International Journal of Pharmaceutical Research and Applications
Volume 9, Issue 5 Sep - Oct 2024, pp: 341-347 www.ijprajournal.com ISSN: 2456-4494

Sulphoraphane: As Health promoting tool

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Date of Submission: 10-09-2024 Date of Acceptance: 20-09-2024

ABSTRACT:
SFN, derived primarily from broccoli and with absolute bioavailability of around 80%, shows promise as a nutrigenomically active compound capable of increasing several endogenous antioxidant compounds via the transcription factor, Nrf2
Sulphur compounds in sulphur rich food have been shown to significantly reduce the risk of cancer development. One such compound is sulforaphane (SF), a cancer chemopreventive agent identified in broccoli (F. cruciferae).Cruciferous vegetable intake may lower overall cancer risk, including colon, lung, and prostate cancer, particularly during the early stages.SFN is a safe and relatively nontoxic chemopreventive agent, and exerts anticancer activities through multiple mechanisms, including regulation of Phase I and Phase II DMEs, anti-inflammatory activity, cell cycle arrest, induction of apoptosis, and the epigenetic regulation on Nrf2-Keap1, cyclins, and CDKs.
Keywords: Sulforaphane, Medicinal plants, Anticancer, Nutraceutical.

I. INTRODUCTION

Sulforaphane was first identified as an antibiotic in the middle of the last century and was isolated from red cabbage and absolute bioavailability is found approximately 80%. (Gielbert et al, 2008).Talalay and Zhang first time isolate it from broccoli and tell about sulforaphane showing anti-cancer properties (Talalay et al, 1999).

It was reported that in one gram florets of broccoli in dried form approximately 507 to 684 µg of sulforaphaneobtained (Campas-Baypoli et al, 2010). A phytochemical glucoraphanin abundantly found in cabbage which acts as a biogenic precursor (Benedict et al, 2010). Glucoraphanin present in higher concentration in the sprouts of broccoli as compared to mature broccoli which act as sulforaphane precursor (Fahey et al, 1997; Zhang et al, 1994).

Isothiocyanate sulforaphane found in broccoli, having a beneficial effect on human health when used in the diet. In the presence of glucoraphanin, sulforaphane is formed through β-thioglucosidase by the actions of myrosinase, present in either the plant tissue or the mammalian microbiome.(G. Shen et al. 2006).It was found that plant-based diets having epidemiologically protective against a range ofdiseases. (Howes et al, 2014).

Isothiocyanates (ITCs), plant-derived chemoprotective constituents, are formed by the hydrolysis of their precursor parent compounds, glucosinolates. The levels of glucosinolate vary greatly within members of the Cruciferae family, depending on the environment and genotype (Saha et al, 2017).

Sulforaphane is reported for several therapeutic and biological activities such as anticancer, antidiabetic, antioxidant, anti-inflammatory, hepatoprotection, antidepressant, cardioprotective, etc.( ). SFN is one of phytochemicals that become a promising anticancer agent because of its low toxicity (Singh et al, 2007).

It is demonstrated that sulforaphane has great antitumor activity and has the ability to inhibit proliferation, viability, migration, malignancy, and epithelial-to-mesenchymal transition of cancer cells.(Cheng et al., 2016; Hu et al, 2005).Sulforaphaneis an isothiocyanate compound that is mainly found in cruciferous vegetables(Noor et al., 2013).

It was reported that sulforaphane is active against various cancer like pancreatic, prostate, breast, lung, cervical, colorectal cancers, etc. (Stephenson K.K, et al , 2002; Min C, et al, 2007; Rose et al., 2005). Sulforaphane shows its therapeutic action by various mechanisms, such as by detoxifying carcinogens and oxidants through blockage of phase I metabolic enzymes, and by arresting cell cycle in the G2/M and G1 phase to inhibit cell proliferation (Zuryn et al, 2016).

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It was found that the ability of sulforaphane to potentiate the activity of various types of anticancer agents like paclitaxel, docetaxel, podophyllotoxin, gemcitabine, etc., through additive and synergistic effects.(Kim et al, 2017).

