

Review Article

Antioxidant and immunomodulatory activities of sericin and its applications in tumor prevention and treatment

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Received February 25, 2026; Accepted May 21, 2026; Epub June 15, 2026; Published June 30, 2026

Abstract: Sericin, a by-product of silk processing, shows great potential in tumor prevention and treatment owing to its excellent antioxidant and immunomodulatory properties. Its structure, which is rich in polar amino acids, endows sericin with high hydrophilicity and biocompatibility, allowing it to suppress cancer cell proliferation and induce apoptosis by scavenging reactive oxygen species and modulating the PI3K/Akt pathway and autophagy-related pathways. In the complex tumor microenvironment, sericin acts as an effective immune modulator. Instead of inducing widespread immunosuppression, it modulates the immune microenvironment by attenuating pro-tumorigenic chronic inflammation and potentially preserving or indirectly enhancing the cytolytic activity of natural killer cells. By balancing macrophage responses and alleviating oxidative stress-induced immune exhaustion, sericin helps restore immune surveillance. The antitumor effect of sericin is not achieved through nonspecific immune activation, but rather by restoring redox homeostasis and reshaping the inflammatory environment, thereby transforming the tumor microenvironment from a pro-cancer state to one conducive to immune surveillance. As a natural antioxidant and drug delivery carrier, sericin shows potential for targeted delivery and low toxicity in combined chemoradiotherapy and nanotechnology-enabled diagnostic and therapeutic systems. However, issues related to stability and production scalability still need to be addressed before its widespread clinical application.

Keywords: Sericin, antioxidant activity, immunoregulation, cancer prevention and treatment

Introduction

Sericin, one of the key components of silk, has been the subject of biomedical research since early studies on silk components and sericin-related genes [1]. The timeline of sericin research is shown in **Figure 1**.

Among the biological functions of sericin, direct in vitro and in vivo evidence of its antioxidant activity first emerged at the end of the 20th century [2, 3]. Subsequently, from the 2000s to the 2010s, research on the immune responses induced by sericin and its application as a biomaterial and tissue-engineering matrix increased significantly [1, 4]. During this period, enzymatically hydrolyzed or lower-molecular-weight sericin was also reported to inhibit the proliferation of tumor cells and induce their apoptosis [5]. The 2020s have witnessed the rise of sericin-based nanocarriers and pH-trig-

gered and charge-reversal drug delivery systems in preclinical cellular and animal models, demonstrating sericin's potential for targeted delivery in tumor prevention and treatment [6]. Meanwhile, as an advanced biomedical material, sericin holds great promise in the fields of tissue engineering, regenerative medicine, flexible electronics, and 3D bioprinting [7]. Nonetheless, despite the diverse functions and promising prospects of sericin, current research on sericin still faces key challenges, such as the in vivo stability of sericin-based biomaterials, the efficiency of targeted delivery, and obstacles to large-scale production for clinical translation. Given these circumstances, this paper aims to provide a credible reference for the clinical translation of sericin by comprehensively and systematically summarizing the latest progress and trends in research on sericin in antioxidation and immunomodulation, thoroughly analyzing its practical applications in

The role of sericin in antioxidant and immunomodulatory effects in tumors

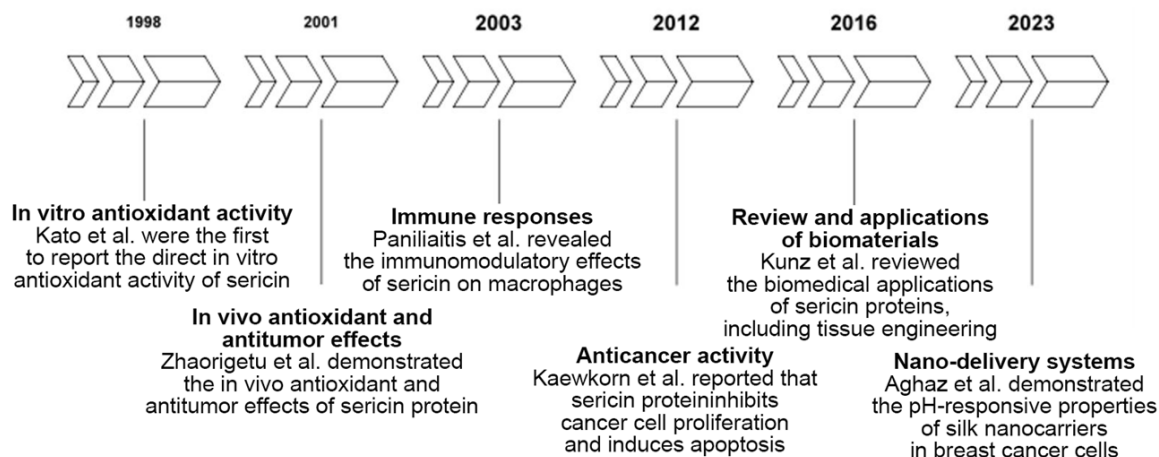


Figure 1. Sericin research timeline.

