The Most Important Pharmaceutical Benefits of Sulforaphane, a Sulfur-Rich Compound in Cruciferous

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ABSTRACT
Natural products have played a key role in drug discovery and development in modern days. Sulforaphane can be found in a wide variety of cruciferous vegetables, including cabbage, Brussels sprouts, cauliflower, broccoli, Chinese broccoli, broccoli sprouts, broccoli raab, Kohlrabi, collards, kohlrabi, mustard, turnip, kale and radish. The most important health benefits of sulforaphane is its effects again breast cancer, lung cancer cells, human liver cancer cells, gastric cancer cell lines, ovarian cancer, prostate cancer, pancreatic cancer, colon cells cancer, treatment of cancer cell senescence, anti-inflammatory properties, antineoplastic agent, reduction of placental and endothelial oxidative stress, potential in mixed granulocyte asthma, treatment of various neurological disorders, protection against skeletal muscle disease, anti-allergic and its impact against oxidative stress.

Keywords: Natural Compounds, Sulforaphane, Health Benefits, Cancer.

INTRODUCTION

Traditional herbal medicines have been considered as a source of curative remedy (Sun et al., 2019a,b; Shahrajabian et al., 2019a,b; Khoshkharam et al., 2020), because chemical components of plants are used to promote health and prevent diseases (Soleymani and Shahrajabian, 2012; Shahrajabian et al., 2019c; Shahrajabian et al., 2020a,b,c,d,e,f; Sun et al., 2020a,b,c), and plants are invaluable sources of new drugs (Soleymani and Shahrajabian, 2018; Khoshkharam et al., 2019). Sulforaphane which is a compound within the isothiocyanate group of organosulfur compounds, obtained from cruciferous vegetables like cabbages, broccoli, and Brussels sprouts. It is produced when the enzyme myrosinase transforms glucoraphanin, a glucosinolate into sulforaphane upon damage to the plant, which allows the two compounds to mix and react. Young sprouts of broccoli and cauliflower are particularly rich in glucoraphanin. The aim of this mini-review article is survey on the most important pharmacological benefits of sulforaphane.
Sulforaphane

Sulforaphane is a natural occurring cancer chemopreventive, the hydrolysis product of glucoraphanin, and the main glucosinolate in broccoli (Kokotou et al., 2017; Akbari and Namazian, 2020). Sulforaphane can be found in a wide variety of cruciferous vegetables, including cabbage, Brussels sprouts, cauliflower, broccoli, Chinese broccoli, broccoli sprouts, broccoli raab, Kohlrabi, collards, kohlrabi, mustard, turnip, kale and radish (Ahn et al., 2010; Liang et al., 2012). Sulforaphane has anticancer and antimicrobial activity (Cierpial et al., 2020), anticarcinogenic compound (Hafezian et al., 2019). It can be also considered as antineoplastic candidate (Arcidiacono et al., 2018). Sulforaphane inhibits proliferation and induces apoptosis decreasing the stemness of nasopharyngeal cancer cells through a mechanism related to STAT3 signaling in vitro (Li et al., 2018). Application of foods rich in sulforaphange can be used in the arena of clinical chemoprevention agent against a variety of cancers such as breast, prostate, colon, skin, lung, stomach, bladder and also cardiovascular disease, neurodegenerative diseases and diabetes (Yang et al., 2016). At the molecular level, sulforaphane modulates cellular homeostasis through the activation of transcription factor Nrf2 (Russo et al., 2018). Lv et al. (2020) recommend both sprouts and seeds as raw materials of functional foods that possess high health-promoting potential. Wang et al. (2018) reported the dual roles of sulforaphane which make this natural compound a valuable agent for prevention against cadmium-induced carcinogenesis. Isaacson et al. (2020) found that activation of the intrinsic antioxidant defense pathway with sulforaphane can partially prevent the effects of olanzapine and may represent a useful strategy to protect against liver injury. Sulforaphane has a potential value as a therapeutic tool in neurodegenerative disease including prion diseases (Lee et al., 2014). The mixture of sulforaphen and chlorogenic are potential nutraceuticals for abdominal pain therapy (Guadarrama-Enriquez et al., 2018). It can also prevent hypoxia-induced impairment of mitochondrial membrane structure (Langston-Cox et al., 2020). Sulforaphane upregulated the expression of Nrf2 and promoted the nuclear translocation of Nrf2 by decreasing DNA demethylation levels of the Nrf2 promoter which leading to antioxidative and anti-inflammatory effects in a cellular model of Alzheimer’s disease (Zhao et al., 2018). Sulforaphane may inhibit the spread of metastatic tumor cells through the stimulation of cell-mediated immune response, upregulation of IL-2 and IFN-γ, and downregulation of proinflammatory cytokines IL-1β, IL-6, TNF-α, and GM-CSF (Thejass and Kuttan, 2007). Alkharashi et al. (2019) reported that intake of sulforaphane-enriched vegetables and fruits are helpful to overcome Cd-induced toxicity in humans. Checker et al. (2015) showed the potent anti-inflammatory effects of sulforaphane which mediated via modulation of PI3K/AKT/GSK3β/Nrf2 and NF-κB pathway in T-cells. It is also effective in preventing estrogen deficiency-induced osteoclastogenic resorption (Lee et al., 2014). Sulforaphane treatment is a promising strategy to reduce intestinal injury in chemotherapy (Wei et al., 2020). The most important epigenetic regulation of sulforaphane in cancer are histone acetylation, histone phosphorylation, DNA methylation, noncoding RNA, CPG demethylation and histone acetylation at the Nrf2 promoter (Su et al., 2018). The structure of sulforaphane is shown in Figure 1.
Figure 1 - The structure of sulforaphane.

