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An epitome on encapsulation of probiotics

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ABSTRACT

Purpose: Nanotechnology is one of the highly evolving fields of research having immense potential in various fields of healthcare sectors. The very advent of nanotechnology lies in its ability to serve as a targeted drug delivery system. The introduction of a new branch namely bionanotechnology has further expanded the scope, especially in the diagnostics and treatment of various diseases. Probiotics being a natural source with a plethora of beneficial properties have been investigated actively in recent days. Probiotics administered into the digestive system have been shown to promote gut health by increasing the microbial balance in the gut. However, the bioavailability of such administered probiotics remains a major concern. These probiotics are protected through microencapsulation techniques, which encapsulate them in small capsules. Several nanoparticles with varied dimensions, forms, surfaces and composites have recently been investigated for probiotic microencapsulation. This has been used for various therapeutic applications, such as drug delivery. This review gives an insight on various materials and strategies used for probiotic encapsulation.

Design/methodology/approach: The main aim of this review is to give a perception of the different types of methods of probiotic encapsulation.

Findings: This review implies the significance of probiotics and subsequent active release in the gastrointestinal system. Different sections of this review paper, on the other hand, may offer up new opportunities for comprehensive research in the field of microencapsulation for boosting probiotic viability and also talks about the various encapsulating materials that has been employed.

Originality/value: This review emphasizes more perceptions about the ongoing and imminent techniques for encapsulating probiotics.

Keywords: Bionanotechnology, Probiotics, Nanoencapsulation, Encapsulation of probiotics, Microencapsulation

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BIOMEDICAL AND DENTAL MATERIALS AND ENGINEERING

1. Introduction

Probiotics are living microorganisms that are delivered into the gastrointestinal tract (GIT) with nourishment in order to ensure better health by boosting intestinal microbial equilibrium. They can sometimes be described as "living microorganisms which are consumed to give medical benefits," while another characterized them as "live microorganisms that provide a significant lead on the host when ingested in sufficient quantities as part of diet" [1]. Increased understanding and perception of the potential advantages of probiotics have resulted in an enormous amount of consumer applications offered in a multitude of formulations. Adverse effects continue to be extremely rare and are largely restricted to significant risk population. There are compelling indications that probiotics are effective for administration in the widespread population [2]. There is growing evidence to substantiate their role as anti-pathogenicity, anti-hyperglycemic, anti-tumour, anti-inflammatory, anti-histamine, obesity-related health issues, as well as angiogenic effects along with their favourable impact on the brain and nerve system [3]. The gut microbiome, along with macrophage as well as dendritic cells of the innate immune system, T and B lymphocytes of the adaptive immune system (responsible for IgA synthesis), and gut-associated lymphoid tissue (GALT), all play a role in immune response development [4]. Several probiotics appear to be negotiated by immunological regulation, namely by the precise management of pro-inflammatory and anti-inflammatory cytokines. Another advantage of probiotics is that they help to maintain and preserve the coherence of the connection between enterocytes, which decreases the probability of SARS-CoV2 infection and the development of COVID-19 [5]. Many investigations on probiotics for their anti-tumour properties are being conducted using mouse models. The majority of this sort of investigation yielded good results and suggested possible clinical applicability. Probiotics-based regimens may be employed in cancer prevention and as a collateral treatment during antitumor therapy owing to their antiproliferative and consequences inducing apoptosis on diverse carcinoma cells (in vitro studies utilising cell lines) and positive impact in animal models (in vivo research) [6]. For the past three decades, nanocomposites have been extensively investigated for treating cancer. The current and ever-broadening nanotechnology tool cabinet, encompasses surface changes, encapsulation and sustained release strategies, as well as tangible asset engineering and alteration. This existent nanotechnology framework can be leveraged to create nanoparticle systems tailored to microbiota manipulation in cancer [7]. For example, probiotic nanoparticles have indeed been implemented to inhibit and relieve neuroinflammation, but also probiotic strains encapsulated with synthetic nanoparticles enhance cancer therapeutic capabilities [8]. Nanotechnology has the ability to deliver the stimulus to its target environment, prolonging its duration, thus enabling the prebiotic to actually support and assist in a thriving intestinal flora. This technological advancement will be extremely beneficial to people suffering from chronic digestive issues and inflammatory bowel disease. Because of its small size, nanotechnology can extend a drug's distribution. The modest ease of interplay, as well as the potential to elude elimination, can boost a drug's efficacy [9]. Assessing the adverse health consequences of nanomaterials is critical for product safety because nanomaterials reach the GIT via the oral route and subsequently into circulation. Also, many crucial organs, including the spleen and liver, as well as metals employed in nanomaterials, may be enduring [10]. Nanoparticles composed of amphiphilic polymers, including namely poly (lactide-co-glycolide) (PLGA) and poly(lactic) acid (PLA)–poly(ethylene)glycol (PEG), hold considerable assurance [11]. This review emphasises on the advances in nanotechnology, which enhanced the therapeutic potential of probiotics in targeted drug delivery.

