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“Foods that prevent cancer”

Diploma thesis

Prague, March 2010

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Master's programme of study

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Date and year of defence: March 2010

Written Declaration

I declare that I completed the submitted work individually and only used the mentioned sources and literature. Concurrently, I give my permission for this diploma/bachelor thesis to be used for study purposes.

Prague, March 2010

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1. INTRODUCTION

I chose the theme of my diploma thesis “Foods that prevent cancer” based on my long-term interest in this subject. I have always been interested in food and after starting my medical degree I have become more and more interested in the healthy aspect of the various fruits and vegetables we have today. Since it is widely known that food has a major influence on our health it is surprising to me why not more people care about their diet. As a medical student practicing in the faculty hospital of Charles University I have witnessed a large number of patients with various diseases-among them cancer- who both by their appearance and history have revealed an extremely poor diet.

In the modern society of today where we have an almost unlimited access to all kinds of foods there should have been more awareness among people about what to eat and what not to eat. However it must be emphasized that there are many different factors that influence people’s choice of food like nationality, traditions, education and socioeconomic status. For example if a child has grown up in a family where the diet consists mostly of fat and carbohydrates it is most likely that this child will continue to eat this kind of food. And if the fruit and vegetables are sold at a high price it is unlikely that persons with low incomes will spend money on this. Another thing to stress is that not all the foods we consider as “healthy” actually have that many benefits. A cucumber for example is healthy to eat but a tomato contains completely different health gaining molecules. So by choosing specific foods with a different composition of health promoting compounds we can prevent diseases like cancer.

Cancer is a disease of genes. However, both epidemiological and experimental evidence shows that only a small proportion of cancers are inherited. Environmental factors are most important and can be modified. These include smoking, infectious agents, radiation, industrial chemicals and pollution, medication and food. Over the long human lifespan our genes are vulnerable to mutations and nutritional factors are important in determining the likelihood of some of these mutations.¹

This thesis will therefore focus on the fruits, vegetables, drinks and spices that have cancer fighting properties.

2. EPIDEMIOLOGY

Lifestyle has a huge influence on the development of cancer. According to the latest statistics published by WHO Hungary and the Czech Republic have the highest incidence of cancer (400 pr. 100 000 inhabitants) followed closely by other industrialized countries like the USA (260 pr. 100 000 inhabitants). India, China and Thailand have on the contrary a much lower incidence of the disease (100 pr. 100 000 inhabitants).²

The type of cancer in the world varies as well. In the US approximately 100 of 100 000 women develop breast cancer in contrast to 8 of 100 000 Thai women. The same is true for colon cancer. While 50 of 100 000 people in certain parts of the Western world are affected, only 5 of 100 000 Indians have this disease. When it comes to prostate cancer the difference is even larger. It affects the Western population ten times more than the Japanese population and hundred times more than the Thai population.³

Studies of populations who have moved to new countries have confirmed that the great variations are not due to genes but rather to different lifestyle and diet. This is exemplified by Japanese immigrants in Hawaii who increased their risk of developing for example prostate cancer by a tenfold (table 1). Also, by comparing the incidence of certain cancers in the Afro-American population and an African population in Nigeria, there are striking differences that can not be explained by genetics (table 2).⁴

Cancer	Japan	Japanese in Hawaii	Original population of Hawaii
Oesophagus	131	46	75
Stomach	1311	397	217
Colon	83	371	368
Rectal	93	297	204
Lungs	268	379	962
Prostate	14	154	343
Breast	315	1221	1869
Cervix	364	149	243
Uterus	26	407	714
Ovaries	53	160	274

(Table 1: Doll, R. & Peto, R. (1981).Journal of National Cancer Institute 66, 1196-1305)

Cancer	Ibadan(Nigeria)	Black(USA)	White(USA)
Colon	34	351	315
Rectal	34	204	225
Liver	272	77	36
Pancreas	55	225	124
Laryngeal	37	193	141
Prostate	134	651	275
Lung	27	1532	981
Breast	337	1187	1650
Uterus	42	407	714
Lymphoma	133	7	4

(Table 2: Doll, R. & Peto, R. 1981, Journal of National Cancer Institute, 66, 1196-1305)

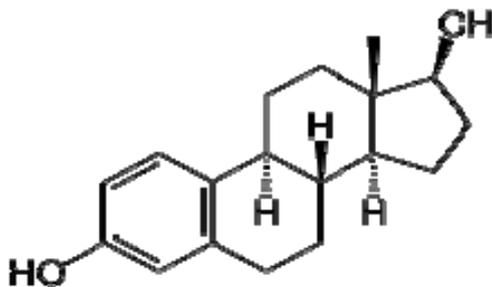
Newer epidemiologic studies suggest that a diet that lacks a sufficient amount of fruit and vegetables is a risk factor for developing cancer. The results that more than 200 of these studies have obtained are sensational (table 3).⁵

