



Microencapsulation: Design, Characterization, and Evaluation

Asmaa Abdelaziz Mohamed

Al-Zahraa University for Women, Karbala, Iraq

asmaa.abdelaziz@alzahraa.edu.iq

ABSTRACT

Any compound can be enclosed inside a specific material utilizing the sophisticated food processing technique known as microencapsulation, creating a tiny sphere with a diameter ranging from 1 μm to several hundred μm . The purpose of microencapsulation is to ensure the safe delivery of sensitive substances by safeguarding them. The material used for encapsulation is known as the encapsulant, and the chemical or active ingredient that is enclosed is known as the core. Polymeric and nonpolymeric substances such as gelatin, cellulose, and ethylene glycol can be used as encapsulants. Microencapsulation is accomplished using a variety of methods. Extrusion, coacervation, fluidized bed coating, spray cooling, and spray drying are a few examples. The characteristics of the encapsulant, core material, and various required capsule morphologies all influence the choice of a certain procedure. A widely used technology in food products is microencapsulation, which can be utilized to create functional foods or as a fortifying agent. This review critically examines and compiles the use of this specific technique in foods, various encapsulation techniques, various capsule properties resulting from the various microencapsulation techniques, and various release mechanisms used to deliver the compounds. It is based on the basic understanding of encapsulation as well as the most recent research and findings from the literature.

Keywords microparticles, core, coacervation, design.

Introduction

The process of encasing a solid or liquid core material by trapping it with a wall-forming or carrier is known as microencapsulation. Typically, this process produces microscopic solid particles that range in size from measurement range between nanometers and micrometers [1, 2 19, 20]. Green and Schleicher created and patented the concept of the development of microencapsulation technology for the factory Cation of capsules with dyes that are specifically made for paper [3 21, 22]. Microencapsulation has since been utilized and studied in numerous fields and sectors, including food, electronics, medicine, and agriculture, biomedicine and cosmetics [4]. The use of microencapsulation has demonstrated a number of benefits, especially in the agricultural pharmaceutical, food, and other industries, and has provided their intriguing characteristics that include the encapsulation of colors, live cells, active enzymes, adhesives, perfumes, and medications, their regulated or postponed release of active ingredients in ingredients, a way to cover any bad tastes, and improved solubility [5, 6]. The microencapsulation method is renowned for its advantages. generating microparticles that are separated into microcapsules or crospheres. These microcapsules are different in size and form according on the materials and process used by combining several polymers or mon mers using various microencapsulation techniques [2]. These microcapsules fall into one of three groups, as mononuclear, as seen in Figure 3 (the core is surrounded by the polynuclear (having many encased core elements), inside the shell), as well as matrix (the cores are similarly or evenly distributed across the shell). [7]

To provide products to market, researchers are currently concentrating on developing new drug delivery systems (DDS) that can reduce adverse effects, be appropriate for site-specific delivery, increase shelf-life, enhance patient compliance, and potentially allow for sustained release [8]. Thus, microencapsulation emerges as a possible technical approach to accomplish the aforementioned objectives. Combinations of biomaterials and active pharmaceutical ingredients (APIs) can form microparticles. With respect to the microencapsulated APIs, these medicinal substances may have a brief half-life and be rapidly hydrolyzed or enzymatically broken down in vivo, which is linked to a more rigorous treatment regimen (several doses). Consequently, microencapsulation methods shield the API from deterioration, enabling these substances to be released in the right amounts over time to achieve the necessary treatment concentration of API [9].

This review discusses in details the several techniques that employed in microencapsulation and purpose of microencapsulation

Design of microencapsulation

The Response Surface approach (RSM) research approach in conjunction with the Central Composite Design (CCD) was used to optimize the microencapsulation process. 10 In the past, a typical method for determining the primary influencing elements in the field of microencapsulation has been to examine the impact of one variable while holding the others constant. This approach, sometimes referred to as one-factor-at-time (OFAT) or one-

variable-at-time (OVAT), results in less-than-ideal procedures or finished goods [11]. This could be explained by factor interactions, which are not taken into account by the OVAT technique. A particular system behavior can be caused by the interaction of multiple variables [12]. The comparatively large number of tests that must be conducted, which makes the OVAT technique a time-consuming approach, is another drawback of the methodology [13]. The primary drawbacks of OVAT processes have recently been addressed by the application of multivariate statistical techniques as design of experiments (DOE) [14]. RSM is the widely employed multivariate statistical technique in the field of microencapsulation. The pharmaceutical and food research industries have mostly described the use of RSM for microencapsulation optimization procedures.

Methods

Coacervation

The most used encapsulating method is coacervation. The process typically involves three steps with constant agitation: (1) creating the reaction medium (a coating polymer solution in which the core is suspended); (2) precipitating and depositing the coating material; and (3) solidifying or stiffening the deposited coating material [15].

