



# Advances in Quality Control Methods for Colla Corii Asini Preparations

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**Abstract:** There are numerous records of Colla Corii Asini from ancient times, which is a good medicine for nourishing yin and moistening dryness, tonifying blood and stopping bleeding. Colla Corii Asini and its preparations are composed of proteins and peptides produced by hydrolysis, amino acids and nucleic acids, polysaccharides, trace elements and other components. The market demand for Colla Corii Asini products has been increasing year by year. This, coupled with natural constraints and the downturn in the donkey farming industry, has led to a shortage in the supply of donkey hides, the raw material for Colla Corii Asini. In order to improve the overall quality and evaluation standards of Colla Corii Asini on the market, it becomes particularly important to study the progress of quality control methods for Colla Corii Asini preparations.

**Keywords:** Colla Corii Asini preparation, quality control, research progress

## 1. Overview of Colla Corii Asini and its preparations

Asini Corii Colla (ACC) is a solid gelatinous drug made from the dried or fresh skin of *Equus asinus* L., a donkey of the family Equidae, by decoction and concentration.[1] ACC is a solid gum made from the dried or fresh skin of the donkey *Equus asinus* L., family Equidae. Records of Colla Corii Asinus from ancient times to the present day are endless, and the description of Colla Corii Asinus in Shennong Ben Cao Jing mentions that it is "sweet in flavor and flat in texture. Main heart and abdomen, internal avalanches, labor, spilling like malaria, waist and abdominal pain, limb pain, women under the blood, to stabilize the fetus, take a long time to lighten the body, beneficial to the gas." This book will be listed as "top grade", "Compendium of Materia Medica" called "holy medicine", medicinal history of more than 2,500 years. Colla Corii Asini is sweet in taste and flat in nature, belonging to the lung, liver and kidney meridians, with the effects of tonifying blood, nourishing yin, moistening dryness and stopping bleeding.[2] It has the effect of tonifying blood, nourishing yin, moisturizing and stopping bleeding. It is often used in blood deficiency and yellowing, palpitation and dizziness, vomiting blood, coughing up blood, coughing up lung dryness, collapse and other blood deficiencies or bleeding disorders, and is a good medicine for nourishing yin and moistening dryness, nourishing blood and stopping bleeding. Colla Corii Asini and its preparations are composed of proteins and peptides produced by hydrolysis, amino acids and nucleic acids, polysaccharides, trace elements and other components. In modern pharmacological research, we found that Colla Corii Asini has the pharmacological effects of accelerating calcium absorption, strengthening immunity, anti-shock, anti-aging, anti-tumor, adjusting the condition of iron-deficiency anemia, nourishing the face and beauty, etc., and it has a wide range of clinical applications.[3] It has a wide range of clinical applications. However, due to the rise of "health culture", people's understanding of sub-health gradually improved, the market demand for Colla Corii Asini products increased year by year, coupled with the natural conditions of the limitations of the donkey industry and donkey farming industry downturn, resulting in a shortage of supply of raw materials for Colla Corii Asini donkey skin. As a result, the Colla Corii Asini products on the market today are a mixture of good and bad. In order to improve the overall quality and evaluation standards of Colla Corii Asini on the market, it becomes particularly important to study the progress of quality control methods for Colla Corii Asini preparations.

## 2. Chemical composition of Colla Corii Asini

Colla Corii Asini and its preparations contain many active ingredients, including proteins and their hydrolyzed peptides and other components such as amino acids and trace elements, each of which will be described next.

### 2.1 Proteins and peptides

The main component of Colla Corii Asini is collagen, and its hydrolysis can produce gelatin, peptides and a variety of amino acids. Its protein content is about 80%. There are three main proteins, donkey serum albumin, donkey collagen a1 and donkey collagen a2, of which donkey serum protein content is particularly high[7] The content of donkey serum protein is particularly high. Liao Feng et al.[8] In the investigation of the pharmacological activity of Colla Corii Asini, 316 recognizable proteins were retrieved by electrophoresis, and it was found that Colla Corii Asini contains leucine-rich small-molecule

proteoglycans such as core proteoglycans, disaccharide-chain proteoglycans, Lumican, and fibronectin, as well as immunoglobulin, collagen, and other active proteins, which provided a theoretical basis for the screening and in-depth exploitation of the pharmacological active ingredients of Colla Corii Asini.

## 2.2 Amino acids

Gum contains 18 amino acids, including 7 essential amino acids, including lysine, histidine, arginine, threonine, serine, glutamic acid, alanine, proline, glycine, valine, methionine, leucine, isoleucine, tyrosine, phenylalanine and so on.[4]. Wang et al.[5] The content of major amino acids including L-hydroxyproline, glycine, alanine and L-proline in Colla Corii Asini Blood Replenishing Oral Liquid was determined rapidly and sensitively by chromatographic method, which provides a theoretical basis for controlling the product quality of Colla Corii Asini Blood Replenishing Oral Liquid.

## 2.3 Other components

Colla Corii Asini contains many other ingredients. The trace elements it contains include K, Na, Ca, Mg, Fe, Cu, Al, Mn, Zn, Cr, Pt, Mo, Pb, Sr, etc.[4] It also contains cytosine, cytosine, and cytosine. It also contains cytosine, cytidine, uracil, hypoxanthine, uridine, guanosine, adenosine and other nucleoside compounds.[6] Glycine Soja. Colla Corii Asini also contains polysaccharide components such as dermatostatin sulfate (DS) and hyaluronic acid (HA), volatile substances, lipids and fatty acids.

