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Review

Nano-encapsulation as a promising approach for targeted delivery and controlled release of vitamins

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A B S T R A C T

Background: Vitamins are bioactive molecules necessary for human health, which are sensible to degradation. During consumption, the bioavailability of these compounds might be limited due to structure break-down and low absorption. Today, nanoencapsulation can be a promising approach for targeted delivery of vitamins and protecting these bioactive components against destructive environment during processing and delivery. Regarding the benefits of utilizing nanotechnology in the food sector, safety aspects of these tiny carriers should also be clarified as this technology develops. Due to the possible negative effects of nanomaterials, several agencies have legislated regulatory policies to prevent potential harms to the consumers, which are underlined in this article.

Scope and approach: Nanoencapsulation-based technologies are a unique and novel field of investigation in the food and pharmaceutical industry with benefits, such as higher bioavailability, high shelf-stability and controlled release of active compounds. This review highlights recent works on these techniques and advances made in nanoencapsulation of lipophilic and hydrophilic vitamins, safety issues and health risks regarding the consumption of these products, which opens new horizons in food technology and nutrition with possibilities of commercialization in the near future.

Key findings and conclusions: Recently, considerable progresses are being carried out in the field of food nanoencapsulation involving novel nanovehicles to encapsulate vitamins. Nanofibers and nanohydrogels are some examples of efficient and modern nanocarriers. Overall, the vitamins encapsulated within nanovehicles are considered safe since they are mostly produced from food components, meanwhile more studies should be performed regarding the safety issues of nanodelivery of vitamins. In near future, it is assumed that nanoencapsulated vitamins will be broadly applied the in the food and beverage products.

1. Introduction

Vitamins and antioxidants are rudimentary elements for human health as they assist the body to grow and develop. Furthermore, they are able to prevent diseases and to promote general health. Unfortunately, most of these bioactive agents are either produced in trifle amounts or not made in the body. Thus, vitamins need to be supplied from food products and through dietary supplements if needed (Wildman, Wildman, & Wallace, 2006). Some of the beneficial functions of vitamins are as follows: enhancing the immune system and vision, supporting skin health and cell growth and helping to prevent cancer (vitamin A); empowering the immune system, alleviate anxiety and depression, reduce stroke risk and relieve PMS (premenstrual syndrome) (vitamin B-complex); raising immunity, treating common cold symptoms, maintaining healthy skin, healing wounds, reducing cholesterol levels and regulating the blood sugar level, reducing neurological disorders (vitamin C) (Hickey, 2009), preventing cancer and cardiovascular diseases as well as promoting vigorous bones and teeth (vitamin D), restraining brain and nervous system diseases; such as, Alzheimer and other dementias, boosting physical endurance and avoiding skin disorders (vitamin E), helping blood clot, nerve signaling, improving bone health and regulating cellular functions (Zempleni, Suttie, Gregory III, & Stover, 2013).

Vitamins are sensitive molecules; therefore they should be

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preserved from harmful agents like heat and oxidants. Encapsulation is a promising and novel method for preserving the innate characteristics of vitamins over time (Sanguansri & Augustin, 2006). This process includes coating or trapping a biomaterial or a combination into another element. The entrapped substance is normally a liquid, while a gas or solid state substance can also be carried. The coating substance is known as capsule, wall material, membrane, or carrier.

Our body has nanoscale structures like DNA, amino acids, etc. (Weiss, Takhistov, & McClements, 2006). Considering these natural nanoparticles, scientists have engineered nanomaterials for the usage in human's food and recently, there has been a tremendous progress in food nanoencapsulation.

In this study, after a brief review on pros and cons of food nanotechnology and microencapsulation of vitamins, we will highlight recent fundamental and novel techniques used to nanoencapsulate different vitamins in the food industry. Besides, issues on the characterization, controlled release and safety-consumption of these vital elements are described. Future trends will also be explained in the last section.

2. Pros and cons of applying nanotechnology in the food industry

Today, the entry of nanotechnology within the food sector has brought new hopes and is expected to be the key to food industry's concerns as it may bring various benefits, nevertheless like the other emerging technologies it could also have risks for consumers. According to Aguilera (cited in Yaktine & Pray, 2009), exerting nanotechnology in food industry may bring about various advantages and opportunities; such as, developing promising nano-processes, fabricating eco-friendly processes and intelligent nano-packaging, manufacturing products with desirable texture and tastes, producing low-calorie food and beverage products with the aim of changing the lifestyles into healthy ones. He also suggested that there are still more opportunities which will be accomplished by carefully studying how food components are formed, disintegrated, ingested and absorbed and without this perception it wouldn't be possible to overcome the potential risks and uncertainties within this technology.

