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Original Article

Analysis of Pathological Factors of Long Head of Biceps Tendinopathy Based on Network Pharmacology

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Abstract

Objectives: To investigate the therapeutic effect and mechanism of Danggui Buxue Tang in the treatment of biceps longus tendon lesions, and to preliminarily explore the relevant factors affecting this injury. **Methods**: Using network pharmacology analysis methods, the potential mechanism of Danggui Buxue Tang in treating key lesions of the long head of the biceps brachii muscle was studied. **Results**: Model analysis revealed 44 protein-protein interactions associated with long head binding. The distribution of 19 strongly correlated targets is Pharmaper>SEA>Stitch>Swiss. Further discovery revealed 17 immune system and inflammation related KEGG pathways with P values less than 0.01. The TNF and sphingolipid signaling pathways are associated with inflammation, while the MAPK signaling pathway is associated with immunity. Finally, it was found that the FoxO and HIF-1 signaling pathways are directly associated with long head restraint injury in the biceps brachii muscle. **Conclusion**: Danggui Buxue Tang inhibits related pathways, regulates the immune system, reduces inflammation, and alleviates disease progression. Danggui Buxue Tang can be an effective choice for treating combined lesions of the long head of the biceps brachii muscle.

Keywords: Biceps Brachii, Traditional Chinese Medicine, Ultrasound

Introduction

Long head biceps (LHB) tendon injury is a common cause of anterior shoulder pain and dysfunction. Arthroscopy can reveal various visible LHB lesions, such as tendinitis, wear, instability (dislocation and subluxation), superior labrum anterior and posterior (SLAP) damage, and partial or complete cleft. However, simple LHB lesions are relatively rare in clinical practice. Most patients with LHB lesions also have other shoulder joint injuries, such as lesions of the long head of the biceps brachii, impingement syndrome, humeral joint instability, and other symptoms. Damage to the upper anterior rotator cuff and biceps pulley in the rotator cuff gap can easily cause LHB instability and related pathological changes. Proper management of LHB lesions discovered before and/or during shoulder surgery is crucial for surgical outcomes. However, due to the unclear function of LHB in complex shoulder joint movements, there is currently controversy and disagreement regarding the treatment of LHB, with no unified standard.

The biceps brachii muscle is a powerful flexor of the elbow and supinator of the forearm. The long head of the biceps tendon (LHBT) originates from the scapula and merges with the short head of the biceps tendon (SHBT) at the insertion in the intertubercular groove. The LHBT attaches to the distal radial tuberosity. Its total length is about 9 cm, with a width ranging from 8.5 to 7.8 mm at the starting point, narrowing down to 4.5-2.6 mm. The LHBT can be divided into three parts: the intra-articular part, the sheath within the intertubercular groove, and the external part stretching from the intertubercular groove to the tendon-muscle transition point.

The starting point and tendon sheath of the LHBT joint are common sites of injury. The shoulder boasts the largest range of motion among all joints in the body; however, it is inherently unstable due to the substantial difference in surface area between the joint and the visceral bone[8].

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Shoulder joint stability relies on a delicate balance between static and dynamic structures. Static stability features the joint lip, shoulder joint band, negative pressure in the articular capsule, and rotator cuff space. Meanwhile, dynamic stability involves the rotator cuff muscle, pectoralis major muscle, latissimus dorsi muscle, periscapular muscles, and the LHBT[9]. An imbalance between these structures can lead to shoulder joint instability.

The LHBT passes through the rotator cuff gap and is stabilized by a pulley structure in the intertubercular groove. Trauma from abduction and arm rotation can damage this pulley, causing LHBT injury. Ultrasonography can diagnose LHB lesions, including LHB synovitis, LHB inflammation, and LHB tear. Synovitis can manifest as irregular thickening of the tendon sheath without a notable increase in blood flow or as local thickening with increased blood flow and fluid accumulation. Inflammation can show disordered tendon echo without significant blood flow increase or increased blood flow with fluid accumulation. Tear is characterized by a discontinuous tendon echo and fluid accumulation. Detecting fluid accumulation around the tendon is difficult in the intertubercular sulcus but easier below it. Elastic imaging technology can effectively distinguish rotator cuff tissue, aid in diagnosing tears, and determine tear edges.

Klauser et al. compared the conventional ultrasound and ultrasound elastography findings of the Achilles tendon with histological diagnosis by performing ultrasound and ultrasound elastography on 14 Achilles tendons from 10 cadavers[13]. As a result, B-ultrasound was categorized into three levels: Level 1, with normal tendons and homogeneous fibrous echoes; Level 2, with local spindle-like or diffuse thickening of tendons; Level 3, hypoechoic areas can be seen within the tendon with or without tendon thickening. Ultrasound elastography is divided into three levels, and the corresponding hardness is: level 1 - blue (the hardest) to green (hard); Level 2 - Yellow (soft); Level 3 - Red (softest).