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<th>Table 2 - The most important pharmacological effects of sulforaphane.</th>
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<td>Sulforaphane</td>
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<td>Its effects against breast cancer</td>
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<td>Its effects against lung cancer cells</td>
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<td>Its effects against human liver cancer cells</td>
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<tr>
<th>Effect against cancer type</th>
<th>Description</th>
<th>References</th>
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<td>Liver damage</td>
<td>LPS significantly increase mortality, serum levels of liver damage markers and inflammatory cytokines.</td>
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</table>
| Gastric cancer cell lines                         | a. Significant changes in expression of CDX1, CDX2, miR-9 and miR-326 in the gastric cancer lines (AGS and MKN45), were found under different concentrations of sulforaphane. It can influence gastric cancer cell lines at specific doses and change their proliferation rate by altering the expression of CDX1, CDX2, miR-9, and miR-326.  
b. Sulforaphane could be a potent natural compound targeting gastric cancer stem cells via suppression of Sonic Hh pathway, which might be a promising agent for gastric cancer intervention. | Kiani et al. (2018)  
Ge et al. (2019) |
| Ovarian cancer                                    | a. Sulforaphane at a concentration of 10 μM effectively inhibits the growth of cancer cells. The effects of sulforaphane on cell growth maybe related to xidation of protein thiols or change in cellular redox status. | Kim et al. (2017) |
| Prostate cancer cells                             | a. Sulforaphane may decrease viable DU145 cell number in large part through the generation of reactive oxygen species (ROS) and JNK-mediated signaling to G2/M arrest and caspase-dependent apoptosis. | Cho et al. (2005) |
| Pancreatic cancer                                 | a. Sulforaphane potentiates the efficacy of 17-AAG against pancreatic cancer through enhanced abrogation of Hsp90 function. | Li et al. (2011)  
Naumann et al. (2011) |
| Colon cells cancer                                | a. Sulforaphane exert a concentration-dependent inhibitory effect on the inflammatory cytokine production by the immune cells.  
b. Sulforaphane has excellent cytoprotective properties in CRL-1790 cells, as it induce Nrf2-dependent expression of MRPI and NAD(P)H quinone dehydrogenase 1 (NQO1). | Zeng et al. (2011)  
Rajendran et al. (2013)  
Lubelska et al. (2016)  
Pocasap and Weerapreeyakul (2016)  
Bessler and Djaldetti (2018)  
Yasuda et al. (2019) |
| Anti-inflammatory properties                      | a. Sulforaphane has function as suppressor of the MALP-2-induced inflammatory response, not only by inhibiting the expression of | Lee et al. (2016)  
Haodang et al. (2019)  
Vuong et al. (2019)  
Liu et al. (2020) |
cytokines and induction of HO-1 but also by diminishing NF-κB activation in cultured monocytes and the lungs of mice.
b. Sulforaphane alleviates pain induced by sciatic endometriosis, which is mediated by inhibiting inflammation.

