# A REVIEW ON ANTICANCER POTENTIAL OF GLUCOSINOLATES

By

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A thesis submitted to the School of Pharmacy in partial fulfillment of the requirements for the degree of Bachelor of Pharmacy (B. Pharm.)

School of Pharmacy
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## Declaration

It is hereby declared that

1. The thesis submitted is my/our own original work while completing degree at Brac University.
2. The thesis does not contain material previously published or written by a third party, except where this is appropriately cited through full and accurate referencing.
3. The thesis does not contain material which has been accepted, or submitted, for any other degree or diploma at a university or other institution.
4. I/We have acknowledged all main sources of help.

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## Approval

The thesis titled "A review on anticancer potential of Glucosinolates" submitted by Mahmuda Khabir (18146084) of summer, 2024 has been accepted as satisfactory in partial fulfillment of the requirement for the degree of Bachelor of Pharmacy.

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## Ethics Statement

This study does not involve any kind of animal trial or human trial.

## Abstract/ Executive Summary

This thesis explores the intricate interplay between glucosinolates, prominent phytochemicals found in the various ways that cruciferous vegetables can help prevent cancer. Glucosinolates are well known for their potential as chemopreventive agents for cancer, have garnered significant attention owing to their ability to inhibit carcinogenesis through various mechanisms. However, recent studies have unveiled a paradoxical aspect wherein certain glucosinolates exhibit antagonistic effects, raising questions about their overall efficacy in cancer prevention. This thesis delves into the intricate molecular mechanisms underlying these opposing actions, shedding light on the complex relationship between glucosinolates and cancer prevention.

## Keywords:

Carcinogenic glucosinolates, Cruciferous vegetables, Cancer prevention, Sulfur containing compounds, Isothiocyanates, Sulforaphane, Epigenetic regulation, Immune modulation, Phytochemicals

## Dedication :

I want to dedicate my project to BRAC University.

## Acknowledgement

Firstly, I want to express my gratitude to Almighty Allah for giving me the perseverance and fortitude I needed to complete my endeavor. Without Allah's direction, I couldn't complete my assigned work.

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List of Acronyms

1. HCG: Hostile to Carcinogenic Glucosinolates
2. CV: Cruciferous Vegetables
3. AA: Antagonistic Effects
4. PC: Prevention of Cancers
5. AMCCA: Apoptosis as a Mechanism of Cancer Chemopreventive Activity
6. ITCs: Isothiocyanates
7. GSTs: Glutathione S-Transferases
8. Nrf2: Nuclear factor erythroid 2-related factor 2
9. KEAP1: Kelch-like ECH-associated protein 1
10. HSF1: Heat shock factor 1
11. NRF1: Nuclear respiratory factor 1
12. HO-1: Heme Oxygenase 1
13. ER: Endoplasmic reticulum
14. ROS: Reactive Oxygen Species
15. NQO1: NAD(P)H:quinone oxidoreductase 1
16. GSH: Glutathione

17. CAT: Catalase

# Chapter 1

## Introduction

The glucosinolates is type with hydrophilic, metabolites of anionic plant that are present on vegetables of the Brassicaceae family. These metabolites make a crucial application to rescue the vegetables from bugs with other environmental stressors. Glucosinolates are synthesized by amino acids, like- phenylalanine, methionine, tryptophan, tyrosine, in a specific order that based on R group side chain within plant.Glucosinolates are not harmful to humans, but they can be decomposed to various consequences through effort by the myrosinase plant enzyme. Myrosinase is present in different compartments of the plant, and when the cell structure is disturbed, it interacts with glucosinolates to form a complex. This complex then breaks down with water presence into aglycone moiety and glucose, producing thiocyanates, isothiocyanates, nitriles like metabolites. It has demonstrated by animal studies that isothiocyanates are operative inhibitors of carcinogenesis that is induced chemically. Therefore, isothiocyanates which is breakdown product of glucosinolates are potentially beneficial for human health.

These glucosinolates based on sulfur-containing glycosides group that are present primarily within Brassicaceae family of plants, also known as the cruciferous vegetables. These compounds are shown to perform biological activities, as well as anticancer, anti-inflammatory effects and antioxidants. Glucosinolates(GLs) biosynthesis starts by conversion of an amino acid into an N-hydroxy-amino acid by the enzyme cytochrome P450. This intermediate is converted into an aldoxime, with

a reaction series to form final glucosinolate molecule. The type of glucosinolate produced depends on the specific amino acid precursor and various enzymes activates in the biosynthetic pathway.When plant tissue is damaged or disrupted, the enzyme myrosinase withstand by glucosinolates, which act as catalyst their hydrolysis producing breakdown product like thiocyanates, isothiocyanates, nitriles and they perform characteristic strong aroma and flavours the cruciferous vegetables.

## 1.1 Rational study:

Research has shown that glucosinolate containing vegetables, for example- cabbage, broccoli, cauliflower, brussels sprouts, can prevent cancer. GLs are a group of hydrophilic, anionic plant natural products acting like defense mechanism as pest remover. GLs are converted into various metabolites when the cell structure is disturbed, including isothiocyanates (ITCs), thiocyanates, and nitriles. Studies have demonstrated that ITCs have potent cancer-preventive properties by inducing apoptosis, a programmed cell death that eliminates abnormal cells and prevent tumor development..

Countless creature and biological inspects have established protective effect of glucosinolates and those extracts against different cancers, such as-, prostate, colorectal, lung, breast cancer. For example, a study of more than 10,000 Chinese women, similarly, a meta-analysis of 87 researched uptaking cruciferous vegetables reduces breast and colorectal cancer risk. The anticancer mechanisms of GLs and their metabolites are complex and involve multiple pathways. One of the most

studied mechanisms is apoptosis induction, which occurs through various pathways, including caspases activation and anti-apoptotic proteins inhibition. For example, ITCs can activate caspase-3, -8, and -9, guiding the multiple cellular substrates cleavage with producing cell arrest. Moreover, ITCs can inhibit the expression of Bcl -2 called anti-apoptotic proteins, and activate Bax called pro-apoptotic proteins.