Consistency between B-ultrasound grading and ultrasound elastography grading was evaluated using the K-test. The results showed that ultrasound elastography detected histological degeneration in all 14 tendons in the distal 2/3 segment, whereas ultrasound only detected 12 of them (86%). The author assumes that LHB, rotator cuff, Achilles tendon, and other tissues are tendon tissues with similar tissue biological characteristics and ultrasound manifestations. The application of ultrasound elastic imaging technology to evaluate LHB lesions based on the ultrasound elastic manifestations of the rotator cuff and Achilles tendon remains to be explored in prospective research[14].

Tohti et al. dissected 101 shoulder joint specimens, confirming a close relationship between the origin of LHBT (biceps brachii muscle anchor) and the anterior and posterior parts of the upper joint, as well as the glenoid brachial ligament (GHL) of the shoulder joint, connecting to the posterior part of the upper joint[15]. A tear near the starting point of LHBT's upper lip is referred to as SLAP (Superior Labrum Anterior and Posterior) injury. Syder et al. classified the upper lip into four categories: Type I, upper lip abrasion and degeneration with no tearing and intact lip margin, LHBT needle; Type II, LHBT avulsion injury of the upper arm and scapula, the most common type; Type III, barrel avulsion of the upper lip. Type A injuries involve the long head of the biceps muscle and part of the upper lip, remaining firmly attached to the scapula. Type B injuries result in a barrel-shaped avulsion of the upper lip, extending to the long head tendon of the biceps brachii muscle. Although part of the upper body remains attached to the scapula, the avulsed part may be transferred to the humeral joint. Complete tearing of the long head tendon of the biceps brachii muscle may also occur in some cases[16].

The embryonic development of the shoulder joint was studied by exploring the joint of three fetuses at 24 weeks of gestation to determine the internal position of the LHBT joint. It was found that there is an aponeurosis tissue connection between the part of the LHBT joint and the upper articular capsule, but no such structure is present in fetuses over 24 weeks of gestation. Dierick et al., after analyzing 2976 videos of shoulder arthroscopic surgeries, classified the variation structures of the intra-articular portion of LHBT into 5 categories and 12 subtypes: tendon sheath type, with a total of 5 subtypes[17].

The LHBT (long head of the biceps tendon) exhibits a suspended mesangial connection with the rotator cuff and the upper joint, allowing it to freely slide between the LHBT and the rotator cuff. There are four subtypes in the adherent type, where the LHBT is closely connected with the articular capsule. The split type comprises two subtypes, wherein the LHBT divides into two parts within the joint. The absence type refers to an intra-articular defect where the LHBT is located in the intertubercular sulcus and surrounded by a fibrous sheath.

The upper part of the intertubercular sulcus is formed by the transverse band of the scapula, while the lower part consists of the biceps muscle pulley composed of the superior digital band, coracoid transverse band, supraspinatus tendon, and subscapular tendon fibers.

Typically, in clinical practice, the LHBT is observed near the upper part of the humeral head. Research indicates that an increase in the width and depth of the intertubercular sulcus, coupled with a decrease in the medial wall angle, is associated with LHBT dislocation and subluxation[18]. Scholars have recently discovered that bone spurs on the inner wall and bottom of the intertubercular sulcus are linked to chronic tendinitis in LHBT. Repeated wear and inflammation contribute to tendinitis, wear degeneration, and, in severe cases, partial tearing or complete rupture. Acute traumatic rupture of LHBT is relatively uncommon, with most fractures occurring due to wear degradation.

Schoff et al.[21] reported four cases of acute LHBT rupture in rock climbers, attributing it to immense pressure from the rotator cuff, intertubercular sulcus, and acromion during intense exercise. Simple LHBT lesions are rare, and approximately 90% of patients with such lesions often have rotator cuff injuries. In a study by Chen et al., 122 patients with long head tendon lesions of the biceps brachii exhibited various types of LHBT lesions, including tendinitis (41%),

subluxation (8%), complete dislocation (19%), partial split (23%), and complete fracture (5%). Murthi et al.[13] found that LHBT is prone to friction with small nodules and the inner wall of the intertubercular sulcus during activity, leading to secondary inflammatory reactions due to repeated wear and tear. Prolonged inflammation can result in tendon degeneration, rendering it more susceptible to wear and tear with minimal external forces.

LHBT instability, encompassing subluxation and dislocation, primarily results from damage to the stable structure of LHBT. Researchers such as Gerber et al. and Lin have proposed that anterior superior impact (ASI) on the shoulder joint can lead to the collision of the pulley structure within the intertubercular sulcus of the LHBT with the subscapular tendon, thereby inducing LHBT instability. Over the years, a combination of Chinese and Western medicine has been recommended for treating critical lesions of the long head of the biceps muscle. Clinically, Danggui Buxue Tang is often prescribed as a combination of Chinese and Western medicine, complemented by painkillers, to regulate and slow the progression of the disease.