Food	Reduced risk	Number of studies	Percentage of studies that suggests reduced risk
Vegetables in general	59	74	80
Fruit in general	36	56	64
Raw vegetables	40	46	87
Vegetables of Brassica family (cabbage, broccoli)	38	55	69
Vegetables of the Allium family (garlic, onion)	27	35	77
Green vegetables	68	88	77
Carrots	59	73	81
Tomatoes	36	51	71
Citrus fruits	27	41	66

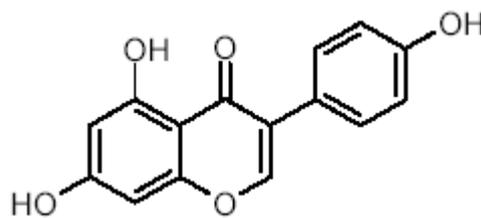
(Table: World Cancer Fund/American Institute for Cancer Research, 1997)

3. PREVENTION OF CANCER THROUGH THE DIET

Research has shown the last couple of years that a large amount of plants and other nutrients which is a part of the daily diet in different cultures are fantastic sources of molecules that can intervene in certain processes of cancer development. These natural molecules are in many ways similar to the synthetic medications used today because they block different phases in cancer progression. A molecule which is found in great amounts of soya for example, genistein, has a huge structural similarity to estradiol. Due to this similarity genistein can occupy the usual site where estradiol binds and reducing the biological effects this hormone has on for example breast cancer. The way genistein works can be compared with Tamoxifen, a drug used to treat this disease.⁶



Estradiol



Genistein

It is important to be aware that the development of tumours is a random event which is quite common in an individual's life. Pathological studies have shown that a great amount of people who have died of other causes than cancer had many tiny tumours hidden in the tissues. However, only a small proportion of these tumours get discovered in the population because they don't reach a clinical stage.⁷

Organ	Tumors found at autopsy (%)	Tumor found clinically (%)
Breast (women 40-50 years)	33	1
Prostate (men 40-50 years)	40	2
Thyroid	98	0,1

Asians have a lower rate of prostate cancer than people in the West, but biopsies performed on Asian and Western populations show that the amount of prostate cells that are in progress of becoming cancer cells is precisely the same in the two populations. The diet at this point is thought to be of crucial importance in preventing these micro tumours from reaching a clinical stage.⁸

Along with surgery, radiation and chemotherapy the diet should therefore be considered as an essential part of cancer therapy. The term nutraceutical has been invented as it combines the words nutrition and pharmaceutical and it comprises various types of foods with cancer preventing properties. Nutraceuticals can be compared to chemotherapy because they use their arsenal of cancer fighting molecules to combat cancer cells that develop spontaneously. *Cancer prevention through diet is however not an alternative type of treatment but it is an additional tool that every person can utilize to prevent cancer from developing.* A regularly intake of fruit and vegetables corresponds to a preventive chemotherapy that stops the micro tumours from reaching a clinical stage with pathological consequences without damaging the tissues. The neutraceuticals works both by acting directly on the cancer cells and by preventing angiogenesis as well as stimulating the immune system.⁹

Not all cancers are genetically inherited, but there are several genetic factors that make certain individuals especially prone to cancer when they are exposed to cancer causing agents. These people should protect themselves by ingesting cancer fighting molecules. This has been proved by a study in Shanghai showing that persons missing two important enzymes to eliminate aggressive toxins had three times big risk to be hit by lung cancer if their diet did not contain vegetables from the Brassica family (cabbage, broccoli, radish, turnip). On the other hand, people with the same mutations but who ate a lot of these greens had a reduced risk of getting cancer compared to the rest of the population.¹⁰

Extracts from garlic, beet root, and different types of cabbage have shown to provoke a full stop of the growth of isolated cancer cells in the very aggressive brain tumour medulloblastoma (see graph next page)¹¹. More investigations are needed in order to confirm what extent these foods can be used in addition to the general cancer therapy as of today, but the results achieved are promising. It seems like garlic especially is very dangerous for these cancer cells.

4. THE ANGIOGENIC BALANCE AND METRONOMICAL APPROACH

Dr. Judah Folkman a surgeon at the medical centre at Harvard university found out in 1971 that angiogenesis is necessary for tumours to grow. This hypothesis led to the development of the first anti-angiogenic drug Avastin in 2004. Until then, it was believed that the war against cancer was limited to destroying cancer cells by using the strongest possible dose of medications. Now it is known that the progression of tumours is the result of an imbalance between molecules that stimulate the formation of new vessels and other molecules that prevent these new vessels from forming.¹²

A new approach to cancer treatment called metronomic chemotherapy is based on a low-dose continuous multidrug therapy that reduces both the number of cancer cells and the angiogenesis. This metronomical strategy can be applied to selected foods with specific anti-angiogenic properties. These natural molecules attack the new vessels and prevent their maturation. Thanks to this anti-angiogenic, metronomic approach cancer is no longer a fatal disease; it is more a chronic disease that needs constant therapy to be under control. And this prevention can be achieved through the diet.¹³