In addition to apoptosis induction, GLs and their metabolites exhibit other cancer-preventive properties, including the adjusting progression of cell cycle, angiogenesis inhibition, inflammation suppression. For example, ITCs can inhibit cyclin-dependent kinases (CDKs) aggregation and their regulatory partners, direct cell cycle death , prevention of uncontrolled cell proliferation. Moreover, ITCs can inhibit new blood vessels formation (angiogenesis), process that is critical to tumor growth also metastasis. Finally, ITCs can suppress inflammation by inhibiting the activity of nuclear factor kappa B (NF-kB) which is a transcription factor controling the appearance of pro-inflammatory genes.

In conclusion, GLs and their metabolites, particularly ITCs, have potent cancer-preventive properties,direct different procedure comprising cell cycle arrest, apoptosis induction angiogenesis inhibition, inflammation suppression. Epidemiological and animal studies have confirmed cruciferous vegetables hostile to various cancers as protective effect, and additional research is required to entirely illuminate the procedure introducting this outcome and to boost the application of GLs as chemopreventive agents.

## 1.2Aim of study:

The study aims about "Anticarcinogenic Glucosinolates in Cruciferous Vegetables and Their Antagonistic Effects on Prevention of Cancers and Apoptosis helps to indicate as a Mechanism of the Cancer Chemopreventive Activity" is to explore the potential role by glucosinolates that is easily build in cruciferous vegetables preventing cancer. According to the research the study aims investigating molecular mechanisms where these compounds perform anticancer actions, with a particular focus on apoptosis for cancer. This study helps to provide how cruciferous vegetables will be utilized preventing cancer, medication and also to identify potential avenues for further research in this area. Mainly it can be said that the goal of the study is contributing developing of huge effective strategies with preventing cancer and treating those cancer patients.

The study also helps to involve biochemical and molecular analyses to identify specific signaling pathways, routes and molecular targets that are affected by glucosinolates and to express the mechanisms by which these compounds inhibit the growth with proliferating cancer cells also inducing apoptosis for any cancer patient. The impact of dietary intake of cruciferous vegetables on cancer occurrence and development also the potential use of glucosinolate supplements or other interventions in cancer helps to overcome cancerous condition.

However, the study aims for the light on the complex communication between glucosinolates and cancer cells and helps patient to provide insights into dormant use of cruciferous vegetables in prevention cancerand treatment of a cancer patient.

### 1.3 Objective of the study:

Reviewing the present scientific biography on anti-carcinogenic properties by glucosinolates found in cruciferous vegetables.

To investigate the mechanism with which glucosinolates perform their cancer chemopreventive actions, specifically focusing on apoptosis (programmed cell death).

To explore the potential effect of glucosinolates in prevention with treatment of different varied cancer.

To identify potential gaps in the current knowledge of glucosinolates and their anti-cancer effects, and suggest areas for future research.

To raise awareness among the general public about the potential health benefits of consuming cruciferous vegetables rich in glucosinolates.

# Chapter 2

## Methodology

The methodology regarding a study investigating the chemopreventive activity of cancer by glucosinolates in cruciferous vegetables would likely involve:

- Selection of cruciferous vegetables containing high levels of glucosinolates, such as broccoli, kale, and cauliflower.
- Extraction of glucosinolates from the vegetables using appropriate procedures like extraction of solid-phase or solvent.

- Purification and identification of the glucosinolates using high-performance liquid chromatography (HPLC) and mass spectrometry methods.
- Testing the anti-carcinogenic activity of the purified glucosinolates in vitro using cell lines, such as A549 lung cancer cells, MCF-7 breast cancer cells. This may involve measuring cell viability, cell cycle arrest, apoptosis.
- Testing chemo preventive activity by glucosinolates in animal models, such as mice or rats. This may involve inducing carcinogenesis in the animals and measuring the effects of glucosinolate treatment on tumor incidence and growth.
- Investigating chemo preventive activity of glucosinolates by the molecular mechanisms, as like their effects on apoptosis, oxidative stress, and inflammation pathways.
- Statistical analysis of the data to determine the significance of the results.

Overall, the methodology of a study investigating the chemo preventive activity by glucosinolates in cancer would involve combination of chemical analysis, cell culture, animal experimentation, and molecular biology techniques.

Some additional points from the methodology section of the study on "Hostile to Carcinogenic Glucosinolates in Cruciferous Vegetables and Their Antagonistic Effects on Prevention of Cancers and Apoptosis as a Mechanism of the Cancer

Chemopreventive Activity" are:

- The researchers used in vitro experiments to assess the anti-cancer properties of glucosinolates. They used human cancer cell lines to investigate the actions of different glucosinolates on apoptosis and cell viability.
- The researchers performed viable experiments applying animal models cancer to investigate chemopreventive effects by glucosinolates in vivo.
- The researchers used various assays to measure different aspects of cell behavior and biochemistry, such as cell proliferation, migration, invasion, apoptosis, production of reactive oxygen species (ROS), and expression by cancer-related genes.
- To assess the significance of their findings and make judgements regarding the efficacy of various glucosinolates in preventing cancer, the researchers employed statical analysis.
- The study also includes a review of the applicable biography on glucosinolates with cancer prevention, which provides additional context and background information for the research.
- In addition to their anticancer effects, glucosinolates and their breakdown products have also been shown to have other health benefits. For example, they have antioxidant and anti-inflammatory properties, which may help to reduce the risk of chronic diseases such as heart disease, diabetes, and Alzheimer's disease.

Overall, the consumption of rich in glucosinolates, cruciferous vegetables have been linked to a decreased risk of many cancers and other chronic illness. Nevertheless, it is necessary reporting  the specific health efficacy of these compounds and the optimal amount needed for health promotion are still the subject of ongoing research.

# Chapter 3

## 3.1 Production of glucosinolate

Production of glucosinolate (GSLs) in plants is important for their defense against

various stresses. The biosynthesis of GSLs is regulated by Myeloblastosis (MYB) transcription factors (TF). Recent studies have identified three orthologous duplicates of AtMYB28 in the Brassica rapa (Br) genome, the increased synthesis of GSL is caused by BrMYB28.1, BrMYB28.2, and BrMYB28.3 when overexpressed. These sulfur-containing secondary metabolites play a crucial role in plant defense mechanisms and interest in their potential health benefits which including anticancer properties.

