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Green Chemo-Prevention: An Integrated Review Between Agriculture and Medicine

Sagar Banik[1], Madhusri Pramanik[2*], Sourav Roy[3], Pabitra Kumar Ghosh[4], Swarnali Duary[5], Soham Bachaspati[6], Ankita Mukhopadhyay Biswas[7], Soham Hazra[8], Soumik Dey Roy[9], Sanjay Mochary[10], Koushik Biswas[11], Bhabani Prasad Mondal[12]

[1,2*,3,4,5,6,7,8,9,10,11,12]*Assistant Professor, Department of Agriculture, Brainware University, Barasat, Kolkata*

***Corresponding Author:** Madhusri Pramanik*
Email id: map.ag@brainwareuniversity.ac.in

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Abstract

The isothiocyanate's chemoprevention properties are reported to be present in cruciferous veggies through a variety of mechanisms. Sulforaphane, a phytochemical found in green leafy vegetables, has shown promise in the prevention and treatment of several cancers, including those of the prostate, breast, colon, skin, urinary bladder, and oral cavities. These malignancies include those that affect these organs. This substance is naturally present in broccoli sprouts, kale, cabbage, cauliflower, and garden cress. Broccoli should be a regular part of your diet because it contains a variety of bioactive substances such as vitamins, polyphenols, sulfides, glucosinolates, and antioxidants. Sulforaphane may be used as an inexpensive replacement or dietary supplement for chemo preventive therapy, according to the findings of epidemiological and experimental studies.

Phase 2 detoxification enzymes like glutathione transferases, epoxide hydrolase, NAD(P)H: quinone reductase, and glucuronosyltransferases, as well as epoxide hydrolase and epoxide hydrolase, are produced when the body is stimulated. This is a useful tactic for preventing cancer and fending off the harm that electrophiles and reactive oxygen species can cause. Isothiocyanates are widely distributed in the Cruciferae family and Brassica genus of food plants, which include both broccoli and cauliflower. The most typical form of these substances is glucosinolate precursors. Sulforaphane and 4-methylsulfinylbutyl isothiocyanate, two of these isothiocyanates, are particularly powerful inducers of phase 2 enzymes.

It is feasible to successfully extract glucosinolates and isothiocyanates from plants by homogenizing them at a temperature of around 50 degrees Celsius in a solution of equal parts dimethyl sulfoxide, dimethylformamide, and acetonitrile. This method avoids the hydrolysis of glucosinolates by myrosinase.

It's interesting to note that glucoraphanin, the precursor to sulforaphane, is 10–100 times more abundant in 3-day-old sprouts of various cruciferous vegetables, including broccoli and cauliflower than it is in fully grown veggies. Dimethylbenz(a)anthracene-treated rats displayed notable reductions in mammary tumor occurrence, quantity, and rate of growth when fed extracts from 3-day-old broccoli sprouts. These extracts' primary enzyme-inducing components were either glucoraphanin or sulforaphane. As a result, crucifer sprouts might provide an equivalent amount of cancer prevention to eating far larger quantities of the same mature vegetable species.

Keywords: broccoli, chemo-prevention, malignancies, polyphenols, sulforaphane, 4-methylsulfinylbutyl, isothiocyanate, glucoraphanin

Introduction

Recent studies have shown that cruciferous veggies can prevent cancer. The first to mention broccoli sprouts' anticarcinogenic activity was Fahey et al. (1997) [1]. Numerous investigations conducted after this discovery have demonstrated that young broccoli and its sprouts contain glucosinolates, which slow the growth of several primary malignancies, including secondary tumors that can occasionally be deadly [2]. Numerous biochemically active compounds, including carotenoids, vitamin C, and glucosinolates, are found in broccoli. One such molecule is glucoraphanin (GPN) precursor sulforaphane (SFN), 1-isothiocyanate-4-[methyl sulfinyl] butane [3].

