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# Clinical Study on the Promotion of Autophagy and Anti-aging Effects of Spermidine Extracted from Wheat Germ

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**Abstract:** Wheat germ is widely regarded as a treasure trove of antioxidants and anti-aging, mainly derived from its abundant spermidine. In recent years, spermidine has received increasing attention as an anti-aging ingredient, and its antioxidant and autophagic promoting effects have gradually been revealed. This study adopted a randomized controlled trial method to conduct clinical research on spermidine extracted from wheat germ, targeting a population prone to skin aging. Research has confirmed that wheat germ extracts containing spermidine can promote cellular autophagy and slow down aging. This indicates that spermidine extracted from wheat germ has a significant promoting effect on cellular autophagy and anti-aging, contributing to the development of anti-aging research. Its profound clinical significance deserves further exploration.

**Keywords:** Spermidine; Extraction of wheat germ; Antioxidant; Autophagy anti-aging

## Introduction

Aging is a natural law that humans cannot escape, but advances in technology and medicine have made it possible for us to slow down this process and even improve some of the adverse effects of aging. Given this theory, some natural nutrients are increasingly being valued in the field of anti-aging, among which spermidine is one of the most concerned. Spermine originates from wheat germ and is like a gemstone hidden in everyday food. With the advancement of scientific research, the antioxidant and autophagic promoting properties of spermidine have gradually emerged to resist aging. However, there is still a lot of work to be explored regarding the specific efficacy and potential clinical applications of spermidine extracted from wheat germ. This study is based on the background that we hope to reveal the specific anti-aging effects of spermidine extracted from wheat germ through precise clinical research, and provide strong empirical support for future anti-aging research.

## 1. Chemical composition and mechanism of action of spermidine extracted from wheat germ

### 1.1 Composition analysis of spermidine extracted from wheat germ

Wheat germ is a natural food rich in various bioactive ingredients, and its spermidine is a polyamine compound with significant antioxidant and anti-aging functions. From a chemical composition perspective, spermidine is an important polyamine molecule in cells, composed of four amino groups and two methylene groups. The concentration of spermidine in wheat germ extract varies depending on factors such as variety and extraction method. Generally, quantitative and qualitative analysis of spermidine is carried out through techniques such as high-performance liquid chromatography (HPLC) and mass spectrometry.

Spermidine can induce autophagy, an intracellular degradation process that is crucial for clearing damaged or aging cellular components. The activation of autophagy is crucial for the survival and health of cells, as it can help cells recover and reuse damaged or aging cellular components, thereby maintaining normal cellular function. Spermine promotes autophagy through various pathways and protects cells from the effects of aging.

Ensuring the activity and purity of spermidine is crucial during the extraction process<sup>[3]</sup>. FNI GROUP only uses water to treat wheat germ and obtain natural spermidine components to ensure food safety and human health. These extraction methods ensure the acquisition of high-quality spermidine and maintain its activity for further functional research and application.

### 1.2 The mechanism of action of spermidine in regulating cellular autophagy

Spermine is a polyamine compound widely present in animal and plant cells, playing a key role in regulating autophagy. Research

has found that spermidine promotes autophagy by regulating the R signaling pathway and AMPK signaling pathway. MTOR (mammalian sirolimus target protein) is a negative regulator of cellular autophagy. When spermidine inhibits mTOR activity, the process of cellular autophagy is activated. On the other hand, AMPK (AMP activated protein 2 kinase) acts as an energy sensor and participates in regulating cellular metabolism. Spermine indirectly promotes the formation of autophagosomes by activating AMPK.

Spermidine also plays a role in autophagy by regulating the expression of autophagy related genes. It can upregulate the expression levels of key phagocytic proteins such as Beclin-1 and LC3, enhancing phagocytic activity. Both in vitro and in vivo experiments have shown that spermidine can significantly enhance autophagosome formation and lysosomal degradation functions, thereby enhancing the ability of cells to clear aging cells and damaged proteins. The above mechanism indicates that spermidine promotes cellular autophagy through multiple pathways, effectively delaying the aging process and providing protection for cellular health.

### **1.3 The effect of spermidine on cellular anti-aging**

As an important component of wheat germ, spermidine has a significant anti-aging effect on cells. The mechanism mainly includes overactivation of the phagocytic pathway to clear damaged or degraded components within the cell, maintain the balance of the intracellular environment, and thus prolong cell lifespan and function<sup>[7]</sup>. Spermidine can also regulate mitochondrial function, reduce oxidative stress and inflammatory response, which is of great significance for the prevention of age-related diseases such as neurodegenerative diseases and cardiovascular diseases. Clinical studies have shown that supplementation with spermidine can improve skin elasticity and texture, slow down the aging process of the skin, and demonstrate significant anti-aging effects.

## **2. The relationship between cellular autophagy and anti-aging**

### **2.1 Concept and regulatory mechanism of autophagy in cells**

Autophagy is a highly conserved process in which cells maintain intracellular homeostasis by breaking down and recovering damaged proteins and cells under specific conditions. The basic mechanism of cellular autophagy involves the formation of autophagosomes with a bi-layer membrane structure, which encapsulate [substances and fuse with lysosomes to form autolysosomes], and degrade the contents through their hydrolytic enzymes.