In summary, despite existing research, there is still no unified understanding of the pathological mechanisms related to the long head key damage of the biceps brachii muscle, especially concerning the specific causes of the lesion and important mechanisms for conditioning and treatment. Many studies have focused solely on efficacy analysis from a clinical standpoint, neglecting the perspectives of pharmacology and pathology. This gap affects the effective long-term treatment of patients with this type of disease, presenting a challenge for the current medical community. This study aims to analyze the pathological factors of the long head key lesion of the biceps brachii muscle using network pharmacology analysis methods, with a focus on examining the mechanism of Danggui Buxue Wan in treating this type of disease. By employing network pharmacology and pathology perspectives, the study aims to identify key factors influencing and inducing the development of long head key lesions in the biceps brachii muscle, providing insights into the pharmacological mechanism underlying the therapeutic effect of Danggui Buxue Wan. This, in turn, can offer guidance for the clinical diagnosis and treatment of such diseases.

Materials and Methods

Data Sources and Search

By reviewing data information recorded in large-scale medical databases such as Prospero, Cochrane, MEDLINE, EMBASE, CINAHL, and the Science and Physical Therapy Evidence Network (Pedro), the selected literature was screened in December 2022 without date restrictions. We conducted a search for studies related to Zhuanggu Pill, Lesions of the long head of the biceps brachii muscle, and keywords such as Zhuanggu Pill and rotator cuff tear. To ensure that no relevant research was missed, we avoided using search restrictions and made additional selections manually. We also verified the relevance of the identified articles and reviewed the references for any additional comments.

Research Selection

The study was assisted by three orthopedic experts who assessed the full text of potentially relevant trials and evaluated the quality of the methods employed in these trials.

Data Extraction

Following the guidelines outlined in the Cochrane Handbook for Systematic Reviews of Interventions 5.1.0 Edition, Chapter 7.6.9, standardized tables were utilized to extract the necessary data for network pharmacology analysis from the selected trials, and the data were subsequently merged for analysis.

Quality Assessment

The quality of methods was assessed using Cochrane's collaborative domain-based evaluation framework. The evaluation process involved assessing the main structural domains in a specific order, which included:

1. Selection bias: evaluating the generation and concealment of random sequences.
2. Performance bias: assessing the blinding of participants and individuals.
3. Detection bias: evaluating the blind method for outcome evaluation.
4. Attrition bias: assessing the completeness of outcome data, including dropouts.
5. Reporting bias: evaluating selective reporting.
6. Other bias. Each bias field was assigned a score, and the final score of the system bias risk was categorized as low, high, or unclear risk.

If multiple high-quality randomized controlled trials consistently show high consistency, the evidence is considered reliable. Conversely, if there are numerous low-quality randomized controlled trials and/or high-quality randomized controlled studies with consistent results, the overall level of evidence is deemed appropriate. However, if these conditions are not met, the evidence is considered inappropriate.

Statistical Analysis

In this study, a random-effects model was employed for the analysis of the effectiveness of chemical components. Heterogeneity was assessed using Q2, T2, and I2 statistical data. I2 values between 0-20% were considered insignificant heterogeneity, 10-60% moderate, 50-90% substantial, and 75-100% indicative of high heterogeneity. For this analysis, the non-standardized "aw" mean difference of changes in results for each study and the combined study sample was calculated to observe differences.