Broccoli that has been cut or chewed causes the naturally existing myrosinase enzyme to interact with the glucoraphanin (GPN) and convert it to sulforaphane (SFN). GPN is more stable than SFN. Compared to mature entire heads, GPN is present in sprouts in much higher concentrations. The heat-sensitive enzyme myrosinase converts glucosinolates into isothiocyanates, which are glucosinolates' active form and which have physiological effects [4]. However, heating for longer than a minute, or even steaming or blanching, destroys this enzyme. Furthermore, it is thought that boiling broccoli and freezing it below -85°C, will destroy its anticancer qualities [5]. The most powerful anti-carcinogenic compounds, SFN, function by raising the levels of liver enzymes that block the effects of chemicals found in food and the environment that cause cancer. A sulfur band that holds SFN to a sugar molecule must be destroyed to release it. The exposed sulfur on SFN will then be removed by a protein that grabs sulfur, rendering SFN inactive. This link is broken by the myrosinase enzyme found in broccoli. The myrosinase enzyme hydrolyzes SFN to produce isothiocyanates when broccoli is chopped or sliced [6]. The production of SFN could decrease as a result of the deactivation of the myrosinase enzyme. The formation of isothiocyanates is not solely dependent on myrosinase; the epithiospecifier protein, which encourages the conversion of breakdown products into nitriles rather than isothiocyanates, also has an impact on it. When broccoli is exposed to temperatures between 60°C and 70°C for a period of 5 to 10 minutes, its effectiveness as a protein may be jeopardized. Under these circumstances, the production of SFN experiences a notable rise of 3 to 7 times [7]. Whenever feasible, opt for raw or recently harvested broccoli. A postponement of 10 days could potentially lead to an approximate 80% reduction in GPN content [8]. Because they are soluble in water, glucosinolates tend to seep into the water while boiling [6]. Therefore, opting for gentle steaming or microwaving might better preserve the highest amount of SFN compared to boiling [5].

In contrast to raw sprouts, numerous supplements accessible in the market lack myrosinase, and encapsulating it is unfeasible due to its functional state being viable only in its fresh form. Eating broccoli alongside a dietary component containing the myrosinase enzyme results in higher levels of SFN. Ingredients like mustard seed powder, daikon radish, wasabi, arugula, and coleslaw are examples of foods rich in myrosinase. Certain amounts of myrosinase enzyme are produced by gut bacteria, a phenomenon that might be absent in individuals with an imbalanced gut microbiome. The myrosinase produced by microorganisms in the intestines then engages with consumed glucosinolates that have managed to avoid the plant's inherent myrosinase activity. It's crucial to remember that this enzyme is not found in mammalian cells by nature [9]. Though in smaller proportions, broccoli extracts also include substances with anti-cancer potential comparable to SFN, such as iberin and erucin [10]. The goal of the study was to determine whether sulforaphane may be utilized as an adjuvant therapy to lessen the cytotoxicity of chemotherapy-related compounds and their negative effects on target cells.

Bio-Availability of Sulforaphane (SFN)

SFN is largely absorbed in the jejunum after consumption and enters the bloodstream via passive diffusion [11]. SFN attaches to thiol groups present in plasma proteins and traverses the cell's outer membrane to gain entry. It interacts with glutathione inside the cells to produce conjugates. These substances are subsequently expelled from the cells by specific transporter proteins, where they undergo metabolism to become mercapturic acid. These metabolites are conveyed to the kidneys for excretion via urine. Importantly, there is a noticeable link between the levels of SFN metabolites found in urine and the amount of SFN consumed in the diet, making them valuable indicators of dietary intake [12-13]. SFN is rapidly assimilated, with its peak concentration occurring within 1 to 3 hours. It takes about 72 hours for the levels to return to their original baseline. The

