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Unlocking the Power of Soybeans: A Promising Ally in Cancer Prevention and Management

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Abstract

Cancer is a huge worldwide health concern, and dietary treatments have gained importance as a viable tool for prevention and management. Soybeans, rich in isoflavones and other bioactive chemicals, have been widely examined for their anticancer potential. This review synthesizes current studies on the role of soybeans in cancer prevention and treatment, emphasizing their bioactive components, modes of action, and therapeutic implications. Soy isoflavones, notably genistein and daidzein, display antioxidant, anti-inflammatory, and anticancer effects, reducing cancer cell growth, inducing apoptosis, and lowering angiogenesis. Epidemiological studies have repeatedly linked increased soy diet to lower chances of hormone-related malignancies, including breast and prostate cancer. The mechanisms behind these benefits include control of estrogen metabolism, antioxidant capabilities, and immune system stimulation. Furthermore, the incorporation of soy isoflavones with traditional cancer therapy has been recommended to boost therapeutic effectiveness while lowering toxicity. This analysis shows the potential of soybeans as a beneficial component in dietary regimens for cancer prevention and control, with implications for individualized dietary advice and integrative oncology.

Keywords: soybeans, isoflavones, anticancer properties, breast cancer, prostate cancer, dietary intervention.

1. Background to the Study

The incidence of cancer continues to rise annually despite advancements in detection and treatment (Wilkinson, Gathani, 2022). This increasing prevalence has prompted extensive research into alternative preventive and therapeutic strategies. Among these approaches, nutritional interventions have gained attention due to their accessibility, affordability, and potential for integration into daily dietary habits (Chatterjee et al., 2021). One dietary component that has attracted significant scientific interest is soybeans. Traditionally revered as a staple food in numerous cultures, soybeans are now recognized for their rich composition of bioactive compounds with promising anticancer properties.

Soybeans are particularly rich in isoflavones, a class of phytoestrogens that structurally and functionally resemble human estrogen. The primary isoflavones in soy-genistein, daidzein, and glycitein – bind to estrogen receptors and act as selective estrogen receptor modulators (SERMs) (Verma et al., 2024). This dual agonist-antagonist mechanism allows soy isoflavones to exert

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estrogen-like effects in low-estrogen environments, such as in postmenopausal women, while mitigating excessive estrogenic stimulation in high-estrogen conditions. Such modulation is particularly relevant in hormone-sensitive cancers, including breast and prostate cancer, where estrogen signaling plays a critical role in tumor initiation and progression (Boye et al., 2024).

Beyond hormonal regulation, soy isoflavones exhibit a broad range of biological activities, including antioxidant, anti-inflammatory, and epigenetic effects. They have been shown to inhibit cancer cell proliferation, induce apoptosis, and suppress angiogenesis, thereby interfering with key processes in tumor growth and metastasis (Ferriere et al., 2024). Additionally, soy protein itself contains bioactive peptides that may enhance immune function and support cellular repair mechanisms. These multifaceted properties make soybeans a valuable component in dietary recommendations for cancer prevention and management.

The health benefits of soybeans have been recognized for centuries, particularly in East Asian populations where soy-based foods such as tofu, miso, and soy milk are dietary staples. Epidemiological data consistently indicate lower incidences of hormone-related cancers, such as breast and prostate cancer, in regions with high soy consumption compared to Western countries (Liu et al., 2022). This cultural variation in dietary habits has spurred scientific exploration into the potential protective effects of soy. Over the past few decades, there has been a surge in research investigating the role of soybeans in cancer prevention and therapy. Meta-analyses of epidemiological studies suggest a consistent inverse relationship between soy intake and cancer risk. For instance, one comprehensive study found that an additional 25 grams of daily soy consumption was associated with a 4 % reduction in overall cancer risk, with more pronounced benefits observed for specific cancer types (Wan et al., 2022). Furthermore, randomized clinical trials have examined the safety and efficacy of soy supplementation in cancer patients, providing valuable insights into its potential as an adjuvant therapy (Wang et al., 2024).

Despite these promising findings, debates and gaps in knowledge persist. Early concerns regarding the estrogenic effects of soy isoflavones and their potential to promote hormone-dependent cancers have largely been dispelled by evidence from population-based studies and clinical trials. However, variability in individual responses to soy consumption, influenced by factors such as genetic polymorphisms and gut microbiota composition, underscores the need for personalized dietary recommendations (Ulusoy-Gezer, Rakıcıoğlu, 2024).

2. Results and discussion

Isoflavones and Cancer Modulation

Soybeans are exceptionally rich in isoflavones, a subclass of phytoestrogens that mimic human estrogen in both structure and function. The predominant isoflavones – genistein, daidzein, and glycitein – bind to estrogen receptors, acting as selective estrogen receptor modulators (Manayi, 2021). This dual agonist-antagonist mechanism enables soy isoflavones to exert estrogenic effects in low-estrogen conditions, such as postmenopausal women, while preventing excessive estrogenic stimulation in high-estrogen environments. This regulatory role is particularly crucial in hormone-sensitive malignancies, including breast and prostate cancers, where estrogen signaling significantly influences tumor development and progression (Orzołek et al., 2022).

Beyond hormonal modulation, isoflavones exhibit various biological properties, including antioxidant, anti-inflammatory, and epigenetic effects. They have been shown to inhibit cancer cell proliferation, induce apoptosis, and suppress angiogenesis, thereby disrupting essential processes in tumor progression and metastasis (Jiang et al., 2020). Additionally, soy protein contains bioactive peptides that may enhance immune function and facilitate cellular repair mechanisms. These diverse bioactivities position soybeans as a valuable component in dietary strategies for cancer prevention and control.

Isoflavones have attracted considerable interest in cancer research due to their potential chemopreventive properties. These compounds, particularly genistein and daidzein, exhibit multiple anticancer mechanisms, including anti-inflammatory, antioxidant, and anti-angiogenic effects (Daman, Miglani, n.d.). The regulation of cancer cell proliferation and apoptosis through various signaling pathways has been a focal point of numerous studies, highlighting the potential role of isoflavones in cancer prevention and treatment. Recent research has elucidated the molecular mechanisms by which isoflavones exert their anticancer effects, particularly in breast and colorectal cancers.

