangiogenic action. Angiogenesis or new blood vessel growth is required for tumors to grow and genistein appears to block that process.

Among others, Potsis et al for example found that at high concentrations (  $IC_{50}$ , 150 $\mu$ mol) genistein inhibited the ability of bovine microvascular cells to invade collagen gels and generate capillary-like structures when stimulated by basic fibroblast growth factor. Development of anti-angiogenesis agents is a highly promising area in cancer treatment because inhibiting the tumor-stimulating growth of new blood vessels prevents tumors from becoming larger than 1-2 mm. Tumors limited to within this size are clinically insignificant.

A study by McMichael-Philips et al found that daily consumption (60g) of a soy-protein product containing 45mg of isoflavones for 2 weeks stimulated DNA synthesis in breast cells taken from biopsies of premenopausal women with benign and malignant breast disease.

Research has also shown that genistein has anti-oxidant and anti-proliferative properties. Genistein potently inhibits oxidant formation and protooncogene expression and this may at least in part be responsible for the anti-carcinogenic mechanism of action. Genistein is also a specific inhibitor of tyrosine protein kinases, topoisomerase II, and protein histidine kinase. Protein tyrosine kinase inhibitors play an important role in cell proliferation and transformation and have been shown to have potential as anti-cancer agents in both as preventative and therapeutic roles. Additionally, genistein inhibits DNA topoisomerase II and ribosomal S6 kinase, both of which may lead to protein-linked DNA strand breaks in cancerous cells, arrest of tumor cell growth, and induction of differentiation of several malignant cell lines into lines that may be benign.

## **Mechanism of Action of Fermented Soy Nutraceutical, Haelan951**

Over the past 16 years there have been a number of investigations done to examine the active components in the fermented soy solution in the Haelan 951 nutraceutical that may play a major role in killing carcinogenic cells. It is postulated that the dietary fermented soy supplementation decreases levels of oxidative DNA damage in humans and that this may be one of the mechanisms behind the anti-carcinogenic effects of soy isoflavones.

There are at least five main cancer preventive or reversal chemical agents in Haelan951, the dietary soy nutraceutical. Firstly, the protease inhibitors prevent the activation of the specific functions of oncogenes that cause the cancer. Secondly, the phytates bind iron in the intestines to prevent it from generating free radicals which have been shown to result in malignancies. Thirdly, the phytosterols are known to neutralize the breakdown products of cholesterol and to reduce the development of certain types of cancers. Fourthly, the saponins stop the cellular mutations that could lead to malignancy. Fifthly, the isoflavones or plant estrogens have strong inhibiting effects in hormone-related malignancies such as prostate, ovarian, cervical and breast cancers. Sixthly, the phenolic acids are powerful antioxidants that help prevent cellular DNA from being attacked by carcinogens. Seventhly, the presence of omega-3-fatty acids, a form of unsaturated fatty acids, has been shown to protect against heart disease and cancer.

The presence of all the above phytochemicals in Haelan951, the dietary fermented soy nutraceutical, has been postulated to have the following direct and indirect effects on the body:

1. Increase the body's production of toxin scavengers, like GSH
2. Enhance Immune System functioning
3. Stimulation of certain detoxifying enzyme systems
4. Shutting down cell oncogene that is responsible for promoting cancer growth
5. Apoptosis
6. Directly killing viruses that may cause cancer and other health related problems

7. By binding up substances such as bile acids that can decay into carcinogenic substance
8. By chelating heavy metals and carrying them out of the body
9. By attaching to fats to prevent the carcinogenic fat oxidation process
10. By providing the known essential and unknown important nutrients that the body needs to better defend itself against pollutants

