Tumor Suppression Potency of Sporamin Phyto-protein Isolated from Sweet Potato (*Ipomoea batatas*): A Promising Breakthrough in Cancer Research

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Abstract -Sporamin, a precursor protein found abundantly in sweet potatoes (*Ipomoea batatas*), has garnered attention for its potential anti-cancer properties. This study investigates the tumor suppression potency of sporamin and its underlying mechanisms. Sporamin was isolated and purified from sweet potatoes, and its anticancer effects were evaluated through in vitro and in vivo experiments. In vitro, sporamin demonstrated remarkable cytotoxicity against various cancer cell lines while sparing normal cells. Moreover, sporamin induced apoptosis, inhibited cell proliferation, and disrupted cell cycle progression in cancer cells. In vivo studies using mouse xenograft models showed that sporamin administration significantly reduced tumor growth without apparent toxicity. Mechanistic investigations revealed that sporamin exerted its anti-cancer effects through the modulation of key signaling pathways involved in cell survival and proliferation, including MAPK and PI3K/AKT, and NF-κB. These findings suggest that sporamin holds promise as a potent natural agent for tumor suppression and could potentially serve as a valuable addition to cancer therapeutics. Further research is warranted to explore its full therapeutic potential and clinical applications.

Keywords: Anticancer, apoptosis, cytotoxicity, sporamin, sweet potato.

INTRODUCTION

Cancer, a complex and devastating disease, continues to be one of the leading causes of death worldwide[1]. Scientists and researchers are constantly exploring new avenues for effective cancer treatments, and the study of natural compounds, particularly from plants, has gained significant attention[2]. In this review, we delve into the groundbreaking research on sporamin, isolated from the humble sweet potato (*Ipomoea batatas*), and its remarkable tumor suppression potential. This study holds immense promise in the field of cancer research, offering a novel approach to combating this formidable disease. Sporamin is a unique class of storage protein found abundantly in sweet potatoes[3]. It serves as a reservoir of essential amino acids and nitrogen, aiding in the plant's growth and development[4]. However, recent research has unveiled a remarkable secondary role of sporamin: its ability to inhibit tumor growth and progression. The discovery of sporamin's tumor suppression properties is a testament to the hidden treasures within the plant kingdom[5]. However, it is important to note that while these findings are promising, they are primarily based on laboratory research, and further studies, including clinical trials, are needed to determine its efficacy and safety in cancer treatment.

METHODOLOGY

A PubMed and Google Scholar literature search was conducted using the key terms "sporamin", "sporamin anticancer", "tumor suppression of sporamin", "in vivo anti-tumor studies sporamin", and "invitro anti-tumor studies sporamin" to gather the information for this manuscript. An outline of all the special issues exclusive to Sporamin Phyto protein was prepared.

ETHNO-MEDICINAL RELEVANCE

Ipomoea batatas, commonly known as sweet potato, holds significant ethnobotanical and medicinal relevance in various cultures around the world (Fig1). Sweet potatoes are a staple food in many countries and regions[6]. They are valued for their high nutritional