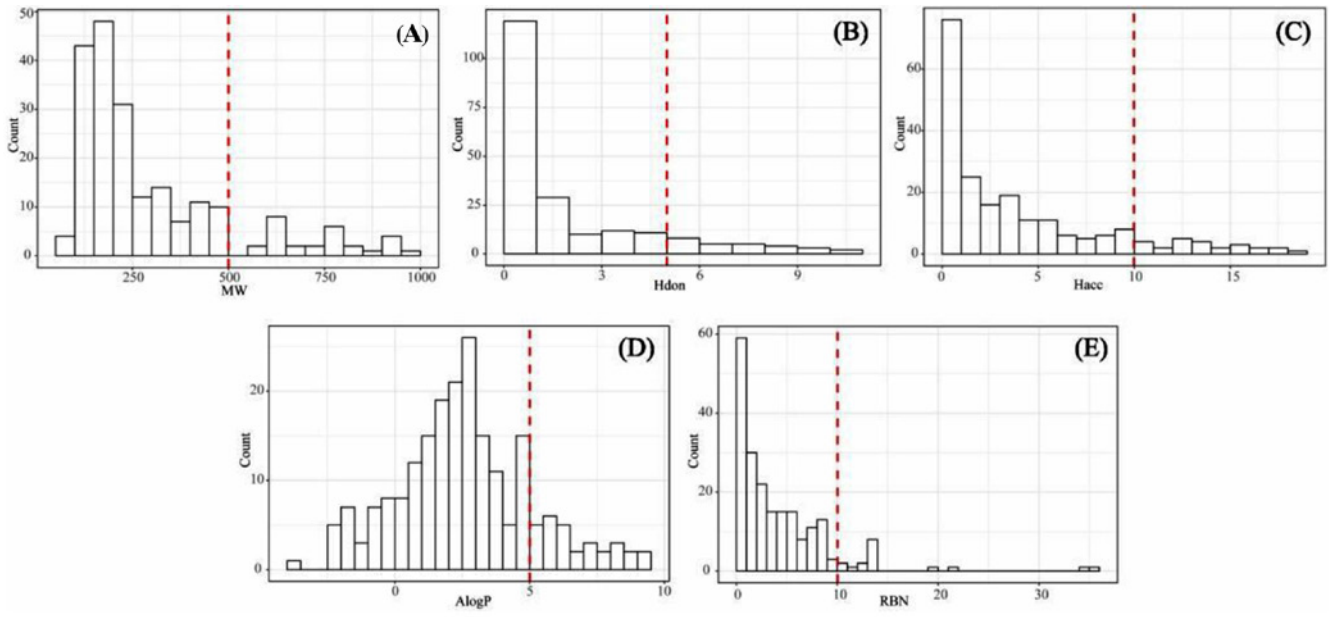

Figure 1. Chemical distribution of effective components in Danggui Buxue Tang for the treatment of long head joint lesions of the biceps brachii muscle, as investigated according to Lipinski's Rule of Five. (A) Molecular Weight (MW); (B) Number of Hydrogen Donors (Hdon); (C) Number of Hydrogen Acceptors (Hacc); (D) Partition Coefficient (AlogP); (E) Rotatable Bond Number (RBN). The red dashed lines indicate the average values of each parameter.

None of the studies included in this analysis reported all three standard deviations (baseline, follow-up, and changes). Therefore, raw data was utilized to calculate the correlation coefficient before and after changes were made to the total constant score. The formula recommended by Cochrane was applied for these calculations.

$$\text{Coefficient} = (\sigma^2_{\text{baseline}} + \sigma^2_{\text{final}} - \sigma^2_{\text{change}}) / (2 \times \sigma_{\text{baseline}} \times \sigma_{\text{final}})$$

The coefficient represents the correlation coefficient before and after, with 'r' as the standard deviation of the sample. The coefficient is 0.52 (0.21-0.79). We use this data for other impact size calculations when needed. Furthermore, this article employs Egger's funnel plot asymmetry test, with a Y-intercept of linear regression for estimating standardization effect and accuracy (¼ 0 is used for testing), to evaluate potential publication bias. The results consistently meet the correlation within a 95% confidence level, indicating high reliability for all included research data.

Results

Analysis of Effective Components of Danggui Buxue Pills

This study analyzed 212 components in traditional Chinese medicine decoction, with 166 of them found to be related to the chemical components in Danggui Buxue Tang. Some compounds, even if they did not meet this requirement, were still included in the study due to their pharmacological activity and high content. Using UHPLC-QTOF-MS/MS and UHPLC-TQ-MS/MS, we characterized 16 components, as shown in Figure 1, making them suitable for network pharmacology analysis according to our results.

MW represents molecular weight, which refers to the sum of the relative atomic masses of all atoms in a compound. Hdon represents the number of hydrogen donors, which refers to the number of hydrogen atoms in a compound that can provide hydrogen bonds. Hacc represents the number of hydrogen acceptors, which refers to the number of atoms or groups in a compound that can accept hydrogen bonds. AlogP represents the partition coefficient, which refers to the equilibrium distribution of a compound between the oil and water phases. RBN stands for Rotatable Bond Number, which refers to the number of bonds in a compound that can rotate freely.

In Figure 1, we can observe that the MW values of different compounds may vary, which reflects their differences in molecular size. Usually, larger molecular weights may correspond to more complex compound structures, Hdon (number of hydrogen bond donors) and Hacc (number of hydrogen bond acceptors) are parameters that describe information related to hydrogen bonds in a molecule. Hydrogen bonding is a strong bond in intermolecular interactions, playing an important role in the stability and interaction of molecules. In Figure 1, we can infer the number of hydrogen bond donors and acceptors that may exist in the compound based on the numerical changes of Hdon and Hacc, and thus understand their interactions with other molecules. AlogP (Distribution Coefficient) is an indicator that describes the equilibrium distribution of molecules between the oil and water phases. It can help us understand the characteristics of

