



Mainland Wasabi Limited

Growers of Nutraceutical Grade Wasabia Japonica

Science and Biomedical information about Real Wasabi

Wasabia japonica - Nature's Gift

Scientific evidence shows us many biomedical applications for the natural products found in *Wasabia japonica*. Existing findings centre on the isothiocyanates with the major areas of interest being:

1. Anti-Cancer (breast, prostate, colon, lung, leukaemia, pancreas oesophagus, bladder and others).

Numerous studies have demonstrated that *Wasabia japonica* contains natural chemicals that are highly efficacious against a variety of cancers. These chemicals are known as isothiocyanates (ITC's), which arise from the enzymatic breakdown of glucosinolate molecules, found in intact cells. When Wasabi cells are disrupted (i.e. macerated) the glucosinolates contact the myrosinase enzyme which catalyses the conversion to isothiocyanates. Wasabi has been shown (Ina *et al.* 1990, Sakura *et al.* 1993) to possess more than twenty different isothiocyanates.



Plantlets from Wasabi tissue culture.

Isothiocyanate extracts from Wasabi have been proven effective against stomach cancers (Tanida *et al.* 1991, Fuke *et al.* 1994, Fuke *et al.* 1997, Shin and Lee 1998, Ono *et al.* 1998), lung cancer (Yano *et al.* 2000) leukaemia (Nakamura *et al.* 2001) and breast cancer (Nomura *et al.* 2005).

Furthermore, isothiocyanates from other sources, but also shown to be present in Wasabi (Ina *et al.* 1990, Sakura *et al.* 1993), have been found to be effective against lung and oesophageal cancers (Stoner and Morse (1997), prostate cancer (Chiao *et al.* 2000, Scott *et al.* 2000) and breast, fore stomach and colon cancers (Wattenberg 1977, 1981). Numerous studies (Stoner *et al.* 1998, Hecht *et al.* 1996a and b, Hecht *et al.* 2000, Chung 2001) have shown isothiocyanates to block the cancer inducing effects of compounds that are associated with cigarette smoke. Included in these findings is the observation that the isothiocyanates may be effective in preventing cancer induction in both smokers and ex-smokers.

Isothiocyanates are easily administered which sets them apart from many pharmaceutically based cancer treatments currently in use. The high efficacies of isothiocyanates against cancer is maintained even when they are administered orally or a part of a diet (Morse *et al.* 1993, Kirlin *et al.* 1999, Hou *et al.* 2000, Fuke *et al.* 2000 [in the drinking water!!], Chiao *et al.* 2004, Tang and Zhang 2004, Tseng *et al.* 2004).

On the other hand, present pharmaceutically based cancer treatments are expensive, difficult to administer, and have many well-documented adverse side effects including toxicity.

There is now a growing base of evidence on how isothiocyanates act against cancerous cells. Isothiocyanates act to inhibit enzymes that cause pre-carcinogenic compounds to turn into carcinogenic ones (Phase 1 enzymes) and they also can induce Phase 2 enzymes which fight against cancerous cells (Yu *et al.* 1996, Hecht 1999, Kirilin *et al.* 1999), possibly through gene expression (Yu *et al.* 1996, Gao and Talalay 2004), inhibit initiation of cancerous growths (Yano *et al.* 2000) and induce glutathione S-transferase (Morimitsu *et al.* 2000). 6-methylsulfinylhexyl isothiocyanate has been shown also to block the cell cycle of cancerous cells (Hashimoto *et al.* 2004). This same molecule has been shown to effect protein production in cancerous cells (Hou *et al.* 2000).



ITCs in Wasabi have been shown to suppress dissemination or metastasis of cancerous tumour cells.

Metastasis, a critical stage in cancer development is blocked by ITCs and in particular 6MITC. Fuke and her co-workers (1997, 2000, 2006) and Manesh and Kuttan (2003) have shown that 6-MITC from Wasabi suppressed dissemination or metastasis of tumour cells. *Wasabia japonica* contains a high concentration of 6-MITC.

