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REVIEW ARTICLE

Title: Research Progress on Mongolian Medicine Improving Tumor Micro environment

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Abstract: Mongolian medicine, rooted in centuries-old traditions, has garnered increasing attention for its potential in improving the tumor microenvironment (TME). This review explores recent research progress in utilizing Mongolian medicinal practices to modulate the TME, focusing on their impact on tumor growth, metastasis, and therapeutic resistance. Key components of Mongolian medicine, including herbal remedies, dietary interventions, and therapeutic approaches such as acupuncture and moxibustion, are discussed in relation to their effects on immune responses, inflammation levels, and angiogenesis within the TME. Additionally, advancements in understanding the molecular mechanisms underlying these effects are highlighted, providing insights into potential synergies with conventional cancer therapies. By elucidating the role of Mongolian medicine in TME modulation, this review aims to contribute to the development of integrative approaches for cancer treatment and management.

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1. Introduction

Cancer encompasses a diverse group of diseases characterized by abnormal cell growth that can invade nearby tissues and metastasize distant organs [1]. According to the World Health Organization (WHO), cancer is one of the leading causes of morbidity and mortality globally, with approximately 10 million deaths attributed to cancer each year [2]. The burden of cancer varies significantly across different regions and populations [3], influenced by factors such as genetics, lifestyle choices, environmental exposures, and access to healthcare. In early detection and treatment have improved survival rates for certain cancers. However, challenges persist, particularly in treating aggressive and metastatic forms of the disease. The emergence of resistance to chemotherapy and targeted therapies further complicates treatment outcomes, underscoring the urgent need for innovative therapeutic strategies.

Central to cancer biology is the concept of the tumor microenvironment (TEM), a complex network of cells, blood vessels, signaling molecules, and extracellular matrix components that surround and support tumor cells [4]. The TME is dynamic and heterogeneous, influencing tumor behavior in profound ways [4]. It is characterized by hypoxia (low oxygen levels), acidity, immune cell infiltration, and chronic inflammation, all of which contribute to tumor growth, invasion, and metastasis [5] [6]. Key components of the TME include cancer-associated fibroblasts (CAFs) [7], immune cells (such as tumor-associated macrophages, T cells, and myeloid-derived suppressor cells), endothelial cells, and various signaling molecules [8] (cytokines, growth

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factors, and extracellular matrix proteins). Crosstalk between tumor cells and these components can promote cancer cell survival, induce angiogenesis (formation of new blood vessels), and create an immunosuppressive environment that shields tumors from immune surveillance.

Understanding the mechanisms that govern TME dynamics is crucial for developing targeted therapies that disrupt tumor-promoting interactions while preserving normal tissue function [9]. Recent research has identified several pathways and molecular mechanisms involved in TME modulation [10], offering potential targets for therapeutic intervention. For instance, the hypoxic conditions within the TME activate hypoxia-inducible factors (HIFs), transcription factors that regulate genes involved in angiogenesis, metabolism, and resistance to therapy. Additionally, inflammatory cytokines such as tumor necrosis factor-alpha (TNF-α) and interleukin-6 (IL-6) contribute to chronic inflammation, which can promote tumor growth and metastasis. Furthermore, the role of immune cells in shaping the TME has garnered significant attention [11]. Tumor-associated macrophages (TAMs) exhibit diverse phenotypes ranging from pro-inflammatory (M1-like) to immunosuppressive (M2-like) [12], influencing both anti-tumor immune responses and tissue remodeling processes. Strategies aimed at reprogramming TAMs towards an anti-tumor phenotype represent a promising avenue for therapeutic development [13][14].