Regarding the risks and disadvantages of applying nanotechnology in food industry, most of the nanoparticles enter the gut through oral administration and absorption via intestine cells (enterocytes) is designed in a way that they do not allow large or foreign particles to pass through them, nevertheless the nano-sized ingredients are able to cross these barriers, therefore there is a potential risk in bringing up gastric diseases which should investigated through *in vivo* and clinical studies.

3. Microencapsulation vs. nanoencapsulation of vitamins

Micro/nanoencapsulation is defined as the creation of a barrier to inhibit unfavorable chemical interactions and for the controlled release of bioactive ingredients especially vitamins. Importance of using the microencapsulation processes for vitamins and their key features could be summarized as below:

- Protection of vitamins from external environment
- Controlled release of vitamins
- Improved flow properties
- Reduce overages
- Measuring the precise level of vitamin delivery
- Forming Light-scattering vitamin solutions
- Being cost effective especially for spray drying method
- Undesirable flavor of some vitamins are masked
- Enriching the food products with a complex of vitamins

While for nano-encapsulation of vitamins, the following advantages can be mentioned:

- ✓ Faster dissociation
- ✓ Higher surface area compared to mass proportion
- ✓ High intracellular uptake
- ✓ Pass along the smallest body fenestrations
- ✓ Enable precision targeting
- ✓ Reduce the reactions between vitamins and other molecules plus surrounding medium
- ✓ Formulating optically transparent vitamin solutions
- ✓ Reduction in the quantity of utilized core-shell material
- ✓ Rendering long-shelf life coated vitamins
- ✓ Reinforced physical stability against coalescence and gravitational separations

The capsule size in microencapsulation ranges between 5 and 300 μm in diameter (Gibbs, Kermasha, Alli, Catherine & Mulligan, 1999). When the particle size reduces to the nanoscale during nanoencapsulation, surface-to-volume ratio increases. Therefore, the reactions are speeded by many folds; moreover, the mechanical, optical and electrical properties of the materials will also change (Neethirajan & Jayas, 2011). Physicochemical characteristics of vitamins strongly depend on the applied nanoencapsulation approach and delivery system. Thus, an appropriate nanoencapsulation technique must be chosen considering the required size, physicochemical properties, nature of the encapsulated vitamin and the wall material. Nanoencapsulation process is more complex than microencapsulation because of the difficulty in acquiring an intricate morphology for the capsule entrapping the vitamin (Chau, Wu, & Yen, 2007).

According to Gutiérrez et al. (2013) casein nanoparticles were found to be more stable, cost efficient and environmentally friendly when compared with microemulsions. Moreover, Danino, Livney, Ramon, Portnoy, and Cogan (2014) and Semo, Kesselman, Danino, and Livney (2007) suggested that nanoencapsulation via β-cyclodextrins produced satisfactory sensory properties and created optically transparent solutions, however, microemulsions tend to scatter light. In a recent investigation, it was suggested that nanoliposomes have the benefits to minimize the reactions between bioactives and other molecules, increasing the shelf-life of food products and reducing the amount of used core-shell material compared to conventional liposomes, which are biocompatible and their surface is easily modified (Fathima, Fathima, Abhishek, & Khanum, 2016).

Fig. 1 presents the forms of microcapsuls. The shell is responsible for protecting vitamins from water, oxygen or sunlight. On the other hand, nanostructured delivery forms applied in nanoencapsulation of vitamins are summarized in Fig. 2.

There are some commercially approved biopolymers for the encapsulation of vitamins. Starches and cyclodextrins are carbohydrate-based biopolymers that protect these sensitive compounds from the outside environment. Gum Arabic is also used in microencapsulating according to its solubility, viscosity and emulsification features. However, economically it is not profitable. Alginates can also be used as a wall material at environment temperatures. Ethylcellulose has been approved to be a good substance for encapsulating water-soluble vitamins, because as the wall materials width rises, the water permeability of the dispersed vitamins is reduced. Protein based shells may also be utilized in encapsulating different vitamins. Nevertheless, their high cost is limiting factor for using them in an industrial scale.

4. Conventional microencapsulation techniques of vitamins

Before explaining the recent nanoencapsulation techniques applied in protection of vitamins, it is necessary to be familiar with