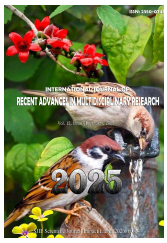
ISSN : 2350-0743

International Journal of Recent Advances in Multidisciplinary Research

Vol. 12, Issue 01, pp. 10639-10645, January, 2025



RESEARCH ARTICLE

SULFORAPHANE: A POWERFUL BIOACTIVE COMPOUND WITH CHEMOPREVENTIVE PROPERTIES AND REMARKABLE THERAPEUTIC BENEFITS

[1]Resta, S., [2]Riccardi, B. and [3]Giacomo Resta

[1]Surgeon, Specialist, Freelancer, 53043 Chiusi (SI), Via Montegrappa, 1 ORCID è: 0000-0001-6950;
[2]Biologistfreelancer, 56022 Castelfranco di Sotto (Pisa), Via dei lazzeri, 33, Italy
[3]Student at the Faculty of Pharmacy of the University of Perugia (Italy)

ARTICLE INFO

Article History

Received 20th October, 2024
Received in revised form
16th November, 2024
Accepted 27th December, 2024
Published online 24th January, 2025

Keywords:

Cancer Prevention, Adjuvant Therapy, Sulforaphane in Cancer Therapy, Therapeutic Properties and Mechanism of Action of Sulforaphane.

****Corresponding author: Resta, S.***

ABSTRACT

Cancer is a multifactorial disease, therefore it is difficult to identify the specific agents responsible for its progression and development, but lifestyle and nutrition have been shown to play an important role. Several natural compounds, especially plant extracts, are demonstrating efficacy in the development of new cancer therapies, among these compounds sulforaphane is the most studied. But one of the main challenges with sulforaphane treatment is its low solubility and oral bioavailability. Several carriers are being studied to overcome these difficulties. Sulforaphane (SFN) is an isothiocyanate derived from cruciferous vegetables, particularly broccoli, known for its powerful antioxidant, anti-inflammatory and anticancer properties. Emerging evidence suggests that sulforaphane acts primarily through the activation of the transcription factor Nrf2, a crucial modulator of the antioxidant response and cellular detoxification. Preclinical and clinical studies have demonstrated that sulforaphane has beneficial effects on several diseases, including cancer, cardiovascular disease, neurodegenerative diseases, and metabolic disorders. In this publication, we review the molecular mechanisms of sulforaphane, its therapeutic effects in various clinical settings, and provide an analysis of the most recent case studies that support its use in the prevention and treatment of chronic diseases.

Citation: Resta, S. and Riccardi, B. 2024. *"*Sulforaphane: a powerful bioactive compound with chemopreventive properties and remarkable therapeutic benefits*", International Journal of Recent Advances in Multidisciplinary Research,* 12, (01), 10639-10645.

INTRODUCTION

The remarkable progress achieved in the treatment of cancer has allowed, in recent years, a progressive improvement in the quality and life expectancy of patients. In addition to the use of antineoplastic drugs, which are increasingly effective and increasingly personalized for the individual patient, adjuvant therapies that use various types of supplements have been spreading for many years [*]. To date, a vast literature has investigated the benefits that can be obtained from the association of various supplements, in particular plant extracts, with conventional antiblastic therapy, with the aim of obtaining a synergism of action and efficacy or at least reducing the debilitating symptoms (the classical oncologic fatigue, tiredness) that is a side effect of pharmacological treatment. Several scientific organizations have emerged aimed at investigating and disseminating, through objective research, the efficacy of various supplements in the adjuvant therapy of cancer and stimulating the comparison of the clinical results obtained by various researchers. For example, we cite the Society for Integrative Oncology (SIO) https://integrativeonc.org/ Despite research efforts, there is no unanimous consensus among clinicians on the actual efficacy and reliability of the protocols that include the associations in question. Although the same principle of understandable caution should be applied about the alleged therapeutic efficacy with antiblastic drugs alone. To what extent are they effective? And to what extent should the supposed efficacy be ascribed entirely to the effect of the drugs?. Having made this necessary premise, in this article we intend to present a cross-sectional and objective examination of the literature regarding one of the most widespread supplements in adjuvant phytotherapy, Sulforaphane. The percentage of patients affected by cancer who turn to non-conventional and complementary medicines is approximately 35.9%. [**] Among complementary medicines, the most used are Phytotherapy and Mycotherapy. In some of the largest and most advanced oncology centers in the world, for example the "Sloan-Kettering" in New York, there have been Departments of Integrative Medicine for several years, precisely to guarantee the complementary contribution of numerous techniques to conventional chemo or radiotherapy.