Genistein, one of the most extensively studied isoflavones, has been shown to inhibit cancer cell growth and induce apoptosis across various cancer types. For example, Goh et al. (2022)

demonstrated that genistein promotes apoptosis in primary cancer cells and embryonal carcinoma cells while upregulating anti-migration proteins such as p38 and p53. Similarly, studies indicate that genistein suppresses nuclear factor kappa B (NF-κB) activation, a key regulator of inflammation and cancer progression, thereby reducing cell proliferation and metastasis (Konstantinou et al., 2024; Konstantinou et al., 2024a; Tuli et al., 2019). Furthermore, research suggests that isoflavones, including genistein, influence signaling pathways associated with cancer cell survival and proliferation, such as the PI3K/AKT pathway (Tuli et al., 2019).

In breast cancer, isoflavones have demonstrated anti-estrogenic effects, which may contribute to reduced tumor growth. Qiu and Jiang (2019) reported that isoflavones inhibit estrogen synthesis and impede cell proliferation, leading to a lower risk of breast cancer recurrence. A meta-analysis by Hatono et al. (2021) supports this finding, showing that higher isoflavone intake is associated with a 17 % reduction in breast cancer risk. This protective effect is believed to be mediated through the modulation of estrogen signaling pathways, particularly in postmenopausal women with diminished endogenous estrogen levels (Xiang et al., 2021).

Isoflavones also exhibit protective effects against colorectal cancer. Studies indicate that isoflavones inhibit colorectal cancer cell proliferation by promoting apoptosis and reducing angiogenesis (Yang et al., 2021). Additionally, high dietary intake of soy isoflavones in Asian populations has been linked to a lower incidence of colorectal cancer, suggesting a potential dietary strategy for cancer prevention (Khankari et al., 2020).

Moreover, the anti-angiogenic properties of isoflavones contribute to their anticancer effects. Wei and Zhang (2024) found that isoflavones inhibit angiogenesis, thereby restricting the tumor's ability to develop a blood supply essential for growth and metastasis. This is particularly relevant in integrative oncology, where isoflavones are being explored for their potential to enhance conventional cancer therapies while minimizing associated toxicities.

Epidemiological Evidence

General Cancer Risk

Epidemiological research has increasingly identified various risk factors contributing to cancer, highlighting the intricate interactions between genetic, environmental, and lifestyle influences. This review consolidates recent findings from multiple studies to illustrate the complex nature of cancer risk.

One of the most critical lifestyle factors associated with cancer risk is tobacco use. Ullah et al. (2024) conducted a Mendelian randomization study confirming the established link between smoking and several cancers, including lung, head and neck, and bladder cancers. This association arises due to carcinogenic compounds in tobacco smoke, such as nitrosamines and polycyclic aromatic hydrocarbons. These findings align with other research, which consistently demonstrates that smoking remains a primary modifiable risk factor for cancer, particularly lung cancer, a leading cause of global cancer mortality (Thandra et al., 2021).

Similarly, alcohol consumption has been implicated in increased cancer risk. The same Mendelian randomization study by Sengupta et al. (2024) identified alcohol consumption as a significant risk factor for esophageal and liver cancers, reinforcing the need for public health initiatives to curb alcohol intake. Moreover, the correlation between obesity and cancer risk has gained attention. Perdomo et al. (2023) found that visceral obesity is associated with higher incidences of both cancer and cardiovascular diseases, suggesting the necessity of integrated health management strategies.

Environmental exposures also play a crucial role in cancer risk. Exposure to environmental chemicals such as DDT and polychlorinated biphenyls during critical developmental stages has been linked to an increased risk of breast cancer, although findings are not entirely consistent across all studies (Rodgers et al., 2018; Kay et al., 2022). Furthermore, occupational exposures to carcinogens contribute significantly to cancer incidence. A review by Hosseini et al. (2021) on epidemiological studies in Iran found notable associations between specific occupational exposures and cancer prevalence.

Genetic predisposition also plays a crucial role in cancer susceptibility. Recent research has explored the genetic mechanisms underlying cancer risk, including the role of vitamin D levels. Meta-analyses suggest that vitamin D supplementation may lower overall cancer incidence and mortality, particularly for digestive tract malignancies (Muñoz, Grant, 2022; Keum et al., 2019). Additionally, studies indicate that diabetes is associated with an increased risk of several cancers, underscoring the importance of metabolic health in cancer prevention (Wang et al., 2020; Abudawood, 2019; Wang, Ding, 2021).

Role of Soybeans in Breast Cancer

The potential role of soy in breast cancer prevention and prognosis has been extensively debated, primarily due to soy's interaction with hormone receptors. This interaction is largely attributed to phytoestrogens, specifically isoflavones, which possess estrogen-like properties. As breast cancer is often hormone-sensitive, researchers have investigated how soy consumption influences breast cancer risk and outcomes (Messina, 2016; Boutas et al., 2022; Fritz et al., 2013; Fraser et al., 2020).

A large-scale study using data from over 300,000 women enrolled in the China Kadoorie Biobank examined the relationship between soy intake and breast cancer risk. The study found no significant association between moderate soy consumption and breast cancer incidence, suggesting that moderate soy intake may not substantially influence breast cancer risk (Wei et al., 2020). This finding may be influenced by cultural dietary habits, where soy is commonly consumed as part of a balanced diet, potentially confounding the results.

However, a dose-response meta-analysis provided a more nuanced perspective. This analysis found that each 10 mg/day increment in soy isoflavone intake was associated with a 3 % reduction in breast cancer risk (Zhang et al., 2020). This suggests that even small increases in soy isoflavone consumption could have protective effects against breast cancer. The results support the hypothesis that soy isoflavones exert a modest yet significant impact on cancer risk, particularly in populations with traditionally low soy intake.

