

Sinigrin: A Cancer Preventing Agent

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Abstract

Various biologically active compounds present in mustard have proved as potential anti-cancerous agents. Sinigrin inhibits angiogenesis and reduces inflammation in tumors. Phenethyl isothiocyanates (PEITC) induces apoptosis in Jurkat T-lymphoma cells over-expressing the oncoprotein Bcl-2. Sulforaphane inhibits cell proliferation and metastasis, block the action of mutagens and induces apoptosis of the transformed cells. High selenium mustard can help in curing breast and prostate cancer. Mustard seeds rich diet has been shown to prevent colon, skin and cervix cancer in animal model. Benzyl isothiocyanate (BITC) suppresses pancreatic tumor growth and angiogenesis. The following review tried to throw light on the mechanism of action and experimental studies conducted on the same.

Keywords: Sinigrin; Cancer; Mustard

Introduction

The importance of mustard has not only been realized in modern times. Mustard is well documented in the classical Ayurvedic literature like Caraka Saṃhitā, Suśruta Saṃhitā, Bhela Saṃhitā and Kāśyapa Saṃhitā [1]. Mustard seeds have been used for thousands of years in traditional medical practices too. They provide an effective remedy for joint pain, common cold, cough, inflammation, rheumatism and arthritis. Various components of mustard have antimutagenic, antidiabetic, antifungal, antimicrobial and antioxidant effects.

Mustard belongs to an angiosperm family i.e. Brassicaceae. This family is known to serve as host for a large group of metabolites called as glucosinolates. GSLs bring a strong flavour and taste in brocolli, cabbage and other brassica vegetables. Approximately 200 GSLs have been reported till date and they all share a common structure consisting of a β -D Glucopyranose residue linked via a sulfur atom to a (Z)-N-hydroximiniosulfate ester, plus a variable R group derived from one of the 8 amino acids.

GSLs themselves have very limited or no biological activity. When the plant tissue is physically damaged by crushing or cutting, the GSLs comes in contact with the endogenous enzyme myrosinase (thioglucoside glucohydrolase), which hydrolyzes them into several compounds like isothiocyanates, organic cyanides, oxazolidinethiones, nitriles and ionic thiocyanates. Among the various hydrolyzed products obtained, ITCs have been reported to be the most biologically active, being commonly used as broad spectrum biocides since 20th century. The type of isothiocyanate generated depends upon the type of GSL being used as substrate (characterized by its side chain) (Figure1). Sinigrin is 2-propenyl Glucosinolate with a molecular weight of 359.03. It is one of the major active members in GSLs group with allyl isothiocyanate and nitriles as its hydrolysis products.

Sinigrin has been reported to stop tumor progression, prevents DNA damage and fights inflammation. Isothiocyanates can inhibit carcinogenesis and tumerogenesis in breast, colon, lung and skin tissue in animals.

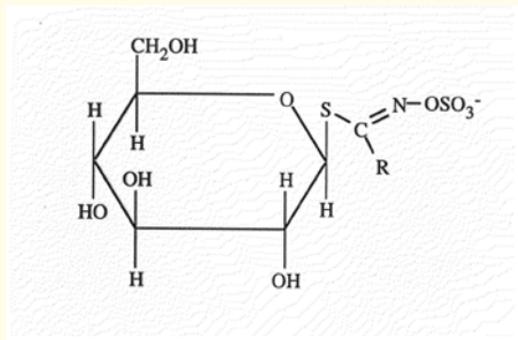


Figure 1: Basic Structure of Glucosinolate (R is an organic aglycone and is an alkyl group) (Source: <https://papyrus.bib.umontreal.ca>).