2. Microencapsulation

Microencapsulation protects probiotics by encapsulating them in tiny capsules. Several nanoparticles with varying magnitudes, forms, surfaces, and composites have recently been studied for probiotic encapsulation. Nanostructured capsules have shown auspicious amendments in preserving probiotics from intense conditions due to their incomparable tangible and chemical features [12]. Various encapsulation techniques, including the spray drying, extrusion, and freeze drying, have demonstrated to microencapsulate or nano-encapsulate probiotic microbes. It has been proven that the simultaneous administration of biopolymers enhances the effectiveness of nanoencapsulation, which also increases probiotic durability rates in foodstuff and also in digestive system experiments [13]. The applications of encapsulated probiotics have been highlighted in Figure 1. Numerous factors must be considered when selecting the appropriate encapsulation method for probiotics in the intension of ensuring the survival of bacteria throughout the process of encapsulation, warehouse conditions, and ingestion, and also sustained release in the precise preferred locus of the gut. Therefore, when it comes to probiotic encapsulation, there are two major concerns to take into account: the magnitude of the probiotics, which precludes the use of nanoencapsulation technologies, as well as the challenges in keeping them functioning [14]. PET is an intriguing topic of biopharmacy, which has grown and advanced dramatically over the last decade. A diverse spectrum of microorganisms has indeed been trapped within partially permeable and biocompatible polymers that control cell delivery using this technique. The coordinated and persistent distribution of cells in the gut is the ideal application of PET in biopharmacy. The possible advantage of this medical technique was that it could keep cells surviving in the stomach regardless of the acidic pH. Probiotics, in their functional stage, may be favourable to the host's health [15]. The following illustration gives the different modes of probiotic encapsulation (Fig. 2).

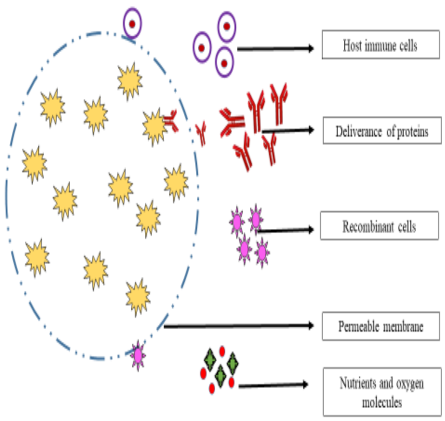

Fig. 1. Schematic illustration showing the applications of nano-encapsulated probiotics (this picture has been adopted from [16])

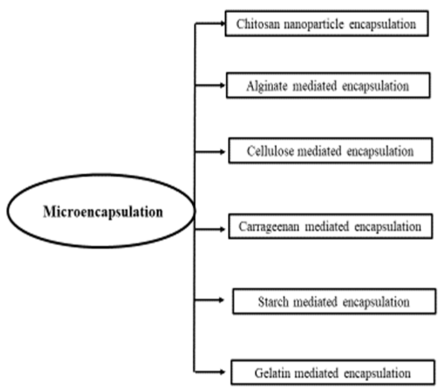

Fig. 2. Different modes of nano-encapsulation strategies available for the encapsulation of probiotics