The benefits of soy may extend beyond prevention to post-diagnosis outcomes. Research by Nechuta et al. (2012) indicated that post-diagnosis soy consumption was associated with improved survival rates and reduced recurrence in breast cancer patients. While the exact mechanisms remain unclear, the antioxidative and anti-inflammatory properties of soy isoflavones likely contribute to cancer suppression.

The role of soybeans, particularly their isoflavones, in breast cancer prevention and treatment has gained considerable attention. Isoflavones such as genistein and daidzein mimic estrogen and are abundant in soy products (Kim, 2021). Epidemiological studies suggest that higher soy consumption correlates with reduced breast cancer risk, particularly in Asian populations, where soy is a dietary staple (Chen et al., 2022; Şahin et al., 2019; Tian et al., 2015). This protective effect is attributed to mechanisms such as estrogen metabolism modulation, antioxidant properties, and immune enhancement (Amaral et al., 2017).

Studies also indicate that soy isoflavones may inhibit estrogen-dependent breast cancer cell proliferation by binding to estrogen receptors (Amaral et al., 2017). A systematic review found that higher soy consumption correlates with a lower risk of breast cancer and improved prognosis, regardless of menopausal status (Lei et al., 2020). Additionally, soy isoflavones may reduce the production of reactive oxygen species (ROS), which are implicated in cancer progression (Sim et al., 2020).

The timing of soy consumption is crucial. Evidence suggests that high soy intake during adolescence and early adulthood significantly reduces breast cancer risk later in life (Wei, Zhang, 2024). This is supported by a large prospective study involving 300,000 Chinese women, which found an inverse relationship between soy intake and breast cancer risk (Wei, Zhang, 2024). However, individual factors such as genetic predisposition and estrogen receptor status may influence the effects of soy consumption (Lee et al., 2021).

Despite promising evidence, inconsistencies remain in the literature regarding soy's protective effects against breast cancer. Variations in study design, population characteristics, and dietary assessment methods may contribute to these discrepancies. A meta-analysis found that while high soy isoflavone intake generally reduces breast cancer risk, the association is weaker in Western populations compared to Asian populations, where soy consumption is higher (Blázovics et al., 2022). Moreover, the interaction between soy isoflavones and breast cancer treatments, such as tamoxifen, requires further investigation. Some studies suggest that isoflavones enhance tamoxifen's efficacy, while others indicate potential adverse effects, highlighting the need for additional research (Blázovics et al., 2022).

Prostate Cancer

The potential protective role of soy in prostate cancer has garnered considerable attention, with research suggesting that regular consumption of soy may significantly reduce the risk of developing this common malignancy (Applegate et al., 2018). Prostate cancer is known to be heavily influenced by androgenic hormones, particularly testosterone, and the androgen receptor

(AR) pathway plays a critical role in both the development and progression of the disease (Vickman et al., 2020). Consequently, dietary interventions that can modulate this pathway have been the subject of extensive research, and soy, with its bioactive compounds, particularly isoflavones, has emerged as a notable candidate for such interventions.

A meta-analysis by Applegate et al. (2018) synthesized data from multiple studies and found that regular soy intake was associated with a reduction in prostate cancer risk by approximately 25 %. This finding is consistent across several population-based studies, highlighting soy's potential as a protective food in the context of prostate cancer. The mechanisms underlying this protective effect are thought to be linked to the bioactive compounds found in soy, particularly the isoflavones genistein and daidzein, which have been shown to interact with multiple biological pathways involved in cancer development.

One of the key mechanisms through which soy isoflavones are believed to exert their protective effects is by modulating androgen receptor activity (Ferriere et al., 2024). Androgens, such as testosterone, bind to androgen receptors on prostate cancer cells, promoting tumor growth and survival. Isoflavones, specifically genistein, have been shown to suppress androgen receptor activity, which may, in turn, reduce the growth-promoting effects of androgens on prostate cancer cells (Manayi, 2021). This suppression of androgen receptor activity suggests that soy consumption could be particularly beneficial for individuals with hormone-sensitive prostate cancer, where androgens drive disease progression.

Another important factor in prostate cancer progression is the expression of prostate-specific antigen (PSA), a protein produced by the prostate gland. Elevated PSA levels are often used as a biomarker for prostate cancer diagnosis and prognosis (Kim, 2021). Isoflavones, particularly genistein, have been shown to inhibit PSA expression, potentially slowing tumor progression and enhancing the effectiveness of other therapeutic strategies. This inhibitory effect on PSA could serve as a marker of soy's potential role in controlling prostate cancer growth, offering both preventative and therapeutic benefits.

Although the protective role of soy in prostate cancer is promising, it is essential to recognize that the effects may vary depending on factors such as genetics, lifestyle, and the form in which soy is consumed. For example, whole soy foods may have a different impact than isolated soy isoflavones, and the bioavailability of isoflavones may vary between individuals (Khankari et al., 2020). Nonetheless, the cumulative body of evidence suggests that incorporating soy into the diet could offer significant benefits in reducing the risk of prostate cancer, particularly when consumed regularly as part of a balanced diet (Verma et al., 2024).

Isoflavones, particularly genistein and daidzein, have been identified as key components contributing to the anticancer properties of soy. These compounds exhibit various biological activities, including antiproliferative and antigenotoxic effects on prostate cancer cells (Liu et al., 2022). The mechanisms through which isoflavones exert their effects include modulation of cell cycle regulation, induction of apoptosis, and inhibition of angiogenesis and metastasis (Wei, Zhang, 2024). For example, genistein has been shown to inhibit the activity of Polo-like kinase 1 (PLK1), a protein involved in cancer progression, thereby reducing the proliferation of cancer cells (Wei, Zhang, 2024). Furthermore, studies have demonstrated that isoflavones can enhance the efficacy of certain cancer therapies, suggesting a potential role in integrative oncology (Liu et al., 2022).

The relationship between soy consumption and prostate cancer is further supported by findings from clinical trials. A randomized controlled trial involving a fermented soy beverage indicated promising results in reducing prostate cancer markers among patients prior to radical prostatectomy (Applegate et al., 2018). Additionally, a prospective study from Japan highlighted that higher intake of soy products was associated with lower mortality rates from prostate cancer, emphasizing the potential protective effects of soy in this context (Khankari et al., 2020).

