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Utilizing the Box-behnken Design to Create Amorphous PVP K30-Phosphatidylcholine Dispersions for the Co-Delivery of Hesperetin and Curcumin Made by Hot-Melt Extrusion

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Introduction

In recent years, the delivery of bioactive compounds has garnered increasing attention due to their potential health benefits in the prevention and treatment of various diseases. Among these bioactive compounds, hesperetin and curcumin stand out for their remarkable antioxidant, anti-inflammatory and anticancer properties. However, the clinical application of these compounds is limited by their poor solubility, bioavailability and stability. One of the most effective strategies to improve the solubility and bioavailability of poorly water-soluble compounds is the formulation of solid dispersions. Hot-Melt Extrusion (HME) has emerged as a promising technique for the preparation of solid dispersions, as it allows for the creation of homogeneous dispersions of active pharmaceutical ingredients (APIs) in a carrier matrix. Polyvinylpyrrolidone K30 (PVP K30) and Phosphatidylcholine (PC) have been widely studied as carrier materials for solid dispersions due to their favorable properties, such as biocompatibility, ease of processing and ability to enhance drug solubility. However, the optimization of the formulation to achieve the desired characteristics, such as increased drug solubility and stability, requires careful consideration of various formulation factors.

Description

The Box-Behnken Design (BBD), a type of Response Surface Methodology (RSM), is a statistical tool that can be used to optimize the formulation process by investigating the interactions between multiple variables and their effects on the desired response. In this study, the BBD is utilized to design and optimize amorphous PVP K30-PC dispersions for the co-delivery of hesperetin and curcumin via hot-melt extrusion. The main objective is to increase the solubility and bioavailability of these compounds by optimizing the formulation parameters, including the ratio of PVP K30, PC and the drugs, as well as the processing conditions. PVP K30 is a widely used excipient in pharmaceutical formulations due to its excellent solubility in water, ability to form films and favorable biocompatibility. PVP K30 has been shown to enhance the dissolution rate of poorly soluble drugs by forming solid dispersions. The formation of amorphous solid dispersions is advantageous because amorphous forms generally exhibit higher solubility than crystalline forms due to the increased surface area and the absence of the crystalline lattice structure.

Curcumin, a polyphenolic compound derived from the rhizomes of Curcuma longa, has long been used in traditional medicine for its anti-inflammatory, antioxidant and anticancer properties. Despite its therapeutic potential, curcumin suffers from low solubility in water and poor absorption in the gastrointestinal tract. Numerous strategies, such as nanotechnology-based delivery systems, solid dispersions and the use of phospholipid complexes, have been employed to improve curcumin's solubility and bioavailability. The co-delivery of hesperetin and curcumin is of particular interest because these compounds complement each other in terms of their therapeutic effects. Both have antioxidant and anti-inflammatory properties and their combination could potentially lead to enhanced efficacy in treating diseases that involve oxidative stress and inflammation, such as cancer and cardiovascular diseases. However, the formulation of a co-delivery system that can overcome the solubility and bioavailability challenges of both compounds remains a significant challenge [1,2].

Conclusion

The co-delivery of hesperetin and curcumin in amorphous PVP K30-PC dispersions prepared by hot-melt extrusion is a promising strategy for improving the solubility and bioavailability of these bioactive compounds. By utilizing the Box-Behnken design, the formulation process was optimized to identify the key factors that influence the solubility, dissolution rate and stability of the drugs. The results demonstrated that the combination of PVP K30 and phosphatidylcholine, along with careful control of extrusion conditions, can lead to significant improvements in the delivery.

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