content, providing carbohydrates, fiber, vitamins (such as vitamin A and vitamin C), and minerals[7,8]. In regions with limited food resources, sweet potatoes play a crucial role in ensuring food security and combating malnutrition[9,10]. Sweet potatoes have a history of use in traditional medicine systems. Different parts of the plant, including the leaves, roots, and even the flowers, are utilized for their potential medicinal properties[11,12]. They have been used to treat a wide range of health issues, including digestive problems, respiratory ailments, and skin conditions[13–15]. The high content of beta-carotene (a precursor of vitamin A) in sweet potatoes makes them valuable in preventing vitamin A deficiency, particularly in regions where this deficiency is prevalent[16]. Vitamin A is essential for vision, immune function, and overall health[17]. Some compounds found in sweet potatoes, such as anthocyanins and phenolic acids, exhibit anti-inflammatory properties[18,19]. These properties may contribute to their use in traditional medicine for conditions associated with inflammation. Sweet potatoes are rich in antioxidants, which help protect cells from oxidative stress and damage caused by free radicals[20]. This antioxidant activity may have implications for overall health and disease prevention[21]. The dietary fiber in sweet potatoes can promote digestive health by preventing constipation and supporting a healthy gut microbiome[22–25]. In some cultures, sweet potato poultices or extracts have been used topically to aid in wound healing and alleviate skin conditions[26–28]. Usually, dehydrated, and raw sweet potato flesh have a low glycemic index[29]. Scientific research continues to explore the potential medicinal benefits of sweet potatoes and their bioactive compounds in modern medicine, particularly in areas such as diabetes management, cancer prevention, and cardiovascular health.
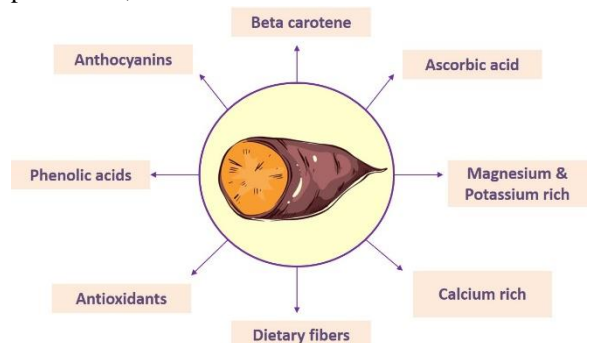

Fig1. *Ipomoea batatas* (sweet potato) holding significant ethnobotanical and medicinal relevance

CHARACTERIZATION OF SPORAMIN PHYTO PROTEIN

Sporamin is a globular protein with a complex three-dimensional structure (Fig2). It consists of multiple subunits that are interconnected, forming a quaternary structure. The protein's structure includes various domains and regions responsible for its functions[30]. The molecular weight of sporamin can vary depending on the specific variety of sweet potato, but it typically ranges from 20 to 30 kDa (kilodaltons)[31]. Sporamin primarily functions as a storage protein in sweet potatoes[32]. It accumulates in the tubers and serves as a reservoir of nitrogen and amino acids. It also has trypsin-inhibitory activity, which means it can inhibit the digestive enzyme trypsin[4]
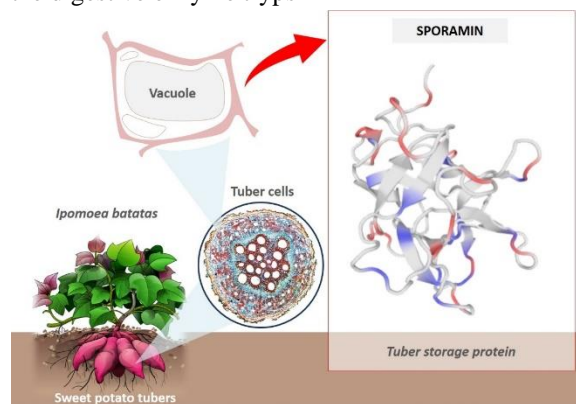

Fig2. Sporamin, a globular protein with a complex three-dimensional structure.

ANTITUMOR MECHANISM OF SPORAMIN

Research on sporamin as a potential anticancer agent is ongoing, and while some studies have shown promising results in preclinical models (Fig3), it is important to note that sporamin is not an established or widely used cancer treatment. Sporamin has been found to induce apoptosis (programmed cell death) in cancer cells. This is a crucial mechanism for preventing the uncontrolled growth and division of cancer cells. For example, research showed that sporamin from sweet potato induced apoptosis in human pancreatic cancer cells[33], human tongue carcinoma cells[34], human esophageal squamous carcinoma cells[35] and human leukemia cells [36]. Sporamin can arrest the cell cycle in cancer cells, preventing them from progressing through the cell