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<tr>
<th>Antineoplastic agent</th>
<th>Negrette-Guzman et al. (2017)</th>
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<tr>
<td>a. The knockdown in the nuclear respiratory factor-1 attenuated sulforaphane-induced effect on prostate cancer cells demonstrating that mitochondrial biogenesis plays an important role in cell death.</td>
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<th>Reduction of placental and endothelial oxidative stress</th>
<th>Cox et al. (2019)</th>
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<tr>
<td>a. Sulforaphane reduce TNF-α mediated HUVEC secretion of endothelin-1, VCAM1, ICAM1 and E-selectin, and prevented increased endothelial permeability. In placental explants, it can reduce the secretion of soluble Flt-1, soluble endoglin and activin A, induce activation and nuclear translocation of NRF2 in HUVECs, including heme oxygenase 1. It may offer a new adjuvant therapeutic approach for the treatment of preeclampsia.</td>
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<th>Therapeutic potential in mixed granulocyte asthma</th>
<th>Al-Harbi et al. (2019)</th>
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<tr>
<td>a. Activation of Nrf2 by sulforaphane may reduce neutrophilic airway inflammation by upregulation of antioxidants and downregulation of inflammatory cytokines in airways.</td>
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<th>Treatment of various neurological disorders</th>
<th>Uddin et al. (2020)</th>
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<tr>
<td>a. Sulforaphane protects various neurological disorders by regulating the Nrf2 pathway.</td>
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<th>Its protection against skeletal muscle disease</th>
<th>Wang et al. (2020)</th>
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<tr>
<td>a. It is a potential drug to prevent skeletal muscle dysfunction in type 2 diabetic mellitus. It may activate the Nrf2/HO-1 signal pathway, and downregulate the expression of inflammatory and apoptotic associated proteins.</td>
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<th>Anti-allergic</th>
<th>Jeon et al. (2020)</th>
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<tr>
<td>a. Sulforaphane has anti-allergic inflammatory effects by intercepting caspase-1/NF-κB/MAPKs signaling pathways.</td>
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<tr>
<th>Its effects against oxidative stress</th>
<th>Yang et al. (2011)</th>
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<tbody>
<tr>
<td>a. Phloretin up-regulate HO-1 and GCL expression through the ERK2/Nrf2 pathway and protect hepatocytes against oxidative stress.</td>
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</table>
CONCLUSION

Sulforaphane can be found in a wide variety of cruciferous vegetables, including cabbage, Brussels sprouts, cauliflower, broccoli, Chinese broccoli, broccoli sprouts, broccoli raab, Kohlrabi, collards, kohlrabi, mustard, turnip, kale and radish. The most important health benefits of sulforaphane is its effects again breast cancer, lung cancer cells, human liver cancer cells, gastric cancer cell lines, ovarian cancer, prostate cancer, pancreatic cancer, colon cells cancer, treatment of cancer cell senescence, anti-inflammatory properties, antineoplastic agent, reduction of placental and endothelial oxidative stress, potential in mixed granulocyte asthma, treatment of various neurological disorders, protection again skeletal muscle disease, anti-allergic and its impact against oxidative stress.

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Authors’ Contribution
All authors contributed equally to literature research, writing manuscript, etc.

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Competing interests
The authors declare that they have no potential conflicts of interest.

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