Biosynthesis of Glucosinolates :

Amino Acid Precursor : This are derived from three major groups of amino acid :

1) Aliphatic amino acid –methionine, alanine
2) Aromatic amino acids – phenylalanine, tyrosine.
3) Tryphtophane- indolic glucosinolates

There are few core biosysthetic pathway mentioning below:

1) Chain Elongation : Which means amino acids undergo chain elongation before glucosinolate synthesis.
2) Involves reactions catalyzed by dehydrogenase and aminotransferase enzymes.

Let’s briefly discuss about the formation of the core structure:

1) CYP79: Convert amino acid into aldoximes.
2) CYP83: Convert aldoxen into aci-nitro compounds.
3) Glutathione-S-transferases: Sulfur groups.

Various enzymes modify the structure which resulting in diverse glicosinolates.

Factors affecting glucosinolate productions:

- Genetic
- Environment Conditions
- Soil Composition
- Plant Development

### 3.2 Endoplasmic reticulam :

The endoplasmic reticulum (ER) is known as the secretory pathway. Trauma centers manage the harmony among obsessive and physiological circumstances. It has been shown that ERS motioning in this pathway advances the fix of the protein reaction of this endoplasmic reticulam. The Bcl-2 protein is a regulatory protein that plays a critical role in the regulation iof programmed cell death or apoptosis. It can be said that it includes both pro-apoptotic and anti-apoptotic members that collectively govern the mitochondrial pathway of apoptosis. This Bcl-2 family prevents apoptosis with hindering apoptotic middle people, like Cytochrome and Bax. Research has revealed that during rodent intervertebral disk degeneration, apoptosis is regulated by ER and mitochondrial pathways. These findings highlight the importance of the mitochondria and ER in chondrocytes. Of the mammalian Sirtuins(SIRTs), seven individuals are known to exist. We can also include the fact that SIRT1 regulates oxidative pressure, metabolic disorders, targeted irritation and maturation.

Clarifying SFN’s role in apoptosis, including its specific mechanisms of action, in H2O2-treated chondrocytes was the aim of the current review. In a mouse model of OA, the effect of SFN on ligament degradation was investigated. SGN actives the ( nuclear factor erythroid 2-related factor 2 ) signaling pathway, which upregulates

detoxifying antioxidant enzymes such as glutathione S-transferase, NADPH.

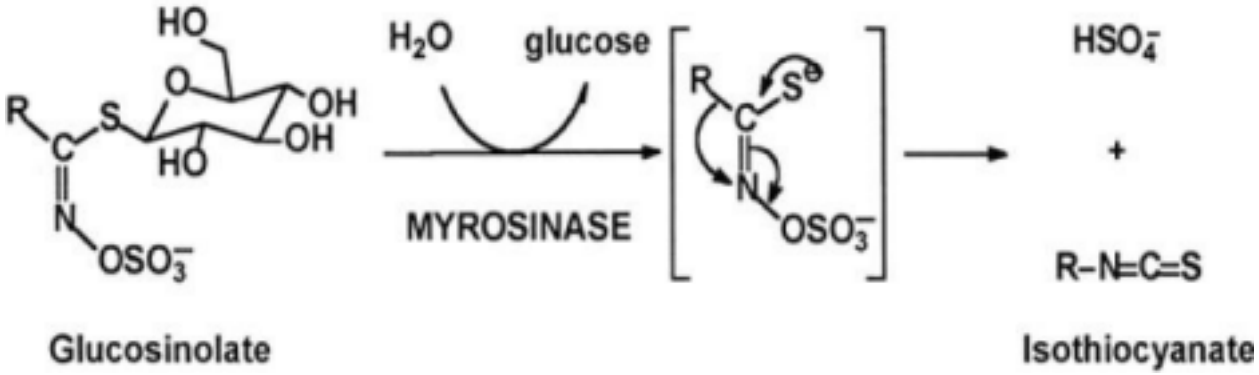


**Figure: 1-** Myrosinase hydrolyzes glucosinolate to produce isothiocyanate(ITC)

Various examinations laid out that isothiocyanates got from glucosinolates are naturally dynamic mixtures. This is also known that the compound glucosinolates are active and idle, it has been also assorted the side chains which records with existence of north of 130 various glucosinolates. Scientists have been accounted for zeroing in on medical advantages of bioactive isothiocyanates of glucosinolates, for example, antimicrobic, cancer prevention agents and antifungal, bio pesticides, anti-carcinogenic and thyroidal exercises Concentrates recommended that glucosinolates and its subsidiaries are generally liable for the fiery flavor and qualities smell of Brassicaceae that contrasts from different types of the comparative family.

### 3.3 Blood:

PEITC obstructed the formation of blood cells by promoting the expression of molecules known as Fas and FasL, along with the production of ROS. However, Fas is a type I membrane protein that is part of the death receptor family, whereas FasL is a type II transmembrane protein classified within the TNF family. The interaction between Fas and FasL is essential for initiating apoptosis, which is responsible for cell death as immune system. This interaction leads to the cytochrome c release and activation of caspase-3 and -9, which is responsible for the cell death. Study also found that in chronic lymphocytic leukemia (CLL), which is a type of cancer that primarily affects adults and is resistant to fludarabine chemotherapy drug, treatment with PEITC resulted in massive cell death in both sensitive and resistant CLL cell lines as it has the glutathione depletion, higher ROS generation, and oxidation of mitochondrial cardiolipin.