Some of the clinical trials done so far have indicated that some of the soy isoflavones such as daidzein, genistein and the saponins may have contributed to the anticarcinogenic activities of the fermented soy nutraceutical, Haelan951. There are also studies that have isolated branched chain fatty acids called small biosynthetic anticancer agents (SBAs) from Haelan, which have significant tumor-inhibition effects. The structural and biochemical analysis has shown that SBAs represent a group of terminally branched-chain saturated fatty acids(C 15-21) and have isolated the active anti-carcinogenic ingredient as largely being contributed by 13-methyltetradecanoic acid and 12-methyltetradecanoic acid. Further research on these compounds have indicated that the mechanism of action of these specific branched –chain fatty acids are associated with the induction of programmed cell death (apoptosis). But just as importantly it was observed that the specific branched fatty acids do not kill normal cells but inhibit the growth of cancer cells without any toxic effects. In animal studies, intraperitoneal injection of 13-methyltetradecanoic acid daily up to 800 mg/kg to mice did not reach the LD50 level (50% lethal dose).

Over the past 10 years a number of both animal and human trials on Haelan were conducted by the manufacturer, Haelan Incorporated. In one clinical study involving 318 cancer patients receiving adjuvant nutrient to chemotherapy and radiation, it was found that when compared with controls, in the group given Haelan 851 Platinum Formula, all of the 119 patients experienced significantly enhanced quality of life, decreased symptoms of nausea and vomiting, improved appetite, improved immune function and decreased toxicity while enhancing the rate of being able to complete the scheduled chemotherapy and radiation treatment regimes. The fermented dietary nutraceutical has

been quite successful in its use along with chemotherapy as an adjuvant therapy. When used with chemotherapy, dietary supplementation with the fermented soy protects the patients from the toxic side effects of the chemotherapy.

### **Addressing the Controversy in Soy and Breast Cancer Studies**

Much of the focus of the epidemiological studies to date on breast cancer have revealed it to be a multifactorial disease; each of the individual risk factors for breast cancer only increases risk by small amounts, about one and a half to three times. The recognized risk factors include age, family history of breast cancer, obesity, high-fat diet, alcohol consumption, and high socio-economic status, reproductive factors such as age of menarche, low parity, late age at first childbirth, and age of menopause. The correlation between greater lifelong exposure to estrogen and increase in breast cancer risk observed in many of these studies have led to the conclusion that there may be a hormonal etiology for the development of breast cancer. A number of these studies have shown a clear association between large lifetime numbers of ovulatory cycles and increased breast cancer risk with a possible mechanism of underlying action thought to be due to their relationship with increased mitotic activity in the breast.

Women diagnosed to have Estrogen Receptor Positive (ER +) breast cancer have traditionally been advised by their oncologists not to use estrogen for fear that estrogen increases their risk of breast cancer. There was concern that soy could have detrimental effects in women with breast cancer because of the weak estrogen-like activity of soy isoflavones. This notion is now being challenged. For example, a study looking at the survival rates among Japanese women diagnosed with breast cancer found that their survival rates were better than the patients in other ethnic groups. Soy consumption was one of the factors associated with the improvement in survival.

Moreover, there have been no studies that found soy or isoflavones actually increase mammary carcinogenesis in rodents given a mammary carcinogen. Thus, these studies help to allay fears about soy being harmful to ER + breast cancer patients. Furthermore,

two studies found that soy acted either additively or synergistically with the breast cancer drug, tamoxifen to inhibit the development of mammary tumor in rats. In fact, the study by Gotoh et al found that this combination inhibited the growth of existing mammary tumors in rats, whereas tamoxifen by itself was ineffective.