reported bioavailability of SFN is 74%. The concentration of SFN in tissues varies according to the specific target organ. SFN levels can differ between distinct plants of the same species as well as within particular parts of a single plant. This variability is also influenced by cultivation methods, climate conditions, and other agricultural factors [11]. When it comes to chemoprevention, it is believed that broccoli sprouts are far more effective than mature broccoli heads, with a potential effectiveness that can be up to 20 to 50 times higher. This increased effectiveness can be attributed to two main factors. Firstly, sprouts contain higher levels of GPN, which is a powerful inducer of Phase 2 enzymes. Secondly, they have a lower potential for toxicity because they contain fewer indole and b-hydroxyalkyl glucosinolates [14]. Additionally, elements including the presence of the myrosinase enzyme, and the bioavailability and pharmacokinetics of SFN are influenced by the epithiospecifier protein's presence and the technique of SFN synthesis. The rapid excretion of SFN metabolites through urine aids in efficiently eliminating harmful carcinogens. However, this method might be influenced by a person's unique genetic variances in metabolism and excretion. The bioavailability of SFN can be increased by using cooking techniques that steaming or microwaving uses less water. Conversely, boiling, employing high-power microwaving (>750 W), and subjecting to high-temperature steaming decrease SFN levels due to the deactivation of the myrosinase enzyme [15].

The Impact of Sulforaphane in Different Cancer Types and Epigenetic Modifications

The role of sulforaphane is complex and necessitates an in-depth analysis in and of itself because of the abundance of studies conducted in this field. Sulforaphane alters susceptibility to carcinogens, encourages programmed cell death (apoptosis), triggers a break in the cell cycle, prevents the growth of new blood vessels (angiogenesis), lessens inflammation, slows the spread and movement of cancer cells, and has antioxidant and anti-inflammatory properties [16]. SFN may also be able to target the epigenetic changes seen in particular cancer types, according to research [17]. By preventing histone deacetylases, inducing widespread demethylation, and regulating microRNA activity, it may be able to correct unusual changes in gene expression. The effect of cruciferous vegetables on changing genetic expressions through epigenetic changes is the current area of intense research.

Genetic and epigenetic alterations within the genome that cause disruptions in transcriptional patterns are involved in carcinogenesis and the progression of cancer. Epigenetic changes cause tumor-suppressing genes to become inactive and oncogenes to become active, which ultimately accelerates the development of cancer [18-20]. Post-translational modifications of histones, widespread hypomethylation of DNA, involvement of non-coding RNAs, and reorganization of chromatin structure are all examples of epigenetic processes. Because epigenetic changes can be undone, unlike genetic mutations, they are appealing targets for chemically induced cancer prevention strategies. The impact of SFN on epigenetic modifications in various cancer types has been extensively studied. SFN has the potential to directly or indirectly increase the transcriptional activity of specific genes to address and reverse epigenetic changes. Due to their capacity to influence epigenetic pathways by focusing on histone deacetylases (HDACs) and DNA methyltransferases (DNMTs), broccoli sprouts and SFN are recognized as components of an epigenetics-focused diet. They start changes in gene transcription and expression within cancer cells through these actions. Additionally, sprouts and SFN seem to affect mitochondrial function and reduce lipid peroxidation. Uneven epigenetic markers may be corrected by SFN [21].

In their study, Meeran et al. (2010) became the first to note a significant decline in the expression of DNMT1 and DNMT3a brought on by SFN, and they discovered that this effect was dose-dependent. Particularly in the MCF-7 and MDA-MB-231 cell lines, as well as to a lesser extent in the healthy MCF10A cells, these findings were visible in human breast cancer cells. SFN dramatically reduced the activity of the human telomerase reverse transcriptase (hTERT) enzyme in breast cancer cells, which ultimately led to the apoptosis, or cell death, of these malignant cells [22].

Li et al. (2014) demonstrated that SFN acts as a strong inhibitor of HDAC, leading to the suppression of hTERT. Epigenetic modification results in the reactivation of estrogen receptors (ERs) in ER-negative breast cancer cells. The authors noted that consuming SFN and broccoli sprouts during maternal and early postnatal stages had a positive impact on reducing the risk of breast cancer in later life. This was attributed to the alteration of gene expressions related to tumor development, such as TERT, c-Myc, p16, and p53, as observed in their study [23-24].