Moreover, the bioavailability and metabolism of soy isoflavones can be influenced by gut microbiota, which may convert these compounds into more bioactive forms, such as equol, enhancing their anticancer effect (Jiang et al., 2020). This interplay between diet, microbiota, and cancer risk underscores the complexity of dietary interventions in cancer prevention.

Despite the promising evidence, some studies suggest that the relationship between soy and prostate cancer may not be straightforward. For instance, certain research indicates that the protective effects of soy may vary depending on the stage of cancer and individual metabolic responses to isoflavones (Khankari et al., 2020). This highlights the necessity for further research to elucidate the conditions under which soy consumption may confer protective benefits against prostate cancer.

Lung Cancer

The intake of soy products has been associated with a reduced risk of several cancers, including lung cancer. A meta-analysis by Fan et al. (2022) found that increased dietary intake of soy isoflavones correlates with a lower incidence of lung cancer among various populations. This finding is supported by Bu (2023), who notes an inverse relationship between soybean consumption and cancer risks, including lung cancer, highlighting the protective effects of soy in dietary patterns. The potential mechanisms behind these protective effects include the modulation of inflammatory pathways and the regulation of gene expression related to cancer progression, as indicated by Talvan et al. (2022).

The beneficial effects of soybeans extend beyond isoflavones. Recent studies have shown that soybean proteins and peptides also exhibit protective properties against chronic diseases, including cancer. Wang et al. (2024) report that specific peptides derived from soy can inhibit the proliferation of non-small cell lung cancer cells by affecting cell cycle regulation and signaling pathways. This suggests that the consumption of soy may not only prevent the onset of lung cancer but also impede its progression.

In addition to the direct effects of soy on cancer cells, the role of nutrition in modulating the tumor microenvironment is increasingly recognized. Dietary factors, including those found in soy, can influence adiponectin levels, which have been linked to cancer prevention (Janiszewska et al., 2021).

Mechanisms of action

Soy's potential protective effects against cancer have been extensively studied, particularly with regard to the bioactive isoflavones found in soy, such as genistein and daidzein (Kim, 2021; Chen et al., 2022; Sahin et al., 2019; Tian et al., 2015; Amaral et al., 2017; Lei et al., 2020). These isoflavones are thought to exert their anticancer properties through a variety of mechanisms, including antioxidant activity and modulation of critical cell signaling pathways. The ability of isoflavones to interact with these molecular processes plays a significant role in their potential as cancer-preventive agents. The most studied isoflavone, genistein, is recognized for its potential to inhibit cancer cell proliferation and induce apoptosis, making it a focal point in research on dietary cancer prevention strategies (Sharifi-Rad et al., 2021). Genistein, the predominant isoflavone in soybeans, has been shown to exert anticarcinogenic effects through multiple pathways. It inhibits receptor tyrosine kinase (RTK)-mediated signaling pathways, which are crucial for cell proliferation and angiogenesis (Sharifi-Rad et al., 2021). Furthermore, genistein's structural similarity to estrogen allows it to bind to estrogen receptors, thereby modulating estrogen-related pathways that are often implicated in hormone-dependent cancers, such as breast and ovarian cancer (Sharifi-Rad et al., 2021). Epidemiological studies have consistently linked high soy consumption with reduced risks of breast cancer, particularly in Asian populations, where dietary patterns include significant amounts of soy (Shin et al., 2023; Cao et al., 2022).

a. Antioxidant Activity

One of the primary mechanisms through which soy isoflavones exert protective effects against cancer is through their antioxidant activity (Kim, 2021). Isoflavones, particularly genistein, have been shown to scavenge free radicals and reduce oxidative stress, which is a key factor in the initiation and progression of cancer. Free radicals are highly reactive molecules that can cause cellular damage by interacting with DNA, proteins, and lipids (Alkhadi, 2020). This damage, if not repaired, can lead to mutations and genomic instability, which are critical steps in the development of cancer (Tubbs, NUssenweiz, 2017). By neutralizing these harmful free radicals, soy isoflavones prevent DNA damage and, therefore, help to reduce the risk of carcinogenesis. The antioxidant properties of soy isoflavones are particularly important in the context of cancers that are driven by oxidative stress, such as lung, prostate, and breast cancers. Oxidative stress has been implicated in a range of cellular processes that contribute to cancer, including inflammation, cell proliferation, and resistance to apoptosis (programmed cell death). By mitigating oxidative damage, soy isoflavones may help to protect cells from becoming malignant and inhibit the progression of early-stage tumors.

Research by Lambert et al. (2007) highlighted the role of isoflavones in reducing oxidative stress. Their findings suggest that genistein and daidzein can directly scavenge free radicals and inhibit the production of reactive oxygen species (ROS), thereby reducing the overall oxidative burden on cells. This action is crucial for maintaining cellular integrity and preventing the initiation of cancerous transformations. Soybeans are rich in bioactive compounds, particularly isoflavones, phenolics, and flavonoids, which contribute to their antioxidant capacity. Isoflavones

such as genistein and daidzein have been extensively studied for their health benefits, including their ability to scavenge free radicals and inhibit cancer cell proliferation (Sharifi-Rad et al., 2021; Wójciak et al., 2024). The antioxidant activity of soybeans is often assessed using various in vitro assays, such as DPPH radical scavenging and FRAP (Ferric Reducing Antioxidant Power) assays, which provide insights into their efficacy in neutralizing oxidative species (Nwachukwu et al., 2021). Research indicates that the antioxidant potential of soybeans varies significantly with seed coat color, suggesting that specific cultivars may offer enhanced protective effects against oxidative damage (Wójciak et al., 2024; Nwachukwu et al., 2021).

Fermentation processes have been shown to enhance the antioxidant properties of soybeans. Studies demonstrate that fermenting soybeans with specific microbial strains, such as Bacillus spp. and Pleurotus cornucopiae, significantly increases their total phenolic content and antioxidant activity (Akyuz et al., 2023, Hamad et al., 2022). This enhancement is attributed to the breakdown of complex compounds into simpler, more bioavailable forms, which can exhibit stronger antioxidant effects (Akyuz et al., 2023). For example, fermented soybean products like tempeh have been linked to improved antioxidant activity, which may contribute to their protective effects against degenerative diseases, including cancer (Ojao et al., 2022).