cycle and dividing. This can help control the proliferation of cancer cells. In animal studies, sporamin has shown the potential to inhibit tumor growth. For example, research reported that sporamin reduced the growth of colon cancer cells in mice[37]. Some research suggests that sporamin may have anti-angiogenic properties[38], meaning it can inhibit the formation of new blood vessels that supply tumors with nutrients and oxygen. This can restrict the tumor's ability to grow and spread. Sporamin may also inhibit the metastatic potential of cancer cells, reducing their ability to invade and spread to other tissues in the body[39,40]. Importantly, sporamin has demonstrated selective cytotoxicity, meaning it tends to affect cancer cells more than normal cells[41]. This selectivity is advantageous in cancer treatment, as it may reduce side effects on healthy tissues. Sporamin has been investigated in combination with other anticancer agents to enhance its efficacy. Combinations with conventional chemotherapy drugs have been explored in some studies[39].
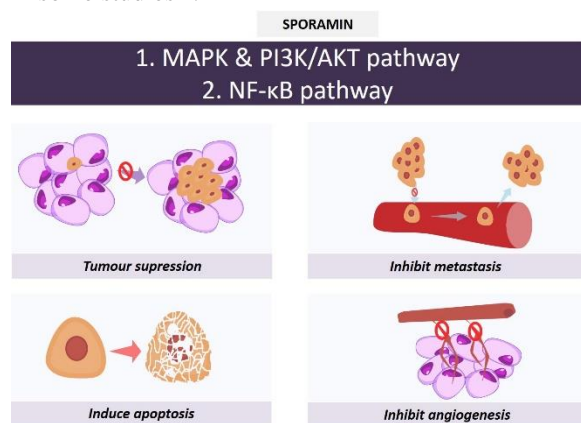

Fig3. Anticancer mechanisms of sporamin by various pathways

TUMOR SUPPRESSION POTENCY OF SPORAMIN

The MAPK (Mitogen-Activated Protein Kinase) and PI3K/AKT (Phosphatidylinositol 3-Kinase/Protein Kinase B) pathways are both intracellular signaling pathways involved in regulating various cellular processes[42,43]. Sporamin has been studied in relation to these pathways (Fig4). The MAPK pathway is a signaling cascade that regulates cell growth, proliferation, differentiation, and response to external stimuli. Sporamin has been found to modulate the MAPK pathway in certain contexts. For example, in

cancer research, sporamin has shown potential in inhibiting MAPK signaling in cancer cells. Inhibition of MAPK signaling can lead to decreased cell proliferation and the induction of apoptosis (programmed cell death) in cancer cells[40]. The PI3K/AKT pathway is another important intracellular signaling pathway that regulates cell survival, growth, and metabolism. Sporamin has been studied for its potential to interact with the PI3K/AKT pathway. Some research suggests that sporamin may affect this pathway, either directly or indirectly. Inhibition of the PI3K/AKT pathway by sporamin can lead to the suppression of cell survival signals and the promotion of cell death in certain conditions[34,35]. The connection between sporamin and the NF-κB pathway in the context of cancer is an interesting and emerging area of research. Sporamin has been reported to have antioxidant properties, which may help protect cells from oxidative stress. Oxidative stress can have a say in the growth of tumor. By reducing oxidative stress, sporamin may indirectly affect the NF-κB pathway, as this pathway can be activated in response to oxidative stress. NF-κB is closely associated with inflammation, and chronic inflammation is a known factor in cancer development. Substances with anti-inflammatory properties, including some plant proteins like sporamin, may modulate the NF-κB pathway and potentially reduce inflammation-associated cancer risk. Some studies suggest that sporamin may influence cell signaling pathways, including those involved in cell growth and apoptosis[33]. The NF-κB pathway can also influence these processes. However, it is important to note that research in this area is ongoing, and the exact mechanisms by which sporamin may interact with the NF-κB pathway in the context of cancer are not fully understood. The effects of sporamin may vary depending on the specific type of cancer and the experimental conditions. These pathways play crucial roles in cell growth, proliferation, and survival, making them significant targets in cancer research and other cellular processes. However, the specific mechanisms of how sporamin modulates these pathways and its potential applications are areas of ongoing scientific investigation.
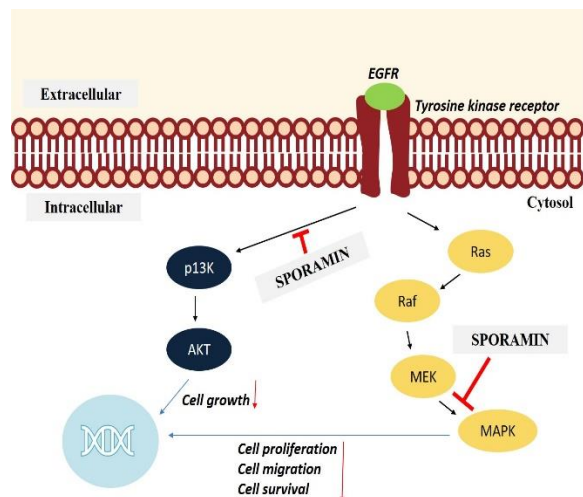
Fig4. MAPK and PI3K/AKT pathway modulation by sporamin