5. THE PHYTOCHEMICAL COMPOUNDS

Food is often described as macro nutrients (carbohydrates, proteins and lipids) and micro nutrients (vitamins and minerals). But such a description is incomplete because fruit and vegetables also contain another group of molecules which are called phytochemicals. These compounds are the reason for the colour and the organoleptic properties of not only fruit and vegetables, but also certain spices and drinks. The bright colour of a raspberry and the characteristic smell of garlic are two examples of phytochemical properties.¹⁴

The phytochemicals are molecules that make it possible for plants to defend themselves against infections and damages which are caused by microorganisms and insects. When for example grapes are attacked by microorganisms, they excrete large amounts of an anti-fungal agent. These surviving properties can be applied also to humans by eating these phytochemicals. Before describing in what way the phytochemicals can prevent cancer, it is important to mention one thing: these molecules are not only antioxidants. Many phytochemicals have an ideal chemical structure that make them able to absorb free radicals and these molecules are much more powerful antioxidants than the vitamins. For example, an apple contain quite small amount of vitamin c (10 mg) but have an antioxidant effect which corresponds to 2250 mg C vitamin. In other words, the antioxidant abilities of fruit and vegetables are attributed to the phytochemicals and not so much the vitamins.¹⁵

The advantage with a diet which is based on a daily intake of nutraceutical nutrients is that the phytochemical compounds work in different ways. Not only do they neutralize the free radicals, they can also work on different levels in the progression towards cancer. A study has shown that a number of phytochemicals activate transcription factors such as NRF2 that regulate expression of phase II enzymes which detoxify carcinogens and protect against oxidative stress. Other prime targets of chemopreventive phytochemicals are the transcription factors NF- κ B and AP1. By blocking the action of these factors the malignant transformation of cells is prevented as well as the normal function of apoptosis is maintained. The multifunctional protein β -Catenin is also a target of many phytochemicals. This protein function as a transcription factor and nuclear translocation of β -catenin has been associated with various human cancers.¹⁶

It is easy to determine the phytochemical properties of foods by their colour and smell. Fruits with extreme colours are for example important sources of molecules called polyphenols. More than 4000 polyphenols have been found until now and there is a high content of these compounds in red wine, green tea, grapes, onions, wild berries and various spices. Other groups of phytochemical compounds are characterized by the smell. The smell of crushed garlic or boiled cabbage is due to their sulphuric compounds while the more pleasant smell of citrus fruits is associated with the presence of certain terpenes. But even though all fruits and vegetables contain phytochemicals the amount and type of these compounds varies between them. It is for example extremely important to include three foods that contain the highest amount of cancer fighting molecules, green tea, soy and turmeric as these basic ingredients are constitute major part of the diet in the countries with the lowest incidence of cancer.¹⁷

The main group of phytochemical compounds in fruits and vegetables:

Family	Class
Polyphenols	Flavonoids Phenolacids Non-flavonoids
Terpens	Carotenoids Monoterpenes
Sulphuric compounds	Allyl sulphides Isothiocyanates
Saponins	Triterpenoids Steroids

6. CABBAGE

A study which analyzed 252 cases of urinary bladder cancer in 47909 health workers over a period of 10 years indicates that by eating 5 portions or more of cabbage weekly (broccoli in particular) halves the risk of this particular cancer, compared to those who only ate 1 portion or less weekly. The same accounts for breast cancer. Chinese women who eat most cabbage-like food have half the risk of developing breast cancer compared to those who don't eat these vegetables. And this is independent on how much soy they eat. Also, in Sweden a study showed that by eating one or two cabbage-like foods a day reduced breast cancer by 40 %. These vegetables have additionally a positive effect on lung, stomach, colon, rectal and prostate cancer. Cabbage like food has actually proved to be better than tomatoes in preventing prostate cancer. All of these facts are important for the western diet, especially in North-America where 50 % of the daily intake of fruits and vegetables consist of potatoes.¹⁸

Of all the plants human beings eat, cabbage like foods contain the biggest amount of phytochemical molecules with cancer preventing capabilities. In addition to many polyphenols, cabbage-like foods also contain compounds called glucosinolates which release two very powerful cancer preventing molecules; isothiocyanates and indoles. By chewing the vegetables the glucosinolates get mixed with an enzyme called myrosinase and these two powerful agents are released. So in the case of chewing broccoli for example we get the important isothiocyante sulforafan after glukorafanin (a glucosinolate) has reacted with myrosinase.¹⁹

An important fact to stress is that the glucosinolates are soluble in water. If cabbage-like foods are cooked in ten minutes, the amount of glucosinolates will be reduced by half . Also, the activity of myrosinase is very sensitive to heat so prolonged cooking of these vegetables will prevent the release of isothiocyanates when chewed. Thus, the vegetables should be steamed instead of boiled for the shortest time possible. Deep frozen vegetables are blanched at a high temperature which is reducing both the content of glucosinolates and myrosinase, so eating fresh products is a much better option.²⁰

The amount of glucosinolates varies among the vegetables and this is important as certain

isothiocyanates are more powerful than others. This is especially true when it comes to sulforafan which is found in broccoli in as much as 60 mg pr. portion. It is also interesting to underline the fact that broccoli sprouts contain over a hundred times more of this compound.²¹

