This edition of “Eye on Excipients” discusses the pharmaceutical applications for zein in film coating and as an excipient.

Pharmaceutical and nutraceutical manufacturers are increasingly seeking natural materials to encapsulate active ingredients. This effort is partly due to an industry trend to reduce the use of synthetics and chemicals and partly to a reevaluation by regulatory authorities in the EU, US, and elsewhere of the health and environmental impacts of materials that pharmaceutical companies currently use for encapsulation.

Natural polymers provide versatility as excipients, are renewable and biodegradable, and offer several advantages in the encapsulation of active ingredients. You can create capsules or films from natural polymers using several techniques, including spray drying, emulsion, coacervation (a chemical method for producing polymer droplets in suspension), and ionotropic gelation (a method of crosslinking oppositely charged ionic polymers). Natural polymers also exhibit attractive chemical properties such as:

- the ability to form films;
- good emulsification properties;
- high resistance to the environment of the gastrointestinal tract;
- biodegradability;
- low viscosity at high solids content; and
- low hygroscopicity.

Food and pharmaceutical companies seeking a vegan alternative to shellac-based coating formulations have investigated the use of zein, a prolamin found in corn, as one such alternative, due to its reputation for being superior to other coatings in terms of resistance to heat, abrasion, and humidity.

Zein demonstrates a wide spectrum of beneficial encapsulation properties while displaying negligible interactions with active ingredients. For encapsulated drug products, zein can provide a zero-order, controlled-release pattern, releasing a constant level of drug for an extended period of time, or a delayed-release pattern, in which a rapid release follows an initial lag time.

Recently, the industry has also been evaluating zein as an excipient in other drug delivery systems, including targeted or sustained drug delivery [1], transdermal patches [2], food-grade capsules [3], and tissue engineering [4]. Recent research has also shown that zein improves the absorption of essential nutrients, such as vitamins D and E and omega-3 fatty acids [5].

Zein as a delivery system

Zein is one of the few hydrophobic, water-insoluble biopolymers that the US FDA has approved for oral use. Because it’s hydrophobic, zein can easily be transformed into colloidal particles by changing the solubilizing capacity of the primary solvent through dilution with a non-solvent [6]. This is due to the excellentmiscibility of ethanol and water, whereas water isn’t a good solvent for the dissolved zein.

Zein micro- and nanoparticles also appear promising for drug delivery, especially for hydrophobic nutrients or drugs. Generally, you can dissolve hydrophobic bioactives together with zein in an aqueous, ethanol binary solvent and then mix the solution with an antisolvent, such as water, to coprecipitate the bioactives with zein.

Zein can create a protective layer because of its extremely high surface area and trapping efficiency. It’s also known for its resistance to digestive enzymes, resulting in slower digestion in the gastrointestinal tract, which you can exploit for the controlled release of functional components loaded in colloidal zein particles. Taken together, these properties make it an attractive novel material in a wide range of applications for protecting bioactive components, such as polyphenols, vitamins, and omega-3 fatty acids [7].

Coating applications

Manufacturers can easily produce zein films by solvent casting, extrusion, and spin casting. An appropriate polymer film for a coating application generally requires ideal mechanical and barrier properties, such as elongation, tensile strength, and water and gas permeability. Manufacturers can tailor these film properties to both the formulation and the process of film formation.

In some cases, manufacturers also use plasticization, chemical cross-
linking, modification, and certain post-treatments to improve the properties of zein films. Other factors that affect the properties of these films include the concentration of zein in the solution, the solution's water-to-solvent ratio, the thickness of the coating or film, and the choice of plasticizers, if required.

**Hybrid solutions**

Zein is also unique in its ability to function cooperatively with many compounds, and hybrid films typically include plasticizers, essential oils, or other natural polymers. Hybrid films can take advantage of the good mechanical and barrier properties of both zein and the other ingredients, bypassing their shortcomings.

Zein-chitosan complex nanoparticles will form a gel at an acidic pH, providing greater protection of the zein protein against enzymatic degradation. The method of combining the two components determines the properties that the complex compound displays, allowing zein's properties to be applied differently with different nutrients and drugs.

For example, a formulator can design a nanoparticle with a chitosan hydrophilic core and a zein hydrophobic shell. This approach provides a higher encapsulation efficiency and a slower sustained release of hydrophilic nutrients or drugs in the gastrointestinal tract.

Alternatively, the formulator can pour the zein nanoparticles, together with hydrophobic bioactives such as fat-soluble vitamins, into a chitosan solution to induce phase separation and form zein-chitosan complex nanoparticles.

Curcumin is a natural polyphenol that is a very powerful antioxidant, but the formulation and delivery of curcumin in oral products is a very challenging task due to a combination of factors. Curcumin mixed with zein colloidal particles has shown enhanced water dispersibility and enhanced stability of the curcumin at various pH levels [8].

As these examples show, the ease with which formulators can enhance the natural performance of zein by adding other ingredients or otherwise manipulating the zein solution makes it a uniquely flexible encapsulator. T&C

**References**


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