### 3.4 Bosom:

In breast cancer cell lines the scientist has discovered that the downregulation of human epidermal growth factor receptor 2 (HER2) and STAT3 leads to the activation of caspase-3 and poly(ADP-ribose) polymerase (PARP) and it is also responsible for the growth of cancer. Also the HER2 belongs to the epidermal growth factor receptor (EGFR) which is a family for the compounds, is overexpressed in many types of cancers in human body. However, HER2 regulates cell growth, survival, and differentiation. Scientists also explained that the compound PARP known as poly ADP-ribose polymerase is involved in DNA repair, genomic stability, and programmed cell death, and is activated under some conditions which is similar to stressful conditions. It is

also noted that excessive activation of PARP leads to ATP depletion at the time of the repair process of damaged DNA in cell which ultimately leads to the termination of a cell grothw. Cdk1 known as cyclin dependent kinase 1 is involved in many stages of cell division which is including the G1/S phase transition, DNA replication in S phase, nuclear breakdown, chromosome assembly and separation, and cytokinesis. As it has been explained before that the members of the bcl family are also involved in anti-apoptosis, but some bcl-2s are also involved in pro-apoptosis. Over all the fact is that the PEITC is an effective HIF inhibitor for stopping the angiogenesis of cancer cells.

### 3.5 Ovary:

The use of PEITC on ovarian cancer cells resulted in a lower rate of phosphorylation of the signaling pathway of EGFR/AKT. Inhibiting the upstream elements of Akt, like EGFR and HER2 can inhibit the proliferation of cancerous cells. In prostate cancer, inhibiting HDAC suppresses the androgen receptor. HDAC plays a role in cell growth, regulation of the cell cycle, and programmed cell death, all of which are associated with the development of cancer. PEITC effectively inhibited cancer-promoting pathways such as EGFR, HER2, and Akt. Additionally, PEITC decreased the levels of chromosomal maintenance 1 (CRM1) proteins, which are crucial for the duplication of centrosomes and the assembly of spindles. These proteins assist in transporting large macromolecules across cell membranes. Ovarian cancer cells that exhibited resistance to cisplatin became more responsive following treatment with metformin and PEITC. Increased levels of reactive oxygen species (ROS) hindered the proliferation of ovarian cancer cells and led to their death.

### 3.6 Colon:

Hostile to carcinogens Antagonistic effect on prevention of cancers Antagonistic effects on the development of cancers. Protective role on cancer initiation or progression Apoptosis (programmed cell death) as a mechanism of cancer chemopreventive activity. In colorectal cancer, the focus is on the potential benefit of glucosinols on this specific type of cancer

### 3.7 Prostate:

To prevent prostate cancer, the levels of 8-oxo-deoxy guanine and pH2AX foci must be decreased. 8-oxo-deoxyguanosine is a modified form of the DNA base guanine which is responsible for the resulting of oxidative damage. This lesion is highly mutagenic because it can mispare with adenine during DNA replication, causing G:C to T:A transversions. There are a few reasons that helps to develop prostate cancer :

8-oxo-deoxyguanosine:

1) Oxidative stress: Chronic inflammation altered metabolism and high ROS level are exhibited by prostate cancer cells.

2) Increased level of 8-oxo-dG in prostate cancer indicates the oxidative damage of DNA.

3) Accumulation of 8-oxo-dG leads to mutation in tumor suppressor genes which drives cancer progression.

4) This-8-oxo-dG can be explored as a cancer progression.

Gamma H2AX :

1) It is the phosphorylated form of the histone variant.
2) It rapidly phosphorylated at Ser139 in response to DNA double-strand break.
3) GammaH2AX foci form around the double-strand break site which indicates as a molecular beacon for the DNA damage repair process.

# Chapter 4

## Mechanism of action of isothiocyanates

Programmed cell death, or apoptosis is a regulated procedure that destroys all of the developed damaged cells  and in mean time it preserves the integrity of surrounding tissue.

### 4.1 Isothiocyanates:

Glucosinolates, which are found in various dietary sources, have been shown to produce a range of metabolites that can induce apoptosis and inhibit cancer progression. Isothiocyanates (ITCs), a hydrolysis product of glucosinolates, have been found to target cancer cells from various organs through several apoptotic pathways, resulting in regulated cell division and death. The potential of glucosinolates and ITCs as chemoprotective agents against common cancers, including lung, prostate, breast, colon cancer, via causing apoptosis is reviewed here.

### 4.2 Phenethyl isothiocyanate (PEITC):

Phenethyl isothiocyanate (PEITC) is a breakdown product of gluconasturtin, which is found in cruciferous vegetables and is released when the tissue is disrupted, such as by chewing or maceration. Watercress is a particularly good source of PEITC. Over the past few decades, numerous epidemiological studies have focused on demonstrating between PEITC and its anti-carcinogenic effects. Recent studies have suggested various mechanisms associated with the effects of PEITC on different stages of cancer that may rising. Scientist also indicated that these mechanisms include biotransformation of phase II detoxification enzymes and also other enzymes like mitochondrial dysfunction and oxidative stress including modification of caspase activity, anti-angiogenesis, and histone deacetylation inhibition on a range of cancer cell lines and animal models, includes those of liver, prostate, blood, lung, colon, and bladder. However, scientist also stated that Gluconasturtin is the precursor of following PEITC with a greater potential to induce ROS and oxidative damage to the cancer cells.

### 4.3 Cell cycle arrest regulation by PEITC:

Cell cycle is a precisely regulated process involving growth and cell division, resulting two daughter cells. Various factors such as growth signals, nutrient availability, and DNA integrity are assessed during cell division. Studies have shown that exposure to PEITC can modify the cell cycle accordingly and helps to come in control of cell proliferation, making it a dormant anti-cancer target in human body. Study shows that the inhibition of cell cycle progression in human body to develop cancer and proliferation is mainly achieved by known as targeting key proteins responsible for the cell cycle and CDK inhibitors I expression in human body. It is known that the cell cycle requires mainly two main phases, G1 and G2, where different cyclin with CDK proteins are in charge of regulating the cell cycle progression. Studies showed that following PEITC can cause cell cycle death at different stages on the cycle which is very important in human body, depending on the used cell type. However, treatment with PEITC, including other ITCs, has been indicated as delay cell cycle progression and inhibit cell growth in HeLa cells at the G2/M phase inside the cell mechanism. Research also indicated that in Caco-2 colon cells, which is responsible for the induced expression of the CDK inhibitor p21waf1/cip1 which is used to treatment with PEITC was responsible to take a part of role in cell cycle arrest at the G2 phase. PEITC has been shown to covalently bind to specific cysteine residues in tubulin, a protein component of microtubules, causing disruption in their growth and breakdown, which triggers cell cycle arrest and apoptosis at the G2/M phase. Moreover, the compound known as PEITC appears to response and act as an electrophile in nature that binds covalently to specific cysteine residues in tubulin, and it is also known that a protein constituent of microtubules.