Scientific research in the last ten years have proved that sulforafan get rid of cancer provoking substances. This effect has reduced the incidence, number and size of breast tumours in rats and mice. Epidemiological studies show that this effect also applies for human beings. It can seem like sulforafan also acts directly on the cancer cells and kill them by triggering apoptosis. A study showed that among substances derived from food the only substance able to kill isolated cells of medulloblastoma was sulforafan. This also applied to other types of tumors of colon and prostate and acute lymphoblastic leukemia.²² Sulforafan has antibiotic properties as well, especially against *Helicobacter Pylori* which is a cause of gastric cancer.²³

Other isothiocyanates and indoles that deserve to be mentioned are phenethylisothiocyanat (PEITC) and indol-3-karbinol (I3C). PEITC is a molecule released from gluconasturtiin, a glucosinolate found in large amounts in water cress and Chinese cabbage. Just like sulforafan PEITC is capable to protect lab animals against cancer after they are being exposed to cancer provoking agents. This applies especially to cancer in oesophagus, stomach, colon and lungs. PEICT has in addition a direct effect on cancer cells by inducing apoptosis. This ability shows that PEITC not only can prevent the development of tumours, but it can also suppress further growth of already existing tumours. I3C on the other hand can change the structure of estradiol which results in the reduction of the hormones ability to promote cancerous growth in breast, uterus and cervix.²⁴

7. GARLIC

Garlic and onion are members of the Allium family. The characteristic aroma and taste is due to the high content of sulphuric phytochemical compounds. While being stored in a cold place garlic gradually accumulates alliin. When crushing the garlic the cells are destroyed and an enzyme called alliinase is released in the process. When this enzyme reacts with alliin a molecule called allicin is formed. Allicin is the reason for the strong smell when we crush the garlic. There can be large amounts of allicin in the garlic but this molecule is very unstable and it is almost immediately transformed into other less complex sulphuric products like diallylsulfid (DAS) and diallyldisulfid (DADS).²⁵

These cancer-preventing molecules have been studied in a laboratory by testing them on animals. As a general rule the results match with the observations done in the population. It seems like garlic is particularly effective against the development of cancer evoked by nitrosamines, a group of chemical compounds that are extremely cancer provoking. These chemical compounds are formed by the bacterial flora in the intestines from nitrites which are compounds used as preservatives in marinades, sausages, bacon and ham. DAS is also able to neutralize the development of lung cancer which is provoked by NNK, a very important nitrosamine formed from nicotine when tobacco is burning. Garlic has a better protecting effect than onions though it has been suggested that onions also reduce the risk of stomach cancer. The compounds in garlic and onions (especially DAS) stop the development of cancer by inhibiting the enzymes responsible for the activation of the cancerous substances at the same time as they stimulate the enzymes that eliminate these substances. The cells are therefore less prone to mutations of DNA. In addition to the direct effect on the cancer provoking substances the garlic's chemical compounds can also attack tumours directly and destroy them by activating the process of apoptosis.²⁶

DAS can also contribute to the death of cancer cells by changing their ability to release special proteins that make the cells capable to resist certain chemo therapies.²⁷

The best way of ingesting as much allicin as possible is by eating fresh garlic. Studies have shown that garlic supplements bought in health food stores contain a lot of alliin that never get changed into allicin because the action of alliinase is not maintained in pills²⁸. Research

up to today has shown that the cancer preventing properties of garlic are directed towards cancer of the gastrointestinal system, especially oesophagus, stomach and large intestine. Epidemiologic studies done in the Yangzhoong province in northeast China where the incidence of stomach cancer is high has showed the benefits of garlic and onions. People eating small amounts of these vegetables have a three times increased risk of developing the disease. Similar results have been obtained in Italy by comparing diets of the inhabitants in north where garlic is much less used than in the south.²⁹ Garlic can also prevent other types of cancer especially prostate cancer. A study performed in Shanghai showed that people who ate more than 10 g pr. day of the vegetables in the Allium family had 50 % less prostate cancer than those eating less than 2 g pr. day.³⁰

When it comes to breast cancer the role of garlic has not been proved to be protecting. A Dutch study suggests that even though onions could reduce stomach cancer, it had no effect on breast cancer. But because the Dutch diet consists of large amounts of fat which is a factor causing breast cancer this particular fact can be held responsible for the result. It is interesting to point out that French scientists on the other hand have proved that the intake of garlic and onion of women in the Lorraine area of France was related to a reduction in breast cancer. The Western population eats much less vegetables from the Allium family than what's necessary for reducing cancer in the prostate and breast. For example, only 15 % of British men eat 6 grams of garlic a week and not more than 20 % of American women ingest 2 grams a week.