Table 1. Amino acid composition of sericin and associated functional characteristics

Amino acid	Approximate proportion	Functional characteristics
Serine	30-33%	Strong hydrophilicity and gel-forming ability
Threonine	8-10%	Enhancement of cell adhesion and signaling
Aspartic acid	18-20%	Provision of negative charges to facilitate drug binding
Glutamic acid	10-12%	Improvement of hydrogel stability
Lysine and arginine	Minor	Formation of hydrogen-bond networks to enhance structural stability

tumor prevention and treatment, and critically discussing its future directions.

Physicochemical properties and biological activities of sericin

Amino acid composition and molecular structural characteristics

As a water-soluble glycoprotein, sericin is of great significance in biomedicine owing to its unique amino acid composition and molecular structure. Sericin contains a high proportion of polar amino acids, with serine and aspartic acid accounting for more than 50%, which explains its strong hydrophilicity and underlies its excellent biocompatibility and solubility [8]. The major amino acid components of sericin and their associated functional characteristics are summarized in **Table 1**. The excellent flexibility of sericin is mainly attributed to its secondary structure, which is composed predominantly of random coils. In addition, its molecular weight range is usually 10-400 kilodaltons (kDa) and varies markedly depending on the extraction method. The dynamic plasticity of this structure provides an important basis

for the functional diversity of sericin [9]. It is noteworthy that its abundant polar amino acids make sericin readily modifiable, enabling its fabrication into carriers, such as hydrogels and nanoparticles, through chemical crosslinking or physical processing. Hence, sericin has the potential to be developed into a highly customizable platform for drug delivery and tissue engineering [8, 10]. This close relationship between structure and function provides a basis for the development of advanced biomaterials. In practical applications, recycling sericin from silk-reeling wastewater can further enhance the industrial value of this sustainable biomaterial and promote its sustainable development [11]. These excellent characteristics lay a necessary foundation for the biomedical utility of sericin.

Antioxidant properties

Sericin is rich in serine and phenolic hydroxyl groups in its molecular structure, which gives it remarkable antioxidant properties and enables it to effectively scavenge free radicals and reactive oxygen species (ROS). To fully utilize the biological activity of sericin, research-

