Research Progress of Mongolian Medicine and Effective Material Basis in the Treatment of Rheumatoid Arthritis

Wuriliga, Cuilan BAI*

College of Mongolian Medicine and Pharmacy, Inner Mongolia Medical University, Huhhot 010010, China

Abstract This paper reviews and summarizes the material basis that contribute to the efficacy of Mongolian medicine, as well as the advancements in research concerning both single drugs and compound prescriptions in Mongolian medicine for the treatment of rheumatoid arthritis (RA). The objective is to provide a reference for further in-depth research and the clinical application of Mongolian medicine in the management of RA, while also offering new insights for the development of more effective therapeutic agents and methods for treating this condition.

Key words Mongolian medicine, Material basis, Single drug, Compound prescription, Rheumatoid arthritis (RA)

1 Introduction

Mongolian medicine, characterized by its distinctive theoretical framework and extensive practical experience, has demonstrated significant therapeutic efficacy in the treatment of a variety of diseases. In recent years, the ongoing advancements in modern science and technology have led to an increasing interest in the study of Mongolian medicine, resulting in notable progress across multiple domains. Rheumatoid arthritis (RA) is classified as a systemic inflammatory disease. According to Mongolian medicine, RA is categorized as "Xieriwusu disease" or "Taolai disease"[1]. The onset of this condition is closely associated with an imbalance among the three roots: Khii, Xila, and Badgan, as well as factors such as Qisu and Huangshui. Treatment strategies emphasize comprehensive regulation and syndrome differentiation, employing methods that include heat clearance, Huangshui desiccation, and the relaxation of muscles to promote blood circulation[2]. The advantages of Mongolian medicine in the treatment of RA are attributed to its multi-component and multi-target mechanisms of action. This approach enables the regulation of the body's immune function through various pathways, enhances the inflammatory response, and facilitates the repair of joint tissues. Currently, it has been documented that there exist over 2 000 varieties of Mongolian single drugs and compound prescriptions[3]. Among these, approximately 30 types of commonly utilized Mongolian medicines are employed in the treatment of RA. The majority of these medicines are sourced from natural plants, animals, and minerals, exhibiting relatively few side effects and demonstrating good safety and tolerability. Consequently, conducting comprehensive research on the material basis underlying the efficacy of Mongolian medicine in the treatment of RA, as well as its mechanisms of action and clinical effectiveness, holds significant practical implications for enhancing treatment means for RA and improving the quality of life for patients.

2 Basic intervention

The efficacy of Mongolian medicine in the treatment of diseases is attributed to the synergistic effects of its diverse active ingredients. The identification and evaluation of these active components necessitate the application of various contemporary methods, including serum pharmacochemistry, serum pharmacology, and network pharmacology. Recent studies indicate that compounds such as flavonoids, alkaloids, and tannins found in Mongolian medicinal materials demonstrate significant anti-RA activity.

2.1 Flavonoids Numerous Mongolian medicinal formulations are characterized by a high content of flavonoids. For example, flavonoid components derived from medicinal plants such as *Xanthoceras sorbifolium*[4] and *Hippophae rhamnoides*[5] exhibit notable antioxidant, anti-inflammatory, and immunomodulatory properties. Research indicates that quercetin, a flavonoid present in *X. sorbifolium*, may serve as an active component in the management of RA. Additionally, isorhamnetin, which is extracted from *H. rhamnoides*, has been shown to effectively inhibit the maturation and migration of bone marrow-derived dendritic cells through mechanisms of immune regulation.

2.2 Alkaloids Certain alkaloid components found in Mongolian medicine exhibit anti-RA activity. For example, the aconitum alkaloids derived from *Aconitum kusnezoffii* demonstrate potent anti-inflammatory and analgesic properties[6]. Furthermore, matrine, which is extracted from *Sophora flavescens*, has been shown to modulate immune cell function, inhibit the release of inflammatory mediators, and significantly improve symptoms associated with RA[7].

2.3 Tannins Tannins utilized in Mongolian medicine demonstrate significant anti-RA activity. For instance, the extract tamarixinin A, isolated from *Myricaria bracteata*, exhibits notable anti-inflammatory properties and mitigates the effects of RA by inhibiting MAPKs and activating the NF-κB pathway[8]. Additionally, chebulanin, extracted from *Terminalia chebula*, also provides a therapeutic effect on RA by suppressing the expression of pro-inflammatory factors via the MAPK and NF-κB signaling pathways[9].

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Wuriliga, master's degree candidate. *Corresponding author. Cuilan BAI, doctoral degree, professor.