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It seems like the cancer preventing properties of garlic is primarily connected to their content of sulphuric compounds. When it comes to onions they contain very important polyphenols like quercetin, which can stop the growth of cancer cells grown in laboratories and that prevents the development of cancer in animals.³²

8. SOY

The average daily intake of soy is about 65 grams per person in Japan and 40 grams per person in China, while it doesn't exceed 1 gram in the West. Soy is rich in proteins, essential fatty acids, vitamins, minerals and fibre and the most important phytochemical compounds in soy are polyphenols called isoflavones. Most soy products contain a big amount of isoflavones except for soy sauce where most of the molecules are reduced during the long fermentation process and soy oil which is completely without. Many people in the West eat soy proteins without being aware of it. There are a lot of products that contain proteins extracted from soy. So rather than being used in its more natural form like in the east, soy proteins are used in various products like hamburgers, sausages, dairy products, bread, cakes and cookies in the West. These products contain a very low amount of isoflavones since the soy concentrate they contain is a result of industrial processing of the beans. The cancer preventing properties of the beans thus disappear during this process.³³

The most important isoflavones in soy are genistein and daidzein while glycitein is found in smaller amounts. An interesting property of the isoflavones is their striking similarity with the female sex hormone estrogen. These molecules are therefore often called phytoestrogens. Genistein is the most important molecule. The phytoestrogens can influence the activity of various proteins that contribute to the growth of tumor cells in breast or prostate cancer. They can also act as anti-estrogen and in that way weaken the cells reaction to these hormones. Genistein is able to bind to the estrogen receptor but this affinity is weaker so the response is not as powerful as the one evoked by the hormone. This mechanism is similar to that of Tamoxifen, an anti-estrogen used to battle breast cancer.³⁴

Until now 14 separate studies have investigated the relationship between the amount of soy in the diet and women's risk of developing breast cancer. The result of the first study which was done in Singapore suggests that there was a connection between the number of breast cancer incidences and amount of soy ingested. The premenopausal women who ate most soy (55 gram and more per day) had half the risk of developing breast cancer compared to those who ate less than 20 gram soy daily. Other similar studies made in Shanghai, Japan and USA have all showed that the intake of soy is related to a reduction of breast cancer.³⁵ Recently a study

on 21 852 Japanese women in a ten year period showed that a daily intake of miso soup and a supply of 25 mg isoflavones each day reduced the incidence of breast cancer.³⁶ But, paradoxically, a study performed in California that included 111 526 female teachers did not show any connection between soy and breast cancer. This has also been the result of three other studies of smaller scales. So what can we conclude after these contradictory findings? First of all it is important to note that the supply of isoflavones was extremely low in the study performed in California. For example, in a study performed in San Francisco among non-Asian women, the intake of soy was only 3 mg isoflavones each day and these came mainly from industrially processed food. Barely ten per cent of these people ate miso or tofu more than one time a month compared to the three daily servings of the Japanese women with low risk of developing the disease³⁷

Another important aspect to look at is at what age the women starts to eat soy. It is crucial to begin at a young age as the protective effect continues to work later in life even though the woman eats less soy then. Even though Japanese women who immigrate to the USA have almost the same risk of developing breast cancer as women born in the USA, it is shown that the risk is less when the women emigrate later in life.³⁸ These observations match with results achieved in laboratories where rats that before puberty got a soy rich diet became more resistant to a cancerous compound causing breast tumours than the rats that only got soy after adulthood.³⁹

Asians have a lower incidence of prostate cancer in the population but relatively few studies have tried to explore the role of isoflavones in preventing this type of cancer. A study who investigated 8000 men of Japanese origin who lived in Hawaii suggested that the intake of rice and tofu was connected to a lower risk of developing prostate cancer. A study on 12395 Adventists in California who drank at least one portion of soy milk showed a 70 % reduction of prostate cancer.⁴⁰

Even though most scientists, doctors and nutritionists agree that soy is beneficial for health there is a controversy about this as well especially in two situations:

a) postmenopausal women

b) women who have or had breast cancer.

a) The climacterium is due to a reduction in the female sex hormones estrogen and progesterone. To reduce the symptoms connected to this period of a woman's life hormone replacement therapy is used by many. But as this therapy is controversial due to its risk of developing breast cancer many Western women use alternative isoflavine treatment instead and it is in this particular situation the phytoestrogens can be dangerous:

Both the scope and frequency of the side effects of the climacterium is reduced in Asian women compared to the women in the West. Only 14 % of Chinese and 25 % of Japanese women complain of hot flushes while 70 to 80 % of Western women complain of the same. As in the case of breast cancer the marked difference in soy intake of women of these two cultures has been taken into account to explain these differences. The pharmacological market has therefore seen an increase in products enriched with isoflavones from soy. These products are controversial because products rich in isoflavones accelerate the development of breast cancer in lab mice where the oestrogen level is low, like in women after menopause. The products are even more questionable after a study showed increased tumour markers and oestrogen in blood and hyperplasia cells in women between 30 and 58 years who got a preparation with soy proteins. These results have made some to suggest that postmenopausal women and those who have or had breast cancer should avoid soy. It is important to separate these two phenomena before drawing a conclusion. In the case of climacterium this allegation is absurd because there is no doubt that soy is healthy for women's health no matter what their age. This is proved by the low incidence of cancer in the Asian countries. The harmful effect is rather due to preparations enriched with isoflavones that has little to do with food based purely on soy. Instead of gradually incorporating soy in the daily diet in order to eventually reach the amounts the Asians have built up, the Western world is more concerned with isolating as much as possible of the active components of soy in order to sell it as pills with the highest economic gain. Some pills sold today without any regulations contain as much as 100 mg isoflavones per tablet. When comparing this to the considerably lower amount Japanese ingest by one daily serving of miso soup (25 mg) it is not surprising that the Western way of using soy can induce breast cancer.⁴¹