2.1. Chitosan nanoparticle mediated encapsulation

Chitosan is a partly deacetylated polymer of N-acetyl glucosamine produced by the alkaline deacetylation of chitin. Chitosan is non-toxic and non-hazardous, and it can combine with polyanions to produce aggregates and gels [17]. It's really a great biocompatible, compostable, and bioadhesive substance. Chitosan has a prolonged shelf life and is possibly generated through an extremely gentle ionotropic gelation process. Under sonication, bacterial solution and a constant volume of normal saline were combined with chitosan solution to decrease the diameter of bacteria for encapsulation in nanoparticles. By this, *Lactobacillus acidophilus* is encapsulated as a probiotic bacteria using chitosan nanoparticles, which improves its durability and survival. Furthermore, encapsulation significantly enhances bacterial survivability in the simulated stomach and intestinal habitats [17]. According to Mawad et al., the alginate-chitosan microcapsule improved EcN survivability [18].

2.2. Alginate encapsulation of probiotics

The most often utilised matrix for microencapsulation is alginate, which has been shown to boost probiotic survival rates from 80 to 95 per cent. Alginate is an anionic polysaccharide comprised of D-mannuronic acid and glucuronic acid that is biocompatible, inexpensive, and non-toxic to the body [19]. Because of alginate's propensity to create hydrogel via calcium crosslinking under mild circumstances, alginate-based microbeads are amongst the most investigated encapsulating technologies for probiotic administration. To enhance the permanence of alginate particles, one strategy seems to utilize natural colloidal materials to form a defensive and consistent barrier on the superficial surface of alginate microbeads. This allows users to customize the ultimate coating's thickness, architecture, and surface attributes. As a result, these surface alterations can lower alginate microbead porosity, thus minimising acid absorption into microbeads in the middle of gastrointestinal transit [20]. Polycations like chitosan, for illustration, can be used to modify the instinctive characteristics and permeableness of alginate capsules by complexing among alginate chains which are negative, thereby affecting the extricate efficacy of encapsulated vital ingredients [21]. Several investigations have demonstrated that calcium alginate immobilised cultures are preserved in the comportment of cryoprotectants through enhanced bacterial durability across diverse circumstances than microorganisms evaluated in the non-encapsulated form [22]. The coating of *L. gasseri* and *B. bifidum* with alginate and chitosan covering provides a powerful technique of delivering viable bacterial cells at colonic levels and assists in their viability throughout mimicked gastrointestinal tract [23].

2.3. Cellulose encapsulation of probiotics

Because of its biocompatibility and biodegradability, cellulose, the most lavishing sustainable natural polymer, has been frequently employed in a group of areas. As encapsulates, numerous cellulose derivatives, namely hydroxypropyl cellulose and also carboxymethyl cellulose, have been broadly utilized [24]. Previous research has shown that revived cellulose macrogels generated comprise spongy architectures and perchance utilised as scaffolds for probiotic loading [25]. The capacity to release individual or combinations of microbes orally, employing cellulose sulphate capsules that safeguard exceptionally potent contrary to highly acidic pH as well as proteolytic enzyme digestion over extended periods of time while liberating bacteria in the small intestines, will indeed make several existing probiotic therapies far more efficient [26]. There have been many investigations on cellulose or its derivative products as probiotic encapsulates, making it inconceivable to be scaffolds with firm supporting qualities [25].