Moreover, germination of soybeans has been identified as another method to boost their antioxidant capacity. Germination increases the levels of bioactive compounds, including isoflavones and phenolic acids, which are associated with enhanced antioxidant activity (Król-Grzymała, Amarowicz, 2020). This process not only improves the nutritional profile of soybeans but also their potential in cancer prevention by reducing oxidative stress and inflammation, both of which are critical factors in cancer development.

Recent metabolomic analyses have revealed that domestication has altered the polyphenolic profiles of soybean seeds, affecting their antioxidant activities (Ullah et al., 2024). Wild soybeans, for instance, exhibit a higher diversity of polyphenolic compounds, which may contribute to their superior antioxidant properties compared to cultivated varieties (Li et al., 2023). This finding underscores the importance of genetic diversity in optimizing the health benefits of soybeans.

b. Modulation of Signaling Pathways

In addition to their antioxidant properties, soy isoflavones also influence critical cell signaling pathways that regulate cell survival, proliferation, and apoptosis. Among the most important pathways affected by isoflavones are the PI3K/AKT and MAPK pathways, both of which are involved in controlling cell cycle progression, survival signals, and responses to stress (Gupta et al., 2021).

The PI3K/AKT signaling pathway is crucial for promoting cell survival and growth. In many cancers, this pathway is dysregulated, leading to uncontrolled cell proliferation and resistance to apoptosis (He et al., 2021). Genistein, a major isoflavone found in soy, has been shown to inhibit the PI3K/AKT pathway, leading to reduced cell survival and growth. By blocking this pathway, genistein can help to restore normal cell-cycle regulation and promote the death of cancer cells, thereby preventing tumor growth and metastasis.

Similarly, the MAPK pathway, which regulates cell proliferation and differentiation, can be modulated by soy isoflavones (Zhang et al., 2020). Dysregulation of MAPK signaling is often observed in various cancers, contributing to unchecked cellular growth and survival. Isoflavones like genistein and daidzein can influence the MAPK pathway, thereby inhibiting cancer cell proliferation and inducing apoptosis (Konstantinou et al., 2024). Moreover, genistein's ability to inhibit tyrosine kinases, which are enzymes that regulate various signaling pathways, further enhances its anticancer potential. Tyrosine kinases play a critical role in signaling networks that control cellular processes such as proliferation, differentiation, and apoptosis (Konstantinou et al., 2024; Chae et al., 2019). By inhibiting these kinases, genistein can reduce the growth of cancer cells and promote the induction of apoptosis. This inhibition of tyrosine kinases contributes to the overall anticancer effects of soy and highlights the importance of genistein in cancer prevention and therapy.

Isoflavones, such as genistein and daidzein, are phytoestrogens that mimic estrogen and interact with estrogen receptors (ERs) in the body. Research indicates that these compounds can induce apoptosis in cancer cells, particularly in prostate cancer models. For instance, Sivoňová et al. (2019) demonstrated that soybean extract containing isoflavones at a concentration of 25 µmol/L significantly increased apoptosis in prostate cancer cells compared to individual isoflavones. Furthermore, the estrogenic activity of isoflavones has been linked to their ability to

modulate signaling pathways associated with cell proliferation and survival, suggesting a dual role in both promoting and inhibiting cancer cell growth depending on the context (Kaufman-Szymczyk et al., 2024).

In addition to isoflavones, peptides derived from soybeans, such as lunasin, have shown promising anticancer properties. Lunasin has been reported to inhibit the proliferation of colorectal cancer cells by inducing apoptosis and modulating cell cycle progression (Kaufman-Szymczyk et al., 2024). Its mechanism of action involves the downregulation of key signaling pathways that promote tumor growth, including the epidermal growth factor receptor (EGFR) pathway (Fernández-Tomé et al., 2020). Phenolic compounds in soybeans contribute to their anticancer effects by exerting antioxidant properties and modulating inflammatory pathways. These compounds can inhibit the expression of cyclooxygenase-2 (COX-2), a key enzyme involved in inflammation and cancer progression (Zappavigna et al., 2020). The anti-inflammatory effects of soy phenolics are crucial in preventing the initiation and promotion of cancer, as chronic inflammation is a well-established risk factor for various malignancies (Kim et al., 2021).

The epigenetic effects of soybean consumption, particularly maternal exposure to genistein, have also been investigated for their long-term implications on cancer risk in offspring. Chen et al. found that maternal genistein exposure could lead to inherited epigenetic changes that lower breast cancer risk in later life (Chen et al., 2022). This highlights the importance of dietary components in shaping cancer susceptibility through epigenetic mechanisms.

c. Epigenetic Regulation

Epigenetic regulation plays a pivotal role in controlling cellular processes such as cell differentiation, proliferation, and apoptosis. In the context of cancer, these processes are often disrupted, leading to uncontrolled cell growth and resistance to cell death (Matthews et al., 2022). Epigenetic changes, such as the silencing of tumor suppressor genes or the activation of oncogenes, can drive the initiation and progression of cancer (Chatterjee et al., 2018).

DNA methylation, a key epigenetic modification, involves the addition of a methyl group to the DNA molecule, typically at cytosine residues in CpG dinucleotides (Acharjee et al., 2023). This modification can lead to the silencing of genes, including those involved in tumor suppression, making it a critical player in carcinogenesis. Similarly, histone modifications, which include methylation, acetylation, and phosphorylation, can alter the structure of chromatin and affect gene expression by making the DNA more or less accessible to the transcriptional machinery (Zhao, Malik, 2022). In cancer cells, abnormal DNA methylation and histone modifications often contribute to the dysregulation of critical genes that control cell growth and survival.