Phytoestrogens can be a significant contributor of nonsteroidal estrogens of dietary origin that may have health effects that are especially relevant to women's risk of hormone-associated diseases. Structurally the plant estrogens share many similarities with endogenous estrogens. Mechanistically, it has been shown that phytoestrogens can bind to estrogen receptors. Due to their weak post-receptor estrogenic properties, many researchers have postulated that isoflavones exert antiestrogenic effects. The evidence to support this theory comes from several observational studies: Firstly, isoflavones can exert their antiestrogenic effects, especially if sufficient amounts of isoflavones are consumed, by competing and occupying the estrogen receptors, thus preventing estrogen from binding. Isoflavones have also been shown to down-regulate estrogen receptors, thus decreasing the availability of estrogen receptors that can potentially bind to estrogen. Thirdly, isoflavones increase circulating serum levels of sex hormone binding globulin (SHBG). These proteins are responsible for carrying estrogen in the serum and the higher their level means that there is less estrogen available to bind to estrogen receptors in the cells. Fourthly, the consumption of soy isoflavones has also been shown to positively alter the metabolism of estrogen itself in premenopausal women by increasing the urinary ratio of 2- to 16 $\alpha$ -hydroxylated estrogens and of 2- to 4-hydroxylated estrogens.

Overall, there is conflicting results whether soy has a predominantly estrogenic or anti-estrogenic effect on breast tissue. The in vitro studies suggest that isoflavones are primarily estrogenic. Researchers have sought to explain this by citing that in vitro systems are incomplete and may not permit an anti-estrogenic effect of isoflavones to be observed. Studies done with intact animal models have not shown that soy feeding increases chemically induced mammary cancer. Rather, most of the evidence reveal a substantial cancer inhibition by with at least a 50% tumor reduction being observed in some cases.

The hormonal etiological theory for breast cancer is also partly based on the findings in studies that show that women who use hormonal replacement therapy are also more likely to develop breast cancer. These studies have found that the use of HRT in these women is associated with a marked increased of lifetime risk of developing breast cancer of between two to three fold, whereas, estrogen by itself is only weakly associated with an increased risk. There are ample experimental and clinical data to show that it's the progesterone component in the HRT rather than its estrogen component that has the carcinogenic effect on breast tissue. Soy isoflavones do not exert any progesterone activity. Recent analyses of these HRT studies that show that HRT does not decrease survival of women with breast cancer but may actually increase it. This provides further evidence that suggests that soy is not harmful to women with breast cancer.

Most of the large randomized controlled clinical trials for breast cancer seek to detect small differences in survival between different modalities of treatment.. By comparison only a small amount of effort is put into trials which look into examining the role of dietary components that may protect against breast cancer or where dietary components such as natural foods or supplements that have been used as adjuvant nutrition in women undergoing conventional treatment for their breast cancers. In fact, there has been no large scale trial done in the US or in the UK to examine the role of dietary components either in prevention or as adjuvant nutrition in breast cancer. This is despite the assertion by the Imperial Cancer Research Fund in the UK that diet may account for some 50 per cent of breast cancers.

Analytical epidemiological studies suggest that diets high in animal proteins and low in fresh fruits and vegetables are associated with increased risk of breast cancer. Prospective studies have shown the association of high meat consumption and breast cancer risk. Many of the major diseases of Western populations are hormone dependent and epidemiological data have shown that a strong association between their incidence and diet. In general, increasing consumption of soy, soy products, and plant-based foods, is consistent with current recommendations to increase fiber and anti-oxidant intakes while

lowering and replacing sources of saturated fat and cholesterol. Issues that still need to be resolved include optimal dosages, possible gender differences in response to the phytoestrogens, demonstration that the observed health benefits can be attributed directly to phytoestrogens rather than to other components of soy and phytoestrogen-rich foods, and the relative impact of the two broad categories of phytoestrogens namely the isoflavones and lignans.

The potential of isoflavones to protect from breast cancer in animal models is well known. Until recently, the epidemiological evidence to date on soy and human breast cancer risk has not been definitive, despite clear association with hormone levels and length of menstrual cycle. Studies of the association of a reduction of breast cancer risk with soya diets in general have reported a reduced risk of developing premenopausal breast cancer. Hiramaya et al demonstrated a significant inverse relationship between consumption of soy bean paste soup and breast cancer risk.