Amidst the complexity of cancer biology, traditional medicine systems like Mongolian medicine offer unique insights and therapeutic approaches that complement conventional treatments. Mongolian medicine, deeply rooted in nomadic culture and the natural environment of the Mongolian steppes, encompasses a rich tradition of herbal remedies, dietary practices, and therapeutic modalities aimed at restoring balance and harmony within the body [15]. Mongolian medicine has integrated knowledge from diverse cultural traditions, including Chinese, Tibetan, and indigenous Mongolian practices [16]. Herbal medicines derived from plants endemic to the region are often central to treatment regimens, with formulations tailored to address specific health conditions, including cancer. Recent research has increasingly explored the potential of Mongolian medicinal practices in modulating the TME and improving cancer outcomes [17]. Herbal remedies, in particular, have garnered attention for their bioactive compounds that exhibit anti-inflammatory, antioxidant, and immunomodulatory properties. These properties are critical for disrupting tumor-promoting pathways within the TME while enhancing anti-tumor immune responses. Studies have highlighted the anti-angiogenic effects of certain Mongolian medicinal plants [18], which inhibit the formation of new blood vessels crucial for tumor growth and metastasis. Moreover, bioactive compounds found in these herbs have been shown to inhibit the expression of pro-inflammatory cytokines and signaling pathways associated with tumor progression [19]. In addition to herbal therapies, other aspects of Mongolian medicine such as dietary interventions and lifestyle practices play a pivotal role in supporting overall health and immune function [20]. Dietary components rich in antioxidants and phytochemicals can mitigate oxidative stress and inflammation within the TME, thereby enhancing the efficacy of conventional therapies.

2. Principles of Mongolian Traditional Medicine

Mongolian medicine views health as a balance between the individual (body, mind, and spirit) and their environment [21]. It emphasizes the dynamic interaction between internal factors (ayu, or vital life force) and external influences (climate, diet, lifestyle) [22]. While treatment focuses not only on curing illness but also on preventing disease by maintaining harmony within the body and its surroundings [23]. Similar to other East Asian medical traditions, Mongolian medicine employs a Five Elements theory (Earth, Water, Fire, Wood, Metal). Each element corresponds to specific organs, seasons, emotions, and qualities. Practitioners use the Five Elements theory to diagnose imbalances in the body and prescribe treatments that restore harmony [24]. For example, an excess of "Fire" element might manifest as fever or inflammation, requiring treatments to cool and balance the body. Similar to Chinese medicine, pulse diagnosis is crucial in Mongolian medicine. Practitioners assess the pulse at different points to detect subtle changes that indicate health imbalances. Basis on examination of the tongue's color, coating, and shape provides further insights into a person's health condition. Mongolian medicine mainly uses herbal medicine for treatment. Medicinal plants and herbs form the backbone of Mongolian medicine. Specific herbs are selected based on their properties (cooling, warming, tonifying) and their ability to restore balance. Key components or herbs commonly used in Mongolian medicine include "Shatar" (Allium polyrhizum), known for its antibacterial properties and use in treating digestive disorders; "Tsagaan ezen" (Rhodiola quadrifida) [25], valued for its adaptogenic effects in reducing stress and enhancing resilience; "Nogoon tsagaan tsetseg" (Astragalus membranaceus) [26], recognized for its immune-boosting properties and support for respiratory health; "Zogan tsegi" (Artemisia spp.), used in moxibustion for its warming and purifying effects; and "Mongol noyon" (Cynomorium songaricum) [27], prized for its aphrodisiac and rejuvenating properties. These herbs are selected based on their therapeutic qualities and are often incorporated into formulations tailored to treat specific health conditions, reflecting the holistic approach of Mongolian traditional medicine in promoting overall well-being and resilience. Mongolian medicine also involves inserting fine needles into specific points on the body to stimulate energy flow (Qi) [28]. Moxibustion uses burning mugwort (moxa) to warm these points, promoting healing and balance. Food is considered medicinal in Mongolian tradition. Recommendations are

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tailored to an individual's constitution and health condition to support healing and prevent illness.

3. Mechanisms of Mongolian medicine for tumor microenvironment

Mongolian traditional medicine represents a holistic healthcare system that integrates ancient wisdom with modern scientific insights to effectively interact with the tumor microenvironment (TME) [29]. This approach is characterized by a diverse array of herbal therapies, diagnostic techniques, and holistic treatment modalities that aim toaddress cancer at its core while promoting overall well-being [30].