Preclinical and clinical studies were both covered in the thorough review by Atwell et al. (2015) [19]. Their review investigated the epigenetic alterations caused by SFN in prostate and breast cancer [20]. The study looked at how SFN affects key processes in cancer cells, including cell cycle regulation, programmed cell death, inflammation, antioxidant defenses, and cellular signaling pathways. It focused specifically on how these factors affect epigenetic processes. In breast cancer cells MCF-7 and MDA-MB-231, treatment with SFN was seen to suppress hTERT and lower levels of DNMT1 and DNMT3a. The hTERT gene's CpG sites lost their methyl groups as a result of the SFN therapy. A change in chromatin structure was also brought about by SFN treatment, as shown by elevated levels of chromatin markers like H3K9ac and acetyl-H4, while concurrently decreased levels of H3K9me3 and H3K27me3 on the hTERT promoter region. These modifications ultimately caused the breast cancer cells to undergo programmed cell death [25]. SFN altered the levels of HDAC and DNMT and decreased the expression of CDK4, cyclin D1, and pRB. These modifications ultimately caused the cancer cells to undergo apoptosis. SFN reduced DNMT expression in prostate cancer, which inhibited methylation-induced silencing of cyclin D2 expression [26].

The enzyme SUV39H1, which is present in prostate cancer cells, is affected by SFN exposure, indicating that it may be a potential target for therapeutic intervention. When used in conjunction with conventional therapies, SFN has demonstrated efficacy in not only treating advanced cancers but also in halting their spread. It helps to reactivate tumor suppressor genes, which slows the spread of cancer and allows for the selective destruction of cancer cells. To confirm the positive effects of SFN, a thorough analysis of clinical human trials is currently being conducted [27].

SFN regulates the apoptosis process by decreasing the anti-apoptotic proteins Bcl-2 and Bcl-XL, increasing the pro-apoptotic protein Bax, triggering the proteolytic activation of caspase-3, and causing the breakdown or cleavage of poly(ADP-ribose) polymerase [28].

Human leukemic cells KG1a and K562 were exposed to SFN, and the amount of apoptosis that resulted was influenced by the exposure's dosage and duration. This result was attained by upregulating Bax and Caspase-3 while downregulating Bcl-2 expression. Significant anti-cancer effects of SFN have been observed in acute myeloid leukemic cells [28].

UV light exposure has been linked to the development of skin cancer and melanoma, but SFN has been shown to modulate STAT3 in cancer cells. SFN starts the epigenetic reactivation of Nrf2 in a mouse model of skin tumors, which then activates downstream target genes like HO-1, NAD(P)H: Quinone oxidoreductase 1 (NQO1), and UGT1A1. SFN might increase the expression of Nrf2's mRNA and protein, which would then activate the downstream target gene NQO1. By lowering DNMT1 and DNMT3a levels, this is achieved. Additionally, SFN promotes the elevation of the active chromatin marker acetyl-histone 3 (Ac-H3) and increases HDACs 1, 4, 5, and 7 both in vivo (using TRAMP mice) and in vitro (using TRAMP C1 cells) during tumorigenesis. As a result, SFN activates the antioxidant stress pathway, partially through changes in epigenetics and also by enhancing the expression of the Nrf2 gene [29].