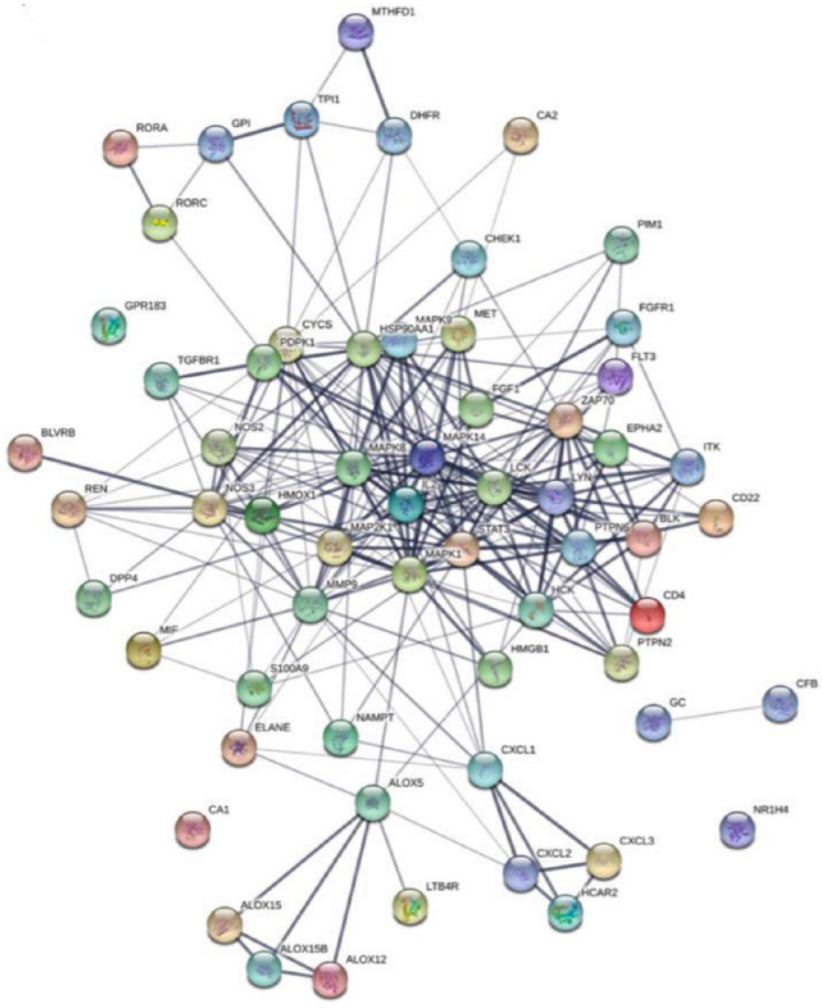

Figure 2. Protein-protein interactions (PPI) of 44 targets.

compounds in terms of absorption, efficacy, and metabolism in the body. In Figure 1, we can observe the changes in AlogP values of different compounds, which can provide information about their lipophilicity and hydrophilicity. RBN (number of rotating bonds) is the number of bonds in a compound that can rotate freely. This parameter can reflect the flexibility of the compound and the number of active parts. In Figure 1, we can use this to determine the number of possible rotational bonds in the compound, and further understand its flexibility and conformational characteristics. Changes in parameters such as MW, Hdon, Hacc, AlogP, and RBN can provide information about the molecular weight, hydrogen bonding, distribution, and number of rotational bonds of the compound. By observing and comparing the values of these parameters, we can have a preliminary understanding of the physical and chemical properties of the compound and some possible pharmacological activities, providing reference for further drug development and activity evaluation.

Analysis of Target Proteins in the Treatment of Long Head Biceps Brachii Lesions with Danggui Buxue Tang

Analyzing the effects of Danggui Buxue Tang on target proteins during the treatment of long head tendon lesions in the biceps brachii muscle using traditional methods is a complex and resource-intensive task. To overcome this, we employed network pharmacology analysis methods to identify potential target substances and analyze the mechanism of the long head bone lesion of the biceps brachii muscle using computer models. Utilizing pharmacophore matching methods, statistical factors, and similarity measurements, we identified 237 Homo sapiens targets, including 92 PharmaMappers, 105 Swiss, 76 SEAs, and 54 Stitches. We then extracted data from published literature to obtain the specific functions of each target. Finally, we analyzed the protein-protein interactions of 44 pathologically related targets of the long head bond of the

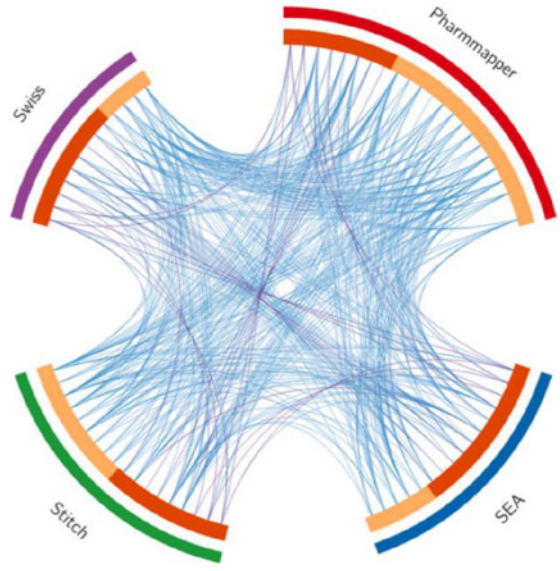

Figure 3. Circos plot of 18 target distributions in PharmaMapper, Swiss, SEA, and Stitch.

biceps brachii, as illustrated in Figures 2 and 3.

Figures 2 and 3 illustrate the strength of the correlation between the results, with thicker lines indicating stronger supported data. Based on our analysis, we identified 19 targets, and their distribution across different databases is displayed using Metascape in the second paragraph of Figure 3. Each arc represents a marker for each gene list, distinguished by different colors: red represents Pharmaper, purple represents Swiss, blue represents SEA, and green represents Stitches. Our analysis reveals that the distribution order of the 19 highly correlated targets selected in this article is Pharmaper > SEA > Swiss > Stitches. In this figure, the number of purple links and the length of deep orange arcs signify greater overlap between predicted targets, while blue links indicate the degree of functional overlap.

