ISSN: 2710-0170

A Comparative Study of Terminalia chebula (Hezi) in the Theoretical Systems of Traditional Chinese and Tibetan Medicine and Its Modern Scientific Interpretation

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Abstract

This study systematically compares the theory and application of Terminalia chebula (Hezi) in Traditional Chinese Medicine (TCM) and Tibetan Medicine. In TCM, Hezi is primarily positioned as an astringent medicinal, mainly used to astringe the lung to suppress cough and astringe the intestines to arrest diarrhea. In Tibetan Medicine, it is revered as the "King of Medicines," broadly regulating the balance of the three humors (rLung, mKhris-pa, and Bad-kan) and is employed for diseases across multiple systems, including digestive, respiratory, nervous, and metabolic disorders, holding a status far beyond its conventional use in TCM. Modern studies indicate that tannin constituents, such as chebulinic acid, exhibit antibacterial, anti-inflammatory, antioxidant, and gut microbiota-modulating activities, providing evidence for traditional efficacy. Furthermore, the "gut–lung axis" mutually corroborates the TCM theory that "the lung and the large intestine are interior–exteriorly related" and the holistic regulatory concept of Tibetan Medicine. However, high-quality clinical evidence is scarce, and the potential hepatotoxic risk of high-dose tannins warrants vigilance. Cross-system comparison can rediscover overlooked values such as tonifying deficiency and moving qi, promoting the integration of traditional medicine with modern science, and offering guidance for new drug development and precision medication.

Keywords

Terminalia chebula; Traditional Chinese Medicine; Tibetan Medicine; Comparative Study; Ethnopharmacology; Tannins.

1. Introduction

Terminalia chebula Retz. (known as Hezi in Chinese and Arura in Tibetan) is acclaimed as the "King of Medicines" in Tibetan medical theory. It is widely used to harmonize disorders of the three humors—rLung, mKhris-pa, and Bad-kan—implicated in a variety of complex chronic diseases, with a status comparable to that of Glycyrrhiza uralensis (licorice) in TCM. Within the TCM system, however, the understanding of Hezi has undergone a marked evolution: herbal classics of the Tang and Song dynasties emphasized its effects of "warming the middle, moving qi, stimulating the appetite, and tonifying deficiency," whereas contemporary TCM clinical practice has relatively narrowed its focus to "astringent" actions, significantly constricting its scope of application. This "temperature difference" between theory and practice raises questions that urgently need answering—has TCM, in its historical evolution, forgotten certain important effects, or has Tibetan medical theory endowed Hezi with unique interpretations and application patterns? Can the cognitions of these two systems find a common empirical foundation through the language of modern science?

ISSN: 2710-0170

Exploring these questions holds multiple levels of significance. First, it helps promote dialogue and mutual learning between TCM and Tibetan Medicine. Comparing the different interpretations of the same drug can reveal the theoretical characteristics and potential blind spots of each system, providing references from fraternal ethnic medicine to enrich the "medicinal property theory." Second, it aims to explore the potential, neglected clinical value of Hezi. The extensive application of Hezi in Tibetan Medicine for tonifying deficiency, moving qi, anti-aging, and treating metabolic diseases offers abundant clues for new drug development. Validating these traditional functions through modern pharmacology holds promise for developing new therapeutic drugs or functional health products. Third, this study represents a typical ethnopharmacological case. It transcends the simplistic "abandon medical theory, merely validate drugs" model; by respecting and understanding traditional theories such as the TCM concepts of zang-fu organs and meridians and the Tibetan three-humor doctrine, it employs modern scientific methods—chemical analysis, network pharmacology, and multi-omics technologies—to verify, interpret, and mutually corroborate, thereby enhancing the scientific connotation of traditional medicines.

To this end, this study will be grounded in the deep excavation of ancient texts and the systematic integration of modern scientific evidence. From a dual perspective, it will compare the historical origins, theoretical connotations, clinical applications, and processing methods of Hezi in TCM and Tibetan Medicine, and, with the aid of modern pharmacology, elucidate the material basis and mechanisms of action underlying its pleiotropic effects, ultimately achieving a multi-dimensional, dynamic, and profound scientific re-evaluation of this ancient drug.