The regulatory mechanisms of cellular autophagy mainly focus on the following aspects. MTOR (mammalian target protein of sirolimus) plays a key role in regulating autophagy through signaling pathway 6. mTOR is a nutrient and energy sensor that activates and inhibits autophagy when nutrient or energy is abundant; When cells are in a state of nutrient depletion or energy stress, mTOR inhibition is eliminated and autophagy is initiated. The regulation of autophagy by AMPK (AMP activated protein kinase) cannot be ignored. AMPK can sense cellular energy balance at low energy levels, activate a series of downstream autophagy related genes, and promote autophagy. Tumor suppressor proteins such as p53 also play an important role in autophagy regulation, affecting the initiation and progression of autophagy by regulating the expression of autophagy related genes.

The latest research shows that cellular stress response, autophagosome generation, maturation, and other processes are strictly regulated by multiple signaling pathways involved in autophagy, such as MAPK signaling pathway 1 and PI3K Akt signaling pathway, all of which play regulatory roles at different stages of autophagy. The changes in the internal environment, such as endoplasmic reticulum stress response and oxidative stress, also have a direct and indirect impact on autophagy.

### **2.2 The role and mechanism of autophagy in anti-aging**

Autophagy is an important cellular process that maintains the stability of the intracellular environment and the normal functioning of cellular functions by breaking down and removing damaged organelles, proteins, and other components. In anti-aging, cellular autophagy plays multiple key roles. Autophagy can effectively eliminate aging cells and damaged mitochondria, preventing them from producing harmful reactive oxygen species and reducing oxidative damage to cells. Autophagy enhances cell survival and repair function by degrading abnormally or misfolded proteins, reducing the impact of protein aggregation on function. Autophagy plays an important role in regulating cellular metabolism, by regulating the recovery and reuse of nutrients, improving cellular tolerance to environmental stress, and delaying the aging process. Research has shown that enhancing cellular autophagy activity can prolong healthy lifespan, reduce the risk of age-related diseases, and has significant anti-aging potential.

### **2.3 The role of autophagy in cellular metabolic balance and clearance of aging cells**

Autophagy plays a crucial role in maintaining cellular metabolic balance and clearing aging cells. The autophagy process maintains the balance of intracellular metabolism by degrading and utilizing damaged proteins and organelles. This mechanism not only prevents the accumulation of harmful substances but also ensures the normal functioning of cells. The self process can identify and eliminate aging cells, avoiding tissue necrosis and functional regulation caused by their accumulation in the body. By activating the autophagy pathway, the clearance of

aging cells can be promoted, thereby delaying the aging process and the occurrence of related diseases in the body, providing new possibilities for anti-aging treatment.

### 3. Clinical study on the use of spermidine extracted from wheat germ in anti-aging

#### 3.1 Clinical study on the promotion of cellular autophagy by spermidine

In recent years, the study of the role of spermidine in cellular autophagy has attracted widespread attention. Based on this, a randomized double-blind controlled experiment was conducted to elucidate the promoting effect of spermidine extracted from wheat germ on cell autophagy and its clinical efficacy in anti-aging. The study selected multiple volunteers aged between 40 and 65, all of whom were at a normal level of physical aging. Participants were randomly divided into an experimental group and a control group, with the experimental group taking 150mg of SPERMD-W® dietary supplement extracted from wheat germ daily, The control group received a placebo.

The experiment lasted for 13 weeks, during which participants were regularly monitored for changes in skin texture, vascular elasticity, and blood routine indicators. Using biochemical detection technology to study the expression of cell related markers LC3 and B-1 in skin biopsy, and combining imaging detection methods to evaluate physiological indicators such as skin aging degree. The results showed that the protein levels of LC3 and Beclin-1 in the experimental group were significantly increased, indicating that their autophagy activity was significantly higher than that of the control group. The experiment specifically demonstrated the improvement of skin texture, vascular elasticity, and vascular growth by spermidine.

#### 3.2 Potential application value of spermidine in anti-aging treatment

Spermidine can effectively reduce the accumulation of senescent cells by promoting autophagy regulation in cells. Research has shown that autophagy can clear damaged proteins and organelles, maintaining normal cellular function and metabolic balance. Spermine activates autophagy related signaling pathways, such as mTOR inhibition and AMPK activation, allowing the autophagy process to proceed smoothly and thus delaying the aging process. Spermidine can also inhibit oxidative stress response, reduce free radical damage to cells, and further enhance the ability of cells to resist aging.

Spermidine has a significant positive impact on skin health. The skin is the first barrier of the human body to the external environment, and its aging not only affects appearance, but may also lead to a series of skin diseases. Wheat germ extract containing spermidine has been found to significantly improve skin quality, including reducing wrinkles, enhancing skin elasticity, and increasing skin moisture and radiance. These effects are mainly attributed to the promotion of autophagy in skin cells by spermidine, which improves the metabolism and function of skin cells.

The potential application value of spermidine in anti-aging treatment is significant, as it can play a role in promoting cellular autophagy, inhibiting oxidative stress, improving skin health, and preventing and treating age-related diseases. This discovery provides new directions and evidence for anti-aging research, and has important clinical significance and application prospects.

### 4. Conclusion

In the future, based on this study, we will further explore the mechanism and scope of action of spermidine extracted from wheat germ, and promote the wider application of such anti-aging substances in clinical medicine. At the same time, research in this area also provides new ideas and references for in-depth analysis of the causes of aging and the search for effective prevention and treatment measures.

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