In Tuscany, in the Careggi Hospital of Florence, there is a phytotherapeutic medicine department where cancer patients are treated with adjuvant phytotherapy.

[*] Helen A. Norman et al; The Role of Dietary Supplements during Cancer Therapy, The Journal of Nutrition, 2003 American Society for Nutritional Sciences.

[**] "Use of complementary and alternative medicine in cancer patients: a European survey." Molassiotis A et Al. Ann Oncol. 2005 Apr;16(4):655-63

Molecular mechanisms of action of Sulforaphane Fig.1: Sulforaphane is a natural phytochemical compound belonging to the class of isothiocyanates, derived from glucoraphanin, a glucosinolate abundantly present in cruciferous vegetables such as broccoli, cauliflower, Brussels sprouts and turnips. Sulforaphane is known for its powerful antioxidant, anticancer and anti-inflammatory properties. Its biological action is mediated mainly through the activation of the transcription factor Nrf2, which regulates the expression of several genes involved in detoxification, oxidative stress response, and inflammation regulation. Many preclinical and clinical studies have highlighted the therapeutic potential of sulforaphane in numerous areas, including cancer chemoprevention, cardiovascular protection, improved neurological function, and modulation of metabolism.

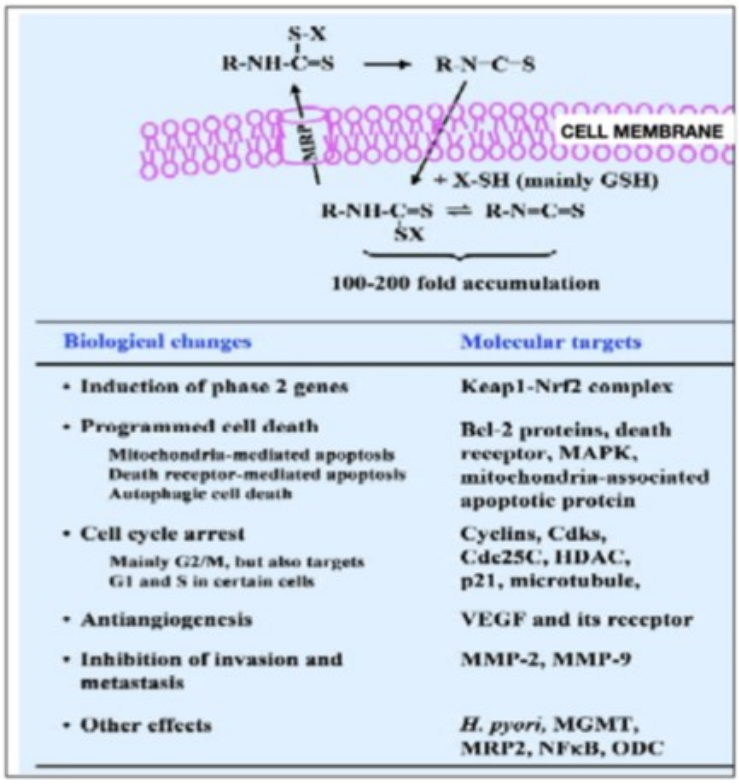


Figure 1. Cellular accumulation and export of SF and its chemopreventive mechanism