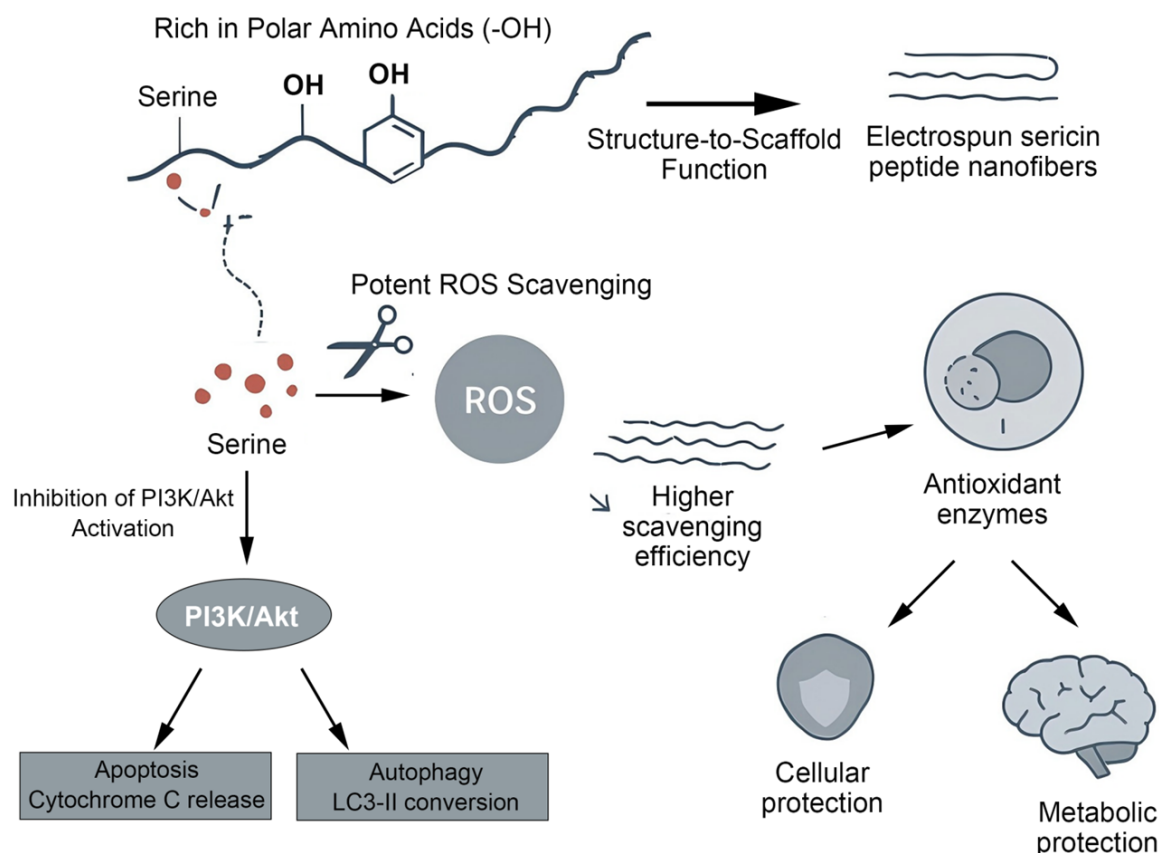


Figure 2. Antioxidant properties of sericin. -OH, hydroxyl group; ROS, reactive oxygen species; PI3K, phosphoinositide 3-kinase; Akt, protein kinase B; LC3, microtubule-associated protein 1 light chain 3.

ers have conducted extensive research on its structural modification. Through limited enzymatic hydrolysis with trypsin, the molecular structure of sericin can be modified to generate low-molecular-weight peptides. This, in turn, significantly enhances its free radical scavenging efficiency and functional performance [12, 13]. In material applications, optimizing the preparation process is an effective way to enhance sericin's antioxidant effects. For example, by using electrospinning to process an aqueous sericin polypeptide solution into nanofibers, the antioxidant performance can be improved [14]. In addition, the combination of sericin and plasma-modified polylactic acid can also enhance antioxidant performance and produce synergistic effects [15].

Sericin has multifunctionality and systemic protective potential. Sericin's biological activity varies notably depending on the source of the silkworm strain. For example, the silk protein from wild silkworms in southern Africa usually

has both antioxidant and antibacterial functions, which are important for the development of multifunctional composite materials [16]. Sericin can not only scavenge local ROS, but also participate in systemic oxidative stress regulation. Flavonoid-rich sericin can significantly alleviate oxidative stress-induced damage by regulating cholesterol metabolism and improving antioxidant enzyme activity, while also preserving metabolic function [17]. **Figure 2** shows the specific mechanism by which sericin exerts its antioxidant effects through free radical scavenging and enzymatic modulation. Sericin exerts its antitumor effects by scavenging ROS, which subsequently suppresses the phosphoinositide 3-kinase/protein kinase B (PI3K/Akt) pathway, leading to tumor cell apoptosis and autophagy. The interaction between sericin's antioxidant capacity and intracellular signaling is complex. While studies in regenerative models focus on its protective effects, evidence in specific cancer models, such as gastric cancer cell lines, suggests that sericin

may modulate the PI3K/Akt axis and induce autophagic responses. However, whether this induced autophagy is cytotoxic or cytoprotective remains to be fully elucidated across diverse tumor types. Also, the unique amino acid profile of sericin allows for the fabrication of electrospun nanofibers that serve as bioactive scaffolds for drug delivery. By neutralizing oxidative stress, sericin safeguards endogenous antioxidant enzymes, thereby providing comprehensive cellular and metabolic protection against oxidative damage [18, 19]. Current mechanistic evidence linking sericin to the PI3K/Akt/mechanistic target of rapamycin axis is often extrapolated from non-oncological models. It is critical to recognize that a signaling response observed in tissue preservation (where sericin acts as a cytoprotectant) cannot be directly equated to its role in a malignant tumor microenvironment (TME). Future research should prioritize pharmacological inhibition assays to confirm whether sericin-induced signaling changes are indeed the drivers of tumor suppression.

Basic immunomodulation

Owing to its special structural properties, sericin has outstanding biological activities in regulating inflammatory responses and the tissue microenvironment. It is a promising immunomodulatory material with broad application potential. Its core function is to effectively regulate the polarization of macrophages. A sericin composite hydrogel can promote macrophage polarization toward the M2 phenotype, thus significantly inhibiting the local inflammatory response, creating an immune microenvironment conducive to bone tissue regeneration, and further promoting the osteogenic differentiation of bone marrow mesenchymal stem cells [20]. This regulation has important practical value: a sustained-release sericin hydrogel scaffold loaded with dexamethasone can effectively repair rat mandibular bone defects by inducing macrophages to polarize toward the M2 phenotype [21]. While M2 polarization is pivotal for tissue regeneration, its role in the TME requires careful context-specific evaluation.