2.4 Others In addition to the aforementioned compounds, substances such as curcumin[10] and lignin[11] have demonstrated therapeutic effects on RA. In terms of compound research, initial findings have been established regarding the material basis of compound treatments, including Sendeng-4[12], Naru-3[13], and Erdun-Wurile[14], for the management of RA. Currently, the investigation into the material basis underlying the efficacy of RA compound medications remains superficial. Therefore, it is imperative to further explore the active component groups and elucidate their mechanisms of action within these compound drugs.

3 Single drug therapy

Mongolian single drug therapy, recognized as the fundamental component of the Mongolian medical treatment system, plays a vital role in the management of RA. Currently, the most commonly utilized and extensively researched Mongolian medicinal substances include *X. sorbifolium*, *S. flavescens*, *Phellodendron amurense*, *etc.* *X. sorbifolium* is a frequently utilized single drug in Mongolian medicine for the treatment of RA[15]. Contemporary research indicates that *X. sorbifolium* is abundant in various bioactive components, including flavonoids, quinones, steroids, and coumarins. These components collectively contribute to a range of pharmacological effects, notably anti-inflammatory and immunomodulatory activities. *S. flavescens*[16], a widely utilized medicinal resource in Mongolian medicine, contains key components such as matrine and oxymatrine, which have exhibited significant efficacy in the treatment of RA through their anti-inflammatory and immunomodulatory properties. *P. amurense* is a widely utilized medicinal plant in Mongolian traditional medicine, particularly for the treatment of conditions associated with toxic heat, Taolai, and Heruhu. This species has demonstrated anti-RA effects through the involvement of multiple components, targets, and pathways[17]. Additionally, there are other traditional Mongolian medicinal substances, such as donkey blood and mercury, which have a long-standing history in the treatment of RA, but current research on these substances remains limited.

4 Compound therapy

In the clinical management of RA in Mongolian medicine, the primary therapeutic approaches involve both oral administration and external application. Treatment may consist of a single Mongolian medicinal compound or a combination of multiple compounds to address the condition effectively. Current research indicates that Mongolian medicine exerts a considerable therapeutic effect on RA. A review of the literature reveals that various Mongolian medicinal prescriptions, including compound Sanzi decoction, Runjiang Wuwei decoction, Naru Sanwei pills, Zhenbao pills, Zhongluna decoction, Garidi Wuwei pills, Yunxiang Shiwuwei pills, Zhachong Shisanwei pills, Sendeng-4, Wuwei Ganlu medicinal bath, Elejigen Chusi-25, Qisu-25 pills, Shouzhangshen Sanshiqiwei pills, Lideri Wuwei decoction, Sendengzhu decoction, Huajiao-6, and Fengtongling capsules, have been shown to play a significant role in the treatment of RA. The management of RA primarily relies on network pharmacology, which involves the construction of network models to analyze pharmacological agents and identify potential active components of drugs. This approach aims to elucidate the relationships between key targets, pathways, and RA[18], thereby facilitating the discovery of effective treatment strategies. Additionally, there are numerous research directions that focus on animal studies and clinical observational trials.

4.1 Research based on network pharmacology The Mongolian medicinal compound comprises a variety of medicinal materials characterized by an exceedingly complex chemical composition. Its mechanism of action involves the synergistic effects of multiple components targeting various pathways, thereby regulating signaling pathways to effectively treat RA. Zhou Jinlong *et al.*[19] conducted a study utilizing network pharmacology and molecular docking technology, revealing that the Mongolian medicinal formulation, Zhenbao pill, comprises 194 active components and 207 intersecting targets. The findings indicate that this formulation primarily modulates immune responses and oxidative stress by influencing the PI3K-Akt and NF-κB signaling pathways and regulating both pro-inflammatory and anti-inflammatory factors, thereby contributing to the therapeutic management of RA. Zhao Zilong *et al.*[20] identified that the Mongolian medicinal formulation, Sanzi decoction, contains 32 active ingredients and interacts with 629 targets, of which 1317 are associated with RA diseases. Among these, 171 targets have been identified as potential candidates for the treatment of RA using Sanzi decoction. The findings suggest that Sanzi decoction may influence critical targets such as MAP2K1 and MAPK3, thereby exerting therapeutic effects through the modulation of the PI3K-Akt and MAPK signaling pathways, *etc.* Enirile[13] employed network pharmacology and molecular docking methods in his research, identifying 10 significant targets, including the phosphatidylinositol-4, 5-bisphosphate 3-kinase catalytic subunit alpha isoform (PIK3CA) associated with Sanwei pill, and 10 critical pathways, notably the PI3K-Akt and MAPK signaling pathways. The mechanism of action of Naru Sanwei pills in the treatment of RA is associated with proteins such as MMP2. Furthermore, Mongolian medicinal formulations, including Garidi Wuwei pills[21], Zhongluna decoction[22], and Runjiang Wuwei decoction[23], have identified key active ingredients, related disease targets and signaling pathways through network pharmacology, thereby achieving therapeutic effects in the management of RA.