The development of novel anticancer drugs with the capability of targeting various molecular pathways is essential for the effective management and treatment of cancer.Identification and subsequent targeting of these pathways showing importance in cancer therapy. MicroRNAs (miRNAs) are small noncoding RNA molecules responsible for post-transcriptional regulation of genes.(A. Buchanan et al, 2017).

It was reported that miRNAs play an important role in various biological processes like proliferation, differentiation, apoptosis, cell cycle regulation, etc.Therefore any impairment in the expression and function of miRNAs is related with the development of some disorders, particularly cancer.(Martin et al., 2017).

Role of sulforaphane in various disease management

As anticancer agent

Cancer development is a multistep process, including initiation, promotion, and progression, and involves genetic and epigenetic changes that disrupt pathways controlling cell proliferation, apoptosis, differentiation, and senescence.(Anfossi et al, 2018; Cheung et al, 2010; Zhou et al, 2018).

It was found that consumption of broccoli related to the lower risk of cancer in various organs like, colon, breast, lung, stomach, prostate, skin, bladder, etc., and anticancer activity due to sulforaphane compound (Ambrosone et al, 2004; Joseph et al, 2004;Xia et al, 2019).

SFN is one of phytochemicals and has become a promising anticancer chemotherapeutic agent because of its low toxicity. (Herman-Antosiewicz et al, 2007).Consumption of broccoli reduces risk of cancer that is related with the ability of SFN to inhibit phase 1 enzymes and induce phase 2 enzymes(Zhang et al, 1992; Clarke et al, 2008).

Sulforaphane act as anticancer agent by induction of apoptosis in (HT-29) cells that is attributed to up-regulation of Bax and release of cytochrome C from mitochondria (Gamet et al, 2000).SFN is a powerful inducer of apoptosis both in vitro and in vivo. (Lenzi et al, 2014)

It was found that treatment with SFN associated with inhibition of histone deacetylase, leading to increased histone acetylation and apoptosisin both the prostate and colon cancer cells. (Myzak et al, 2006; Myzak et al, 2004).Sulforaphane act by various mechanism including, inhibition of cell cycle progression, induction of apoptotic cell death via activation of AP-1 and MAPK pathways, inhibition of angiogenesis etc., in a variety of cancer cell types(Shen et al, 2006; Jeong et al, 2004).

It is also reported that sulforaphane induces the activation of nuclear factor erythroid-2(Nrf2) that is a critical transcription factor during the antioxidant stress response, responsible for the activation of cytoprotective genes with anticarcinogenesis activities (Agyeman et al, 2013; Li et al, 2015). Over the years, sulforaphane (SFN), found in cruciferous vegetables, has been shown to have chemopreventive activity in vitro and in vivo. SFN protects cells from environmental carcinogens and also induces growth arrest and/or apoptosis in various cancer cells. (Watson et al,2013; Juengel et al, 2017; Xu et al, 2006).

SFN reported for induction of apoptosis, or programmed cell death, both the p53-positive and p53-negative human colon cancer cell lines, prostate cancer DU145 cells(Gerhauser et al, 2006; Cho et al, 2005). In both the prostate and colon cancer cells, SFN treatment was associated with inhibition of histone deacetylase, leading to increased histone acetylation and apoptosis (Wang et al, 2006; Myzak et al, 2004).

SFN Inhibits Cell Cycle Progression and Enhances the Ability of Paclitaxel to Induce Cell Cycle Arrest. Anticancer effects of SFN have been demonstrated in several malignancies including human colon, bladder, prostate, ovarian, lymphoblastoid, pancreatic, cervical cancer, and lung cancers (Hedley et al, 2004; Andelova et al, 2007; Shan et al, 2006).

As antimicrobial agent

It has also been a few reports that the antimicrobialpotential of ITCs depends on their chemical structure (Dias et al, 2014).Aromatic and indolyl groups show a higher antibacterial effect compared with aliphatic groups against plant pathogenic bacteria (Aires et al, 2009).Initial in vitro evaluations of the antibacterial activities of glucosinolate enzymatichydrolysis products against plant pathogenic bacteria (Wilson et al, 2013).