SFN effectively starts detoxification procedures by boosting glutathione synthesis, an antioxidant. As a result, Phase 1 enzymes like cytochrome P450, which are involved in cell proliferation and tumor growth, are inhibited. SFN aids in the removal of chemicals that can harm DNA by starting the activation of Phase 2 enzymes through a variety of mechanisms. Mitogen-activated protein kinase (MAPK) and nuclear factor erythroid-2 (NF-E2-) related factor 2 (Nrf2) are both regulated by SFN. Besides that, an overexpression of Nrf-2 can make cancer cells resistant to particular chemotherapy drugs [30]. To effectively control this pathway in cancer treatment, the authors recommended more investigation to determine the ideal timing and dosage for SFN administration. The goal of this research is to increase SFN's anticancer benefits while minimizing the possibility of negative effects. SFN increases the efficacy of chemotherapy drugs even when used sparingly, minimizing damage to healthy, normal cells [30].

Researchers found that people who regularly consumed broccoli, even if not daily, had higher levels of the tumor suppressor gene p16 compared to those who consumed few or no of these vegetables.
SFN is normally excreted from the body within 24 hours, so this finding was unexpected. This finding raises the possibility that SFN and its byproducts may affect the body's epigenetic processes, increasing the risk of cancer even after the substance has been eliminated [31]. A protein known as Nrf2 is stimulated by SFN, and

it is thought that this protein may support tumor growth and aid in the formation of arterial plaque in more advanced stages of cancer progression. Therefore, in-depth research into the function of Nrf2 in the contexts of both cancer and cardiovascular disease is required.

The ability of SFN to trigger apoptosis in mouse models of various cancers, including colon, prostate, breast, liver, and lung cancer, has been demonstrated. Despite the benefits of SFN having been established through cell-based research, animal testing, and specific human trials, the usage recommendations currently in place are still limited. SFN's current application is primarily restricted to that of a complementary therapy used in addition to conventional radiotherapy and chemotherapy. It might have the ability to help those who have successfully treated head and neck cancer prevent relapses.

Sulforaphane helps protect the body from prolonged exposure to toxins and carcinogens in the environment. In a study involving both mice and people, it was identified that the specific negative effects related to the consumption of this compound [32]. Cancer cells are thought to undergo autophagy in response to SFN. Prostate cancer cell lines PC-3 and LNCa p showed increased levels of microtubule-associated protein light chain 3 expressions, processing, and mobilization to autophagosomes when subjected to SFN [33].

Nuclear factor-kappa B (NF-κB) controls processes like cell proliferation, angiogenesis, and invasion to prevent the growth of tumors. It is well known that inflammation promotes tumor cell proliferation while inhibiting apoptosis, which raises the possibility of tumor growth. According to SFN, blood cells secrete fewer inflammatory cytokines less frequently, which prevents NF-κB from affecting DNA [34].

Contrary to healthy cells, cancer cells bypass DNA repair mechanisms and divide quickly, which promotes the spread of incorrect mutations. Additionally, they are unresponsive to signals that ordinarily cause normal cells to undergo programmed cell death (apoptosis). By interacting with mitochondria, broccoli extracts cause cancer cells to undergo apoptosis and cause cell cycle arrest at the S and M phases. This effect is not specific to any one type of cell or tissue. Cell division cycle 25C expression is reduced as a result, and the development of mitotic spindle structures is interfered with. The ability of SFN to prevent tubulin polymerization is well-known [35].
In various cell lines, including PC3 cells, activation of the MAPK/ERK pathway has been seen after SFN therapy. The activator protein-1 (AP-1) transcription factor, which aids in promoting apoptosis, is stimulated during this activation [36].
According to research by Tang et al. (2006), the presence of isothiocyanates in broccoli extracts gives them the ability to prevent the growth of cancer cells [9]. In addition, the broccoli compound SFN induced the synthesis of Phase 2 enzymes. Broccoli extracts exhibited anti-proliferative characteristics that were comparable to those of SFN, indicating that they might be used and evaluated in clinical settings instead of SFN. Therefore, compared to pharmaceutical agents, using naturally occurring SFN from sources like broccoli is not only more accessible but also requires less complicated preparation techniques. This makes it more affordable and cost-effective. However, the consumption of sprouts may deplete SFN due to the presence of the epithelia-specifier protein. Therefore, more research is required to look into ways to maintain the stability of these [9].