In numerous cases the ITCs from Wasabi have been shown to cause cancerous cells to undergo apoptosis or cell death. This has been shown in leukaemia cells (Nakamura *et al.* 2001, Fimagnori *et al.* 2004), breast cancer cells (Nomura *et al.* 2005), lung cancer (Kuang and Chen 2004), colorectal cancer (Lund *et al.* 2001) and cancerous cells of other cell types (Watanabe *et al.* 2003, Fimognari *et al.* 2005).

An important point to be made here is that ITCs are efficacious against the cancerous cells but do not harm healthy cells. No side effects have been encountered. Musk and co-workers (1993, 1995) showed that AITC was selectively toxic towards colorectal tumour cells. Nakamura *et al.* (2001) found in the case of leukaemia that the isothiocyanates from Wasabi inhibit the growth of leukaemia cells but do not inhibit normal cells. From this finding Nakamura *et al.* suggested that a remarkable therapeutic effect could be expected.

2. Antibiotic - infections, oral hygiene, cavity prevention and ulcers

It has long been known that Wasabi contains natural antibiotics and it was this feature that brought Wasabi into Japanese cuisine 1300 years ago.

Isothiocyanate vapours inhibit the growth of several strains of bacteria, yeast and mould (Depree *et al.* 1999). Other scientific studies (Hasegawa *et al.* 1998, Ono *et al.* 1998, Shin and Lee 1999) have shown that 6-MITC from Wasabi extracts have potent anti-bacterial properties against *Staphylococcus aureas* and *Escherichia coli*, common types of bacteria leading to infections and food poisonings.



Wasabi is a powerful, natural antibiotic.

Isothiocyanates in Wasabi have demonstrated an inhibitory effect against *Streptococcus mutans*, the bacterium responsible for dental cavities. Wasabi has also been found to interfere with the sucrose-dependent adherence of cells. As recently as December 2000, Japanese scientist Hideki Masuda, Ph.D. presented evidence of these findings at an international meeting of chemists in Honolulu, Hawaii (The 2000 International Chemical Congress of Pacific Basis Societies, Hawaii, December 2000). These results may lead to the possibility of Wasabi extracts to be used in a variety of products (i.e. toothpastes

and mouthwashes) for cavity prevention. More recent research has proven Wasabi extracts to be efficacious against mutant strains of *Staphylococcus* (Hasegawa 2002).

Another disease causing bacterium that Wasabi and ITCs are effective against is *Helicobacterium pylori* (Kinae *et al.* 2001, Haristoy *et al.* 2003, Masuda *et al.* 2004, Shin *et al.* 2004, Haristoy *et al.* 2005) This bacterium is known to be responsible for ulcers and ensuing stomach cancers. Wasabi extracts have been shown to kill the bacterium, even if the bacterium has entered a cell lining the stomach. Under this condition pharmaceutical antibiotics have proven themselves ineffective. Ulcers affect a large percentage of the population in certain cultures.

3. Anti-Coagulant - blood thinning for circulation and prevention of strokes, treatment of atherosclerosis (blood vessels narrowed by plaque), surgical uses.

The 6-MITC of Wasabi has been found to inhibit platelet aggregation thus making it an effective anti-coagulant (Kumagai *et al.* 1994, Morimitsu *et al.* 2000, Morimitsu *et al.* 2002). These anti-coagulant properties could be used in the treatment of the elderly, and during surgery where preventing platelet aggregation is vital. Platelet aggregation is recognized to be a precipitating factor in cardiovascular diseases. 6-MITC may inhibit platelet aggregation by a number of different mechanisms including the inhibition of lipoxigenase, cyclooxygenase, cAMP phosphodiesterases and CGMP phosphodiesterase.