Sericin-mediated immunoregulation has broad applications in skin and soft tissue repair. According to recent reviews, sericin has application potential in skin wound healing because

of its biocompatibility and anti-inflammatory and antioxidant properties [22, 23]. When sericin is combined with other components, synergistic enhancement of biological activity can often be achieved. For example, a 3D biological scaffold prepared by combining sericin, collagen, and flavonoids further expands its versatility in wound healing [24]. Anti-inflammatory actions are further observed in certain pathological models. In diabetic wound healing, for instance, sericin-based plant extract-enriched hydrogels promote wound contraction by modulating pro-inflammatory/anti-inflammatory cytokine levels [25]. Sericin also demonstrates efficacy in regulating epidermal immunity and attenuating cell hyperproliferation in rats, thus alleviating psoriasis symptoms [26]. Therefore, instead of acting merely as an immune stimulator or inhibitor, sericin's clinical significance also stems from its precise reshaping of the local immune microenvironment and its adaptation to the needs of tissue regeneration or inflammation mitigation.

Sericin in tumor prevention and treatment

Antioxidant effects of sericin in tumor models: research progress

In various tumor models, sericin has shown marked therapeutic potential through its antioxidant effects. It inhibits cancer cell proliferation by regulating oxidative stress and related signaling axes. In colon cancer cell models, sericin reduces ROS to induce cancer cell apoptosis and inhibit tumor cell proliferation [5]. Sericin, as well as the complex it forms with silver nanoparticles, shows antineoplastic and tissue-preserving effects in 7,12-dimethylbenz[a]anthracene-induced breast cancer models by substantially mitigating oxidative stress-induced tissue damage [27]. It further exhibits targeted therapeutic potential in triple-negative breast cancer, evidenced by its ability to alleviate oxidative stress-driven cell proliferation through PI3K/Akt axis inhibition [28]. In MKN45 cells, a gastric cancer cell line, sericin activates autophagy-related pathways and regulates the expression of oxidative stress-related proteins to effectively inhibit tumor spread [29]. Regarding the mechanistic sequence, the suppression of PI3K/Akt signaling likely acts as a pivotal mechanism connecting sericin's antioxidant properties to its pro-apoptotic effects. While sericin's immediate action may stem

from ROS scavenging, the sustained downregulation of Akt suggests a deeper modulation of cell survival signaling. Furthermore, sericin-induced autophagy in triple-negative breast cancer and MKN45 cells appears to be cytotoxic rather than cytoprotective, as it coincides with profound Akt inhibition and increased cleaved caspase expression, indicating that sericin-induced stress eventually overwhelms cellular adaptive capacity.

Sericin in tumor prevention and treatment via immunomodulation

During tumor occurrence and development, the complex tumor immune microenvironment (TIME) plays a crucial role by altering the dynamic interactions of multiple immune cells and signaling molecules. By regulating TIME, sericin acts as an immunomodulatory agent. For example, a receptor tyrosine kinase-like orphan receptor 1 small interfering RNA (siRNA)-equipped nano-targeted delivery system can inhibit triple-negative breast cancer cell proliferation and enhance antitumor immune responses [30]. In this system, sericin serves as a functional delivery vehicle, using its high biocompatibility to shield receptor tyrosine kinase-like orphan receptor 1 siRNA from degradation. While the primary antitumor effect is driven by siRNA-mediated gene silencing, sericin's inherent properties provide a supportive microenvironment for treatment. Although studies have observed that sericin itself has the potential to inhibit the PI3K/Akt pathway, this inherent biological activity should be regarded as auxiliary support for major therapies, such as siRNA-mediated gene silencing, rather than an independent antitumor mechanism [31]. Complex signaling networks, such as imbalances in cytokines and chemokines in the TME, will further inhibit effector T cell recruitment and activation, exacerbating the immunosuppressive state [32]. In the psoriasis model, sericin inhibits the excessive proliferation of epidermal cells and significantly ameliorates the local immune response by downregulating pro-inflammatory cytokines [26]. Sericin-based biomaterials, by virtue of their favorable biocompatibility and regulation of inflammatory responses, help accelerate wound healing by modulating adaptive immune responses, providing a new approach for the repair of wounds or tissue defects after tumor surgery [33]. How-

ever, it is necessary to carefully distinguish the immunomodulatory logic of sericin in different pathological scenarios. In bone defect or skin wound models, sericin attenuates inflammation and promotes tissue regeneration by inducing macrophage polarization toward the M2 phenotype. However, in the TME, M2-type macrophages are usually associated with immunosuppression and the promotion of tumor progression. Therefore, the true potential of sericin in the tumor context may not stem from simple induction of M2 polarization, but rather from its antioxidant properties that clear ROS, thereby indirectly alleviating the immune exhaustion of natural killer (NK) cells or T cells and maintaining basic immune surveillance capacity.

