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Nano-encapsulation of Bioactive Compounds: a diminutive review

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Abstract
Bioactive compounds are non-nutritive and functional nutrients of food commodities. They play a vital role in human health and reduce the chances of chronic diseases including cancer. Plants, animals and microbes are all source of different bioactive compounds. The conversion of macro particles in small particles to nano-meter is termed as nanotechnology. Encapsulation is the process of covering the active ingredient in protective core and the process at nano level is termed as nano-encapsulation. The active material is made safe from outer environmental threats and the bioactivity of bioactive compounds is extended. Emulsification, coacervation, nano-precipitation and emulsification-solvent evaporation techniques are important techniques to achieve nano-encapsulation. Nanoencapsulation of bioactive compounds may also decrease the degradation and improves solubility and availability of bioactive compounds. Techniques for encapsulation may be develop keeping in view their biosafety issues. Efficiency of nano-encapsulation may depend upon the choice of best technique for encapsulation. Different techniques for encapsulation have been discussed within this review.
Keywords: anti-oxidant activity, cardiovascular diseases, sodium glutamate, transglutaminase, chocolates.

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Introduction

Bioactive compounds are present in minute quantities but are functional constituents of food commodities, and have benefits beyond the traditional nutrients in food (Kris-Etherton et al., 2002). They impart several biochemical and physiological effects on cellular activities. They belong to wide range of classes including flavonoids, anthocyanin, betaines, carotenoids, sterols, and glucosinolates (Walia et al. 219; Table 1). These compounds have less nutritive property but add a functional value to human body. They have several functions including anti-oxidant activity, LDL-C oxidation, eicosanoid synthesis and prevent cardiovascular diseases, Alzheimer's, cancers, ulcers. (Kris-Etherton et al., 2002). Some of the important bioactive compounds includes colors, flavors, vitamins, minerals, bioactive carbohydrates, bioactive lipids, bioactive peptides and phenolic compounds (Tolve et al., 2016). These bioactive compounds act as antimicrobials, anti-inflamators, anti-scavengers and cholesterol absorbers. The main sources of bioactive compounds are plants, animals and microorganisms. Plant source for bioactive compound includes fruits, vegetables, tubers, roots, cereals and pulses. Animal source for bioactive compounds are kidney and liver. The microbiota provides antibiotics from gram positive bacteria, lactic acid from lactic acid bacteria and short chain fatty acids are also provided by microorganisms (Septembre-Malaterre et al., 2018).

Table 1. Sources and example of various bioactive compounds in various species

Species	Extract	Compounds	Functions	Reference
Ziziphus lotus	Leaf	Quinic acid and Rutin	Antimicrobial activity	Yahia et al. (2020)
Medicinal plants	Fruits	Phenols, aldehydes, and terpenes	Aflotoxin reduction	Loi et al. (2020)
Tomatoes	Fruit	Vitamin A, lycopene, ascorbic acid, tocopherols, hydroxycinnamic acid	anticarcinogeni, cardioprotective and hepatoprotective	Pinela et al. (2016)
Mushrooms	Hyphae	Selenium, D2, glutothiane, ergothionine	Decreae in human age	Beelman et al. (2019)
Sunflower	Seed and vegetative	Tocopherols, phytosterols, etc.	Prevent chronic disease	Rauf et al. (2020)
Moringa Olifera	root leaves, flowers and fruits	carotenoids, sterols, and glucosinolates	Prevent chronic diseases	Chhikara et al. (2020)

Nano is a Greek word that means dwarf. It is the technology of this century, which arises as results of significant progress in the field of nanoscience. It provided a novel way for the development of consumer products and many of which have been moved from evaluation to commercial scale production. One nanometer is 10^{-9}m, which is about sixty thousand (60,000) times smaller than a human hair in diameter. In terms of a nanometer, the size of virus is two thousand (2000) nm (Sekhon, 2010) while a red blood cell is five thousand (5000) nm. Moreover, diameter of DNA is about 2.5 nm diameter. The size of nanoparticles may be understandable by comparing with these micro cells and particles (Paredes et al., 2016). It utilizes about 1-100 nm atoms or molecules having novel properties, which have external dimensions to deliver compounds at nano-scale (Singh et al., 2017).