## 3. Advances in quality control methods for Colla Corii Asini preparations

There are many quality control methods for Colla Corii Asini. In recent years, the more mature ones that have been studied include chromatography, chromatography-mass spectrometry (LC-MS) and nuclear magnetic resonance hydrogen spectrometry.

### 3.1 Chromatography

The hydrolysis products of collagen, the main component in Colla Corii Asini, are amino acids, so the type and content of amino acids can be tested to determine the quality of Colla Corii Asini products. Li Wanshi et al.[9] The determination of 17 amino acids in Colla Corii Asini was accomplished using HPLC technology, among which threonine, valine, methionine, isoleucine, leucine, phenylalanine, lysine and histidine are essential amino acids, and these essential amino acids accounted for 17.0% of the total amino acids. The method is simple and reliable, with good precision and reproducibility, and the distribution and proportion of amino acids contained in 10 batches of Colla Corii Asini are relatively stable, and the application of fingerprinting and cluster analysis to the quality identification of Colla Corii Asini from different sources can provide a basis for the establishment of a method for the characterization of the medicinal herbs. Liu Wen et al.[10] Simultaneous determination of L-hydroxyproline, glycine, alanine and L-proline in Colla Corii Asini by one-measurement-multi-assessment method with accurate and reliable results, which can be used for the quality control of Colla Corii Asini. Ge Chongyu et al.[11] The contents of 17 amino acids in 18 batches of Colla Corii Asini from 18 enterprises were determined by fully automatic amino acid analyzer, and it was found that the total contents of amino acids in marketed Colla Corii Asini varied greatly, and the contents of various amino acids in Colla Corii Asini from different enterprises also differed to a certain extent.

### 3.2 Chromatography-mass spectrometry

The proteins contained in different skin sources are highly homologous and have similar amino acid compositions, so it is difficult for common methods such as gel electrophoresis, amino acid fraction analysis, and chromatography to effectively determine the small differences in amino acid composition. Deoxyribonucleic acid (DNA) degradation is inevitable during the processing of Colla Corii Asini into preparations, so it becomes difficult to identify the quality of Colla Corii Asini through the determination of DNA. In recent years, the identification of characteristic peptides by liquid chromatography-mass spectrometry (LC-MS) has gradually become a mainstream technique to identify the quality of Colla Corii Asini. Guo Shangwei et al.[12] used HPLC-MS/MS to determine the contents of 17 amino acids in Colla Corii Asini, Colla Corii Asini and Colla Corii Asini, thus realizing the easy operation, rapidity and accuracy, as well as good reproducibility and stability, which can be applied to the analytical quality detection of amino acids in Colla Corii Asini, Colla Corii Asini and Colla Corii Asini.

### 3.3 Other methods

JIANG Jiaojiao[13] Using low-field nuclear magnetic resonance (LF-NMR) technology for the rapid detection of different brands of Colla Corii Asini and adulterated Colla Corii Asini, the contents of four major amino acids in three kinds of gelatine could meet the standards stipulated in the 2015 edition of the Chinese Pharmacopoeia, and the contents in Colla

Corii Asini Juice were the highest, followed by Colla Corii Asini and Colla Corii Asini were the lowest, which could serve as an intrinsic quality index for distinguishing between different kinds of gelatine. For the first time, the content of four major amino acids in Colla Corii Asini juice without excipients was determined by HPLC-ELSD method, and the minimum limit standards were established. The interference of excipients on the determination of amino acids after hydrolysis was eliminated, and the results were more accurate and efficient, which can be used to control the quality of Colla Corii Asini from the source. Ji Guoxia et al.[14] Microwave digestion coupled with inductively coupled plasma mass spectrometry (ICP-MS) was utilized to determine 14 elements in Colla Corii Asini, including 3 macronutrients (K, Ca, Mg), 5 trace elements (Fe, Zn, Mn, Ba, Sr) and 6 heavy metal elements (Cr, As, Cd, Pb, Cu, Hg).

#### 4. Summary and outlook

As of now, there has been great progress in the study of the composition and quality control methods of Colla Corii Asini and its preparations. We found that Colla Corii Asini is composed of collagen, the main component, and other components such as amino acids, trace elements, nucleoside analogs and polysaccharides. The quality control of Colla Corii Asini has also made great progress, especially the liquid chromatography mass spectrometry (LC-MS) technique can be used to identify the characteristic peptides for the quality control of Colla Corii Asini.

However, the components of Colla Corii Asini that cause medicinal effects are still not precise enough. At the same time, the quality control methods of Colla Corii Asini still need further research, and the current methods used to identify the quality control of Colla Corii Asini are still limited to many single compounds that exist in many substances at the same time, while its exclusive active ingredients are still unknown, and it is one-sided to evaluate the quality control of Colla Corii Asini by these ingredients. Therefore, the research on Colla Corii Asini still has a long way to go. It should be combined with the latest modern research technology to carry out multi-faceted research and development to maximize the value of Colla Corii Asini.

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