Opportunities and challenges of sericin in tumor immunomodulation

Research on the potential of sericin in tumor immunomodulation remains a burgeoning field characterized by promising biochemical properties but a notable lack of direct in vivo immunological evidence. Current hypotheses regarding its efficacy often rely on extrapolations from non-oncological models, necessitating a cautious interpretation. Oxidative stress is recognized as a key driver of immune cell dysfunction within the TME, particularly regarding the inactivation of NK cells. While some studies suggest that antioxidants can restore NK cell cytotoxicity in various pathological states [34], direct evidence demonstrating that sericin preserves NK cell killing activity specifically within a tumor-bearing host remains scarce. In this context, sericin is more accurately characterized as a homeostatic stabilizer rather than a direct immune activator. Its primary contribution may lie in mitigating chronic oxidative stress, thereby theoretically preventing the functional exhaustion of effector cells, though this requires further validation through direct tumor-immunology assays. In tissue repair and bone regeneration, sericin's ability to promote an anti-inflammatory M2-like macrophage phenotype is an advantage. However, in the TME, M2-polarized tumor-associated macrophages are predominantly pro-tumorigenic and facilitate immune evasion [35, 36]. Therefore, the narrative that sericin optimizes the immune landscape via M2 induction is inherently con-

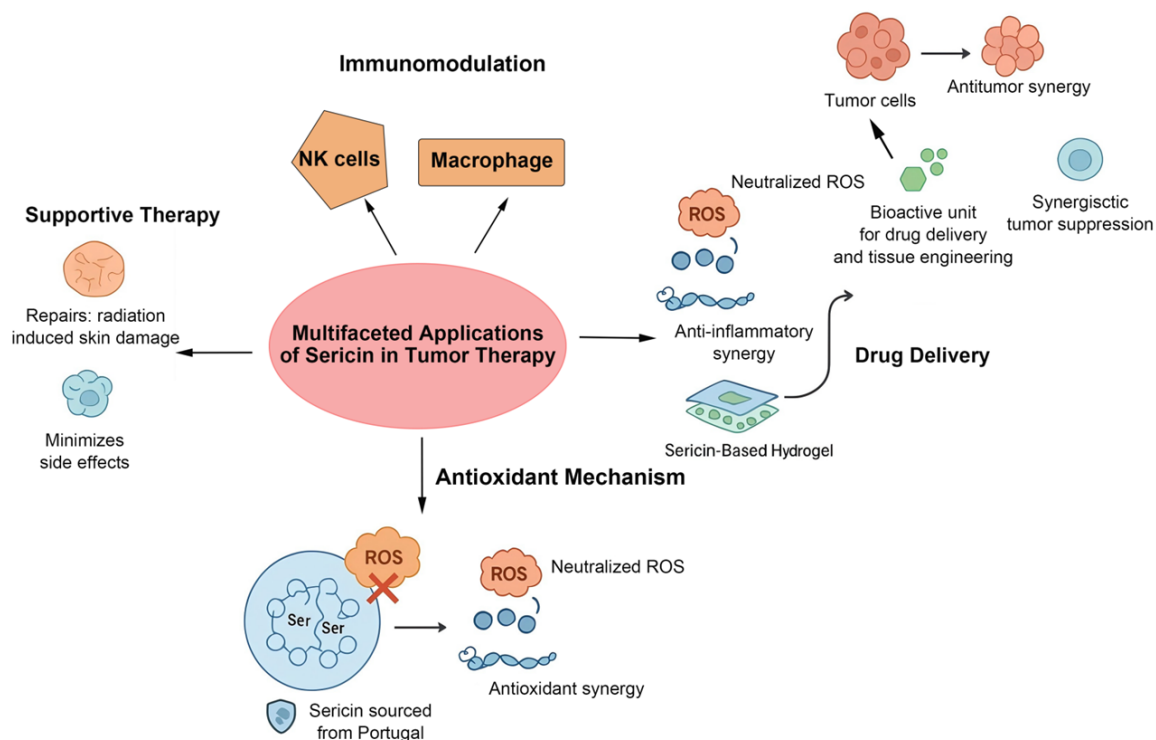


Figure 3. Sericin's adjuvant applications as a natural antioxidant. NK, natural killer; ROS, reactive oxygen species; Ser, Sericin.

tradictory. Its true potential may be confined to the pre-malignant stage, where it inhibits DNA damage caused by chronic inflammation, potentially preventing the initial transformation of macrophages into a tumor-promoting phenotype.

