Technology Summary: Polysaccharide-Modified Gelatin Nanoparticles

Opportunity Statement

Gelatin is a translucent, colorless solid substance prepared by either alkaline or acidic hydrolysis of collagen obtained from animal sources. It is generally prepared by the Maillard reaction between an amino acid and a reducing sugar. Gelatin is organic, biocompatible and non-immunogenic, and is considered a "generally regarded as safe (GRAS)" material by the USFDA. Nanoparticles made of gelatin can be used to encapsulate different compounds and have applications as drug- or gene-delivery carriers, food additives and cosmetic ingredients.

The potential market for gelatin nanoparticles is expected to be huge. In the pharmaceutical industry alone, the nanotechnology-enabled drug delivery market is expected to reach $220 billion by 2015.

Problem

Although they possess a wide range of applications, unprocessed gelatin nanoparticles (without surface modification) encounter the problem of being phagocytosized by the mononuclear phagocyte system (MPS) in the body. Surface modification of gelatin nanoparticles is usually required to prevent phagocytosis, and this can be done through the use of synthetic polymers, generally polyethylene glycol (PEG). The process of grafting PEG over gelatin nanoparticles, however, is complex and involves the use of organic chemicals as well as toxic chemical reagents. The use of these chemicals can increase the cost of the process, endanger human health and cause environmental pollution.

Recent research suggests that polysaccharides can be a viable material for surface modification of gelatin nanoparticles. It also has been found that polysaccharide-modified nanoparticles have low plasma protein adsorption and long circulation times.

Therefore, there is a need for a technology that can produce polysaccharide-modified gelatin nanoparticles without the issues associated with PEGylation of gelatin nanoparticles.

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360ip Partner's Solution

360ip partner's invention relates to a method of preparing stable polysaccharide-modified gelatin nanoparticles and its applications. The nanoparticles are formed by a cross-linking mechanism and have a gelatin core and polysaccharide shell. The method for preparation involves two steps:

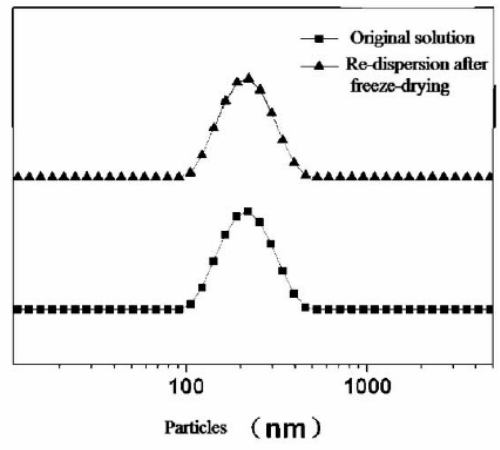
i. A Maillard reaction carried between gelatin and polysaccharide to form a protein-polysaccharide covalent composite

The Maillard reaction is performed under dry heat without the addition of other chemical reagents; the reaction condition is moderate and is safe and nontoxic. Also, the Maillard reaction serves to reduce the preparation cost and achieve better nanoparticle stability. The product of the Maillard reaction needs no further separation and can be subjected to the next step reaction directly.

ii. A globular protein used as a cross-linking agent is mixed with the protein-polysaccharide covalent composite

The gelatin and the globular protein tend to aggregate under the action of intermolecular force. The mixed solution obtained is heated to denature the protein. This causes nanoparticles having the structure with the protein as the core (the main component is gelatin) and the polysaccharide as the shell to be formed. The pH value of the gelatin-polysaccharide covalent composite solution can be regulated within a predefined range.

The nanoparticles prepared have excellent monodispersity. They can be preserved for long durations in a water solution as well as processed into powder form by freeze drying for storage. Nanoparticles in a freeze-dried powder form can be distributed in water later to recover the original size and size distribution (as shown in the figure below).



Laboratory experiments have shown that a variety of compounds can be encapsulated in the gelatin nanoparticles. (See Table below)

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Polysaccharide Type	Encapsulated Compound	Drug Loading Efficiency %	Encapsulation Efficiency %
Glucan	Ibuprofen	28	56
Glucan	Tamoxifen	14	29
Glucan	Topotecan	44	88
Glucan	Indometacin	24	48
Glucan	Naproxen	23	46
Glucan	Adriamycin	15	53
Glucan	Ibuprofen	40	80
Glucan	5-fluorouracil	11	28
Glucan	Calcein	31	76
Glucan	Fhodamine	11	22
Glucan	Vitamin E	24	59
Glucan	Tea polyphenol	25	51
Glucan	Irisone	18	46
Mannogalactan	Ibuprofen	29	58
Pullulan	Ibuprofen	33	67

The gelatin nanoparticles have the following benefits:

- Use of polysaccharide as a surface modifier prevents the gelatin nanoparticles from being phagocytosized , thereby providing long circulation properties in the body
- Stable nanoparticles due to the use of Maillard reaction and cross-linking agent (globular protein)
- Long-term stability as nanoparticles can be preserved in water solution for a long period of time, or they can be processed to powder form
- Reduced cost as only heat and organic chemicals are used
- Possess monodispersity property
- Environmentally friendly, non-toxic and safe due to the absence of organic solvents and toxic chemical reagents in the preparation

Patents

360ip's partner has filed one patent application on this technology and plans to seek protection in multiple jurisdictions.

360ip is seeking interested parties for the licensing, further development and commercialization of this technology-based product.

For additional information, contact:
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