

# Advance on delivery nanocarriers of piperine: nanoparticles

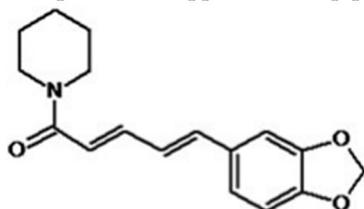
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**Abstract.** Piperine is a kind of natural functional active components with spicy flavor and varies pharmacology effects. It has wide application in the food and medicine industries. However, the solubility of piperine is low, and it was easy to be transformed or degraded during the conditions of acid, alkali, light, heat and oxygen which lead to the vanish of its function. In order to enhance the stability of piperine, the nanotechnology was utilized to fabricate the delivery carrier of piperine. In this paper, the latest research progress of piperine nanoparticles was reviewed by summarizing domestic and foreign literature. The characteristics, preparation methods, preparation materials and stability of nanoparticle delivery carriers were systematically discussed. Finally, the present problems and future development of piperine delivery carrier were analyzed and forecasted in order to provide a reference for profound process and study of piperine.

## 1 Introduction

Pepper is a kind of tropical vines. Its main active component is piperine which can endow food spicy flavor and improve our appetite<sup>[1]</sup>. In addition, it contains various physiology function, such as antibacterial, anti-inflammatory, hypoglycemic, prevention of tumor and treatment of convulsion<sup>[2]</sup>. Piperine has been widely used in food and medicine industries. However, piperine has some defects. For example, in acid environment, C<sub>17</sub>H<sub>19</sub>O<sub>3</sub>N acidate to C<sub>17</sub>H<sub>19</sub>O<sub>4</sub>, while in alkaline condition piperine hydrolysis into C<sub>15</sub>H<sub>11</sub>N and other substance. The piperine can transfer into chavicine and isopiperine in light condition. These transformed products will attenuate or lose the original spicy and pungent effect of piperine and the pharmacological function of piperine<sup>[3]</sup>. The structure of piperine molecule contains benzene ring, alkene, carbonyl and other hydrophobic groups (Fig. 1), which leads to it has the properties of low polarity, water insoluble, difficult to digest and absorb by human body, and low bioavailability. Only a little of piperine could realize its pharmacology activation, and these defects limited the development and application of piperine.



**Figure 1.** Chemical structure of piperine

To solve these problems, many new method and technology are used in improving the solubility, stability

of physics and chemistry and bioavailability, such as chemical modification technology<sup>[4]</sup>, nanotechnology<sup>[5]</sup> and emulsification technology<sup>[6]</sup>. Compared with other technologies, the particle size of delivery carrier prepared by nanotechnology is small. It can transport piperine through membrane which could realize targeting and controlled release to increase the bioavailability of piperine. In addition, to make piperine stable in nano carrier during the process of transportation and storage, we can prepare smart response delivery carrier with nano technology. Based on these technologies, we can improve its storage stability and bioavailability that piperine can release slowly during in vivo metabolic process<sup>[7-10]</sup>.

## 2 Delivery nanocarriers of piperine

Currently, the researches of piperine mostly focus on the extraction process, detection method, chemistry modify, bioavailability and physiology function. However, the studies of piperine's delivery carrier were lacked. In recent years, many delivery nanocarriers were prepared from starch, oil, protein, polysaccharose and other natural biomacromolecule using nanotechnology<sup>[11-14]</sup>. These nanocarriers not only embedded and protected piperine efficiently, but also improved the stability of piperine. Besides, these nanocarriers had the merit of excellent biocompatibility, digestibility and degradability, safe and non-toxic, and so on<sup>[15]</sup>.

According to the difference of structural property in these delivery carriers, they could be divided into nanoparticles, nanoemulsion, nanomicelle, liposome and so on<sup>[16-18]</sup>. These delivery vehicles are either used to increase the water solubility of piperine, or to increase the stability of piperine, or to increase the bioavailability of piperine. Among them, nanoparticles can expand the

application of piperine in the solid matrix. This article will focus on the nanoparticle of piperine.

### **3 Nanoparticles of piperine**

#### **3.1 Preparation material and preparation method of piperine nanoparticles**

The nanoparticles in delivery system referred to particle size less than 1000nm, and the inner place of these solid particle was used to embed and deliver active substance. The natural materials which used to prepare delivery carriers of nanoparticles contained whey protein isolate, soybean protein isolate, casein, zein and other protease materials; starch, chitosan, sodium alginate, pectin and other polysaccharide materials; even solid fat, structured oil gel, other biomolecule polymer, polylactic acid, glyceride and so on<sup>[19-21]</sup>. The preparation of piperine nanoparticles included antisolvent precipitation method, complex coagulation method, spray-drying process, freeze-drying and so on<sup>[22]</sup>. The antisolvent precipitation method was dissolving piperine and base material of delivery carriers in proper solvent advancedly, then adding the obtained solution into another different polarity solvent to make the base material of delivery carriers self-assembled into nanoparticles. The particle range of nanoparticles prepared by antisolvent precipitation method was comparable small<sup>[23-26]</sup>. However, these nanoparticles had no need for complex manufacture machine with wide spread in application. Complex coagulation method requires base material with positive and negative opposite charge molecular assembled into nano particles. It had the merit of controlling the particle range and consuming less solvent. Spray-drying process and freeze-drying mainly was made the dispersing liquid of prepared nanoparticles drying into solid powder particles which was benefit for transportation, storage and application.