Despite the extensive scientific literature documenting the benefits of sulforaphane, the clinical efficacy of this natural compound is still under investigation to determine optimal doses and administration methods. The chemical structure of SF is abbreviated as R– N=C=S, where R represents CH3-SO-(CH2)4. Cdc25C, cell division cycle 25C; HDAC, histone deacetylase; Keap1, Kelch-like ECH-associated protein 1; MAPK, mitogen-activated protein kinase; MMP, matrix metalloproteinase; MGMT, O6-methylguanine-DNA methyltransferase; MRP2, multidrug-resistance-associated protein 2; NF-κB, nuclear factor-kappa B; Nrf2, nuclear factor erythroid 2-related factor 2; ODC, ornithine decarboxylase; VEGF, vascular endothelial growth factor; X-SH, X stands for the side chain of a sulfhydryl molecule. From: Yuesheng ZHANG, Li TANG; Discovery and development of sulforaphane as a cancer chemopreventive phytochemical, Acta Pharmacol Sin 2007 Sep; 28 (9): 1343–1354

Activation of Nrf2: The main mechanism of action of sulforaphane is the activation of Nrf2 (NuclearFactorErythroid 2-Related Factor 2), a key transcription factor in the antioxidant response and protection against oxidative stress. Under physiological conditions, Nrf2 is bound to Keap1, a protein that inhibits its activity. When sulforaphane enters cells, it interacts with Keap1, causing a conformational change that releases Nrf2, which moves to the nucleus and activates the expression of antioxidant and detoxifying genes. These genes include glutathione S-transferase (GST), superoxide dismutase (SOD), and catalase, which contribute to reducing oxidative damage and enhancing the inflammatory response (Dinkova-Kostova& Kostov, 2012). These enzymes are involved in restoring redox balance and removing free radicals that can damage DNA and contribute to carcinogenesis. Protection against oxidative stress is essential to prevent genetic mutations and DNA damage that could lead to cancer development (Dinkova-Kostova& Kostov, 2012).

Induction of Programmed Cell Death (Apoptosis)

Inhibition of Tumor Proliferation and Apoptosis: Sulforaphane has been studied for its anticancer effects, particularly for its ability to inhibit cell proliferation and induce apoptosis in tumor cells. In preclinical models, sulforaphane has shown inhibitory effects on several tumor cell lines, including colon, breast, lung, and multiple myeloma. The mechanism by which sulforaphane inhibits tumor growth includes inhibition of signaling pathways involved in cell growth, such as the PI3K/Akt pathway, and induction of programmed cell death by modulating pro-apoptotic genes (Zhao & Wang, 2017). Sulforaphane has a direct effect on the induction of programmed cell death or apoptosis, a process that allows damaged or mutated cells to self-destruct before they become tumorous. Sulforaphane works by modulating several cellular signaling pathways that regulate apoptosis, including the p53 and Bcl-2 genes.

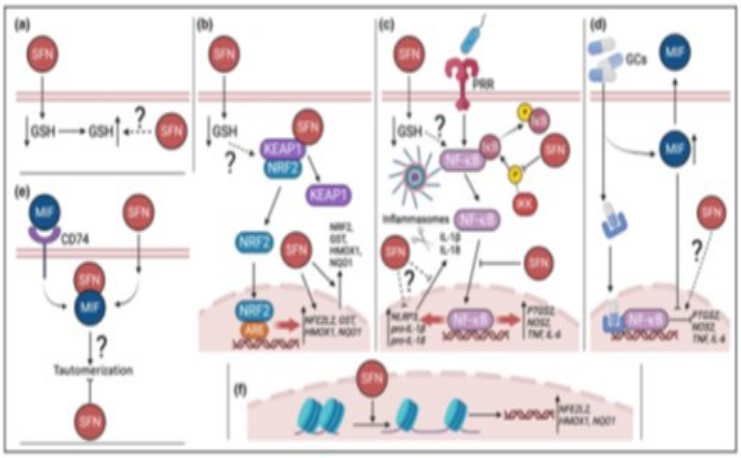
p53: Sulforaphane stimulates the activation of p53, a gene that plays a crucial role in the response to DNA damage. When DNA is damaged, p53 can either arrest the cell cycle to allow repair, or activate apoptosis if the damage is irreparable. In many tumors, p53 is mutated or inactive, but sulforaphane can restore its function, increasing the sensitivity of tumor cells to cell death.