When it comes to women who suffers from breast cancer or who have survived it the situation is a bit more complicated. More than 75% of the cancer incidences are diagnosed in women over 50 years and most of these cancers are related to oestrogen. Since the combination of oestrogen and progesterone increase the risk of breast cancer some scientists have postulated a

hypothesis saying that the isoflavones ability to bind with oestrogen receptors can promote tumours in the breast in women who have low oestrogen levels and remaining tumours left in the breast tissue. This hypothesis is strengthened by the fact that mice with breast tumours that got preparations enriched with isoflavones got bigger tumours. Therefore it is absolutely necessary that women who are diagnosed with breast cancer should avoid these preparations.⁴²

9. TURMERIC

Turmeric is a bright yellow powder which comes from the dried root of the plant *Curcuma longa* found mainly in India and Indonesia. It is a very important spice in the Indian cuisine. It is also used to cure gastrointestinal problems, fever, infections, arthritis, dysentery and jaundice in the traditional Indian medicine practice called Ayurveda. Chinese medicine use turmeric to treat liver problems, constipation and bleeding. It is also interesting to find that Indians have the lowest rate of Alzheimer's in the world, 5 times lower than in the West. There are no epidemiologic studies made on the possible relation between the intake of turmeric and the development of cancer. However, there is a wide agreement in scientific circles that turmeric can be the reason for the enormous differences between the incidence of certain cancers in India and countries in the Western world for example the USA. The hypothesis is based on the fact that turmeric is mainly eaten in India.⁴³

	Men, India	Women, India	Men, USA	Women, USA
All cancers(-skin)	99	104	361	283
Lung	9	2	59	34
Colon/Rectal	5	3	41	31
Breast	-	19	-	91
Ovarian	-	5	-	11
Endometrial	-	2	-	16
Prostate	5	-	104	-
Liver	2	2	4	2
Urinary bladder	3	1	23	5
Kidney	1	0.5	11	6

(based on a population of 100 000 persons. GLOBOCAN 2000: Cancer incidence, mortality and prevalence worldwide Lyon,France: IARC Press; 2001

Curcumin is the main ingredient in turmeric. Its molecule is not only responsible for its yellow color but also for its diverse health promoting abilities. Curcumin has several pharmacological activities (antithrombotic, anticholesterolemic, antioxidant) as well as a powerful cancer preventing potential. The curcumin's effect on lab animals is well known because it prevents tumours from developing in mice. These studies have shown that curcumin can be useful in the prevention and treatment of stomach, intestinal, skin and liver cancer. These effects are due to both curcumin's ability to induce apoptosis of cancer cells and to inhibit angiogenesis. Experiments have shown that curcumin is mostly effective against cancer of the large intestine as it reduces the amount of COX 2 which is the reason for inflammatory reactions in the gut. ⁴⁴

10. GREEN TEA

Tea is the world's most popular drink after water. Black tea is favoured by 78 % and is mostly drunk by the Western population while green tea is consumed by 20 % and mostly in the East where black tea is uncommon. Despite the fact that green and black teas have a common origin, their chemical composition is completely different as the polyphenols in black tea leaves are changed drastically during the fermentation process. The oxidation leads to the production of compounds called theaflavins and this has serious consequences when it comes to the ability of fighting cancer since it is the polyphenols in the fresh leaves that accounts for this. ⁴⁵

One third of the weight of green tea leaves consists of a special group of polyphenols called flavonols or catechins and these are the main molecules responsible for the cancer preventing property of green tea. One particular catechin called epigallocatechin-3-gallate (EGCG) is especially important. ⁴⁶

The composition of catechins in green tea varies according to where it is grown, the season of harvesting and the manufacturing process. Experiments have shown that green tea from Japan contains a lot more of EGCG than the Chinese tea. It is also crucial to allow the tea leaves to steep in hot water long enough so that the highest portion of catechins are released. Tea that is

left in the pot for only two minutes contain 60 times less polyphenols than tea that has steeped for ten minutes. 47

Several studies have shown that green tea has a favourable effect when it comes to preventing especially cancer of the urinary bladder and prostate. It is also postulated that green tea has a protective effect on breast and stomach cancer as well, but the results are contradictory at this point. This is probably due to the extreme variations of polyphenols found in green tea around the world.⁴⁸