PEITC may be a viable option for anti-cancer treatment because of its electrophic actions on tubulin and its capacity to control the cell cycle and suppress cell proliferation by targeting important proteins involved in cell cycle progression and CDK inhibitor expression.

### 4.4 Protection against oxidative stress and mitochondrial dysfunction :

In aerobic cells, scientists has declared that mitochondria play significant regulative role in human body which is responding to intracellular death signals, like oxidative stress, DNA damage, starvation, and persuade by chemotherapy drugs and cause to form tumor or cancer. It is obvious that mitochondrial function is disrupted by a decrease in the mitochondrial inner transmembrane potential (Dy) and an increase in the permeability transition (PT) and responsible to form a violation in balance or an imbalance in the redox potential which is responsible to form a cancerous cells. This leads to a decrease in ATP production, oxidation of redox molecules like NADH, NADPH, and glutathione, and generation of harmful free radicals that mediate and enhance apoptotic pathways.

However, Isothiocyanates (ICTs) control the levels of glutathione (GSH) either by inducing phase II biotransformation proteins or by increasing the volume of GSH levels in cells, which is responsible for the cell's antioxidant defense mechanism.

### 4.5 Anti-angiogenesis effected by PEITC:

Isothiocyanates (ICTs) control the levels of glutathione (GSH) either by inducing phase II biotransformation proteins or by elevating GSH levels, which is responsible for the cell's antioxidant defense mechanism. This mechanism was supported by a study conducted on altered ovarian epithelial cells that were exposed on PEITC, resulting of the GSH antioxidant system inactivation and it indicates the aggregation of compounds of ROS especially in the converted cells in body which is responsible for leading cancerous cell death. This process has also been seen in animal models, where hepatic GSH levels rose after seven days of PEITC treatment adult male F344 rats.

### 4.6 Sulforaphane (SFN):

Sulforaphane is another isothiocyanate that has garnered significant attention from researchers worldwide. It is derived from glucoraphanin, which belongs to a group of phytochemicals called glucosinolates, which is also established in cruciferous vegetables like broccoli known as vegetable. SFN is extensively studied like anti-cancer agent due to its ability to regulate biological conversion enzymes and inducing cell cycle arrest. However, scientific literature has pertained to SFN like anti-mutagenic mechanism, and its potent properties have been introduced to radish roots which is also known as vegetable. Current biological studies also have discussed the function of consuming vegetables holding SFN in preventing individual cancer susceptibility or tumor forming.

### 4.7 Mind with SFN (Sulforaphane):

When brain cancer cells were treated with SFN, it caused Nrf2 to move to the nucleus. This led to the ERK1/2 activation and the MMP-2 and CD44v6 downregulation, which inhibited invasion of cerebrum tumors. CD44v6 is an essential component for the invasion, migration, and generation of metastatic tumors. The decreased expression of CD44v6 can significantly impede the proliferation of cancer cells.

### 4.8 Mechanism of Bosom:

SFN treatment is applied as  agent which interfere with breast cancer cells growth by affecting various pathways. Researchers said that one of the pathways involves the interaction between HDAC5 and LSD1 which is responsible for linking the breast cancer cell lines abnormal growth of a human body. It is also known that the compound SFN

inhibits the demanding regulator USF1 of HDAC5, thereby inhibiting growth of ductal carcinoma cells. When SFN is used as a LSD1 inhibitor, it particularly inhibits cancer cells growth. In addition, SFN in combination with Withaferin A (WA) promotes breast cancer cell death by reducing the upregulation of pro-apoptotic protein Bax and the downregulation of anti-apoptotic protein BCL-2.

### 4.9 Mechanism of Colon:

Researchers said that SFN can cause DNA obstruction in colorectal cancer cells by acetylating the DNA repair protein. This leads to apoptosis activation and rise of proapoptotic protein bax expression, detoxifying enzymes, and release of cytochrome c , which ultimately bring about the proteolysis of PARP. When SFN and 3,3'-diindolylmethane are coupled, the stimulation of Phase II enzymes promotes the phosphorylation of ERK1/2 and Akt kinases, which increase the effectiveness of colon cancer growth arrest.

## Chapter 5

## Analyzing tests on different leaves and animals

The scientist found that the inhibitory effects of different extracts from Moringa oleifera, including methanolic extract (ME), aqueous extract (AE), glucosinolates-rich hydrolyzed extract (GEH), glucosinolates extract (GE) which are key extractions on cell proliferation of HCT116 and HT-29 individual colorectal cancer cells. It is also found that the previous studies have published that glucosinolate educe alone can't apply preventive effects although shows the according conversion or hydrolysis into isothiocyanates, such as benzyl isothiocyanate (BITC) which is responsible for the antiproliferative effects on cancer cells in human body. However, scientists indicated that the result of this investigation showed that most physiologically active chemicals are isothiocyanates derived from hydrolyzed glucosinolates, while GEH and BITC had lower IC50 values than GE.

### 5.1 Results on Moringa oleifera leaves extricates:

It is also mentioned by scientist that no cytotoxic actions were observed on CCD-33Co normal colorectal cells with such as Moringa extracts. The research found that IC50 values were resolved using Prism 7 software which is different letters include columns indicate significant differences ($p < 0.05$) based on Tukey Kramer's test in given conditions. Also it has been found that, for cytotoxicity or LDH action, the data are formulated as ± SD of three independent experiments, where letters indicate significant differences ($p < 0.05$) based on Tukey Kramer's test among the different treatments that has been applied as a test.