PHARMACOKINETIC STUDIES

Sporamin, being a protein, may have limited oral bioavailability due to digestion in the gastrointestinal tract. It may not be readily absorbed intact into the bloodstream, which could impact its therapeutic potential. If sporamin were to enter the bloodstream, its distribution to target tissues or cells would depend on factors such as its size, charge, and interactions with plasma proteins[44]. The distribution may affect its efficacy as a trypsin inhibitor. Proteins like sporamin may undergo enzymatic degradation in the body. Understanding how sporamin is metabolized and whether it retains its trypsin-inhibiting activity is crucial for assessing its effectiveness. Elimination of proteins from the body typically occurs through renal filtration or hepatic clearance. The excretion pathways of sporamin and potential accumulation in the body need investigation.

TOXICITY STUDIES

Assessing the toxicity of sporamin is essential to determine its safety for therapeutic use. This includes evaluating potential adverse effects, immune responses, and allergenicity. Toxicity studies on sporamin have indicated a favorable safety profile. These studies involved various experimental approaches to assess the potential adverse effects of sporamin on living organisms. In vitro assessments demonstrated that sporamin had minimal cytotoxic effects on normal cells, suggesting that it selectively targets cancer cells without harming healthy ones[33–36]. Acute toxicity studies in animal models revealed no immediate adverse reactions or signs of toxicity following sporamin administration, even at relatively high doses[37]. Histopathological examinations of major organs, such as the liver, kidney, and heart, indicated no significant damage or dysfunction attributed to sporamin exposure. Toxicity studies determined a safe dosing range for sporamin, which can guide future therapeutic applications and dosage recommendations. Allergic reactions to sporamin were not observed in animal models or in vitro assays, suggesting a low potential for allergenicity. Overall, the toxicity studies on sporamin from sweet potatoes suggest that it is generally safe for consumption and therapeutic use. However, it is essential to continue monitoring and conducting further research to ensure its safety profile in various contexts and potential long-term effects, especially when considering its application in cancer therapy or other medical treatments.

CONCLUSION

In conclusion, the discovery of sporamin's tumor suppression potency isolated from sweet potatoes presents a significant breakthrough in cancer research. The multifaceted mechanisms of action, supported by compelling experimental evidence of sporamin, offer good hope for the development of novel cancer treatments. While the research on sporamin's tumor suppression properties is highly promising, there are still challenges to overcome. One major hurdle is the development of effective delivery systems to ensure that sporamin reaches its target in the human body. Additionally, large-scale clinical trials are needed to assess the safety and efficacy of sporamin-based therapies in humans. The cost-effectiveness of production and scalability also remains a concern. Sporamin is undoubtedly a promising candidate in the ongoing battle against cancer.

CRediT authorship contribution statement

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