In a study conducted, the major biologically active compounds in the methanolic extract of mustard genotype were found to be methallyl cyanide; allyl isothiocyanate; Oxime-methoxy-phenyl; 1-butene-4-isothiocyanato; 4HPyran-4-one,2,3-dihydro-3,5-dihydroxy-6-methyl;2-Furancarboxaldehyde;5-(hydroxym-ethyl)-ethylbeta-d-galactopyranoside. Moreover, the genotype also showed allyl isothiocyanates in small percentage. Fatty acid analysis of Indian mustard also showed the presence of good amount of oleic acid, linolic acid and palmitic acid. Also, major phenolics identified were caffeic acid, gallic acid, chorogenic acid, ferulic acid and sinapic acid. The detection of these compounds in seeds of mustard genotypes highlights the pharmaceutical properties of this crop [2].

Black mustard seed: the best source of sinigrin

Stops tumors

Scientific work has shown that sinigrin inhibits bladder cancer growth by 34 percent, and stopped muscle tissue invasion by 100 percent. The effect of sinigrin to stop tumors comes with its ability to stop vascular endothelial growth factor from helping tumors to develop new blood vessels.

Sinigrin has also been tested against liver tumors. It boosts the activity of a tumor suppressing gene called p53, and restores the function of the liver. In one case from an Ethiopian species of the plant, *Brassica carinata* sinigrin has protected the DNA damage in colon cancer cells and leukemia cell lines.

Fights inflammation and free radicals (both are critical to control in cancerous cells)

Leading edge research in Korea has found that sinigrin suppresses inflammatory pathways and reduces the body's production of inflammatory markers, including COX-2, prostaglandin E2, tumor necrosis factor- α , and IL-6 – all of which are active in various diseases.

Besides inflammation, sinigrin can stop oxidative damage too.

Cancer prevention by isothiocyanates

Organic isothiocyanates protect the cancer by number of mechanisms:

- In a study conducted on neuroblastoma cell lines, mustard juice inhibited benzo[a]pyrene (B[a]P)-induced DNA damage in human-derived cells and it also induces detoxifying enzymes.
- In another study conducted, the organic isothiocyanates enhanced the efficacy of cancer chemotherapy by inhibiting the P-glycoprotein- and MRP1-mediated efflux of daunomycin and vinblastine in MDR human cancer cells. Both P-glycoprotein and MRP1 (multidrug resistance-associated protein) are involved in the bioavailability, distribution, and elimination of many drugs [3].

Phenethyl isothiocyanates (PEITC) are even able to induce apoptosis in numerous cells including Jurkat T-lymphoma cells overexpressing the oncoprotein Bcl-2 [4].

Sulforaphane as a promising molecule for fighting cancer

Sulforaphane (SFN) is the most recognized isothiocyanate with potential anti cancerous activity. SFN is simultaneously able to modulate multiple cellular targets involved in cancer development, including: (i) DNA protection and blocking the action of mutagens; (ii) inhibition of cell proliferation and induction of apoptosis, thereby retarding the clonal expansion of transformed neoplastic cells; (iii) inhibition of neoangiogenesis and metastasis [5].

Prevention of various types of cancer

Breast cancer

White and black mustard seeds are an excellent storehouse of melatonin. Melatonin protects against breast cancer by reducing

estrogen production by decreasing aromatase activity within the breast.

A little association exists between levels of selenium in breast tissue and breast cancer risk. In a study conducted it was found that selenium intake could reduce the number of DNA breaks typically associated with mutations in BRCA1 carriers. Moreover, selenium disrupts estrogen signaling by altering estrogen receptor expression and ligand binding in human breast cancer cells [6].

Prostate cancer related study

Indian mustard is has a tendency to incorporate heavy metals and minerals (e.g., cadmium, arsenic and lead) from its soil. Using this knowledge, a high-selenium mustard was developed by growing Brassica juncea in soil with high levels of selenium. This mustard can be used in combating prostate and other cancers.

Brazil nuts contain the highest percentage of selenium of any food source.