### 5.2 SFN cytotoxicity on mice chondrocytes:

Scientists discovered that the cytotoxic actions of SFN, a CCK-8 assay was

examined under conditions. However, cells being treated by rising concentrations (0.0, 12.5, 25.0, 50.0, 100.0, and 200.0 μM) of SFN for 24 and 48 hours. It is also clear that SFN displayed cytotoxic actions of ≥100 μM after both 24 and 48 hours accordingly under conditions, it will not exhibit if the concentrations lower than 100 μM (Fig. 2E and F). Therefore, a concentration of 50 μM was chosen for apply in successive experiments to follow up properly.

### 5.3 Apoptosis effect of SFN in H2O2-treated chondrocytes:

**Apoptosis:** This is known as a critical biological process or programming cell death that helps regulate tissue homeostasis which is responsible for eliminating damaged or unwanted cells. Imbalance of apoptosis can contribute to various diseases, including cancer.

**H2O2-treated chondrocytes**: Chondrocytes are the cells responsible for creating producing and maintaining cartilage. However, the factor is obvious that H2O2 is hydrogen peroxide, a reactive oxygen species (ROS) often used to minimize in effect or induce inflammation or oxidative stress in cell culture experiments which is essential for the experiments. Treating chondrocytes with H2O2 mimics oxidative stress conditions, which can lead to cell damage and apoptosis.

**Cancer treatment:** It is also obvious that the query that is meant to have experimented with the results indicated that the effects of compound as SFN on cell death in H2O2-treated the chondrocytes which could have an important implications for cancer treatment. However, the outcome suggests that the research may be exploring the active and potential molecules of SFN in mitigating cell damage and promoting

apoptosis in cancer cells for the patients.

### 5.4 SFN alleviates ERS (European Respiratory Society) and apoptosis of H2O2-treated chondrocytes

**Alleviates ERS and apoptosis**: Scientist stated the fact that SFN has an important and mitigating effect on endoplasmic reticulum stress (ERS) and also on apoptosis within chondrocytes treated through H2O2. It should be remind that the endoplasmic reticulum stress happens during variance connecting protein-folding load also the capacity on the endoplasmic reticulum to process unfolded proteins, which can trigger apoptosis (programmed cell death) if unresolved. SFN may help alleviate these stress responses, potentially by modulating cellular signaling pathways involved in ERS and apoptosis.

**H2O2-treated chondrocytes**: Chondrocytes are the specialized cells found in cartilage tissue, and treating them with hydrogen peroxide (H2O2) induces oxidative stress. H2O2 is knows and familiar as a reactive oxygen species (ROS) which is responsible for leading cellular damage and trigger various cellular responses, including ERS and apoptosis.

**In cancer treatment:** The statement suggests that the observed outcome of the compounds of SFN on ERS also apoptosis in H2O2-treated chondrocytes may have an important role and also implications for cancer treatment in human body. This implies that SFN's ability to alleviate cellular stress and apoptosis could be beneficial in cancer therapy, potentially by promoting cell survival or inhibiting cancer progression.

### 5.5: SIRT1 activity in H2O2-treated chondrocytes is increased by SFN pretreatment:

Researchers discovered that SIRT1 ensures a critical part in cell signaling passages concerned in DNA repair and help to prevent cancer cell formation in human body and also helps to prevent cell proliferation, invasion, metastasis as well as chemotherapeutic resistance and long-term survival that are relevant in human malignancies and will continue to be a positive therapeutic study for years to come. Enhances SIRT1 activity: SIRT1 (sirtuin 1) which a protein which is responsible and also involved in different cellular processes and helps various ways including DNA repair, apoptosis, stress response. It is also associated with longevity and has been implicated in cancer development and treatment. Enhancing SIRT1 activity may have protective effects on cells, potentially promoting their survival and reducing the risk of cancer.

# Chapter 6

## Limitations

### 6.1 Dose-dependent effect:

The chemopreventive activity of glucosinolates in cruciferous vegetables may vary depending on the dosage, with higher doses not always correlating with increased efficacy.

The dose-dependent effect refers to the phenomenon where the effectiveness of glucosinolates in cruciferous vegetables in preventing cancer may not always increase proportionally with higher doses. In other words, consuming a higher amount of glucosinolates may not necessarily result in increased efficacy in cancer prevention.

Research studies have shown that the relationship between the dose of glucosinolates and their chemopreventive activity may not follow a linear pattern. It is possible that the

mechanisms of action of glucosinolates may reach a saturation point at higher doses, where further increase in dosage does not lead to increased cancer-preventive activity. Additionally, higher doses of glucosinolates may also result in potential adverse effects, such as gastrointestinal discomfort or interference with thyroid function, which may offset their beneficial effects. However, it's necessary to focus on the point that the optimal dosage by glucosinolates for cancer prevention could be responsible and may vary depending on various factors, such as individual genetics, type of cancer, and overall health status. Therefore, primary work is to discuss with a healthservice professional or else registered dietitian before considering glucosinolate additives or making significant changes to your cruciferous vegetable consumption, especially if you are using them for cancer prevention purposes.

### 6.2 Variability in glucosinolate content:

The amount and type of glucosinolates in cruciferous vegetables can vary depending on factors such as plant species, growing conditions, and storage methods, which may impact their chemopreventive activity. The variability in glucosinolate content refers to the fact that the amount and type of compounds knows as glucosinolates, the bioactive compounds located at cruciferous vegetables, can show various elements like plant breed, growing conditions, and storage methods. This variability can impact the chemopreventive activity of vegetables as like cruciferous  in cancer prevention in human body. Furthermore, growing conditions, such as soil composition, temperature, light exposure, and water availability, can also influence the content of glucosinolates in cruciferous vegetables. For example, stressors like drought or nutrient deficiencies may lead to changes in glucosinolate content in plants. Similarly, post-harvest storage

methods, such as temperature, humidity, and duration of storage, can also impact the glucosinolate content of cruciferous vegetables.

The variability in glucosinolate content can have implications for the chemopreventive activity of cruciferous vegetables. Different types and amounts of glucosinolates may have varying bioavailability, metabolism, and efficacy in cancer prevention. Therefore, the variability in glucosinolate content in cruciferous vegetables should be taken into consideration when interpreting research findings or recommending dietary intake for cancer prevention purposes. Consuming a variety of cruciferous vegetables, with a diverse array of glucosinolates, can help to mitigate the potential impact of variability in glucosinolate content and ensure a balanced intake of these beneficial compounds.