Role of Isoflavones in Epigenetic Modulation

Isoflavones, particularly genistein, have been shown to influence both DNA methylation and histone modification processes, making them important modulators of gene expression in cancer cells (Sharma et al., 2021). One of the key mechanisms through which genistein impacts epigenetic regulation is by inhibiting DNA methyltransferases (DNMTs), the enzymes responsible for adding methyl groups to DNA (Akone et al., 2020). By inhibiting DNMTs, genistein can prevent the silencing of tumor suppressor genes, such as p53, which play a critical role in regulating the cell cycle and inducing apoptosis in response to cellular stress. The reactivation of these genes may help to restore normal cellular function and prevent the transformation of normal cells into cancerous ones.

Furthermore, genistein has been shown to influence histone modifications, which can alter the chromatin structure and affect gene expression (Dutta et al., 2018). By modulating histone acetylation and methylation, genistein can promote a more open chromatin structure that favors the expression of tumor suppressor genes. This effect is particularly important in cancer cells, where histone modifications are often altered, leading to the silencing of critical genes involved in growth regulation (Perri et al., 2017). Through its ability to modify histone marks, genistein can help to reverse these changes and promote the expression of genes that inhibit tumor growth. Soy isoflavones, particularly genistein, could modify the expression of genes involved in cell cycle regulation and apoptosis through epigenetic mechanisms (Sharma et al., 2021). The researchers found that genistein's ability to alter DNA methylation and histone modifications contributed to its anticancer effects, particularly by reactivating the expression of genes that suppress tumor growth.

Isoflavones and Oncogenesis

Isoflavones not only affect tumor suppressor genes but can also influence oncogenes, which are genes that, when activated, promote cancer cell proliferation and survival (Ziaei, Halaby, 2017). Epigenetic silencing of tumor suppressor genes and the activation of oncogenes are common events

in the progression of many cancers. Moreover, the ability of soy isoflavones to modulate the expression of key regulatory genes through epigenetic mechanisms may also influence other processes involved in cancer, such as angiogenesis, metastasis, and immune surveillance (Eren et al., 2024). Angiogenesis, the formation of new blood vessels, is a critical process for tumor growth and metastasis. By modulating gene expression related to angiogenesis, soy isoflavones could potentially inhibit the ability of tumors to establish a blood supply, thereby limiting their growth and spread (Ajdžanovic et al., 2019). Additionally, by influencing immune-regulatory genes, isoflavones may enhance the immune system's ability to recognize and eliminate cancer cells.

Isoflavones, particularly those derived from soybeans, have garnered significant attention in the context of cancer prevention due to their diverse biological activities and mechanisms of action. Isoflavones such as genistein and daidzein are recognized for their phytoestrogenic properties, which allow them to interact with estrogen receptors (ERα and ERβ) and modulate various signaling pathways involved in oncogenesis (Kaufman-Szymczyk et al., 2024; Messina et al., 2022). This inhibition leads to decreased expression of proteins that promote cancer cell proliferation, such as cyclin D1 and PCNA, while enhancing the expression of cell cycle inhibitors like p21 and p27 (Singh et al., 2017). Additionally, isoflavones can induce apoptosis in cancer cells by activating caspases and modulating the expression of pro-apoptotic and anti-apoptotic proteins (Jeong et al., 2024).

Moreover, isoflavones have demonstrated the ability to inhibit the activity of various enzymes involved in cancer progression, such as protein tyrosine kinases and topoisomerases (Sarkar et al., 2021; Ivashkevich, 2023). These enzymes play critical roles in cell signaling and DNA replication, respectively, and their inhibition can lead to reduced tumor growth and enhanced sensitivity to chemotherapeutic agents (Coutinho et al., 2023). For example, studies have indicated that genistein can enhance the efficacy of radiotherapy by sensitizing cancer cells to radiation while protecting normal tissues from radiation-induced damage (Komorowska et al., 2022).

The antioxidant properties of isoflavones also contribute to their anticancer effects. By scavenging reactive oxygen species (ROS) and reducing oxidative stress, isoflavones can mitigate DNA damage that may lead to cancer initiation and progression (Sarkar et al., 2021). Furthermore, the anti-inflammatory effects of isoflavones, mediated through the inhibition of nuclear factor-κB (NF-κB) signaling, can reduce the chronic inflammation associated with cancer development (Subedi et al., 2019).

Epidemiological studies have supported the protective role of isoflavones against various cancers, particularly hormone-related cancers such as breast and prostate cancer. Populations with high soy consumption, such as those in Asia, exhibit lower incidences of these cancers compared to Western populations (Messina et al., 2022). This correlation underscores the potential of dietary isoflavones as chemopreventive agents.

Soy Combination Therapies for Cancer Treatment

The integration of soy-based interventions, particularly soy isoflavones such as genistein and daidzein, into cancer treatment has gained significant attention. These phytoestrogens exhibit estrogen-like activity and interact with molecular pathways involved in cancer progression (Goleij et al., 2024; Ivashkevich, 2023). As adjuncts to conventional therapies, including chemotherapy, radiation therapy, and immunotherapy, soy isoflavones have shown potential in enhancing therapeutic efficacy and mitigating treatment-related side effects. However, further research is needed to confirm their safety and effectiveness (Ivashkevich, 2023).

The anticarcinogenic properties of soy isoflavones stem from their dual role in hormonal modulation and antioxidant activity. Isoflavones can bind to estrogen receptor beta (ERβ), inhibiting estrogen receptor alpha (ERα), which is often associated with tumor growth in hormone-sensitive cancers like breast and ovarian cancers (Goleij et al., 2024). Epidemiological studies have consistently linked higher dietary intake of soy to reduced risks of breast, prostate, and ovarian cancers, especially in populations with high soy consumption (Messina et al., 2022).

Soy isoflavones also exhibit antioxidant properties, scavenging free radicals and reducing oxidative stress, a known contributor to cancer development (Sarkar et al., 2021). These compounds enhance the activity of antioxidant enzymes and modulate inflammatory pathways, mitigating the risk of cancer associated with chronic inflammation (Subedi et al., 2019). These properties make soy isoflavones promising candidates for integrative oncology, where they may complement conventional therapies to enhance efficacy and reduce toxicity (Ivashkevich, 2023).