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Central to the therapeutic efficacy of Mongolian medicine are its herbal components, each selected for their specific medicinal properties and therapeutic effects within the TME. Herbs such as "Shatar" (Allium polyrhizum) and "Tsagaan ezen" (Rhodiola quadrifida) are renowned for their potent antioxidant and anti-inflammatory properties. These herbs play critical roles in reducing oxidative stress and chronic inflammation within the TME, creating an environment that is less conducive to tumor growth and metastasis. By scavenging free radicals and modulating inflammatory pathways, they help to maintain cellular homeostasis and inhibit the proliferation of cancerous cells. In addition to their antioxidant and anti-inflammatory effects, such herbs in Mongolian medicine as "Mongol noyon" (Cynomorium songaricum) and "Nogoon tsagaan tsetseg" (Astragalus membranaceus), exhibit significant immunomodulatory properties. These herbs enhance the body's immune responses against cancer cells by activating cytotoxic T cells, natural killer (NK) cells, and dendritic cells within the TME. By bolstering immune surveillance and promoting cytotoxicity against tumor cells, these herbs contribute to the body's natural defense mechanisms against cancer. Complementary therapies in Mongolian medicine further support these effects. Moxibustion, a technique utilizing "Zogan tsegi" (Artemisia spp.), is used to enhance local circulation and lymphatic drainage. Improved circulation facilitates the delivery of immune cells and therapeutic agents to the site of the tumor, while enhanced lymphatic drainage aids in the removal of metabolic wastes and toxins from the TME. These therapies not only support the efficacy of herbal treatments but also contribute to overall immune function and systemic health (Table 1).

Diagnostic methods play a crucial role in Mongolian medicine, providing insights into the underlying imbalances contributing to cancer progression. Pulse diagnosis, for instance, involves the assessment of pulse qualities at various points on the radial artery [31].

Practitioners interpret pulse characteristics to identify systemic imbalances such as stagnation, deficiency, or excess, which may influence cancer development and progression. Tongue examination is another diagnostic tool used to assess the body's internal state, with changes in tongue appearance indicating specific health conditions and guiding herbal prescriptions [32].

Personalized treatment strategies in Mongolian medicine are tailored based on diagnostic findings and individual patient needs. By addressing underlying imbalances identified through diagnostic methods, practitioners aim to restore harmony and balance within the body [33]. Herbal formulations are customized to target specific aspects of cancer pathophysiology, whether it be reducing inflammation, enhancing immune function, or supporting detoxification processes within the TME.

Beyond its specific therapeutic interventions, Mongolian medicine emphasizes a holistic approach to health and well-being. This approach acknowledges the interconnectedness of body, mind, and spirit, emphasizing the importance of lifestyle factors, diet, and emotional health in cancer prevention and treatment. Recommendations for dietary modifications, stress management techniques, and supportive therapies are integral components of holistic cancer care in Mongolian medicine.

Scientific research into the mechanisms of Mongolian traditional medicine's efficacy in cancer treatment is advancing, with studies exploring the biochemical pathways, molecular interactions, and clinical outcomes associated with herbal therapies and integrative treatments. Emerging evidence supports the role of Mongolian medicine in enhancing conventional cancer therapies, improving patient outcomes, and reducing treatment-related side effects.

Challenges remain in integrating Mongolian traditional medicine into mainstream oncology, including issues related to standardization, quality control [21], and cross-

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cultural understanding of diagnostic and treatment practices [34].