2. Hezi in Ancient Texts of TCM and Tibetan Medicine

2.1. Historical Origin and Medical Records

The historical status of Hezi differs fundamentally between TCM and Tibetan Medicine. In the TCM system, Hezi is a relative "newcomer": it is not recorded in the Shennong Bencao Jing (Divine Farmer's Materia Medica). It was only officially incorporated into the national pharmacopoeia with the Xinxiu Bencao (Newly Revised Materia Medica) of the Tang Dynasty, marking its entry into the official medicinal system. Although it was mentioned earlier in the Nanfang Caomu Zhuang (Records of Southern Plants and Trees), the focus was on botanical description rather than medicinal use. Subsequent herbal works in successive dynasties gradually deepened understanding, with later generations largely inheriting and developing on the basis of Ming and Qing herbals such as the Bencao Gangmu (Compendium of Materia Medica). In contrast, Hezi has occupied a core position in Tibetan Medicine from its very origins. The fundamental classic, the rGyud bzhi (Four Medical Tantras), reveres it as the "King of Medicines." Legend holds that the Medicine Buddha holds a branch of Hezi, symbolizing the cure of all diseases, elevating the drug beyond a mere medicinal substance to a cultural symbol, and making it the most basic ingredient in almost all Tibetan compound formulas. This supreme status, conferred right from the source, constitutes the most fundamental historical divergence from TCM.

2.2. Clinical Application Classification

2.2.1. Clinical Application in TCM

Based on its core action of "astringing the lung and astringing the intestine," the clinical application of Hezi in TCM primarily targets diseases caused by deficiency and chronicity leading to the loss of containment and consolidation, with application concentrated in chronic stages rather than acute phases. In the digestive system, Hezi is an essential medicine for treating chronic diarrhea and dysentery. For chronic diarrhea and rectal prolapse caused by spleen-kidney yang deficiency with failure to govern containment, classic formulas such

ISSN: 2710-0170

as Zhenren Yangzang Tang (True Man's Viscera-Nourishing Decoction) combine it with poppy capsule and nutmeg to warmly astringe and secure the intestines, while Hezi Pi San (Terminalia Peel Powder) combines it with highly acrid and hot medicinals like dried ginger and aconite to simultaneously warm the middle, disperse cold, and astringe to stop diarrhea. In the respiratory system, it is used for chronic cough, deficiency-type dyspnea, sore throat, and loss of voice caused by lung qi depletion and failure of qi to return to its root, capable of astringing dissipated lung qi to calm dyspnea and benefit the throat. Although the "Hezile San" (Terminalia Powder) from the Jingui Yaolue (Essential Prescriptions of the Golden Cabinet) mainly treats qi dysentery, it also embodies its qi-regulating function. Notably, the "warming the middle and moving qi" effect emphasized during the Tang and Song dynasties persists in some formulas. For example, in the well-known emergency formula Suhexiang Wan (Storax Pill), Hezi is combined with various aromatic, warm, and unblocking medicinals to synergistically open the orifices and move qi, while its astringent nature prevents excessive acrid dispersal. This suggests that, under specific combinations, Hezi can simultaneously possess a qi-moving function—a complexity worthy of re-examination.

2.2.2. Clinical Application in Tibetan Medicine

In stark contrast to the "specialized" application in TCM, the use of Hezi in Tibetan Medicine is distinguished by its "broad" characteristics. It covers almost all internal miscellaneous diseases and is one of the most frequently occurring drugs in Tibetan formulas. Its application logic lies in restoring the body's balance by regulating the "three humors," rather than directly targeting symptoms. In the digestive system, Hezi enhances digestive function by "increasing the stomach fire," used for symptoms like poor appetite and gastric distension caused by Bad-kan disorder, and is a core high-frequency drug for treating gastric diseases like chronic atrophic gastritis. Even for chronic diarrhea, it is not confined to deficiency-cold patterns but focuses on restoring the functional balance of the intestinal tract. In the respiratory system, Hezi is a vital medicine for treating various lung disorders, including lung-deficiency cough and dyspnea, lung heat syndromes, and lung abscesses. Formulas such as "Hezi Seven-Ingredient Formula" and "Hezi Ten-Ingredient Formula" are used to clear the liver, quiet the lung, cool the blood, and stop cough. In hepatobiliary and metabolic diseases, Hezi is a core drug for clearing heat and promoting bile secretion against heat-induced liver diseases, jaundice, and hepatitis caused by an excess of mKhris-pa. Simultaneously, as the cornerstone of the "Three Fruits" (Triphala) combination, it is widely used for joint and metabolic diseases like "serous humor disease" (chu ser) and gout, functioning to clear blood heat, dry up serous humor, and regulate qi movement. In the cardiovascular, cerebrovascular, and neurological fields, Hezi is used for hypertension and high-altitude polycythemia caused by disorders of rLung and blood, exerting effects of clearing blood heat and unblocking vessels. It also plays a role in calming the mind and harmonizing qi movement for rLung-induced disorders such as mania, insomnia, and post-stroke sequelae. Furthermore, Hezi is extensively used for detoxification, improving vision, wound healing, and treating skin diseases. This difference in application breadth from "specialized" to "broad" profoundly reflects the fundamental philosophical and formula-strategic divergence between the linear logic of "medicinal nature–efficacy–indication" in TCM and the holistic, systemic three-humor doctrine of Tibetan Medicine.