4. Anti-Inflammatory (asthma, arthritis, allergies, anaphylaxis - aids in the healing process)

Isothiocyanates of Wasabi and other crucifers are effective anti-inflammatory (Depree *et al.* 1998) and anti-asthmatic (Dorsch *et al.* 1985) agents. Depree *et al.* (1998) were so impressed with their results when testing isothiocyanates that they made the following statements: 'The anti-inflammatory effects and inhibition of platelet aggregation by omega-methylthioalkyl isothiocyanates is perhaps of more interest given the rapid action of the compounds and the low levels at which they are effective. This could potentially be used to counter inflammatory conditions such as asthma or even anaphylaxis. The ability of the Wasabi isothiocyanates to inhibit platelet aggregation could also have medical applications, particularly in the treatment of heart attacks. Further work on the pharmacology of these compounds and their possible medicinal use, as well as other medicinal properties of Wasabi seems warranted.'



Wasabia japonica - with its powerful nutraceutical attributes, truly a miracle plant.

Other inflammatory conditions that may be treated with Wasabi's isothiocyanates include rheumatoid arthritis, inflammatory bowel disease (Crohn's Disease and ulcerative colitis), allergies and septic shock.

5. Aids in Bone Calcification (fights/prevents Osteoporosis).

Suzuki and his co-authors have found that a small molecular weight compound in *Wasabia japonica* leaf stalk extract has a significant stimulatory effect on bone calcification in vitro (Suzuki *et al.* 1997) and in vivo (Suzuki *et al.* 1999). The authors' findings revealed that the compound was easily extracted from the plant tissue, is of small molecular weight and functions at low concentrations. However, the authors did not report on the identity of the active compound, nor on its mode of action.

6. Phase 1 and Phase 2 Liver Detoxification

Cruciferous vegetables are high on the list of foods that support detoxification. These Brassica family foods contain several chemical constituents that induce both Phase I and Phase II detoxification enzymes. The more commonly investigated isothiocyanates are primarily responsible for having exceptional detoxification actions within the liver. Specifically, two important Phase II enzymes induced by isothiocyanates which catalyse conjugation reactions are glutathione S-transferase (GST) and quinone reductase.

Wasabia japonica, in particular, is distinctive in the Brassica family in that the rhizomes contain high concentrations of many standard isothiocyanates (allyl, benzyl) found in more commonly consumed vegetables (broccoli, cauliflower, Brussels sprouts, etc.). In addition, it contains high concentrations of a unique group of isothiocyanates - long chain isothiocyanates, which are not routinely found in the foods people consume. These long chain methyl isothiocyanates have important medical benefits, but the effects are complex.

They are associated with inducing Phase I and Phase II detoxification enzymes in the liver. The rhizomes exhibit antioxidant and free radical scavenging activities. Wasabi was also found to induce glutathione S-transferase (GST), a Phase II enzyme, more effectively than any other plant investigated. These unique long chain methyl isothiocyanates have been shown to be up to 40 times more effective than common isothiocyanates in inducing Phase II enzymes.

One in vitro assay system was developed by researchers to demonstrate that sulforaphane (4-methylsulfinylbutyl isothiocyanate) has been identified as the principal Phase II inducers in broccoli extracts. Wasabi was identified as containing the highest source of an analogue of sulforaphane called 6-methylsulfinylhexyl isothiocyanate (6-HITC). This compound induced GST activity with great potency. (Morimitsu 2002), (Guengerich 1995) and (Percival 1997)

7. Other Health Benefits of Wasabi/Isothiocyanates

In addition to the above health benefits there is now evidence showing that Wasabi and the isothiocyanates act: 1. To prevent diarrhoea (Nakayama et al. 1998); 2. To protect nephrons in diabetes (Fukuchi et al 2004); 3. As antioxidants (Gao et al. 2001, Lee et al. in review); 4. As immune boosters (Manesh and Kuttan 2003); 5. As inhibitors of cancer treatment toxicities (Manesh and Kuttan 2005); 6. As cardiovascular defenders (Wu et al. 2004)