2.4. Carrageenan encapsulation of probiotics

Carrageenans (CGs) are hydrophilic polysaccharides found as mould components in a variety of Rhodophyta species, the most prominent of which is Irish moss. In the past, research articles on CGs were published to flourish reviews of their immunological impacts, toxicological consequences, structure-property interactions, chemical alterations and equivalent structural analysis, implementations in delivery of drugs, therapeutic benefits, as well as relevance as nutritional supplements [27]. Considering its increased resistance to organic acids, the k-carrageenan-locust bean gum combination often acts as encapsulating substance in favour of probiotic micro-organisms. The compound-based method necessitates a temperature range of 40 to 50 degrees Celsius when the cells are put to the polymer solution. Gelation happens when the solution is cooled to room temperature. Bifidobacteria encapsulation in k-carrageenan enhanced as well as even after months of storage, the number of live encapsulated cells in yoghurt was kept constant. [28]. The probiotic cell encapsulation in j-carrageenan beads maintains the bacteria alive; however, the resulting gels are brittle and unable to endure pressures [29]. Furthermore, carrageen may enhance the viscosity of gastric substances, extending the gastric evacuating time, thus favouring the distribution and action of probiotics encapsulated with carrageenan [30].

2.5. Gelatin encapsulation of probiotics

Gelatin is a protein generated from contaminated collagen that comprises elevated quantities of proline, hydroxyproline, and also glycine, which is beneficial as a thick two-sided stiffen emulsifier for encapsulation. It possesses good membrane-forming potential, biocompatibility, and is harmless. Because of its poor network stiffness, gelatin's application as a hydrogel matrix is circumscribed [31]. Duck feet gelatin (DFG) and chicken skin gelatin (CSG) are two poultry gelatins with exceptional film-forming capabilities [32]. Microbial encapsulation with ricotta, while associated with gelatin along with parsed collagen, presented substantial defence, particularly below gastric environment of acidic pH as well as the existence of pepsin, where survivability of both LA-5 and BB-12 has been significantly greater than those of non-encapsulated microbes [33]. Advanced research has commenced to synthesise nanocomposites that combine the most noticeable properties of hydrogels and nanoparticles. In the latest report, Ghibaudo et al. coupled pectin with iron oxide nanoparticles and accomplished performing two crucial functions: sheltering probiotic lactic acid bacteria from mimicked gastrointestinal system fluids and transporting iron effectively to the colon [34]. Bifidobacterium adolescentis 15703T survival in the gastrointestinal tract was improved by enveloping it in alginate-coated gelatin microspheres [35].

2.6. Starch encapsulation of probiotics

Starch is a polysaccharide generated by all green plants that is made of -D-glucose units connected by glycosidic linkages [36]. There is a substantial accumulation of research regarding using starch-based delivery methods for drug encapsulation. When building starch-based encapsulating systems for the distribution of foodstuffs, this may be referred to. A comprehensive method should be used to investigate not just the encapsulation procedure but rather its influence on sustained release implementations. Food components have now been encapsulated successfully in starch-based systems with high encapsulation productivity [37]. Native starch is often employed in spray drying microencapsulation, in which an internal structural solution is delivered into a spray dryer along with a starch emulsion. It has been demonstrated, for example, that large surface area induces high Bifidobacterium adherence per gramme of starch. Maltodextrins and octenylsuccinate-starch are two popular encapsulation alterations. Maltodextrin is a starch-based substance that is produced through acidic or enzymatic hydrolysis. OSA-starch is a lipophilic matrix capable of encapsulating along with retaining microbes, colours, proteins, tastes, and other components [38]. Encapsulation of probiotics in the starch system may be achieved without the use of gelling agents or the modification of pH, whereas ionic polysaccharides can create gel/matrix that can entrap the bacteria in the presence of proper salt or ionic condition [39]. The overall advantages of using nano-encapsulated probiotics are highlighted in Figure 3.

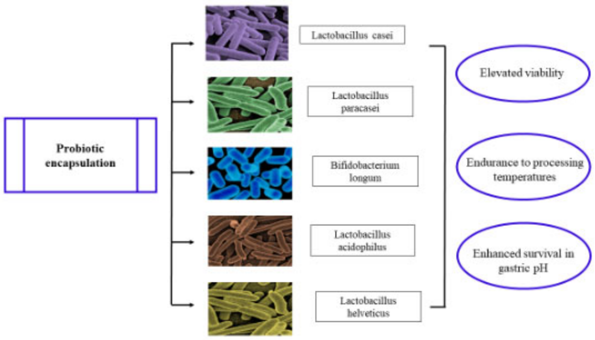

Fig. 3. The picture depicts the advantages of nano-encapsulation of probiotics in increasing the bioavailability of probiotics