There are however many indications that green tea can reduce the chance of getting cancer. EGCG prevents the in vitro growth of many different cancer cells like leukaemia, kidneys, skin, breast, and mouth. These results are important because studies made on animals have shown that green tea prevents the development of tumours provoked by cancer promoting agents, especially skin cancer, breast, lung, oesophagus, stomach and large intestine. It doesn't seem like the protecting effect is limited only to tumours developed from cancer promoting agents since also genetically modified mice that spontaneously developed prostate cancer also reduced their tumours considerably. These findings are sensational because the dose of green tea the mice got can easily be obtained by humans if drinking green tea regularly.⁴⁹

Green tea has a very powerful effect on angiogenesis. Of all molecules derived from food EGCG is the most effective in blocking the activity of the VEGF receptor which is an important element in the process of angiogenesis. The most interesting finding is that the inhibition of the receptor is extremely fast and only very low concentrations of the compound are necessary. This can be achieved by drinking a few cups of green tea every day.⁵⁰

11. WILD BERRIES

Berries contain three important phytochemical compounds called ellagic acid, antocyanides and proanthocyanides. Ellagic acid is probably the most powerful of these. Raspberries and strawberries contain especially high amounts of this polyphenol. The cancer preventing potential of these berries has been tested in laboratories on both isolated cancer cells and lab animals that have been exposed to cancerous compounds. The effects of these berries are connected to the amount of polyphenols they contain and not to their antioxidant potential. The ellagic acid not only prevents the cancerous agents to cause mutations of DNA. It also inhibits two proteins, VEGF and PDGF that are necessary for the development of angiogenesis.⁵¹

Antocyanides is a class of polyphenols that are responsible for the intense colour and antioxidant potential of berries and is found in particularly high amounts in raspberries and blueberries. Several studies have pointed out that the antocyanides not only are molecules with antioxidant properties. They can also stop the DNA synthesis in isolated tumor cells grown in laboratories and thereby induce apoptosis. And delphinidin, an antocyanidin found in blueberries, prevents the activity of the VEGF receptor responsible for angiogenesis. It is interesting to note that this activity is not connected to the antioxidant property of delphinidin, because a similar molecule found in blueberries, malvidin, is not able to interfere with the VEGF receptor.⁵²

Proanthocyanides are complex polyphenols found in cranberries and blueberries with an unusually high amount of antioxidants. They can prevent the growth of isolated tumor cells (especially those that origin from the colon) and also prevent angiogenesis.⁵³

12. OMEGA -3

The polyunsaturated fatty acids- omega-3 and omega-6- are essential because the human body is not able to produce them. Omega -6 is found in large quantities in meat, egg, vegetables and various oils. The intake of the most important lipid of this category, linoleic acid (LA), is therefore sufficient. It is much more difficult on the other hand to get enough of omega-3. The ratio of omega-6 to omega-3 intake today is 20/1. This imbalance which favours omega-6 can

have negative consequences and lead to chronic diseases like cardiovascular diseases and cancer as omega-6 can produce molecules that lead to inflammations.⁵⁴

Omega-3 on the other hand is important because it produces anti-inflammatory molecules. Fat fish is the main source of two omega-3 acids, eicosapentaenoic acid (EPA) and dokosahexaen acid (DHA). These fish synthesize the two fatty acids from alpha linolen acid (LNA) which is an omega-3 found in plankton. LNA is also found in linseed, soy and nuts. However, the production of EPA and DHA from LNA is not particularly effective in humans when there is an increased amount of omega-6 in the diet. The reason for this is that the enzymes that produce these acids out of LNA are the same that transforms the LA in omega-6 to inflammation causing molecules. Studies have shown a reduced risk of developing breast, prostate and colon cancer in people eating fish. This finding is strengthened by the results from laboratory animals and isolated cancer cells. While omega-6 fatty acids are known to be a triggering factor of cancer, omega-3 has the opposite effect on laboratory rats because it reduces tumour development in breast, colon, prostate and pancreas.⁵⁵

13. TOMATOES

Lycopene is a member of the carotenoid family which is a huge group of phytochemicals responsible for the strong colours of many fruits and vegetables. The role of lycopenes is still not yet completely known, but several observations suggest that it is the most cancer preventing of all carotenoids. Tomatoes are the best source of lycopene. It is best to eat cooked tomatoes rather than raw, since the cells have then been broken down and the molecules are more available for absorption. Fat increases the availability of lycopenes. The ideal product is therefore tomato sauce since it has a high concentration of molecules and it contains olive oil.⁵⁶

Countries with the highest intake of tomatoes like Italy, Spain and Mexico have a lower rate of prostate cancer than the USA. It seems like this connection applies in a higher extent to those over 65 years, something that suggests that lycopene is more likely to counteract prostate cancer occurring at a higher age than in younger age which is more likely to be of genetic origin. In what way the lycopenes work in order to prevent cancer is not fully understood. It is a powerful antioxidant just like its related family member beta-carotene but it can also prevent the development of prostate cancer by its direct effect on certain enzymes like androgens that cause the tissue to grow.⁵⁷

14. CITRUS FRUITS

Citrus fruits are much more than a rich source of vitamin C. They contain many phytochemicals as well. An orange contains almost 200 different compounds and among them are important polyphenols called flavanone, flavone O- and C- glycosides and methoxylated flavones. Each of these groups of compounds exhibits a number of in vitro and in vivo anti-inflammatory and anticancer actions due to their effect on the microvascular endothelial tissue. Evidence suggests that the biological actions of the citrus flavonoids are linked to their interaction with key regulatory enzymes involved in cell activation and receptor binding.⁵⁸

Studies made in different parts of the world have shown a correlation between citrus fruits and a reduced risk of developing certain cancers of the esophagus, mouth, larynx and stomach. Recent findings have also revealed a reduced risk of getting leukemia by drinking orange juice regularly⁵⁹.