### 6.3 Bioavailability:

Glucosinolates need to be converted into their active forms, such as isothiocyanates, to exert their anticancer effects, and the bioavailability of these active forms may vary among individuals. In the case with glucosinolates, these are the bioactive compounds located on cruciferous vegetables, they need to be converted into their active forms, such as isothiocyanates, in order to exert their anticancer effects. Glucosinolates are relatively stable compounds that are converted into isothiocyanates through an enzymatic reaction, typically triggered by mechanical disruption or enzymatic activity during food processing, cooking, or digestion. Isothiocyanates are known to possess potent anticancer properties, such as inhibiting carcinogen activation, inducing detoxification enzymes, and promoting in cancer cells the apoptosis (programmed cell death). Nevertheless, bioavailability with those active isothiocyanate compounds may vary among individuals due to factors such as genetics, gut microbiota composition,

and individual differences in metabolism and digestive processes. Some individuals may have higher or lower capacity to convert glucosinolates into isothiocyanates, which may affect the efficacy of the anticancer effects of glucosinolates in cruciferous vegetables.

Additionally, the bioavailability of isothiocyanates may also be influenced by food processing and cooking methods. For example, boiling cruciferous vegetables for a prolonged period of time may result in significant loss of glucosinolates and reduced formation of isothiocyanates, while other cooking methods like steaming or microwaving may help to better retain the bioactive compounds.

The variability in bioavailability of active isothiocyanates from glucosinolates may impact the overall chemopreventive activity of these vegetables in preventing cancer, the extent on which these compounds are absorbed and utilized by the body can affect their effectiveness.

### 6.4 Genetic factors:

Individual genetic variations can affect the metabolism and effectiveness of glucosinolates in cancer prevention.

Those genetic factors performs functions in the metabolism and effectiveness of glucosinolates in cancer prevention. Glucosinolates were bioactive substances included in cruciferous vegetables that been linked to anticancer properties. However, individual genetic variations can impact how these compounds are metabolized in the body, which may in turn affect their effectiveness in cancer prevention. Enzymes are responsible for converting glucosinolates into their active forms, such as isothiocyanates, which

possess anticancer properties. The activity of these enzymes can be influenced by genetic variations, which can result in different rates of conversion of glucosinolates to their active forms among individuals. Genetic polymorphisms (variations) in genes encoding for these enzymes, such as myrosinase and glutathione S-transferases, have been shown to affect the metabolism of glucosinolates and their anticancer effects. For example, some individuals may carry genetic variations that result in lower activity of the enzyme myrosinase, which converts glucosinolates to isothiocyanates in the gut. This can result in reduced conversion of glucosinolates to their active forms, potentially impacting the overall effectiveness of cruciferous vegetables in cancer prevention. Similarly, genetic variations in glutathione S-transferases, which are involved in the detoxification of isothiocyanates and other compounds, can affect their efficacy in cancer prevention. Some individuals may have genetic variations that result in lower activity of these enzymes, leading to reduced detoxification of isothiocyanates and potentially increased effectiveness in cancer prevention.

On the other hand, some individuals may carry genetic variations that result in higher activity of these enzymes, leading to more rapid metabolism of glucosinolates and their active forms, potentially impacting their cancer preventive effects.

Overall, genetic factors can influence the metabolism and effectiveness of glucosinolates in cancer prevention by affecting both the detoxification of these active forms and the transformation of glucosinolates into their active forms. To learn more about how genetic variables affect metabolism, more research is required, effectiveness of glucosinolates in different populations and individuals, and to optimize their potential health benefits in cancer prevention strategies.

### 6.5 Interaction with other dietary components:

Cruciferous vegetables are often consumed as part of a mixed diet, and interactions with other dietary components may affect their chemopreventive activity.

### 6.6 Timing of exposure:

The timing of cruciferous vegetable consumption in relation to cancer development may be crucial, and the efficacy of glucosinolates may vary depending on when they are consumed in the cancer development process.

**Variability in cancer stages**: The stage of cancer development at which glucosinolates are administered may impact their efficacy, with potential differences in chemopreventive activity between early and late stages of cancer.

**Inter-individual variability**: Individual differences in metabolism, absorption, and excretion of glucosinolates may affect their cancer-preventive activity.

**Animal studies vs. human studies**: Majority proof on cancer-preventive activity on glucosinolates derives from animal history, and the results may not always directly translate to humans.

**Lack of long-term human studies:** Long-term studies investigating that glucosinolates have few cancer-preventive effects in humans, and further study is required to determine their long-term safety and effectiveness.

**Potential adverse effects:** High consumption of cruciferous vegetables or glucosinolate supplements may have potential adverse effects, such as gastrointestinal discomfort or interference with thyroid function, which may limit their use.

**Individual preferences and tolerances**: Taste preferences, tolerances, and cultural differences may impact the consumption and efficacy of cruciferous vegetables and glucosinolates in different populations.

**Variability in cooking methods:** Cooking methods, such as boiling or microwaving, can affect the bioavailability and efficacy of glucosinolates in cruciferous vegetables.

**Interactions with medications**: Cruciferous vegetables and glucosinolates may interact with medications, and caution should be exercised, especially in individuals taking medications for cancer treatment or other health conditions.

**Lack of standardized dosages:** There is a lack of standardized dosages of glucosinolates or isothiocyanates for cancer prevention, which makes it difficult to compare studies and establish optimal dosages.

Confounding factors: Factors such as smoking, alcohol consumption, physical activity, and other dietary components may confound the effects of glucosinolates on cancer prevention.

# Chapter 7

# Controlling

## 7.1 Breeding and choosing plants:

Cruciferous vegetables types can be created through plant breeding and selection methods with higher levels of anti-carcinogenic glucosinolates, and optimize their content and profile for cancer prevention.

## 7.2 Optimal growing conditions:

Providing optimal growing conditions, such as appropriate soil fertility, adequate water supply, and optimal temperature and light conditions, can promote the accumulation of anti-carcinogenic glucosinolates in cruciferous vegetables.