The current literature suffers from a lack of high-resolution immunophenotyping regarding sericin's influence on critical populations such as CD8⁺ T cell infiltration or the modulation of regulatory T cells. To bridge this gap, future research must move beyond indirect inferences. Until direct interventional data in tumor-bearing models are available, sericin's role in tumor immunity should be viewed as a supportive mechanism for maintaining microenvironmental homeostasis rather than a stand-alone immunotherapy. Future research should clarify, through high-resolution immunophenotypic analysis, whether macrophages modulated by sericin in tumor tissues have unique functional subtypes distinct from the conventional M2 phenotype, thus avoiding the direct application of findings from regenerative immunity to tumor immunity.

Application prospects of sericin in comprehensive tumor prevention and treatment strategies

The adjuvant application of sericin as a natural antioxidant

Sericin shows unique potential in the comprehensive prevention and treatment of tumors, and its serine-rich structure enables it to efficiently scavenge ROS and reduce oxidative stress-induced damage. This natural antioxidant activity supports its role as an important building block of advanced treatment modalities [37]. **Figure 3** provides a detailed illustration of sericin's antioxidant mechanisms and various applications in tumor adjuvant therapies. Its potent antioxidant activity has been verified in sericin from different sources. Portugal-sourced sericin, for example, effectively inhibits tumor cell-induced oxidative damage [38]. In addition, in vitro antioxidant and anti-inflammatory synergy has been reported in bacterial silk-like biopolymer-derived sericin [39]. This basic activity makes it possible for sericin to optimize tumor treatment planning: the sericin-based hydrogel and antioxidant bio-

adhesive combination is able to lower the risk of breast cancer recurrence while effectively repairing radiation-induced skin damage; hence, sericin is promising in comprehensive adjuvant treatments [40]. Additionally, sericin and melatonin are prepared as wound-healing patches, which exert antioxidant effects to inhibit melanoma progression, demonstrating sericin's value in postoperative or local adjuvant therapies [41].

Owing to its characteristics as a multifunctional biomaterial building block, the adjuvant antioxidant effect of sericin has been further explored. Its excellent structural characteristics, properties, and biological activity make it stand out in the selection of biomedical materials [8, 42]. By virtue of its amino acid composition and chemical groups, sericin shows unique functions in nanotechnology, such as acting as a reducing, capping, or stabilizing agent in the synthesis of silver nanoparticles or other advanced carriers [43]. Chemical modifications can also be used to process it into novel amphiphilic molecules, such as a lipopeptide surfactant, effectively enhancing its utility in drug delivery systems [44]. Given its high modifiability, sericin has become central to complex biological interface construction: as an established multifunctional biomaterial, it is capable of promoting tissue-engineered heart valve endothelialization via the regulation of cellular activity [45]. Sericin is expected to be applied beyond traditional biomaterial applications, such as in next-generation cardiovascular electronic devices, by leveraging its asymmetric amino acid structure to develop implantable and degradable piezoelectric thin-film energy harvesters [46]. Therefore, sericin has broad application breadth and depth in biomedical engineering.

Multifunctional roles of sericin in combined radiotherapy and chemotherapy

Sericin facilitates combined radiotherapy and chemotherapy through a dual contribution: acting as a robust structural scaffold to optimize drug delivery and serving as a bioactive adjuvant to modulate survival signaling. This synergy significantly enhances therapeutic efficacy while minimizing systemic off-target effects.

Sericin as a structural scaffold for precision and safety: As a biocompatible and modifiable carrier, sericin improves the pharmacokinetics

and safety profiles of conventional therapies. For instance, engineered sericin-tagged layered double hydroxide nanocarriers have been utilized for the co-delivery of pemetrexed and zinc oxide quantum dots, enhancing both chemotherapy precision and tumor diagnostic imaging [47]. Furthermore, sericin-modified zeolitic imidazolate framework-8 nanoplateforms increase the delivery efficiency of chemotherapeutic agents, thereby promoting tumor cell apoptosis while concurrently reducing systemic toxicity [48]. The high biocompatibility of self-stabilized sericin-based nanoparticles also provides a safety advantage, significantly attenuating toxicity induced by potent agents such as adriamycin [49].