3. Modern Pharmacological Analysis of Hezi

3.1. Identification of Core Chemical Constituents

Tannins are the most abundant and pharmacologically central constituents of Hezi, with content reaching 20%–40%, primarily as hydrolyzable tannins. Among them, chebulinic acid and chebulagic acid are characteristic marker compounds, serving as the main contributors to antiviral, anti-inflammatory, and immunomodulatory activities. Studies show that their direct

ISSN: 2710-0170

antiviral activity against herpes simplex virus type 2 is superior to that of acyclovir. Chebulagic acid can also reduce inflammatory cytokines such as TNF-α and IL-1β by inhibiting the MAPK signaling pathway, proving effective in rheumatoid arthritis models. Gallic acid and ellagic acid, as basic structural units of hydrolyzable tannins, are renowned antioxidants that effectively scavenge free radicals, resist lipid peroxidation, and simultaneously exhibit various activities including anti-tumor and antibacterial effects. Additionally, Hezi contains other polyphenolic compounds such as corilagin and 1,2,3,4,6-penta-O-galloyl-β-D-glucose (PGG), which jointly contribute to its complex network of antioxidant and anti-inflammatory activities.

Using techniques such as gas chromatography-mass spectrometry, researchers have identified various volatile and semi-volatile components in Hezi. Although present in lower quantities, they may contribute to its overall aroma and some pharmacological actions. These components mainly include fatty acids and their esters (e.g., palmitic acid, linoleic acid), aldehydes and ketones (e.g., phenylacetaldehyde, furfural, phytone), and other compounds (e.g., ethyl trans-cinnamate, pentadecane). It should be noted that independent pharmacological data on these single volatile components are currently far less abundant than for tannins. Their reported antibacterial and anti-inflammatory effects are often evaluated at the level of volatile oil or total extracts, and their specific contribution to the overall pharmacodynamics of Hezi requires more in-depth investigation to clarify.

3.2. Key Pharmacological and Clinical Mechanisms

3.2.1. Regulation of the Digestive System

Modern research provides a solid scientific basis for the traditional effects of Hezi in "astringing the intestine to stop diarrhea" and "increasing the stomach fire to aid digestion." Hezi extracts and their tannin components exhibit broad-spectrum inhibitory activity against various enteric pathogens, including Staphylococcus aureus, Escherichia coli, Salmonella typhi, Shigella dysenteriae, and Helicobacter pylori. Simultaneously, large quantities of tannins can bind to gastrointestinal mucosal proteins to form a protective layer, reducing exudation and inflammatory irritation. Animal experiments have also confirmed its significant inhibition of small intestinal propulsive motility, completely consistent with the TCM description of "astringing the intestine". Furthermore, Hezi protects the integrity of the intestinal mucosal barrier through antioxidant and anti-inflammatory effects. Recent research has further revealed that it can modulate the gut microbiota, increasing the abundance of beneficial bacteria such as Lactobacillus and regulating the ratio of Bacteroidetes, thereby suppressing inflammation and improving metabolism. This offers a novel perspective for understanding its treatment of chronic functional intestinal disorders and also resonates with the Tibetan medical concept of "harmonization."