Beyond improving therapeutic efficacy, soy isoflavones may alleviate treatment-related side effects. Genistein, for instance, exhibits anti-inflammatory properties that help reduce

chemotherapy-induced inflammation and tissue damage (Goleij et al., 2024). These protective effects contribute to better patient tolerance and quality of life during treatment.

Soy isoflavones are particularly effective in hormone-sensitive cancers, such as breast and prostate cancer. Their estrogenic activity can counteract endogenous hormones that promote tumor growth. Meta-analyses have shown that higher intake of soy-based foods is associated with reduced recurrence rates in breast cancer (Messina et al., 2022). However, individual responses to soy isoflavones vary due to genetic polymorphisms and gut microbiome differences, which influence their metabolism and bioavailability (Ashrafi-Dehkordi et al., 2024). This variability underscores the importance of personalized approaches to incorporating soy-based therapies into cancer treatment.

Soy Isoflavones in Combination with Radiation Therapy

Radiation therapy is another common treatment for cancer, but it can cause significant damage to normal tissues surrounding the tumor, leading to side effects such as skin irritation, fatigue, and organ dysfunction. Research suggests that soy isoflavones, particularly genistein, may be able to enhance the therapeutic effects of radiation therapy while also reducing its toxicities (Goleij et al., 2024).

Genistein has been shown to have radiosensitizing properties, meaning that it can increase the sensitivity of cancer cells to the damaging effects of radiation. By inhibiting the repair of radiation-induced DNA damage, genistein may enhance the cytotoxicity of radiation, leading to greater tumor cell death. Genistein increased the radiosensitivity of human prostate cancer cells, making them more susceptible to radiation-induced apoptosis (Komorowska et al., 2022). This sensitization was mediated through the inhibition of the PI3K/AKT pathway, which is often activated in cancer cells to promote survival after radiation.

Soy Isoflavones in Combination with Immunotherapy

Immunotherapy, which harnesses the body's immune system to fight cancer, has revolutionized cancer treatment in recent years. However, not all patients respond to immunotherapy, and the mechanisms underlying this resistance are still being explored (Bai et al., 2020). There is growing interest in the potential of soy isoflavones to enhance the effectiveness of immunotherapy, particularly by modulating immune system activity.

Genistein has been shown to modulate the immune response in several ways. It can enhance the activity of immune cells, such as T cells and natural killer (NK) cells, which are critical for recognizing and destroying cancer cells (Goleij et al., 2024). Genistein has also been shown to increase the production of cytokines, signaling molecules that help coordinate the immune response (Čoma et al., 2021). This immunomodulatory effect may help boost the effectiveness of immunotherapies, such as checkpoint inhibitors, which rely on stimulating the immune system to recognize and attack cancer cells.

In addition to their use in combination with conventional therapies, soy isoflavones may also have synergistic effects when combined with other natural compounds that possess anticancer properties (Mia et al., 2023). For example, studies have investigated the combined use of genistein with curcumin, a compound found in turmeric, which has well-documented anti-inflammatory and anticancer effects. A study by Mia et al. (2023) found that the combination of genistein and curcumin synergistically inhibited the growth of prostate cancer cells and promoted apoptosis. This combination worked through multiple mechanisms, including the suppression of NF-kB signaling, which is often activated in cancer cells to promote survival and metastasis. By combining genistein with other natural compounds like curcumin, it may be possible to enhance the overall anticancer effect while reducing the likelihood of resistance developing during treatment.

Combination of Soy with Other Plant-Based Compounds for Cancer Treatment

Research on combining soy with other plant-based compounds for cancer treatment has garnered significant interest due to the potential synergistic effects of these combinations. Soy isoflavones, particularly genistein and daidzein, have well-documented anticancer properties, including inhibiting cell proliferation, inducing apoptosis, and suppressing metastasis (Ashrafi-Dehkordi et al., 2024). When combined with other bioactive compounds found in plants, such as curcumin, green tea catechins, resveratrol, and compounds from cruciferous vegetables, these effects may be enhanced. The combination of soy with other plant-based compounds has garnered significant attention in cancer treatment due to the synergistic effects that enhance therapeutic efficacy while minimizing side effects.

Soy isoflavones have been shown to exert anti-cancer effects through multiple mechanisms, including the modulation of cell signaling pathways, induction of apoptosis, and inhibition of tumor growth. For instance, studies indicate that soy isoflavones can influence the expression of genes involved in cell cycle regulation and apoptosis, thereby promoting cancer cell death (Sauter, 2020). Furthermore, the incorporation of soy isoflavones in combination therapies has been reported to enhance the sensitivity of cancer cells to conventional chemotherapeutics, leading to improved therapeutic outcomes (Wang et al., 2021). This is particularly relevant in the context of resistant cancer types, where traditional therapies often fail to achieve desired results.

Moreover, the immunomodulatory effects of soy and its phytochemicals contribute to their therapeutic potential. Studies have indicated that soy isoflavones can enhance immune responses, which may play a role in tumor suppression and prevention of metastasis (Kaufman-Szymczyk et al., 2024). This is particularly important as effective cancer therapies not only target tumor cells but also aim to bolster the body's immune system to fight cancer more effectively.

Soy Isoflavones and Curcumin

Curcumin, a bioactive compound found in turmeric, is known for its anti-inflammatory, antioxidant, and anticancer properties. Research has explored the synergistic effects of combining curcumin with soy isoflavones, particularly genistein, for enhanced anticancer outcomes. Curcumin works by inhibiting key signaling pathways involved in cell survival and proliferation, such as NF-kB, PI3K/AKT, and MAPK (Coutinho et al., 2023). Soy isoflavones, particularly genistein, also target these pathways, providing a complementary mechanism of action.

Additionally, curcumin has been shown to enhance the bioavailability of genistein, further increasing its therapeutic potential (Gan et al., 2018). This is particularly important in cancer treatment, where ensuring effective absorption and distribution of anticancer compounds is crucial for achieving therapeutic efficacy.