Target GO enrichment analysis during the Lesions of the long head of the biceps brachii muscle

Figure 6 displays the results of GO enrichment analysis conducted on the 19 targets uploaded to DAVID bioinformatics resources. The top 15 terms for molecular function (MF), biological process (BP), and cell component (CC) were selected for the enrichment analysis.

Moreover, our analysis of the 68 KEGG pathways revealed 17 pathways with P values of 0.01 or less, all related to the immune system and inflammation. Inflammation and immune response are complex signal structures that play a crucial role in the pathological changes of the long head of the biceps brachii muscle, where inflammatory reactions decrease the body's immune system. Prolonged inflammation can lead to severe inflammatory lesions, making immune system and inflammation-related pathways a crucial focus of this research. We ultimately identified 16 pathways, as shown in Figure 5. Among them, the TNF signaling pathway and sphingolipid pathway are closely related to inflammation, the MAPK signaling pathway is closely related to immunity, and the FoxO signaling pathway and HIF-1 signaling pathway are directly associated with long head binding injury of the biceps brachii muscle.

Based on the above analysis, Danggui Buxue Tang has the potential to regulate the inflammatory response, peptide tyrosine phosphorylation, T cell receptor signaling pathway, plasma membrane and intracellular protein binding, CXCR chemokine receptor binding, and iron ion binding in the affected area of the long head joint of the biceps brachii muscle through cytoplasmic sol. This mechanism may help alleviate inflammation and reduce pain in patients by regulating the inflammatory response in the affected area.

Analysis of the Composite Target Pathway Network of Danggui Buxue Tang in Treating Long Head Bone Lesions of the Biceps Humerus

Traditional Chinese medicines typically contain hundreds or more compounds, each of which may target one or more targets and work together synergistically to achieve therapeutic effects. Given this complexity, our analysis employed a multi-compound and multi-target analysis model. Using Cytoscape 3.2.1, explores the pathway mechanisms involved in the effectiveness of Danggui Buxue Tang in treating long head bond lesions of the biceps brachii muscle, we constructed a compound-target pathway network. Figure 6 visually represents the targets of Danggui Buxue Tang and the corresponding number of targets associated with the 16 pathways related to the long head bond lesion of the biceps brachii.

Figure 6A presents the target and participant count for Danggui Buxue Tang, while Figure 6B illustrates the number of targets associated with the 16 pathways related to the long head bond lesion of the biceps brachii muscle. Figure 7 provides a more comprehensive analysis of the pathway network connecting these targets and pathways.

Figure 7A illustrates the composite target pathway network of Danggui Buxue Tang, while Figure 7B depicts the composite target pathway network associated with the Lesions of the long head of the biceps brachii muscle. In the outermost circle of Figure 7B, 16 pathways associated with the long head key lesion of the biceps brachii muscle are illustrated. It is evident that several compounds in Danggui Buxue Tang, such as Z-ligustrazine, Z-butylphthalic acid, and ferulic acid, as well as purslane and ononin in HQ, are effective influencing agents. Moreover, these compounds are linked to most targets, as evidenced by the top ten influencing compounds shown in Figure 8.