3.2.2. Respiratory System Protection

The TCM effect of Hezi in "astringing the lung to suppress cough" has also been supported by modern pharmacology. Animal experiments demonstrate that Hezi extracts possess significant central and peripheral antitussive effects and can relieve bronchospasm through anti-inflammatory action to alleviate dyspnea. Its core component, chebulagic acid, effectively inhibits the production and release of multiple pro-inflammatory cytokines such as TNF-α, IL-1β, and IL-6, thereby reducing airway inflammation and relieving cough symptoms. For respiratory diseases caused by bacterial or viral infections, Hezi's broad-spectrum antibacterial and antiviral activities can directly target the etiology. These actions collectively interpret its traditional efficacy in astringing the lung, suppressing cough, and calming dyspnea from three dimensions: antitussive, anti-inflammatory, and anti-pathogen.

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3.2.3. Neuroprotective and Cardiovascular Effects

The application of Hezi in treating neurological and cardiovascular diseases in Tibetan Medicine has also begun to attract modern scientific attention. The tannins and phenolic acids enriched in Hezi are potent antioxidants capable of scavenging free radicals and inhibiting lipid peroxidation, thereby protecting neurons from oxidative damage. This provides a potential mechanistic explanation for the Tibetan medical treatment of neurological dysfunctions associated with rLung disorders. Concurrently, constituents like chebulagic acid have been found to possess immunomodulatory effects, such as inhibiting CD8+ T cell activity, reducing IgG and IL-6 levels, and increasing the concentration of the anti-inflammatory cytokine TGF-β. This bidirectional immunomodulatory capacity holds significant importance for treating autoimmune-related neurological or cardiovascular inflammatory diseases. Moreover, studies suggest that Hezi extract exerts a protective effect against myocardial injury, with mechanisms possibly related to antioxidation, anti-inflammation, blood lipid regulation, and improvement of vascular endothelial function. This provides preliminary pharmacological clues for the Tibetan medical use of Hezi in treating hypertension and high-altitude heart disease.

4. Mutual Verification between Traditional Theories and Modern Research across Medical Systems

4.1. Theoretical Verification: A Cross-System Dialogue Centered on "Lung, Intestine, and Qi"

Hezi's characteristic of acting simultaneously on the respiratory and digestive systems provides an excellent case for the convergence of the TCM theory of "interior–exterior relationship between zang-fu organs" and the Tibetan medical three-humor doctrine. The TCM theory that "the lung and the large intestine are interior–exteriorly related" posits that these two organs are interconnected by meridians and mutually influence each other physiologically and pathologically. Hezi's ability to "treat both the lung and intestine" is a classic embodiment of this concept. In Tibetan Medicine, rLung governs respiration, circulation, neural sensation, and intestinal peristalsis; its functional state directly links the breathing of the lung and the conveyance of the large intestine. As an essential medicine for regulating rLung, Hezi pacifies upper rLung to treat cough and dyspnea while harmonizing lower rLung to stop diarrhea. This unified concept of "regulating rLung" encompasses the two seemingly separate TCM actions of "astringing the lung" and "astringing the intestine," offering cross-system collateral evidence for the lung–intestine correlation. Similarly, the TCM notion that "the spleen is the source of phlegm and the lung is the receptacle of phlegm" strongly echoes the Bad-kan disease theory in Tibetan Medicine, which considers Bad-kan closely related to bodily fluids, mucus, digestion, and metabolism; spleen-stomach weakness and excessive phlegm all fall under the category of Bad-kan disorders. Hezi, by "increasing the stomach fire and aiding digestion," enhances digestive function, treating both diarrhea and, at its root, reducing the generation of Bad-kan to address respiratory diseases. This aligns highly with the TCM approach of "treating phlegm by first treating the spleen," validating TCM's profound insight into the spleen as a root cause of lung disease.

4.2. Modern Research: Scientific Evidence as a "Common Language"

Modern science provides a quantifiable and verifiable material basis for the comparison of traditional theories, becoming a "common language" for cross-system dialogue. The "gut–lung axis" theory revealed by modern medicine indicates that the gut microbiota and its metabolites can regulate pulmonary immune responses through the blood circulation. Hezi exerts a dual action precisely on this axis—it can directly suppress pulmonary inflammation while significantly modulating the gut microbiota and repairing the intestinal barrier, thereby

ISSN: 2710-0170

indirectly mitigating lung inflammation by improving the intestinal microecology. This perfectly connects the TCM zang-fu theory and the Tibetan medical holistic regulatory view with the modern "gut–lung axis" doctrine. At the level of anti-inflammation and immunomodulation, Hezi's powerful anti-inflammatory activity serves as the common pharmacological foundation for treating multiple diseases. Its tannin constituents, by inhibiting key inflammatory signaling pathways such as NF-κB and MAPK, regulate various inflammatory cytokines and immune cell functions, achieving broad-spectrum therapeutic effects across different systems and diseases at the molecular level. This scientifically explains why Hezi can act as the "King of Medicines" in Tibetan Medicine for treating a range of seemingly unrelated "heat disorders" and three-humor imbalance diseases.