Sericin as a bioactive adjuvant in signaling modulation: Beyond its role as a physical vehicle, sericin's intrinsic biochemical properties contribute directly to tumor suppression. In composite nanoplateforms such as sericin/propolis/5-fluorouracil, sericin does not function merely as an inert matrix; rather, it actively aids in enhancing chemotherapy by suppressing the PI3K/Akt/mechanistic target of rapamycin signaling axis to inhibit colorectal cancer cell proliferation [50].

Context-dependent redox homeostasis in therapy: The therapeutic utility of sericin's antioxidant capacity must be evaluated through a context-dependent lens to avoid interfering with ROS-dependent treatments. While high intracellular ROS levels are essential for triggering immunogenic cell death during certain chemotherapies, chronic low-level oxidative stress in the TME typically drives tumor progression and immune exhaustion. Therefore, in the therapeutic phase, sericin does not function as a broad-spectrum antidote that quenches all ROS; instead, it acts as a homeostatic regulator. It reduces pro-tumoral chronic stress in the microenvironment without necessarily neutralizing the localized, high-intensity ROS bursts required for the therapeutic induction of apoptosis [51].

Utility of sericin in drug delivery systems

Sericin has emerged as a versatile drug delivery platform, with its role shifting from that of a simple encapsulation matrix to that of a sophisticated, responsive vehicle. Its high content of polar amino acids, inherent biodegrad-

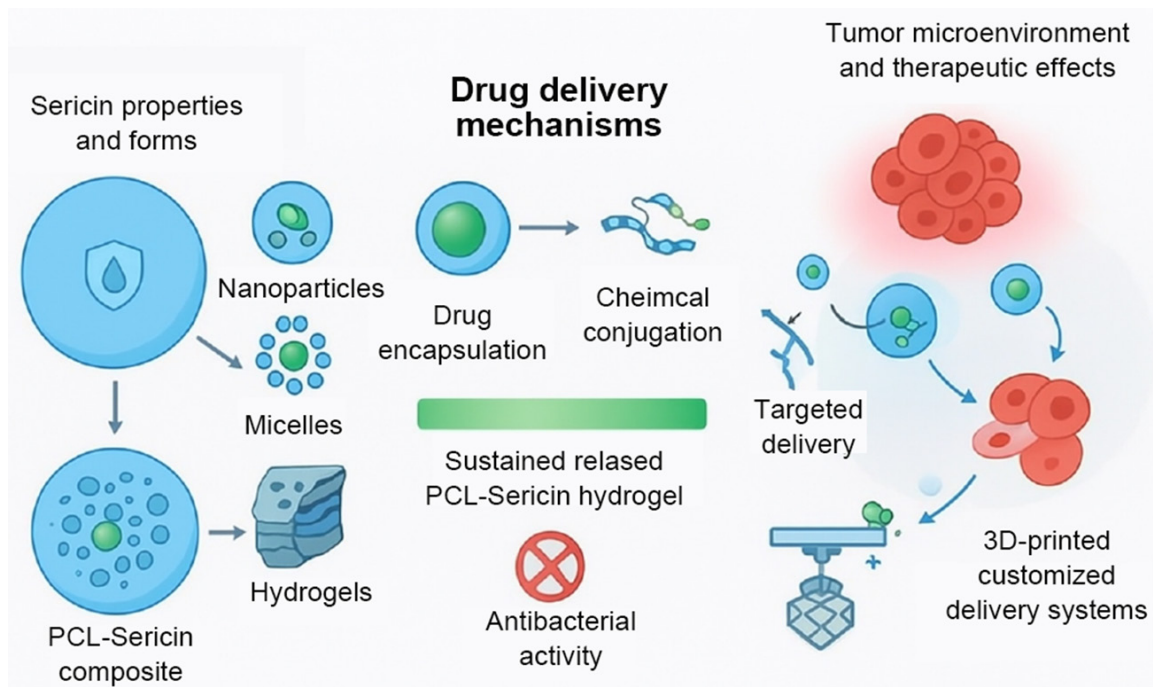


Figure 4. Applications of sericin in drug delivery systems. PCL, polycaprolactone; 3D, three dimensional.

ability, and low immunogenicity provide a unique chemical basis for both physical scaffolding and precise molecular targeting [19], as shown in **Figure 4**.

Sericin as a structural matrix and composite scaffold: In its foundational role, sericin serves as a biocompatible matrix for stabilizing therapeutic agents. When combined with synthetic polymers such as polycaprolactone, sericin forms a hydrogel matrix that ensures the sustained release of drugs while providing ancillary antibacterial activity [52]. Furthermore, sericin is frequently utilized alongside fibroin to construct composite scaffolds, using the mechanical strength of fibroin and the biological signaling of sericin to create a biomimetic environment for tissue-integrated delivery [53].