Soy Isoflavones and Green Tea Catechins

Green tea catechins, especially epigallocatechin-3-gallate (EGCG), are well-known for their antioxidant and anticancer properties. EGCG has been shown to inhibit cancer cell proliferation, induce apoptosis, and reduce metastasis (Ohishi et al., 2022). Research has explored combining soy isoflavones like genistein with EGCG to enhance the anticancer effects of both compounds (Kundur et al., 2019).

A study by Kundur et al. (2019) demonstrated that the combination of genistein and EGCG exhibited enhanced anticancer effects in breast cancer cells. The results indicated that the combination promoted apoptosis and inhibited cell proliferation more effectively than either compound alone. Both genistein and EGCG target key signaling pathways such as PI3K/AKT, which regulates cell survival and proliferation. The study highlighted the potential of combining soy isoflavones with green tea catechins for more potent anticancer activity.

EGCG also complements soy isoflavones by modulating the tumor microenvironment. EGCG has been shown to inhibit angiogenesis, the process through which tumors develop blood vessels to supply nutrients, and reduce oxidative stress (Mokra et al., 2022). When combined with genistein, EGCG may not only enhance cancer cell sensitivity to therapy but also protect normal tissues from damage during cancer treatment.

Soy Isoflavones and Resveratrol

Resveratrol, a polyphenolic compound found in grapes and red wine, has garnered attention for its anticancer properties (Kursvietiene et al., 2023). It has been shown to inhibit cancer cell proliferation, promote apoptosis, and reduce inflammation. When combined with soy isoflavones, resveratrol may provide a complementary mechanism of action, as both compounds target similar signaling pathways involved in cancer progression.

Research by Tuli et al. (2019) examined the effects of combining genistein and resveratrol in prostate cancer cells. The combination of these two compounds resulted in significant inhibition of cell proliferation and induction of apoptosis. The study suggested that the synergy between genistein and resveratrol was due to their ability to modulate key pathways such as PI3K/AKT and MAPK, which are often dysregulated in cancer cells. Resveratrol also plays a role in reducing inflammation and oxidative stress, which are common in cancer and can contribute to tumor progression (Aggarwal et al., 2019). By combining resveratrol with soy isoflavones like genistein, it is possible to target not only cancer cells but also the tumor microenvironment, further enhancing the therapeutic effect.

Soy Isoflavones and Cruciferous Vegetables

Cruciferous vegetables, such as broccoli, cabbage, and kale, contain compounds like sulforaphane, which have well-established anticancer properties. Sulforaphane has been shown to inhibit cancer cell growth, promote apoptosis, and reduce inflammation through the modulation of various signaling pathways, including the Nrf2 pathway (Sharma, Tollefsbol, 2022). Research has explored combining soy isoflavones with sulforaphane to enhance the anticancer effects of both compounds.

A study by Sharma and Tollefsbol (2022) investigated the combined effects of genistein and sulforaphane in prostate cancer cells. The results showed that the combination of genistein and sulforaphane led to a significant reduction in cell proliferation and an increase in apoptosis. The synergistic effect was attributed to the activation of Nrf2, which enhances antioxidant activity and reduces oxidative stress in cancer cells. By combining genistein with sulforaphane, it may be possible to target multiple pathways involved in tumorigenesis, improving the overall therapeutic effect. Moreover, sulforaphane has been shown to modulate the immune response and inhibit tumor angiogenesis (Mahn, Castillo, 2021). This makes it an ideal partner for soy isoflavones, which also have immunomodulatory properties. Together, they provide a comprehensive approach to cancer treatment, targeting both cancer cells and the tumor microenvironment.

Recommendations for Soy Consumption

Current recommendations suggest that incorporating soy foods into the diet may provide a variety of health benefits, including potential cancer prevention. Soy foods, such as tofu, tempeh, edamame, and soy milk, are rich in isoflavones, which exhibit antioxidant, anti-inflammatory, and anticancer properties. Health organizations such as the American Institute for Cancer Research (AICR) and the World Cancer Research Fund (WCRF) generally encourage the consumption of plant-based foods, including soy, as part of a diet that emphasizes fruits, vegetables, whole grains, and legumes. Soy foods are considered safe for most people when consumed in moderate amounts, and they may offer a nutritional alternative to animal-based products.

Incorporating soy as a part of a balanced diet, particularly in populations at higher risk for certain cancers, such as breast, prostate, and colorectal cancer, may help to lower the incidence of these cancers. Soy isoflavones are thought to exert their protective effects by interacting with estrogen receptors, modulating cell signaling pathways, and exhibiting antioxidant properties. These mechanisms make soy a promising dietary component for cancer prevention. However, it is important to note that the effects of soy may vary depending on individual factors, including health conditions and lifestyle choices.

While the general population may benefit from including soy in their diet, it is essential for individuals with specific health concerns, such as thyroid disorders or hormone-sensitive cancers, to consult with a healthcare provider before making significant dietary changes. The interaction between soy isoflavones and estrogen receptors, for example, has raised concerns for individuals with estrogen-sensitive conditions, though the overall evidence is still inconclusive. Therefore, personalized dietary recommendations that take into account individual health factors are necessary.

3. Conclusion

The integration of soybeans into the diet holds promise for cancer prevention and management, largely due to the bioactive isoflavones found in soy, which exhibit antioxidant, anti-inflammatory, and anticancer properties. Epidemiological and clinical studies provide supportive evidence for the health benefits of soy, particularly in reducing the risk of hormone-related cancers such as breast and prostate cancer. However, the mechanisms through which soy isoflavones exert their anticancer effects are not fully understood, and more research is needed to clarify these processes. Additionally, while moderate soy consumption is generally considered safe, the long-term safety of high-dose isoflavone supplementation remains uncertain, and further investigation is warranted.

Ultimately, incorporating soy foods into a balanced diet can be a beneficial strategy for cancer prevention and management. However, it is essential to consider individual variability in isoflavone metabolism, the potential risks of high-dose supplementation, and the need for personalized dietary recommendations. As research progresses, a more comprehensive understanding of the role of soy in cancer prevention and treatment will help to inform dietary guidelines and therapeutic approaches for cancer patients.

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