4.3. Dialogue between TCM and Tibetan Medicine: Complementation and Inspiration in Differences

Differences in comparative studies often contain valuable complementary information. Regarding the breadth of application, modern TCM tends to "narrow" the use of Hezi, strictly limiting it to the "astringent" category and even considering early-stage excess pathogenic patterns as contraindications. In contrast, Tibetan Medicine has maintained its "broad-spectrum" application, using it not only for heat and infectious diseases but even as a core component of the "Three-Fruit Decoction" to treat pestilential febrile disorders. Regarding the recognition of its "tonifying deficiency" effect, Tibetan Medicine places great emphasis on Hezi's nourishing and health-promoting properties, frequently using it to treat fatigue and bodily weakness. Modern TCM almost completely ignores this action. This cognitive divergence suggests that modern TCM needs to re-examine Hezi's value in regulating overall bodily function and enhancing immunity. In terms of processing methods, TCM commonly uses techniques such as simmer-roasting, stir-frying, and bran-roasting to moderate its sour-astringent nature and enhance its astringing and antidiarrheal effects, with different processing methods influencing the content of chemical components. Tibetan Medicine adopts a unique approach, often using Hezi as an adjuvant or detoxifying agent, processing highly toxic substances such as aconite and Euphorbia fischeriana with Hezi decoction. Recent research has revealed that its detoxification mechanism lies in the reaction of tannins and the acidic environment with toxic alkaloids or diterpenoids through hydrolysis, complexation, and precipitation, significantly reducing the content of toxic components and their absorption rate in the body. This unique function has not been fully recognized within the TCM system, providing new ideas for developing safer aconite-based analgesic drugs and further confirming Tibetan Medicine's profound understanding of Hezi's "harmonizing" properties.

5. Conclusion

This study reveals the common challenges faced by the modernization of traditional medicines. A vast gap exists between basic pharmacology and clinical application; it is urgent to conduct high-quality randomized controlled trials targeting dominant diseases such as chronic diarrhea and chronic obstructive pulmonary disease. Although animal experiments have already warned of the hepatotoxicity of high-dose Hezi, clinical safety data are absent, necessitating systematic research into the "dose–time–toxicity" relationship and exploration of toxicity-reducing processing mechanisms. In terms of quality control, a multi-index quantitative standard using marker compounds such as chebulinic acid and chebulagic acid should be established to replace current crude quality assessment methods. At the level of theoretical translation, multi-omics technologies can help translate the holistic effect of "harmonizing the three humors" in Tibetan Medicine into measurable molecular network changes, thereby achieving a deep integration of traditional theory and modern science.

ISSN: 2710-0170

The core conclusions of this study are threefold. First, the contemporary mainstream TCM application has narrowed Hezi to an astringent drug, whereas Tibetan Medicine has consistently esteemed it as the "King of Medicines," maintaining its broad-spectrum, holistic regulatory application. Tibetan medical practice may have preserved a more complete historical profile of Hezi. Second, Hezi, through multiple mechanisms including anti-inflammatory, antioxidant, antibacterial, and gut microbiota-modulating activities, provides scientific mutual corroboration for the traditional efficacy recognized by both medical systems. The "gut–lung axis" particularly offers a modern annotation for the TCM theory that "the lung and the large intestine are interior–exteriorly related" and the Tibetan medical holistic view. Third, the applications of Hezi in Tibetan Medicine—tonifying deficiency, moving qi, and detoxifying—prompt a re-examination of its neglected clinical potential. Looking forward, the macroscopic wisdom of Tibetan Medicine, the pattern-differentiation experience of TCM, and modern evidence-based methods should be combined. Through standardized preparations and high-quality clinical research, this "King of Medicines" can be revitalized within the modern medical system to radiate new value.

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