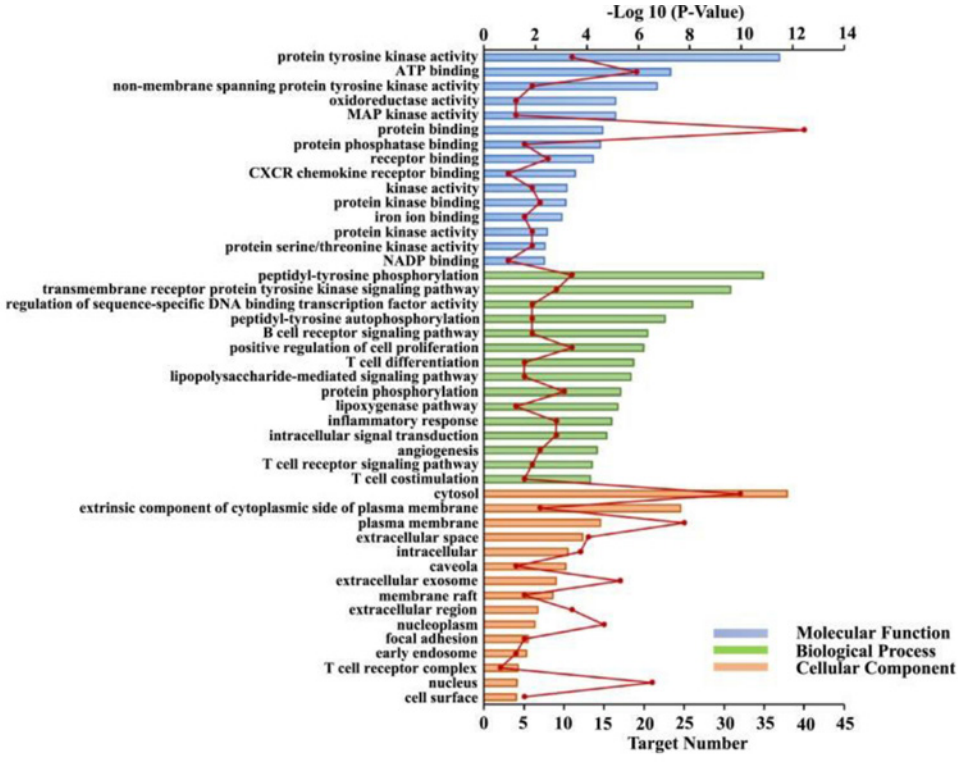

Figure 4. GO enrichment analysis of DBD targets.

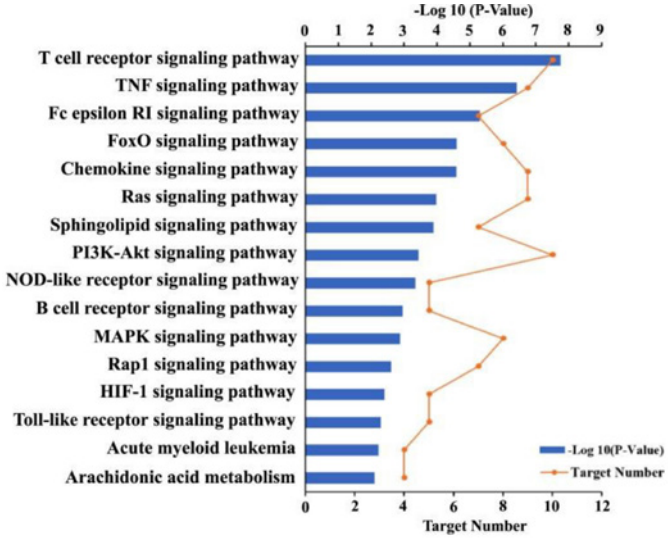

Figure 5. The KEGG pathway related to the long head bone lesion of the biceps brachii muscle is the target of Danggui Buxue Tang.

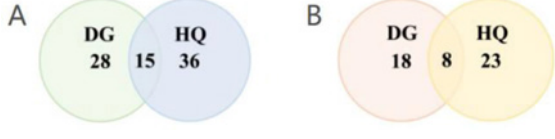

Figure 6. The target of Danggui Buxue Tang and the number of targets involved in 16 pathways related to the long head bone lesion of the biceps brachii muscle.

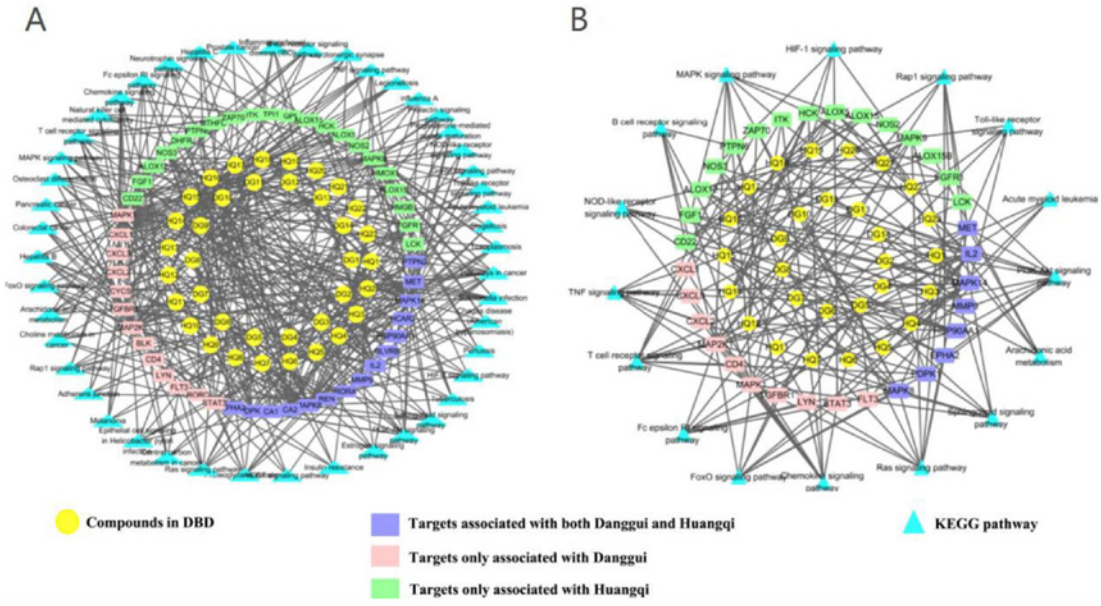

Figure 7. The composite target pathway network of Danggui Buxue Tang and the composite target pathway network related to the long head bone lesion of the biceps brachii muscle.