#### **3.2 Piperine nanoparticles based on polylactic acid/glyceride matrix**

Pachauri et al.<sup>[27]</sup> prepared piperine nanoparticles based on polylactic acids, and their particle size were very small (131.1 nm). These nanoparticles were comparable stability but had a low embedding rate of 37%. Embedding rate (%) was the percentage between the weight of piperine embedding in nanoparticles and the total weight used during the whole preparation process. It was a crucial standard to measure the ability of embedding in nanoparticles. The assay of piperine in nanoparticles was tested by reverse liquid chromatography and detectability could be reached to 0.1mg/kg<sup>[28]</sup>. To improve the embedding rate of piperine, the glyceride was used as matrix. Preparing the solid fat particles with glyceride as matrix, the embedding rate of piperine reached to 78.71% and the oral bioavailability and stability were improved<sup>[29]</sup>. In addition, there are many other advantages on preparing piperine nanoparticles through glyceride as matrix. For example, the particle size was small, only 100-150nm. And through cell experiment and animal model

experiment, it proved that glyceride nanoparticles could enhance the bioavailability of piperine and other active components<sup>[30]</sup>. When piperine and curcumin embedded in glyceride nanoparticles simultaneously and adjusted the particle size less than 60nm, these nanoparticles could pass through blood brain barrier and cure parkinsonism<sup>[31]</sup>.

#### **3.3 Piperine nanoparticles based on polysaccharide matrix**

To improve the embedding rate of piperine, the polysaccharide could be used as matrix. As the only cation polysaccharide in nature, chitosan was able to enhance the embedding rate of piperine to 53%<sup>[32]</sup> while the piperine nanoparticles prepared by chitosan. Cyclodextrin is a kind of special oligosaccharide with annular cavity structure. It could form clathrate compound whose particle size was nanometer scale with piperine inside. The nanoparticles could be obtained after spray drying or freeze-drying. The embedding rate of piperine could be reached to 88.12% with saturated solution method and microwave assisted as cyclodextrin-piperine clathrate compound. The water solubility of piperine increased 2.6 times after embedded, and its thermal stability was also obviously improved.

#### **3.4 Piperine nanoparticles based on protein-polysaccharide composite matrix**

Protein used as delivery carrier matrix of piperine had many advantages. Because protein was safe, non-toxic, digestible and degradable, the molecule of protein was comparable giant in order to embed piperine inside and its surface could absorb piperine.

In addition, protein in water solution system had some emulsion stability which could be used to steady piperine nanoparticles. For example, the embedding rate of piperine in nanoparticles produced by BSA as matrix could be reached to 77.8% which made piperine release slowly in vivo and improved bioavailability<sup>[33]</sup>. Due to the piperine was a kind of hydrophobic molecule, the interaction force with almost protein in water system was not strong. But it could form stable nanoparticles with hydrophobic protein by hydrophobic interaction. Zein, with over 50% hydrophobic grouping, was insolubility but dissolved in 60%-90% alcohol water solution. It was the ideal material to prepare piperine nanoparticles. However, the isoelectric point of zein was 6.2, dispersing solution of zein was easy to gather as sediment in neutral pH circumstance. Therefore, it could use polysaccharide and zein composite in order to decorate surface nature and particle structure. For example, with the assay of chitosan increasing, the particle size of piperine nanoparticles which produced by electric spray method using zein and chitosan as matrix became larger. And the embedding rate of piperine could increase gradually too. The maximum of particle size was 527 nm, and the supreme embedding rate could reach to 87%<sup>[34]</sup>. In addition, piperine and other active components had a synergistic effect. For example, the bioavailability of curcumin could improve over 9 times through simultaneously embedding curcumin and

piperine in zein-chitosan nanoparticles [35].

## 4 Conclusion

Piperine, as one kind of flavoring component and functional active substance, is adored by people for its spicy flavor. In addition, piperine has prosperous application prospect among food and medicine industries because it has the effect of bacteriostat, anti-inflammatory, curing convulsions and so on. However, poor solubility, unstable nature and low bioavailability limited the development and usage of piperine. Based on nano technology, structuring nanoparticles delivery carrier of piperine, not only can it increase the solubility of piperine, but also improve the anti-degradation capability during the condition of acid, alkali, light, heat and oxygen which extend the application range of piperine among food and medicine industries. Now, nanoparticles in delivery piperine aspect belongs to the leading edge of scientific research, it still has a long way to actual production and application. And we believe that delivery carrier of piperine will get more concern and study among food and medicine industries in the future. With the improvement of scientific technology, delivery carrier of piperine will obtain more application among food and medicine industries.

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