Bcl-2 and Bax: Sulforaphane can also modulate the expression of Bcl-2 and Bax, two proteins that regulate mitochondrial membrane permeability and cytosol release that induces apoptosis. Bcl-2 is an oncoprotein that promotes cell survival, while Bax is a pro-apoptotic protein. Sulforaphane reduces Bcl-2 levels and increases Bax levels, promoting apoptosis in tumor cells (Zhao & Wang, 2017). Sulforaphane can reduce cell proliferation and inhibit the invasiveness of tumor cells. This effect is achieved through interaction with critical signaling pathways involved in cell growth, such as the PI3K/Akt pathway and the MAPK pathway:

PI3K/Akt pathway: The PI3K/Akt pathway is one of the major signaling pathways involved in cell proliferation, survival, and chemotherapy resistance. Sulforaphane has been shown to inhibit this pathway, reducing tumor cell proliferation and increasing the sensitivity of tumor cells to therapeutic treatments (Sharma & Agarwal, 2011).

MAPK pathway: The MAPK pathway is involved in the regulation of numerous cellular processes, including differentiation, proliferation, and stress response. Sulforaphane can activate the p38 MAPK pathway, which inhibits tumor cell growth and promotes cell differentiation (Jang & Park, 2014). Another important mechanism through which sulforaphane fights cancer is its ability to inhibit neoangiogenesis, or the formation of new blood vessels that feed tumors. Neoangiogenesis is a crucial process for tumor growth and metastasis. Sulforaphane reduces the expression of VEGF (vascularendothelialgrowthfactor), a protein that stimulates the formation of new blood vessels. By inhibiting VEGF, sulforaphane limits the supply of nutrients and oxygen to the tumor, reducing its ability to grow and spread (Zhao & Wang, 2017).

Modulations of Metastasis



Sulforaphane (SFN) is a modulator of cell signaling in multiple pathways. (a) Upon immediate entry into the cell, SFN lowers intracellular glutathione (GSH) levels. (b) nuclear factor-erythroid factor 2–related factor 2 (NRF2) activation, which may occur through SFN-mediated GSH depletion or structural modification of Kelch-like ECH-associated protein 1 (KEAP1), upregulates transcription and translation of phase II detoxification enzymes which serve to restore intracellular redox homeostasis. (c) Activation of nuclear factor j-light-chain–enhancer of activated B cells (NF-jB) occurs following detection of numerous pathogenic stimuli via cell surface pathogen recognition receptors (PRRs). This signals for phosphorylation of nuclear factor of kappa light polypeptide gene enhancer in B-cells inhibitor alpha (IjB) by IjB kinase (IKK). NF-jBtranslocates to the nucleus and regulates the transcription of numerous proinflammatory cytokines. SFN has been shown to inhibit phosphorylation of IjB and nuclear translocation of NF-jB. (d) Following entry to the cell, glucocorticoids (GCs) bind to a glucocorticoid receptor to induce nuclear translocation. The glucocorticoid–glucocorticoid receptor complex binds nuclear DNA to repress transcription of proinflammatory genes. Paradoxically, GC entry increases intracellular levels of macrophage migration inhibitory factor (MIF) levels. (e) Exogenous MIF binds the major histocompatibility complex class II invariant chain receptor CD74. In a cell-free environment, MIF catalyzes a tautomerase reaction, which is potentially inhibited by SFN. However, an endogenous substrate for MIF tautomerase is yet to be identified. (f) DNA transcription is upregulated by retaining acetyl groups in histone lysine residues. SFN acts as a histone deacetylase inhibitor to prevent the removal of acetyl groups. ARE, antioxidant response element; GST, glutathione-S-transferase; IL, interleukin; HMOX-1, heme oxygenase 1; NQO1, NAD(P)H quinone dehydrogenase 1. From: Katie Treasure et al: Exploring the anti-inflammatory activity of sulforaphane , Immunology & Cell Biology 2023; 101: 805–828

Figure 2. Mechanism of the anti-inflammatory activity of Sulforaphane

Sulforaphane also exerts an inhibitory effect on tumor metastasis, the process by which tumor cells spread from a primary site to other organs. Studies have shown that sulforaphane can reduce the expression of MMPs (matrix metalloproteinases) and enzymes that are involved in the degradation of the extracellular matrix, allowing tumor cells to invade surrounding tissues and migrate distantly (Zhang &Talalay, 1994).