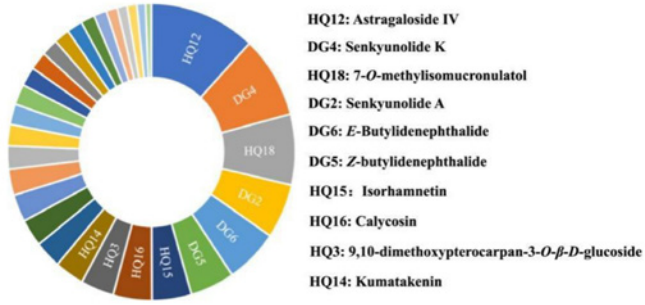

Figure 8. Top 10 Effective Compounds for the Treatment of Long Head Bone Lesions in the Biceps Humerus Muscle.

Discussion

This article utilized network pharmacology to analyze the pathological factors underlying long head tendon lesions in the biceps muscle. The study aimed to comprehend the drug mechanism and pathways involved in the treatment of these lesions using Danggui Buxue Tang. From a pathological perspective, the study systematically analyzed the influencing factors and pathways associated with long head tendon lesions in the biceps muscle. The results of the study will contribute to a deeper understanding of the mechanisms driving the development of the disease and offer new insights for the clinical treatment of such conditions.

This study conducted a comprehensive search and data analysis on six major databases in the medical community. Standardized methods were used to evaluate and analyze the quality of the research data to ensure the credibility of the data used in the study and ultimately ensure the reliability of the research results. The study targeted 28 targets and 14 components related to long head bond lesions of the biceps brachii in Danggui Buxue Tang, including LYN, CYCS, MAPK8, MMP9, ALOX15, FGF1, HSP90AA1, and others, for in-depth research and analysis. Through this investigation, the study identified multiple components within Danggui Buxue Tang that may have potential effects on CA1 and CA2 related to long head

tendon lesions in the biceps brachii muscle. These findings provide valuable insights into the potential therapeutic effects of Danggui Buxue Tang and could facilitate the development of more targeted treatment strategies for patients suffering from this condition.

According to research conducted by Benarroch EE[16], the study found that CA1 and CA2 could potentially serve as crucial factors in distinguishing autoimmune long head tendon lesions from other types of lesions. This distinction arises from the observed low expression of CA1 and CA2 in hemolytic multi head lesions within the biceps brachii muscle, whereas they exhibit high expression in other lesion types. Despite the relatively low protein-protein interaction scores of CA1 and CA2, based on the findings of this study, they can still be considered as relevant targets associated with the long head bond lesion of the biceps brachii muscle. The results of the pathway enrichment analysis reveal that LYN, a non-receptor tyrosine protein kinase, plays a significant role in EPO receptor signal transduction and muscle histiocyte homeostasis. LYN influences various stages of muscle histiocyte expansion, growth, and survival signal transduction, thereby promoting the production of normal muscle histiocytes. Furthermore, this study identified 17 KEGG pathways related to the immune system, inflammation, and other factors, among the total of 68 KEGG pathways analyzed.

Inflammation and immune responses are intricate signal pathways evolved to resist diverse external and internal factors. Lesions in the long head of the biceps brachii muscle may disrupt these pathways, providing valuable insights into the underlying mechanisms of long head bond lesions. This understanding could facilitate the development of more targeted treatment strategies[17]. Persistent inflammation may exacerbate pathological changes by harming muscle histiocytes. Consequently, pathways related to the immune system, inflammation, signal transduction, and hematopoiesis were specifically chosen for investigation[18]. Drawing from existing research, our study identified and retained 16 pathways. Notably, the TNF signaling pathway and sphingolipids signaling pathway emerged as key players in inflammation, while the MAPK signaling pathway and Ras signaling pathway were associated with intracellular signaling. Additionally, the FoxO signaling pathway and HIF-1 signaling pathway were directly linked to long head binding injuries of the biceps brachii.

To summarize, this study provides a comprehensive analysis of the mechanisms and principals involved in long head key lesions of the biceps brachii muscle. With a pharmacological approach, the efficacy of Danggui Buxue Tang in regulating these lesions is examined by investigating its active ingredients and pathway mechanisms. Specifically, the analysis centers around systemic immunity and inflammation, shedding light on valuable insights that can support future clinical treatments for long head key lesions in the biceps brachii muscle.

Conclusion

This study aims to explore the pathological and underlying mechanisms associated with long head lesions of the biceps brachii muscle in a systematic manner. The study found that a decrease in autoimmune function is the key factor leading to pathological changes in the long head, resulting in sustained inflammation. Interestingly, Danggui Buxue Tang was found to contain effective chemical components that regulate these pathological changes, primarily by regulating the immune pathway of the body to alleviate inflammation and alleviate the lesion. Further analysis confirmed that inflammation and immunity are key factors affecting the pathological changes of the long head of the biceps brachii muscle. These findings provide insights into the development of more effective treatment strategies for patients suffering from this condition.

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Authors' contributions

WD, YL and JC designed the work and wrote the paper; YL, JC, NC XZ and JG revised the paper; All authors read and approved the final version of the manuscript.

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