Chemopreventive effects of mustard (*Brassica campestris*) on chemically induced tumorigenesis in murine forestomach and uterine cervix

In the present study, cancer chemo preventive potentials of different doses of mustard (*Brassica campestris*) seed mixed diets were evaluated against benzo(a)pyrene [B(a)P]-induced forestomach tumorigenesis and 3-methylcholantrene (MCA)-induced uterine cervix tumorigenesis. Results showed a significant inhibition of stomach tumour burden (tumours/ mouse) by mustard seeds [7].

Skin cancer

The components of mustard seeds were proved to possess anticancer activity as they decrease the incidence of 7,12-dimethylbenz(a)anthracene-induced skin cancers and their trans-placental and trans-lactational spreading in Swiss albino mice [8].

Colon cancer

In a study conducted, colon tumors were induced by administering azoxymethane (AOM) in Kummung mice. The mice were then fed with mustard seeds and the tumors were checked for signs of proliferation, apoptosis, and beta-catenin expression. a clear inhibitory effect on colon tumorigenesis was reported with significant reduction in proliferation activity and enhanced apoptosis. Moreover, mustard seeds rich diet enhanced the anti-oxidant status of the animals and depressed peroxidative damage in a dose-dependent way. It was also found that an emulsion of extracted mustard seeds (EMS) had the ability to significantly reduce production of reactive oxygen species (ROS) from peritoneal macrophages when exposed to oxidized LDL (ox-LDL), to prevent growth and to induce apoptotic death of SW480 cells (a human colon cancer cell line), [9].

Pancreatic cancer

Benzyl isothiocyanate (BITC) suppresses pancreatic tumor growth and angiogenesis by inhibiting STAT-3 dependent pathway. BITC blocks the migration and invasion of BxPC-3 and PanC-1 pancreatic cancer cells in a dose dependant manner. Moreover, secretion of VEGF and MMP-2 in normoxic and hypoxic BxPC-3 and PanC-1 cells was significantly suppressed by BITC. Both VEGF and MMP-2 play a critical role in angiogenesis and metastasis [10-22].

Phytochemical	Bioavailability	Role in cancer prevention	Chemical Formula
Erucin	Isothiocyanates have high bioavailability being 90% absorbed in the GI tract.	Modulates activity of detoxifying enzymes in tissues.	$C_6H_{11}NS_2$
Sulforaphane		Protects DNA and block the action of mutagens, inhibits cell proliferation and induces apoptosis, inhibits progression of benign tumors to malignant tumors (metastasis).	$C_6H_{11}NOS_2$
Phenethyl isothiocyanate		Induce apoptosis of Jurkat T-lymphoma cells overexpressing the oncoprotein Bcl-2	C_9H_9NS
Allyl isothiocyanate		Inhibit the proliferation of lung, pancreatic, and prostate cancer cells.	C_4H_5NS
Benzyl isothiocyanate		Prevents pancreatic tumor growth by inhibiting angiogenesis.	C_8H_7NS

Table 1: Major Isothiocyanates, functions and their structures.

Conclusion

In the fast growing world of technology and ill-food habits, cancer has become a major concern influencing a major part of the society. Dietary supplements serve as the safe and convenient way for reducing the risk and prevention of the deadly disease. Indian meals contain lots of spices including mustard whose nutritional value has been realized since ancient times.

Glucosinolates and their hydrolysis products present in mustard are pharmacologically active compounds with potent anticancerous activity. Sinigrin is well known to stop tumor growth by inhibiting the formation of new blood vessels. Benzyl, allyl and phenethyl isothiocyanates have shown the potential to be formulated as anti cancerous drugs. Moreover, sulforaphane seems to be a promising molecule to fight with cancer. Several experiments conducted across the world have proved that consuming a diet rich in mustard seeds helps in prevention of colon, breast, prostate and other types of cancer. The review thus helps in emphasizing the importance of mustard as dietary supplement.

Conflict of Interest

The authors declare that there are no conflicts of interest.

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