It was demonstrated that broccoli sprouts suppressed the up regulation of the inflammatory

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markers, TNF-α and IL-1β in the gastric mucosa by H. pylori infection in a wild type but not in Nrf2−/− mice, suggesting a systemic protective effect against gastritis that was the result of Nrf2 activation (Yanaka et al, 2009).

The presence of a double bond in the chemical structure of the ITCs seemed to increase the antimicrobial activity. For example, sulforaphene (CH3-SO-CH=CH-CH2-CH2-), which is similar in structure but has one double bond, showed higher antimicrobial activity (0.344 mg/ml) against C. albicans than sulforaphane (CH3-SO-CH2-CH2-CH2-CH2-) (1.000 mg/ml) (Wilson et al, 2013; Leodolter et al, 2001). Sulforaphene, which is similar in structure, but has one double bond, showedhigher antimicrobial activity than sulforaphane. (Dufour et al, 2015)

Erucin, which has a thiol group, showed higher antimicrobial activity than sulforaphane, which has a sulfinyl group. BITC and iberin with a short chain exhibited higher antimicrobial potential than PEITC and sulforaphane with a longer chain, respectively. ITCs have strong antimicrobial activities and may be useful in the prevention and management of dental caries.(Wilson et al, 2013; Zhang et al, 2001).

As Neurodegenerative

Various age-related neurological disorders are multifactorial and that no drugs are available to stop their progression, intervention strategies using phytochemicals have been proposed as an alternative form of treatment for their prevention.

It was reported that sulforaphane (isothiocyanato-4-(methylsulfinyl)-butane) (SF) have neuroprotective effects in various experimental paradigms.(Middleton, 1998; Eastwood, 1999).

It was found that SF increased the expression of Nrf2 and of downstream targets HO-1 and NQO-1 in Neuro2a cells and the sciatic nerve of diabetic animals. (Negi et al, 2011).

Sulforaphane prevented oxidative stress-induced cytotoxicity in rat striatal cultures by raising the intracellular GSH content via an increase in γ-GCS expression induced by the activation of the Nrf2-antioxidant responsive element pathway (Muto et al, 2011). SF was also effective in counteracting oxidative stress induced by antipsychotic drugs in human neuroblastoma SK-N-SH cells, increasing GSH levels and inducing NQO1 activity (Mas et al; 2012).

The ability of SF to exert neuroprotective effects in different acute and chronic neurodegenerative diseases could be ascribed to its peculiar ability to activate the Nrf2/ARE pathway. Nrf2 is a recent therapeutic target in neurodegenerative diseases because it regulates several genes that have been implicated in protection against neurodegenerative conditions(Ma et al, 2012; Townsend et al, 2009).

As anti-inflammatory:

Chronic inflammation and carcinogenesis are thought to be closely related, and SFN has been found to have anti-inflammatory properties.(Shimizu et al, 2016)

Constitutive activation of NF-κB is common in various human malignancies, including breast and prostate cancer, and leads to the up regulation of genes encoding adhesion molecules, inflammatory cytokines, growth factors, and antiapoptotic genes.(Kolberg et al, 2015).

Expression of several proinflammatory genes including, nitric oxide, inducible nitric oxide synthase, Cox-2, and TNF-α, regulated by a transcription factor known as NF-κB(Lozanovski et al, 2014).

It was also found that elevated levels of Cox-2 monitored in various tumors and may account for excessive production of prostaglandin. In human malignant glioblastoma cells, SFN can also significantly decrease NF-κB expression compared to control cells, suggesting that NF-κB is an important molecular target of SFN(Karmakar et al, 2006; Thejass et al, 2006).

II. CONCLUSION:

It was found that the SFN is a safe and relatively nontoxic chemopreventive agent, and exerts anticancer activities through multiple mechanisms, including regulation of Phase I and Phase II DMEs, anti-inflammatory activity, cell cycle arrest, induction of apoptosis, and the epigenetic regulation on Nrf2-Keap1, cyclins, and CDKs. It was reported that SFN effectively inhibited tumor growth and increased the sensitivity of cancer cells to chemotherapeutics in patients with advanced pancreatic ductal adenocarcinoma.

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International Journal of Pharmaceutical Research and Applications
Volume 9, Issue 5 Sep - Oct 2024, pp: 341-347 www.ijprajournal.com ISSN: 2456-4494

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