Anti-Inflammatory Effects: Sulforaphane has been shown to reduce the production of inflammatory cytokines such as IL-6 (inflammatory cytokine that plays a major role in the immune response and chronic inflammation. Sulforaphane reduces IL-6 levels, contributing to the reduction of systemic inflammation and tissue damage -Zhao & Wang, 2017), TNF-α (TNF-α Tumor necrosis factor alpha is a central cytokine in acute and chronic inflammation.

Sulforaphane has been shown to reduce the expression of TNF-α in immune cells and in various animal models of inflammation) and IL-1β (pro-inflammatory cytokine that plays a central role in the regulation of the immune and inflammatory response. It is a major cytokine involved in acute and chronic inflammation and, if not properly regulated, may be implicated in a wide range of inflammatory and autoimmune diseases), which are involved in the inflammatory response. Chronic inflammation is a risk factor for many diseases, including cardiovascular disease, diabetes, and cancer. Sulforaphane exerts anti-inflammatory effects by modulating several signaling pathways, including the NF-κB pathway, a central regulator of inflammation (Hayes &Dinkova-Kostova, 2007) Fig.2.

Efficacy of Sulforaphane in Clinical Studies: Case Studies and Therapeutic Applications

Sulforaphane and Cancer Prevention: Many preclinical studies have suggested that sulforaphane may have a significant role in cancer prevention. A study on transgenic mice showed that treatment with sulforaphane reduced the incidence of colon tumors (Shapiro et al., 2001).

In a clinical study conducted on patients with breast cancer, sulforaphane intake showed positive effects in reducing cell proliferation and improving the immune response (Clarke et al., 2008). Another clinical study, conducted in patients with prostate cancer, reported that taking sulforaphane in combination with a chemotherapy regimen improved drug sensitivity and reduced chemotherapy side effects (Zhang &Talalay, 1994). Although the results are promising, further study is needed to determine the optimal dosage and duration of treatment Fig.3.

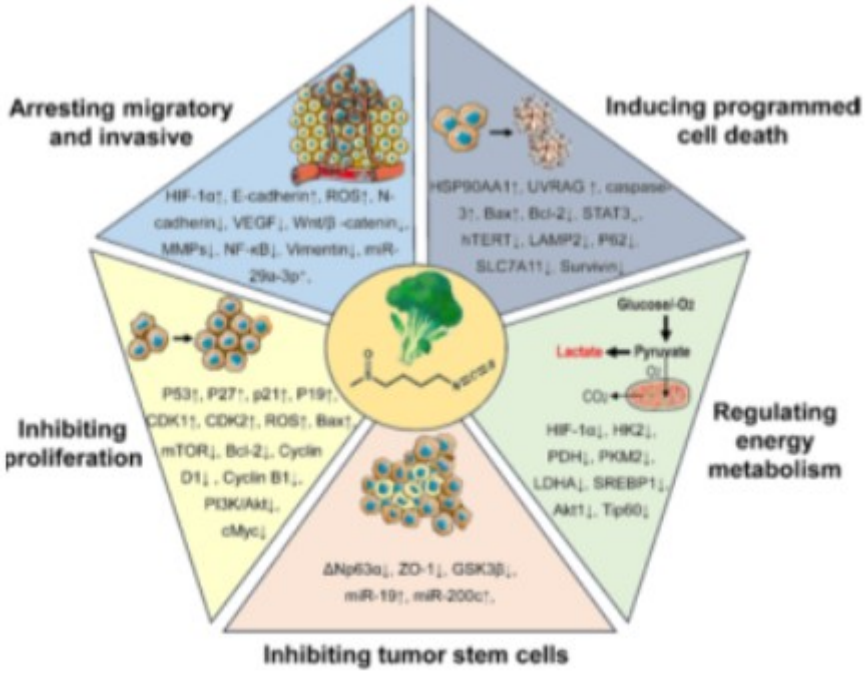


Figure 3 . Overview of the multiple molecular mechanisms of the plant natural compound sulforaphane for cancer prevention and treatment.From: Liu et al. Potential mechanisms of cancer prevention and treatment by sulforaphane, a natural small molecule compound, Molecular Medicine (2024) 30:94

Lung Cancer: Preclinical studies have suggested that sulforaphane has a protective effect against lung cancer, one of the most common and deadly cancers in the world. Sulforaphane can inhibit the proliferation of lung cancer cells and reduce the formation of metastases. Additionally, sulforaphane increases the sensitivity of lung cancer cells to chemotherapy (Jang & Park, 2014).