It seems like the most important cancer preventing property of citrus fruits is connected to their ability to detoxify cancerous agents. Monoterpenes, another phytochemical compound found in citrus fruits have antitumor activities as well. Evidence suggests that the blocking chemopreventive effects of monoterpenes during the initiation phase of mammary carcinogenesis are likely due to the induction of Phase II carcinogen-metabolizing enzymes, resulting in carcinogen detoxification. The tumour suppressive chemopreventive activity in the post-initiation phase may be due to the induction of apoptosis and/or inhibition of cell-growth regulating proteins.⁶⁰

15. RED WINE

Red wine has a positive effect not only on cardiovascular diseases but also cancer. A Danish study of 13 064 men and 11459 women between 20-98 years of age found that a moderate intake of red wine not only reduced the risk of dying of cardiovascular diseases by 40 % , it also reduced the risk of dying of cancer by 22%.⁶¹

Red wine is not like other alcoholic drinks. The complex content of molecules is due to the long fermenting process of the grapes which leads to important changes in their chemical composition. There are hundreds of different molecules and the group of polyphenols

constitutes a great part. Resveratrol which is only found in red wine is the polyphenol of most interest even though it is found in very small amounts compared to the other phytochemicals. The wine plants production of resveratrol is a part of the plants defense mechanism against environmental stress like pollution or microorganisms such as fungi⁶².

In 1996 resveratrol was identified as the first molecule of nutritional origin that could interfere with tumour growth because it was able to prevent the three stages necessary to develop cancer; initiation, promotion and progression. Resveratrol was found to act as an antioxidant and antimutagen and to induce phase II drug metabolizing enzymes (anti-initiation activity); it mediated anti-inflammatory effects and inhibited cyclooxygenase and hydroperoxidase functions (antipromotion activity) and it induced human promyelocytic leukemia cell differentiation (antipromotion activity).⁶³

Just like turmeric resveratrol is a very powerful cancer fighting molecule and its mode of action is at least as effective as many medicines of synthetic origin. Studies of laboratory animals have shown resveratrol can prevent cancer of breast, colon and esophagus. The concentration of resveratrol in the blood of these animals was between 0,1-2 μmol s per liter which is an amount that can be achieved by a moderate intake of red wine.⁶⁴

16. CHOCOLATE

One bite of dark chocolate contains twice as much polyphenols as a glass of red wine and just as much as green tea that has steeped for a long time. The most important polyphenols in cocoa are the same as the one found in green tea (catechins) and the polymers made of these molecules, proanthocyanides can constitute up to 48 % of the cocoa beans weight.⁶⁵

Since the content of phytochemical compounds in cocoa is similar to that of other foods described in previously it is most likely that chocolate has cancer fighting properties as well.⁶⁶ Even though studies are in the beginning phase the results are promising. It has been observed that the proanthocyanides are capable of delaying certain cancers that have been induced in laboratory animals especially lung cancer. The intake of polyphenols results in a marked reduction in a receptor (EGFR) which is crucial for cell growth and angiogenesis.⁶⁷

Source	Polyphenols (mg)
Dark chocolate (50 g)	300
Green tea	250
Cocoa (2 tablespoons)	200
Red wine (125 ml)	150
Milk chocolate (50 g)	100

	Green tea	Turmeric	Soy	Cabbage	Garlic and onion	Grapes and berries	Citrus fruits	Tomatoes	Omega-3	Chocolate
Reduction of cancerous agents				•	•	•	•			
Growth inhibition of tumour cells	•	•	•	•	•	•	•	•	•	•
Induction of tumour death		•	•	•	•	•				
Interference of angiogenesis	•	•	•			•			•	
Effect on immune system		•					•		•	

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17. CONCLUSION

The aim of this thesis has been to highlight the importance of including specific foods in the diet to prevent diseases like cancer. Even though many of the interesting findings described yet has to be confirmed there is no doubt that many cancers worldwide could have been prevented if people ate more fruits, vegetables and fibre and less sugar, fat and red meat. This applies especially for the Western population. A great part of the Western world has shown a profoundly lack of interest in diet. A result of this is that fantastic sources of cancer fighting molecules have and never will be included in the daily food. I am interested in the preventive aspect of medicine and as a future medical doctor I will emphasize this to my patients. I think it is my duty to try to influence people's habits and not only to treat their diseases. This will not only benefit the patient but the society as well considering the huge amount of money diseases costs annually.

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