Angiogenesis plays a crucial role in cancer development by supporting the nourishment of fast-dividing cancer cells. SFN is said to impede the creation of new blood vessels, thus depriving tumor cells of essential nutrients and restraining tumor growth. SFN also serves as a barrier to tumor invasion and metastasis, or the spread of cancer to different parts of the body. SFN can therefore prevent the growth and expansion of tumors that are hormone-sensitive, such as those found in breast and prostate cancer. In cultured prostate cancer cell lines, the breakdown of glucosinolates triggers apoptosis, which effectively inhibits tumor growth.

Cancer stem cells (CSCs) play a key role in the development and progression of the disease [37]. They are also linked to drug resistance and cancer recurrence. SFN can counteract these effects, potentially delaying the recurrence of CSCs and the development of drug resistance. SFN was found to inhibit the growth of cancer stem cells (CSCs) connected to oral squamous cell carcinoma [38]. The dosage of SFN determined how strong this effect was. Additionally, after receiving SFN treatment, CSCs linked to oral cancer displayed diminished capacities for migration, invasion, clonogenicity, and in vivo tumor formation. According to the amount of SFN administered, this was linked to an increase in the expression of the tumor-suppressing miR200c. These

results suggested that SFN inhibited the development and maintenance of stem-like properties in cancer CSCs, ultimately resulting in a reduction in tumor growth and the avoidance of the development of new tumors. Both animal studies and laboratory-based cell culture experiments (in vitro and in vivo) showed evidence of these effects. SFN has the potential to affect NF-B, the epithelial-mesenchymal transition, and Wnt/β-catenin pathways, which in turn may affect cancer stem cells (CSCs) in different cancer types. To improve outcomes, researchers have pushed for the addition of SFN to traditional chemotherapy as an additional treatment [38].

The limited examination of how SFN affects the regulation of miRNA expression in the currently available literature emphasizes the need for additional study to gain a thorough understanding. In colorectal cancer cells treated with SFN, miR-23b, and miR-27b expression was noticeably upregulated [39].

Both gastric cancer brought on by Helicobacter pylori and cervical cancer brought on by HPV are well-known diseases. SFN has demonstrated efficacy in preventing these particular cancer types.

Significantly, SFN was successful in delaying the development of cervical cancer in mice from intraepithelial neoplasia [40]. Furthermore, in both mouse and human trials, SFN in its purified form was successful in eradicating the strain [41]. Another recognized chemo preventive property of SFN is its capacity to influence TLR activation and signaling. Zhu et al. (2013) discovered that SFN suppressed TLR3 and demonstrated the capacity to regulate NF-κB signaling and the ensuing gene expression. Interleukin 8 and tumor necrosis factor-alpha expression were both reduced as a result [42].

Studies using the UM-UC-3 cells, a particular type of bladder cancer cell line, showed that the isothiocyanates present in broccoli extracts, when combined with SFN, have potent anti-proliferative properties that inhibit tumor growth. The authors have hypothesized that comparable effects might be seen in several different cancer types. Notably, urothelial and bladder cancer susceptibility was markedly increased in people with genetic variations in the glutathione S-transferase (GST) or NQO1 genes, resulting in either absent or insufficient enzyme activity. This result is in line with what was expected because both GST and NQO1 play a crucial role in cellular defense against oxidants and carcinogens [43]. Numerous studies have demonstrated that SFN can increase the susceptibility of drug-resistant cancer cells to TNF-related apoptosis-inducing ligand (TRAIL)-induced apoptosis. Studies have shown that SFN can enhance TRAIL-induced apoptosis, particularly when human hepatoma cells are involved [44].