Colon Cancer: Sulforaphane has also been studied for its ability to prevent colon cancer. Animal models have shown that sulforaphane can reduce the formation of intestinal polyps, which are precursors to colorectal cancer. Sulforaphane inhibits cell proliferation and stimulates apoptosis in colon cells, preventing tumor formation (Michaud & Martel, 2015).

Breast Cancer: Sulforaphane reduces tumor growth and inhibits metastasis in breast cancer by modulating the Wnt/β-catenin pathway, which regulates cell growth and spread (Zhao & Wang, 2017).

Prostate Cancer: Sulforaphane has also shown anticancer activity in prostate cancer, a type of cancer that primarily affects older men. Sulforaphane reduces tumor cell proliferation and promotes apoptosis. Additionally, sulforaphane inhibits the PI3K/Akt pathway, which is frequently activated in prostate cancer cells, contributing to tumor growth (Zhao & Wang, 2017).

Cardiovascular Effects of Sulforaphane: Sulforaphane has shown protective effects against cardiovascular disease. A study in patients with hypertension found that sulforaphane treatment reduced LDL cholesterol levels and improved endothelial function, promoting blood vessel dilation (Ferguson & Harris, 2007). Additionally, sulforaphane has been shown to reduce the risk of atherosclerosis and improve cardiovascular health in animal models of coronary artery disease (Talalay& Fahey, 2015). Oxidative stress is a key factor in the pathogenesis of many cardiovascular diseases, including atherosclerosis and hypertension.

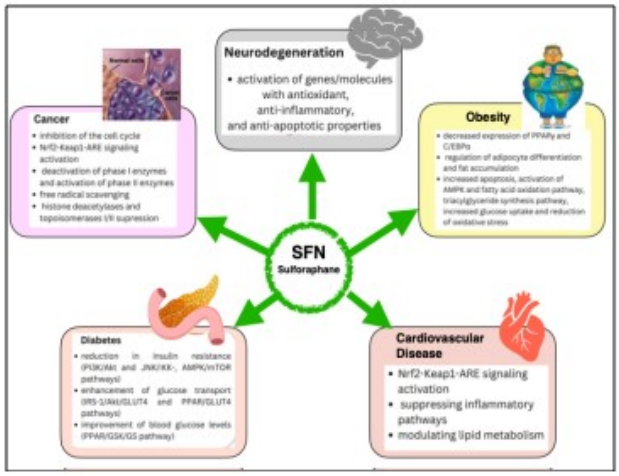


Figure 4. Potential Health Benefits for Disease Prevention whit Sulforaphane

Free radicals generated during oxidative stress damage endothelial cells and promote the formation of atherosclerotic plaque. Sulforaphane, thanks to its antioxidant action, reduces oxidative damage and lipid peroxidation, which are the basis of plaque formation in the arteries. The endothelium is the cellular lining that lines the inside of blood vessels and plays a crucial role in regulating vascular tone, vasodilation and blood clotting. Nitric oxide (NO) is an important mediator of vasodilation, and its production is regulated by the endothelium. Sulforaphane increases the production of nitric oxide, thus improving vascular function and contributing to cardiovascular health.

Neurological and Neuroprotective Benefits: Sulforaphane has also shown neuroprotective properties in clinical and preclinical studies. In mouse models of Alzheimer's and Parkinson's disease, sulforaphane reduced oxidative damage and improved cognitive function (Zhao & Wang, 2017). Furthermore, a clinical study in patients with neurological disorders suggested that sulforaphane supplementation improved cognitive parameters and reduced neuroinflammation.