The nanotechnology has wide range of applications. The scope of nano-technology is widening with the advancement in the field of science and technology. However, its scope encompass three main fields; nanocomposites, nano-biosensors and nano-encapsulation. Nano-composites deals with the technology of nano food packaging. Nano-encapsulation deals with encapsulation of bioactive compounds (Bernela et al., 2018). In recent years, nanotechnology has gained significant growth and attracted an investment of 150 billion USD during year 2016. Nanotechnology has been exploited in more than 1800 products from 622 companies of 32 countries(Vance et al. 2016). It was reviewed that nano- technology was most frequently applied in the development of health and fitness products while silver particles were designed as nano-particles (Vance et al., 2016). It has been applied in various food processes such as processing, packaging, functional food, investigation of food pathogens (Singh et al., 2017).

Background for Nano-encapsulation

The last four decades can be termed as the age of synthase. Everything was a synthetic including coloring agents, flavoring compounds and most important packaging material. The use of mono sodium glutamate is now banned all over the world due to its cancer causing hazards. The use of synthetics in such huge numbers became a real threat for the world. The last decade world started to think about the naturals. People started to think about eating natural foods including use of natural food colors and flavors. The use of natural foods was not easy. It is difficult to use natural bioactive compounds just after extraction. These bioactive compounds digest easily before reaching to their site of action and this procedure is similar for almost all of the bioactive compounds. Moreover, the shelf life of bioactive compound is far lesser as compared to basic components of foods. These "extra active" components are present in foods in very minute quantities (Kris-Etherton, et al., 2002). A Latest technology and research made gigantic exploration in the field of nanotechnology. There was a need for encapsulation of bioactive compounds for their safe and easy transfer to the body. Therefore, many of the encapsulation techniques were developed for this purpose (Toniazzo et al., 2014; McClements, 2014).

Nano-encapsulation

Encapsulation is a process of covering of bioactive compound around a core making it safe from environmental stresses and hazards, when this process is done at nano level it is called nano-encapsulation (Ramsden, 2005). Two materials are involved in process of nano-encapsulation. First one is bioactive compound that has to be encapsulated and called as active material. This bioactive material is also called as core material, nucleus and internal phase. The material that covers the active ingredient is termed as carrier material (Gunasekaran, 2014). The carrier material that carries bioactive components could be of starch, pectin, protein, guar gum, chitosan, cellulose and alginates (Liu et al., 2015). There are some selection considerations and properties of carrier material that can be summarized as, the carrier material must be resistant to pH changes. It must bear mechanical stress. It must bear high temperature and enzymatic activity. The carrier material must be inert and inexpensive. Most important property of carrier material is to be food grade and regarded as safe from the food certification bodies (Shah et al., 2016).
There are so many benefits of nano-encapsulation technology (Fig 1). Some of the major benefits are it protects the bioactive compounds from environmental hazards. It provides more balanced foods with in limiting time frame. It enhances the nutritional value of food. It releases nutrients slowly. (Khare and Vasisht, 2014)
The Nano encapsulates act on particular site of action. Nano encapsulates increases the shelf and storage life of bioactive compounds. Nano encapsulates improves food quality includes organoleptic and functional properties (Paredes et al., 2016).