In conclusion, numerous studies have highlighted the fact that SFN triggers apoptosis via mitochondria-mediated pathways, causes cell cycle arrest, acts as an antioxidant to reduce oxidative stress, activates Nrf-2 to inhibit inflammatory and cytokine production, and inhibits histone deacetylase and DNA methylation processes, thereby affecting epigenetic mechanisms. Additionally, SFN activates Phase 2 enzymes like GST and quinone oxidoreductase 1, protecting cells from reactive oxygen species and carcinogens that can damage DNA. These actions ultimately interfere with oncogenic signaling pathways.

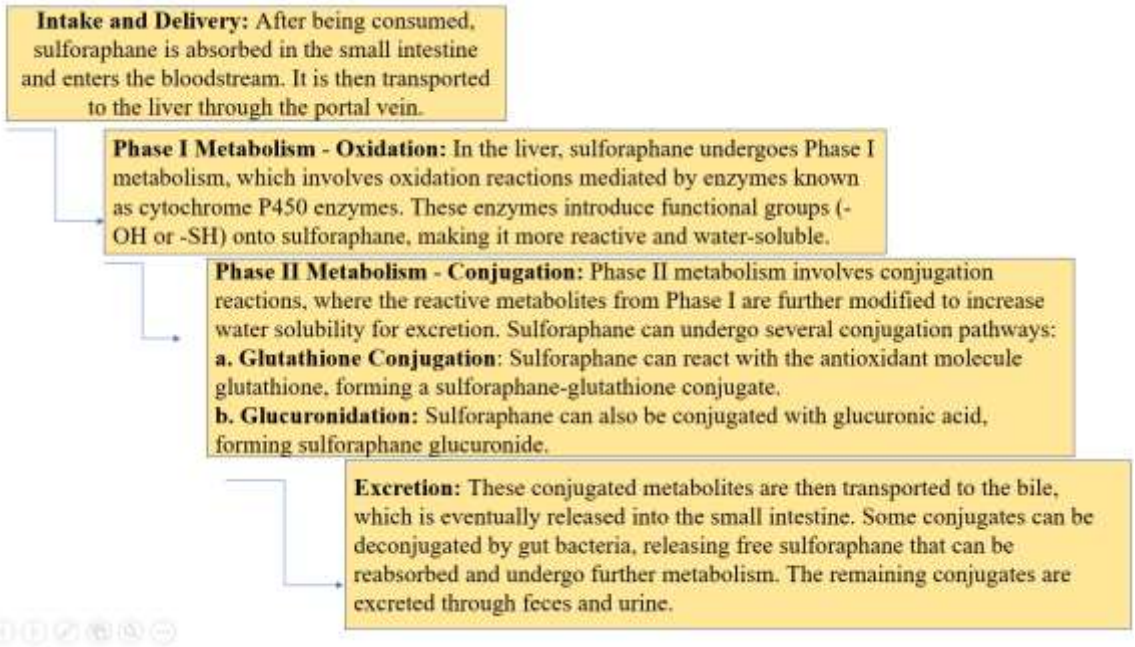

Fig 1. Overview of the pathway of sulforaphane metabolism in the liver

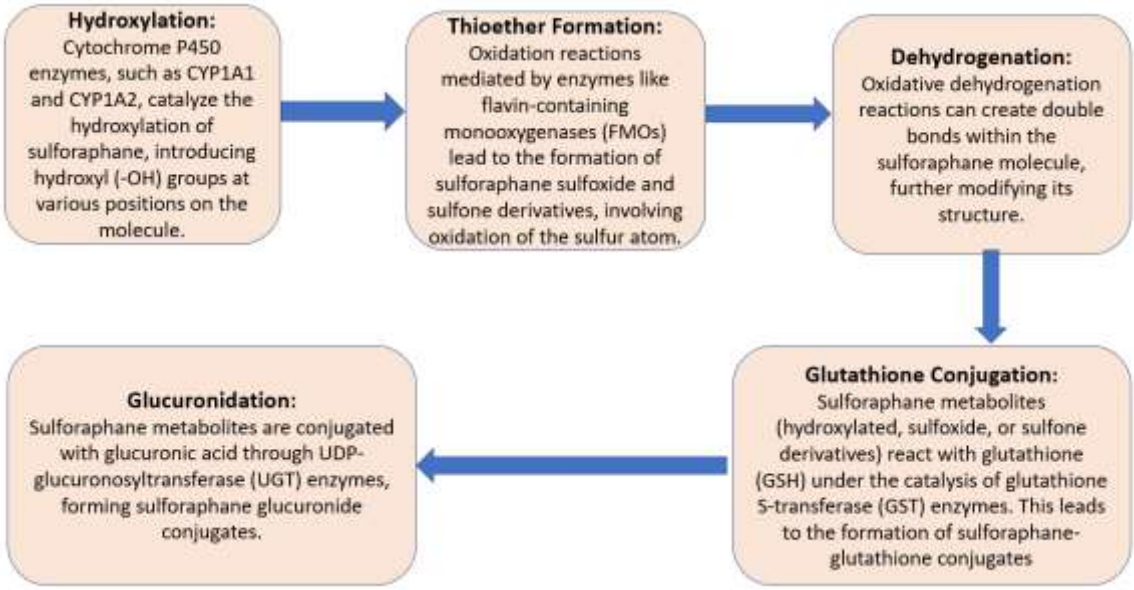

Fig 2. Stepwise breakdown of the Phase 1 and Phase 2 metabolism of sulforaphane:

Adverse Effects

SFN exhibits a dual nature, serving as a double-edged sword. Consuming broccoli in moderate amounts can yield benefits, but excessive intake could result in certain side effects. Particularly, an excessive intake in diabetic patients might lead to the occurrence of hypoglycemia. Several reports are there regarding potential liver toxicity associated with the consumption of extremely high doses of SFN.

Additionally, side effects like irritable bowel syndrome, excessive gas, stomachaches, and diarrhea have been documented, which can be attributed to the high fiber content of SFN-containing foods. The isothiocyanates present in broccoli are considered to be goitrogens, substances that can influence the uptake of iodine. This can consequently affect the function of the thyroid gland, potentially increasing the chances of hypothyroidism [6]. Broccoli may contain traces of various pesticides, including carcinogenic formaldehyde. In some individuals, consumption of broccoli could lead to allergic reactions like skin rashes, itching, nasal congestion, wheezing, and headaches.