The microglia are the main type of immune cell in the central nervous system. In pathological conditions, microglia can become overactive, contributing to neuroinflammation and neuronal damage. Sulforaphane reduces microglia activation and the production of pro-inflammatory cytokines such as IL-1β and TNF-α, which are involved in neurodegenerative processes (Luo & Zhao, 2016). Sulforaphane has been shown to improve mitochondrial function, reducing free radical production and improving the energy efficiency of brain cells. Additionally, sulforaphane promotes autophagy, a process of removing damaged cellular components, including defective mitochondria (Zhao & Wang, 2017).

Sulforaphane in the Management of Diabetes and Metabolic Disorders: Sulforaphane has shown positive effects in the management of type 2 diabetes. A clinical study in patients with diabetes found that sulforaphane supplementation improved insulin sensitivity and reduced blood glucose levels (González & Abarca, 2010). Additionally, sulforaphane has been shown to reduce systemic inflammation and improve metabolic parameters in obese patients, suggesting a potential role in the treatment of metabolic syndrome. Sulforaphane inhibits the NF-κB pathway, an important signaling pathway involved in systemic inflammation. Reducing NF-κB activation helps reduce the production of inflammatory cytokines such as TNF-α, IL-6, and IL-1β, which are known to be elevated in patients with diabetes and metabolic syndrome.

Oxidative stress: Sulforaphane reduces lipid peroxidation and mitochondrial damage, improving mitochondrial function and reducing insulin resistance (Zhao & Wang, 2017). Insulin resistance is a condition in which the body's cells no longer respond adequately to insulin, leading to increased blood glucose levels and type 2 diabetes. Sulforaphane may improve insulin sensitivity through several mechanisms, including: - Regulation of the PI3K/Akt pathway: The PI3K/Akt pathway is critical for proper insulin function. Sulforaphane has been shown to activate this pathway, improving glucose uptake into cells and reducing blood glucose levels (Sharma & Agarwal, 2011). Increased expression of glucose transporters (GLUT4): Sulforaphane increases the expression of GLUT4, which is an insulin-dependent glucose transporter. Increased GLUT4 in muscle and fat cells helps improve glucose uptake and reduce blood glucose levels.

Improved Lipid Profile

Sulforaphane benefits lipid profiles, which are often disrupted in metabolic disorders. Specifically, ithasbeenshown to:

- Reduce levels of LDL cholesterol ("bad cholesterol") and triglycerides, which are frequently elevated in patients with type 2 diabetes and metabolic syndrome.
- Increase levels of HDL cholesterol ("good cholesterol"), which helps reduce the risk of cardiovascular disease.

DISCUSSION AND CONCLUSION

From the review of the properties of sulforaphane, resulting from the vast literature reported in the previous paragraphs, sulforaphane emerges as a powerful therapeutic agent with applications in numerous areas of human health, from cancer prevention to cardiovascular protection, from the prevention of neurodegenerative diseases to the management of metabolic disorders.

Although preclinical and clinical results are promising, further research is needed to determine the optimal administration routes, bioavailability, and dosimetry to ensure therapeutic efficacy of sulforaphane.

Disclosure: The authors declare that they have no conflicts of interest in this article

REFERENCES

Dinkova-Kostova, A. T., & Kostov, R. V. (2012). "Mechanisms of cancer chemoprevention by sulforaphane: A comprehensive review." Antioxidants & Redox Signaling, 16(1), 57-69. DOI: [10.1089/ars.2011.4084] (https://DOI.org/10.1089/ars.2011.4084)

Zhao, J., & Wang, Y. (2017). "Sulforaphane as a potential anticancer agent: Mechanisms and therapeutic applications." Frontiers in Pharmacology, 8, 109. doi:[10.3389/ fphar.2017.00109] (https://DOI.org/10.3389 /fphar.2017.00109)

Shapiro, T. A., Fahey, J. W., &Dinkova-Kostova, A. T. (2001). "Chemoprotective properties of cruciferous vegetables and their bioactive constituents." Toxicology and Applied Pharmacology, 172(3), 137-148. DOI: [10.1006/taap. 2000.9107](https://doi.org/10.1006/taap.2000.9107)

Clarke, J. D., Hsu, A., & Riedl, K. (2008). "Pharmacokinetics of sulforaphane: In vivo evidence of bioavailability and chemoprotective effects in humans." Clinical Cancer Research, 14(13), 4179-4186. DOI: [10.1158/1078-0432.CCR-08-0590](https://doi.org/10.1158/1078-0432.CCR-08-059 0)