4.2 Basic research Animal experiments are grounded in the investigation of fundamental biological principles, primarily aimed at simulating biological conditions to observe the progression of diseases in both humans and animals. In contemporary research, these experiments have expanded into various disciplines, including genomics, physiology, pathology, and pharmacology[24]. Animal experiments play a critical role in understanding the pathogenesis, pharmacological and toxicological mechanisms, as well as in the drug screening processes for RA[25]. In the domain of Mon-

golian medicine aimed at treating RA, it has been observed that conducting experiments to validate the therapeutic effects through animal studies is of paramount importance. Zhao Zilong *et al.* [20], Zhao Haiyue *et al.* [26], Ao Limei *et al.* [27], Wang Xiye[28], and Qu Hong[29] employed collagen-induced arthritis (CIA) animal models in their research. Their findings indicated that Mongolian medicinal formulations, including Sanzi decoction, Naru-3, Zhongluna decoction, and Sendeng-4, were effective in alleviating and controlling the progression of disease in CIA-affected animals. Chang Chun[21] and Wang Siriguleng *et al.* [30] conducted a study utilizing an animal model of adjuvant RA. Their findings indicated that the Mongolian medicine Garidi Wuwei pills exhibited a beneficial intervention effect on adjuvant RA. Additionally, the Mongolian medicine Hata capsules demonstrated efficacy in treating and managing adjuvant RA by inhibiting the levels of IL-1, IL-6, and TNF-α. Furthermore, the Mongolian medicinal compounds Lideri Wuwei decoction[31], Huajiao-6[32], and Sendeng-4[33] all play a role in mediating immunotherapy for RA.

4.3 Clinical research Clinical research is defined as a scientific inquiry that involves patients as research subjects. Its primary objective is to investigate the causes, progression, prevention, and treatment methods of diseases. This research enables physicians to more accurately assess disease trends, formulate precise diagnostic and therapeutic strategies for patients, and provide a robust scientific foundation for the discipline of clinical medicine. Research indicates that Mongolian medicine demonstrates both safety and efficacy in the clinical management of RA. Specifically, the Mongolian medicinal compounds Naru Sanwei pills[34] and Shouzhangshen Sanshiqiwei pills[35] have been shown to significantly enhance clinical outcomes when used as single treatments for RA. Mongolian compounds such as Zhenbao pills[36], Zhongluna decoction[37], Yunxiang Shiwuwei pills, and Zhachong Shisanwei pills[38], Elejigen Chusi-25[39], Sendengzhu decoction[40], and Fengtongling capsules[41], are utilized in conjunction with Western medications, including methotrexate, loxoprofen sodium, and leflunomide, for the treatment of RA. The findings indicate that this combination can significantly enhance clinical efficacy while reducing adverse reactions, thereby improving the safety profile of RA treatment. Furthermore, the Mongolian medicinal bath Wuwei Ganlu[42], when administered alongside oral Mongolian medicine, has demonstrated effectiveness in the management of menopausal arthritis.

5 Outlook and conclusions

Mongolian medicine is founded on the principles of three fundamental roots and seven essential elements of the human body, which are organized according to specific rules to create a cohesive and interdependent system that operates in harmony. By observing and analyzing the patterns of diseases that arise during human existence, Mongolian medicine seeks to achieve prevention, accurate diagnosis, and effective treatment, and develops treatment plans tailored to the unique circumstances of each individual case[43]. Mongolian medicine categorizes RA as "Xieriwusu disease" or "Taolai disease"[1]. Within this framework, it is posited that RA results from an imbalance in Xieriwusu, which subsequently leads to deformities in limb muscles and lesions in the joints[44]. Mongolian medicine is informed by theoretical frameworks, and treatment is administered through the compound integration of various Mongolian medicinal practices, guided by syndrome differentiation. Currently, the clinical application of Mongolian medicine demonstrates favorable efficacy when employing a combination of internal administration and external application. Furthermore, the pathogenesis of RA is currently understood to be associated with genetic factors, environmental influences, and immune disorders[45]. Currently, the pharmacological agents employed in Western medicine for the treatment of RA primarily include glucocorticoids and antirheumatic drugs. To date, no effective and reliable therapeutic alternatives have been identified. Nevertheless, the emergence of traditional ethnic medicine holds the potential to introduce safe and effective treatment options for RA in the future.

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