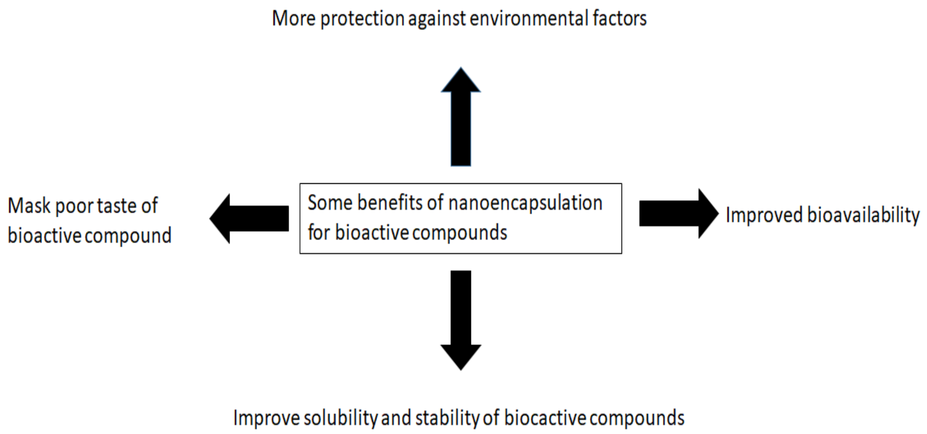

Figure 1. Some benefits of encapsulation of bioactive compounds

Table 2. Review of encapsulation material as carrier for bioactive material

Carrier	Function	Technique	Reference
Pectin	Protection, increase shelf life and stability	Hydrogels, liposomes Pectin uses along with protein and lipids	Rehman et al. (2019)
Sodium alignate and Chitosan	Improve functioning of bioactive compound	Alignate and chitosan dissolved in deionized water	Mahmoud et al. (2018)
Porous Calcium carbonate	Protection and improved shelf life	Layer by layer adsorption of polyelectrolytes into $CaCO_3$ fine particles of 5 µm	Sukhorukov et al. (2004)
Ascorbic acid (10 g kg^{-1}) and maltodextrin (30 g kg^{-1})	High water solubility index, antioxidant capacity, and phenolic compounds	Drying spray	Ahmed et al. (2010)
Gum Arabic (GA), maltodextrin (MD) blend	High phenolic and anthocyanin contents	Drying spray	Collin-Cruz et. (2019)
Ultrafine fibers of zein prolamine	Improved light stability	Electrospinning	Fernandez et al. (2009)
Ultrasound and gum arabic	High Gerranylgeraniol oxidative stability	Freeze drying and spray drying	Silva et al. (2019)
Novel starch-based nanoparticles	Improved solubility and retention in intestine	Horse chestnut, water chestnut and lotus stem	Ahmad et al. (2019)

Nano-encapsulation techniques

There are numerous techniques of nano-encapsulation whch have been reviewed in various sections below and some examples have been cited in Table 2.

Emulsification technique

It is one of the most famous techniques used now a day. In this technique two different immiscible liquids are mixed with the help of emulsifier. The two immiscible liquids can be water and oil solution. Water soluble may be active compound or may be core material. After the complete mixing homogenization is done at 1000-1500 rpm at 200 bar pressure (Solans & Solé, 2012). After the process of homogenization 50-100 nm sized droplets are achieved. These nano encapsulates are dried via using the techniques of freeze or spray drying (Mosquera, 2014).

Coacervation

In this technique the carrier material is termed as coacervates. The coacervates material is homogenized at high temperature to convert it into small droplets. After making the coacervates active ingredient is added and these coacervates are covered on active ingredient. Transglutaminase enzyme is added to make strong linkage between coacervates and active ingredient. Jyothi et al. (2010) described that drying is done with spray or freeze technique. Tannin is applied for finishing and regular shape but the disadvantage of the use of tannin is it decreases the blood pressure and increases the blood clotting (Zuidam and Shimoni, 2010).

Nano precipitation

It is a single step technique in which organic solvent is used to make the solution of solvent and active ingredient. After making the solution, the organic solvent is diffused by the process of diffusion and spray or freeze drying is used to dry the precipitates (Galindo-rodriguez et al., 2004). This is one of the simplest technique used for the process of nano-encapsulation (Ezhilarasi, et al., 2013).

Emulsification- solvent evaporation technique

It is another technique used for the nano-encapsulation process. In this technique solvent is used with immiscible liquid. An emulsifier is used to make solution. After complete mixing, solvent is evaporated by the use of heat and encapsulates are collected (Mukerjee and Vishwanatha, 2009).

Food stuff with bioactive compounds encapsulation

There are many foods used for the encapsulation process. Some of the foods are listed as follow. Fruits, vegetable (Golding et al., 2011), milk, cheeses (Angiolillo et al., 2014), yoghurt (Mousa et al., 2014), ice cream, chocolates (Dordevic´ et al., 2014), bakery and meat products are encapsulated with probiotics, garlic oil, iron, vitamin c, vitamin D, fish oil, β-carotene, phenolics, Ꞷ 3, linseed oil, flaxseed oil and canola oil (Tolve et al., 2016).

Conclusion

Bioactive compounds are important to human health. They reduce the chance of many diseases including cancers but are sensitive to environment and have very short shelf life. Nanotechnology is an important technique to make food nutritious. Core material protects the bioactive compound and make it available in body to perform important body functions. Emulsification, coacervation, nano-precipitation and emulsification-solvent evaporation techniques are much important to achieve nano-encapsulation.

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