Talalay, P., & Fahey, J. W. (2015). "The role of isothiocyanates in cancer prevention and therapy." Cancer Letters, 356(2), 125-130. DOI:[10.1016/j.canlet.20 14.10.006] (https:/ /doi.org /10.1016/j.canlet.2014.10.006)

González, S., & Abarca, C. (2010). "Sulforaphane and its role in the prevention of chronic diseases." Journal of Nutritional Biochemistry, 21(7), 582-588 DOI:[10.1016/j.jnutbio.2009.09.006](https://doi.org/10.1016/j.jnutbio.2009.09.006)

Hayes, J. D., &Dinkova-Kostova, A. T. (2007). "The Nrf2 regulatory network provides an interface between redox and detoxification control." Trends in Biochemical Sciences, 32(6), 218-226. DOI: [10.1016/j.tibs.200 7.03.001](https://doi.org/10.1016/j.tibs.2007.03.001)

Ferguson, L. R., & Harris, P. J. (2007). "Sulforaphane: Its role in cancer prevention and treatment." Journal of Nutritional Biochemistry, 18(1), 5-11. DOI: [10.1016/j.jnutbio. 2006.08.003] (https://doi.org /10.1016/j.jnu tbio.2006. 08.003)

Matusheski, N. V., Juvik, J. A., & Jeffery, E. H. (2004). "Concentration of sulforaphane in broccoli sprouts: Influence of growth conditions, processing, and storage." Journal of Agricultural and Food Chemistry, 52(3), 565-571. DOI: [10.1021/jf034820j] (https:// doi.org/10. 1021/ jf034820j)

Jang, J. Y., & Park, S. H. (2014). "Sulforaphane inhibits the proliferation of human lung cancer cells by modulating the Akt signaling pathway." Cancer Letters, 347(2), 232-238. DOI: [10.1016/j.canlet.2014.02 .029](https:// doi.org/ 10.1016/j.canlet.2014.02.029)

Sharma, S. D., & Agarwal, C. (2011). “Sulforaphane: A potential cancer chemopreventive agent.” Journal of Cancer Research and Clinical Oncology, 137(5), 703-711. DOI: [10.1007/s00432-010-0972-4](https://doi.org /10. 1007/ s00432-010-0972-4)

Michaud, M., & Martel, J. (2015). “Sulforaphane and its anticancer effects: A review.” Journal of Cancer Therapy, 6(1), 1-9. DOI: [10.4236/jct.2015.6 1001](https ://doi.org/10.4236/jct.2015.61001)

Borek, C. (2003). "Antioxidant health effects of aged garlic extract." Nutrition, 19(5), 561-566. DOI: [10.1016/S0899-9007(03)00081-X](https://doi.org/10.1016/S0899-9007(03)00081-X)

Fahey, J. W., Talalay, P., &Dinkova-Kostova, A. T. (2009). "The role of dietary sulforaphane in cancer chemoprevention." Journal of Nutritional Biochemistry, 20(1), 1-12. DOI: [10.1016/j.jnutbio. 2008.08.002] (https://doi.org/10.1016/j.jnutbio.2008.08.002)

Zhang, Y., &Talalay, P. (1994). "Mechanism of action of chemopreventive isothiocyanates: A study of the effects of sulforaphane on enzyme induction." Proceedings of the National Academy of Sciences, 91(8), 3147-3150. DOI: [10.1073/pnas.91.8.3147](https://doi.org/10.1073/pnas.91.8.3147)

Lai, H. C., & Chen, L. (2015). "Sulforaphane-induced chemoprevention in lung cancer." Pharmacology & Therapeutics, 146, 1-10. DOI: [10.1016/j.pharmthera.2014. 09.004](https://doi.org/10.1016/j.pharmthera.2014.09.004)

Luo, X., & Zhao, Z. (2016). "Sulforaphane attenuates oxidative stress and neuroinflammation in neurodegenerative diseases." CurrentDrug Targets, 17(4), 460-471. DOI: [10.2174/13894501176661 61012125529] (https://doi.org/10.2174/138945011766616101212552 9)

****