Table 1. Effects of Mongolian Medicines on Tumor Microenvironment

Mongolian Medicine	Main Components	Mechanism of Action	Effects on Cellular Composition	Effects on Extracellular Matrix	Effects on Vascular Network	Immune Regulation	Metabolic Environment	Inflammatory Response
Ginseng	Ginsenosides	Promotes apoptosis	Reduces tumor cell proliferation	Alters ECM structure	Inhibits angiogenesis	Activates immune cells	Lowers metabolic rate	Inhibits inflammation
Notoginseng	Notoginsenosides	Antioxidant effects	Enhances immune cell activity	Strengthens ECM support	Enhances vascular integrity	Inhibits immune evasion	Increases oxygen supply	Alleviates inflammation
Astragalus	Astragalus polysaccharides	Inhibits proliferation pathways	Enhances T cell function	Reduces ECM stiffness	Inhibits angiogenesis	Enhances immune surveillance	Regulates pH levels	Reduces chronic inflammation
Ganoderma	Ganoderma polysaccharides, Ganoderic acids	Regulates gene expression	Enhances NK cell activity	Promotes ECM degradation	Increases vascular permeability	Inhibits immunosuppressive cells	Reduces acidic environment	Inhibits inflammatory factors
Salvia miltiorrhiza	Tanshinones, Salvianolic acids	Anti-angiogenesis	Inhibits tumor cell migration	Inhibits ECM remodeling	Inhibits angiogenesis	Enhances immune response	Regulates tumor metabolism	Inhibits inflammation
Coptis chinensis	Berberine, Coptisine	Anti-proliferation, pro-apoptosis	Inhibits tumor cell proliferation	Inhibits ECM synthesis	Inhibits angiogenesis	Activates immune cells	Improves hypoxic environment	Inhibits inflammation
Dandelion	Taraxacin, Flavonoids	Antioxidant, anti-proliferation	Enhances immune cell activity	Enhances ECM degradation	Inhibits angiogenesis	Enhances immune surveillance	Regulates tumor metabolism	Inhibits inflammatory response
Atractylodes	Atractylodes lactone, Atractylodin	Anti-inflammatory, immune regulation	Promotes immune cell proliferation	Strengthens ECM structure	Promotes angiogenesis	Inhibits immune evasion	Increases metabolic efficiency	Inhibits chronic inflammation
Shatar	Allium polyrhizum	Antioxidant, anti-inflammatory	Inhibits tumor growth	Modulates ECM structure	Inhibits angiogenesis	Enhances immune cell activity	Regulates oxidative stress	Reduces inflammation
Tsagaan ezen	Rhodiola quadrifida	Adaptogenic, anti-tumor	Enhances immune response	Stabilizes ECM	Inhibits angiogenesis	Modulates immune system	Improves metabolic function	Reduces oxidative stress
Nogoon Tsagaan tsetseg	Astragalus membranaceus	Immunomodulatory, anti-proliferative	Enhances T cell function	Enhances ECM integrity	Inhibits angiogenesis	Enhances immune surveillance	Modulates pH and hypoxia	Reduces inflammation
Zogan tsegi	Artemisia spp.	Anti-tumor, anti-inflammatory	Inhibits tumor cell proliferation	Alters ECM composition	Inhibits angiogenesis	Modulates immune response	Regulates oxidative environment	Reduces chronic inflammation
Mongol noyon	Cynomorium songaricum	Anti-tumor, immunomodulatory	Inhibits tumor growth	Modulates ECM dynamics	Inhibits angiogenesis	Enhances immune function	Improves metabolic resilience	Reduces inflammation

Efforts to validate traditional knowledge through rigorous scientific inquiry and collaborative research partnerships are essential for expanding the evidence base and enhancing the acceptance of Mongolian medicine in cancer care [35].

4. Conclusion

The tumor microenvironment represents a complex and dynamic milieu that plays a pivotal role in cancer progression and therapy resistance. Understanding the molecular mechanisms underlying TME modulation is crucial for developing effective therapeutic strategies that target tumor-promoting interactions while preserving normal tissue function.

Mongolian medicine, with its rich tradition of herbal remedies and holistic healing practices, offers promising avenues for TME modulation and cancer treatment. By harnessing the bioactive compounds and therapeutic principles of Mongolian medicinal plants, researchers aim to develop innovative therapies that complement existing treatment modalities and improve patient outcomes.

Moving forward, continued research efforts are needed to elucidate the specific mechanisms by which Mongolian medicinal practices influence the TME and to evaluate their efficacy in clinical settings. Integrating traditional medicine systems with modern oncology holds great potential for advancing personalized cancer care and addressing the multifaceted challenges posed by this complex disease.

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