Intelligent responsiveness and targeted engineering: The true clinical potential of sericin lies in its transition into an intelligent, stimuli-responsive system tailored for the TME. By exploiting the acidic pH of the TME, sericin-assisted nanocarriers achieve site-specific drug release, thereby increasing intracellular drug concentrations while minimizing systemic exposure. For example, pH-responsive sericin-based nanocarriers have successfully co-delivered resveratrol and melatonin to synergisti-

cally suppress breast cancer cell proliferation [6]. Beyond passive accumulation, sericin can be engineered as a coating for magnetic nanoparticles to facilitate externally guided delivery. Surface modifications of these sericin-coated platforms enable the recognition of specific cancer cell receptors, significantly enhancing treatment specificity and stability [54]. The versatility of sericin extends to digital light processing 3D printing technology [55]. As a highly customizable silk by-product, sericin can be used to fabricate personalized drug delivery systems with complex architectures, representing a shift toward precision drug delivery.

Structure-function relationships: impact of extraction and source heterogeneity

The biological efficacy of sericin is intrinsically linked to its molecular weight (MW) distribution, which is largely dictated by the extraction technique [56]. Thermal extraction generally preserves a broad MW range (10-300 kDa), maintaining the protein's native secondary structure, whereas acidic or alkaline processing yields low-MW peptides (<20 kDa) through extensive hydrolysis [57]. These lower-MW hydrolysates often exhibit enhanced antioxidant activity due to the increased exposure of polar amino acid residues, yet they may elicit differ-

ent immunogenic profiles compared to their high-MW counterparts. Furthermore, source materials varying from domesticated *Bombyx mori* to diverse wild silkworm species introduce distinct amino acid polarities and glycosylation patterns. A rigorous understanding of these extraction-dependent heterogeneities is essential for ensuring the reproducibility and safety of sericin-based clinical interventions.

Challenges in clinical translation and safety

Despite the versatility of sericin as a biomaterial, its clinical implementation is fundamentally constrained by unresolved safety concerns, particularly regarding its long-term immunotoxicological profile. As a non-human protein, sericin necessitates a more rigorous evaluation than that provided by simple biocompatibility assays. Regarding immunogenicity and hypersensitivity, a primary translational hurdle is the risk of immunoglobulin E-mediated hypersensitivity and the potential formation of anti-sericin antibodies upon repeated exposure. Future studies must identify specific allergenic epitopes within sericin structure and assess the risk of complement activation-related pseudoallergy to ensure patient safety. Regarding standardization and good laboratory practice (GLP) compliance, most current evidence is derived from academic laboratory settings. To bridge the translational gap, it is mandatory to establish standardized, clinical-grade extraction and purification protocols. Furthermore, comprehensive toxicological assessments, including chronic toxicity and reproductive toxicity, must be conducted under GLP standards to meet regulatory requirements. Regarding biological complexity, moving beyond small animal xenograft models is essential. Large animal studies are required to accurately evaluate pharmacokinetics, biodistribution, and the complex interaction between sericin and a more human-like immune system.

Conclusion

Sericin has excellent biocompatibility, good modifiability and a unique molecular structure rich in polar amino acids. It has transitioned from a silk by-product to a multifunctional biomaterial that can help prevent and treat tumors. Based on the antioxidant and immunoregulatory effects of sericin, this paper systematically summarizes its latest application ad-

vances: sericin modulates macrophage polarization to rebalance the TIME. It modulates the inflammatory landscape to support immune surveillance, bridging the gap between potent antioxidation and targeted immunoregulation. Sericin is multifunctional and can be used to build intelligent nanocarriers and achieve precise delivery based on pH responsiveness. It is also promising in combined chemotherapy/radiotherapy strategies and nanodiagnostic and therapeutic systems. However, the leap from the laboratory to the clinic requires moving beyond fragmented mechanistic inferences. The field must prioritize addressing the “translational valley of death” by focusing on systematic immunotoxicological evaluations and GLP-compliant manufacturing. Only by establishing a rigorous safety and standardization framework can the therapeutic potential of sericin observed in preclinical settings be successfully realized in clinical oncology.

Authors' contributions: Chen Songning determined the review theme and research framework, conducted the systematic literature search and screening, organized and analyzed the literature, and drafted the paper; Lv Ping was in charge of paper revision, quality control, proofreading, supervision, and management; Yang Fengbo and Ding Daxiong prepared the figures; Deng Yi and Gao Yang assisted in literature screening and quality evaluation, while providing suggestions for modifying the paper's logical framework. He Linli edited and organized the tables.

Disclosure of conflict of interest

None.

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