## 7.3 Post-harvest handling:

Proper post-harvest handling practices, including careful harvesting, handling, and storage of cruciferous vegetables, can help to minimize the loss of glucosinolates and maintain their anticancer properties.

**Cooking methods:** Different cooking methods can have varying effects on glucosinolates in cruciferous vegetables. For example, steaming, microwaving, and stir-frying have been shown to retain more glucosinolates compared to boiling or prolonged high-temperature cooking, which can result in loss of these bioactive compounds.

**Food processing techniques**: Various food processing techniques, such as chopping, crushing, and blending, can activate the enzymes responsible for converting glucosinolates into their active forms, enhancing their bioavailability and anticancer effects.

**Proper storage:** Proper storage of cruciferous vegetables, such as refrigeration and avoiding prolonged exposure to light and air, can help to maintain their glucosinolate content and prevent degradation.

**Consumption of fresh, raw cruciferous vegetables**: Raw cruciferous vegetables, such as in salads or as garnish, can provide higher levels of glucosinolates compared to cooked vegetables, as some glucosinolates may be heat-sensitive.

**Balanced diet:** Consuming a good and preferred diet which consists of different cruciferous vegetables can provide a diverse array of glucosinolates, maximizing their cancer preventive effects.

**Avoiding overconsumption**: While glucosinolates have cancer preventive properties, overconsumption of cruciferous vegetables, particularly in the form of supplements, can result in excessive intake of certain glucosinolates and their breakdown products, which may have adverse effects.

**Individualized nutrition plans**: Taking into consideration individual variations in genetics, health status, and dietary preferences, developing personalized nutrition plans that incorporate cruciferous vegetables can optimize their anticancer effects and overall health benefits.

**Blanching:** This entails briefly submerging cruciferous veggies in boiling water by rapid cooling, can help to retain their glucosinolate content and prevent loss during storage or further processing and help to reduce dangerous factors.

### 7.4 Fermentation and combinations with other foods:

Fermenting cruciferous vegetables, such as cabbage in the form of sauerkraut or kimchi, can enhance the bioavailability of glucosinolates and their conversion into active forms, as fermentation activates enzymes that break down glucosinolates. Combining cruciferous vegetables with other foods that contain certain enzymes, such as myrosinase, which help to convert glucosinolates into active forms, can enhance their anticancer effects. For example, consuming cruciferous vegetables with mustard, radishes, or daikon can increase the conversion of glucosinolates into bioactive compounds.

Glucosinolate-rich extracts obtained from cruciferous vegetables can be used in the form of supplements or food additives to provide standardized doses of these bioactive compounds for cancer chemoprevention.

# Chapter 8

## Futuristuc purpose

### 8.1 Precision cancer prevention:

With advancements in genomic medicine and personalized nutrition, the identification of specific genetic markers or biomarkers related to glucosinolate metabolism and efficacy could lead to tailored cancer prevention plans. Individuals with certain genetic profiles may benefit more from specific cruciferous vegetables or glucosinolate-rich extracts based on their ability to convert glucosinolates into active forms and their

overall metabolic response.

- **Nutrigenomics**: The field of nutrigenomics aims to understand how nutrients, including glucosinolates, interact with genes and influence their expression to prevent diseases, including cancer. Futuristic research may uncover novel mechanisms by which glucosinolates modulate gene expression, leading to personalized cancer prevention strategies based on an individual's genetic makeup.

- **Nanotechnology-based delivery systems**: Nanotechnology offers potential futuristic approaches for delivering glucosinolates in cruciferous vegetables to target cancer cells specifically. Nanoparticles loaded with glucosinolates can be engineered to deliver the bioactive compounds directly to cancer cells, maximizing their therapeutic effects and minimizing side effects.

- **Combination therapies:** Future research may explore application of glucosinolates combining other cancer preventive agents, like drugs, radiation, or immunotherapies, to enhance their synergistic effects and provide more effective cancer prevention strategies.

### 8.2 Machine learning and artificial intelligence:

The incorporation of machine learning and artificial intelligence(AI) into cancer prevention research may enable the identification of patterns, correlations, and predictive models related to glucosinolate efficacy, dosage, timing, and other factors. This could help optimize personalized cancer prevention strategies based on an individual's unique characteristics and health status. Future research may explore

advanced techniques to enhance the bioavailability of glucosinolates, such as using nanotechnology, microencapsulation, or other innovative methods to improve their absorption, distribution, and metabolism in the body.

# Chapter 9

## Conclusion:

Glucosinolates and isothiocyanates play a crucial role in our daily diet, and extensive scientific research suggests that these compounds have significant potential in

preventing cancer through their metabolites. PEITC, BITC, SFN, and AITC are some of the glucosinolates that have been closely associated with chemopreventive effects by modulating various cellular. However, further research is needed to elucidate and provide evidence for the association between glucosinolates and their target molecules, as well as the mechanisms involved in apoptotic events. Cruciferous vegetables have gained preferences for health-promoting qualities and effective clinical trials can reduce the incidence of cancer. Proteins linked to homeostasis and cell proliferation are targeted by BITC, PEITC, SFN. They engage in interaction which help proteins that repair DNA damage, helps in important stimulation cell cycle arrest and it also helps and assists with the factors which induce programmed cell death, Scientists also found that they play an important role to target various pathways including the adaptive stress response also adding those phases known as phase I/II protein modulation. Scientists also included that many in vivo studies have demonstrated the bioavailability of isothiocyanates and their anti-tumoral effects under preferred conditions. It is also important to know that vegetables are prone to prevent cancerous cell formations in human bodies as they have anti cancerous compounds. Although human studies are limited, they support the oral bioavailability of isothiocyanates with reasonable plasma and urine concentrations achieved. Overall, both cell and animal studies support a potential role for isothiocyanates in bladder cancer prevention and treatment. However, it is clear that SFN, an isothiocyanate found in cruciferous vegetables which has been shown to important indications and proves of exhibition of anti-anxiety, sedative-hypnotic, and anti-depressant effects.

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