There's a potential concern for smokers who consume excessive amounts of broccoli, as the surplus

antioxidants might raise the risk of lung cancer. Excessive consumption of broccoli has been linked to an increased risk of hemorrhagic stroke due to the presence of Vitamin E. Moreover, overconsumption of potassium-rich broccoli could potentially result in hypotension. Vitamin K presence in broccoli sometimes interferes with blood clotting and also increases the risk of bleeding among patients who are taking blood thinners. Therefore, extreme consumption of broccoli has been shown to have some associated side effects [45]. Indeed, the health benefits of consuming broccoli outweigh the potential side effects when it is taken in appropriate and moderate amounts.

3. Conclusion

Broccoli sprouts and Broccoli itself are naturally rich sources of isothiocyanates like SFN, which possess powerful properties for combating cancer. Extensive in vitro and animal experiments have been conducted to investigate the role of SFN in the treatment of different categories of cancers, as well as its potential effects on other diseases. Moreover, ongoing research is focused on comprehending the pharmacokinetics and potential side effects of SFN. Further studies on clinical laboratories and various human trials are essential to gain a deeper understanding of its safety, side effects, optimal isolation methods, therapeutic dosages, and recommended frequency of intake. Such investigations will contribute to a more comprehensive understanding of the advantageous effects of these isothiocyanates. These vegetables offer a readily accessible and very low-cost alternative for chemoprevention, which has comparatively minimal side effects than traditional chemotherapy. Therefore, it is valuable to keep these vegetables in one's diet in appropriate quantities regularly to enhance overall health and diminish the risk of cancer.

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