Researchers in Singapore have observed that the incidence of breast cancer has been on the increase for the past 20-30 years. The period with increase in cancer rates coincided with the diets among the young and affluent becoming richer. Lee et al in a study of premenopausal women also found an inverse correlation between breast cancer risk and consumption of soy proteins as well as soy products. In their study comparing the diets of Singapore Chinese women diagnosed with breast cancer with the diets of women who did not have breast cancer, they were able to show that a diet high in Soya proteins might be protective against breast cancer. The findings suggested that a diet low in fat and high in vegetables containing carotene would also confer a low risk of breast cancer. Conversely, a diet high in animal proteins and red meats were associated with increased risk.

There is also clear evidence for an inverse association between timing of soy intake during the adolescence period and breast cancer risk. One explanation for the conflicting results seen in different studies may possibly be the focus on soy intake at later periods in life.

A recently conducted study also showed evidence that soy consumption reduced risk of premenopausal breast cancer but mainly in women who were ER + and overweight suggesting that soy exerted its effect through its antiestrogenic effects. Studies examining the effects of isoflavones on breast tissue density are especially important since breast tissue density is an excellent marker of breast cancer risk and can easily be determined by a mammogram. Factors such as hormone replacement therapy that increase breast tissue density also increases the risk of developing breast cancer. On the other hand factors that decrease risk such as the breast cancer drug, tamoxifen, also decrease density which can be determined by a mammogram. Some of the studies showed that isoflavones had no effect on breast tissue density in younger women and moderately decreased the breast tissue density of postmenopausal women.

## **Conclusion**

This paper supports the contention that fermented soy isoflavones could be used in the treatment of existing tumors, especially breast cancers, either alone or in conjunction with conventional chemotherapeutic agents. Researchers have found that the chemotherapy agents significantly increased Nuclear factor-kappaB (NF-kappaB) activity affects cell survival and determine the sensitivity of cancer cells to cytotoxic agents such as cisplatin, docetaxel, and adriamycin as well to ionizing radiation. Data is now emerging to show that soy isoflavone supplementation may protect cells from oxidative stress-inducing chemotherapeutic agents by inhibiting NF-KB activation and decreasing DNA adduct levels. The phytochemical ingredients in the dietary fermented soy nutraceutical, Haelan951 act as biological response modifiers by promoting immunostimulation, redifferentiation of malignant cells, and inhibiting tumor neovascularization.

Current research in the area of soy and breast cancer is focused on the effects of soy exposure early in life, the influence of phytoestrogens before and after menopause, and interactions with genetic polymorphisms. Breast cancer survivors who presently rely on

tamoxifen to inhibit endogenous estrogen or on aromatase inhibitors to prevent its production need to know how phytoestrogens in fermented soy nutraceuticals such as Healan951, can benefit them. Urgent action is needed and the focus to reconcile the different and conflicting results may well lie in taking a deeper look at understanding the benefits and mechanism of action of fermented soy supplementation both in chemoprevention and as a therapeutic dietary supplementation to support the nutritional requirements of patients diagnosed with breast or any other type of cancers.

Future research in advocating dietary supplementation with fermented soy nutraceutical such as Healan951, in patients diagnosed with cancers need to address pertinent issues such as: (1) the role of the fermented soy supplement in the prevention and reversal of cancer related asthenia, anorexia and cachexia. (2) The role of the phytochemicals in the fermented soy supplement that may help reduce toxicity and improve the efficacy of conventional cancer therapy and (3) the identification of the nutritional factors in the fermented soy nutraceutical that selectively help to arrest tumor cell growth and metastasis.

#### **Acknowledgement.**

The author wishes to thank Walter Wainright and Andrea Cohen, MD for their comments on the paper. As well as the two patients, PS and JH for their invaluable dedication to have their case narratives be available to all.

#### **Reference:**

**NOTE: REFERENCES NOS. 1 THRU 368 NOT INCLUDED IN THIS UNPUBLISHED MANUSCRIPT. TOTAL PAGES WITH REFERENCES TOTAL 41 PAGES.**