3. Elements influencing the viability of probiotics amid encapsulation

3.1. Habitat circumstances

Probiotics are treated to intense temperatures in a variety of probiotic encapsulation techniques. Heat may cause severe cell damage, with lower temperatures being more likely to disrupt the cell membrane. Despite the fact that, capsules may be desiccated at lower conditions, even mild heating dramatically reduces the amount of live bacteria [40]. Water activity (aw) and moisture content are known to affect not only the survivability of microorganisms during the procedure and moreover, their survivability in prolonged storage [41]. It has been established that pressure increases of up to 50 MPa disrupted the proliferation of E.coli cells as well as the overall protein production rate. Pressure can have a negative effect on spray drying; as the liquid is atomized, shear forces can destroy the probiotic cells [42]. Probiotics survival has also been proven to be affected by pH. To survive and grow, bacteria must assert a steady pH in the cytoplasm [43].

3.2. Encapsulation components

The feasibility of encapsulation and the survivability of microbes are affected not only by culture, physiology and processing factors but also by the materials employed for encapsulation [44]. The reduction in the concentration of calcium chloride during the production of calcium alginate capsules had no effect on the capsules' ability to protect live cells; nonetheless, greater yields of immobilised cells may be generated [40,45]. Cationic humectants are the most destructive to microbes, whereas non-ionic surfactants are the least harmful. Surfactants have the ability to alter the cellular structure, the cytoplasmic membrane, and the cytoplasm themselves. Non-ionic substances, like Tween 80, are utilised for encapsulation for this reason [40].

3.3. Characteristic feature of capsules

Larger particle creation is dangerous due to the likelihood of deleterious impacts on the structural and sensory qualities of the product to which they have been introduced. A suitable range of 100-200 µm has been proposed [40]. The dimensions and forms of capsules are mostly determined by the encapsulating technology used. The size of a capsule is determined not just by technology but also by the substances utilized. The larger the capsules, the greater the viscosity of the encapsulating suspension [46]. The following are the various factors that influence the efficiency of encapsulated probiotics (Fig. 4).

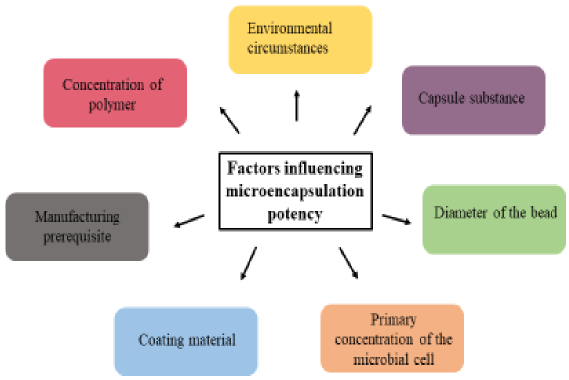

Fig. 4. Various factors that influence and determine the efficiency of encapsulated probiotics in exerting their effect

4. Conclusions

The significance of probiotics and subsequent active release in the gastrointestinal system is illustrated in this review study. Microencapsulation is the most important modern and improved method for preserving probiotics against harmful environmental factors. The technique also employs a variety of encapsulating materials, including alginate, chitosan, carrageenan, gelatin, cellulose, and starch. The most significant component to be given special attention is the protective action of the encapsulation material, since capsules sufficiently preserve the encapsulated cells from severe environmental conditions. Longitudinal investigations should look at the release rate of probiotics from capsules. Furthermore, novel polymers must be developed in order to find the appropriate protection elements. Finally, a significant number of in vivo research, followed by drug trials, are required to assess the potency of encapsulated probiotics in health care. The clinical significance of encapsulated probiotics relies on the survival rate of the probiotics, the maintenance of curative potency of the probiotic after encapsulation, and also the enhanced tolerance to environmental stress. Different sections of this review paper, on the other hand, may offer up new opportunities for comprehensive research in the field of microencapsulation for boosting probiotic viability.

Additional information

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