Coating deposition

With the help of careful blending of the polymer and the core substance in the solvent. By lowering the system's overall interfacial energy, the polymer is encouraged to adsorb at the interface that forms between the solvent and core. To help the created coat over the core material solidify or harden, step three involves adding cross-linking agents or using heat or desolvation processes [16, 17].

Ionotropic gelation

One popular technique for producing hydrogels is ionotropic or ionic gelation. This method produces enclosed particles through the hydrophilic polymer-based interaction of an oppositely charged molecule with a cationic or anionic polymer [18]. This method frequently makes use of biodegradable polymers such as gellan gum, chitosan, sodium alginate, gelatine, and carboxymethylcellulose [19, 20]. At concentrations below the gel point, these polysaccharides form gels. Large amounts of water or other fluids can be absorbed by the hydrophilic, three-dimensional matrix that forms. This technique is ideal for encasing hydrophilic core materials and is non-toxic [21, 22]. It is straightforward, affordable, and perfect for low molecular weight substances, but one of its disadvantages is that it is not very mechanically stable in acidic environments [23].

Pharmaceutical and wastewater applications have documented the use of sodium alginate hydrogel beads with divalent cations including calcium, and barium salts as well as polyvalent cations such as Al^{3+} . In drug encapsulation applications, sophisticated coacervation involving two polymers, such as chitosan and alginate [20].

Solvent evaporation

Core materials that are hydrophilic or hydrophobic can be encapsulated using this technique. There are two steps in it [24]. The polymer and the core material to be encapsulated are dissolved by a volatile solvent during emulsification. At the same time, distilled water alone is utilized as the aqueous phase in a basic evaporation process, with additives such as surfactants in complex emulsification procedures to create a stable emulsion. Then, the organic solvent is removed to generate nanospheres, which can then be collected as a free-flowing powder, coated onto a substrate, or used in suspension. After being separated by ultracentrifugation, the generated nanoparticles are rinsed with distilled water to remove any leftover additive residues or free, non-encapsulated core material. They are then freeze-dried and kept as a freeze-dried powder. [25]

Supercritical fluid assisted encapsulation technique

Upper their critical temperature and pressure, supercritical fluids are very compressed gases that can exist as liquid and solid [26]. Their density varies significantly, with a minor variation in temperature and pressure. Because they are environmentally friendly, carbon dioxide (CO_2) and water are frequently utilized as supercritical fluids in industrial and laboratory settings. Supercritical carbon dioxide, or SCO_2 , is frequently used in pharmaceutical and food encapsulation processes. SCO_2 is a great solvent for encapsulation because of its special qualities, which include viscosity, excellent solubility, non-toxicity, non-flammability as well as its affordability [27].

Sol-gel method

A colloidal suspension (sol) is formed in the sol-gel process, and then a network is built in an external liquid phase (gel). This procedure utilizes core and polymer suspension formation (Sol), which converts a sol into a gel and then solidifies [28]. Metal substances include metal alkaloids, metal chlorides as oxides, water as hydrolysis agents, and alcohol as a solvent. The sol-gel technique often involves hydrolysis and polycondensation processes. Near room temperature, metal compounds quickly go through hydrolysis and polycondensation reactions, producing sols that contain small particles or polymers [29].

Liposomal encapsulation

A liposome is a spherical vesicle made up of water molecules encased in one or more phospholipid bilayers. It has a structure very similar to that of the human cell membrane and can be made from natural phospholipids [30]. A hydrophilic head and a hydrophobic tail make up a phospholipid bilayer, with the polar head arranged as inner and exterior aqueous phases. Liposomes are frequently employed as a nanocarrier because of their structure, which is both hydrophilic and hydrophobic [31].

Characterization

The morphology of microparticles is recognized by scanning electron microscopy (SEM). Their chemical composition by Fourier transforms infrared spectroscopy (FTIR), thermogravimetric analysis (TGA), and first-derivative curves (DTG) [32,33].

CONCLUSION

A microparticle is a flexible drug delivery system that can be administered orally or parenterally. It should ideally generate the necessary plasma level and keep it constant for an extended amount of time, solve issues with traditional therapy, and increase the therapeutic efficacy of a particular drug. The development of colloidal and nano drug delivery systems for a range of drugs was made possible by the methods for producing microparticles through the microencapsulation process.

References

1. Dubey R, Shami T, Rao KB. Microencapsulation Technology and Applications,” *Defence Science Journal*, vol. 59, no. 1, pp. 82–95, 2009.
2. F. Paulo F, Santos L, “Design of experiments for microencapsulation applications: A review,” *Materials Science and Engineering: C*, vol. 77, pp. 1327–1340, 2017.
3. Agnihotri N, Mishra R, Goda C, Arora M. Microencapsulation—a novel approach in drug delivery: a review,” *Indo Global Journal of Pharmaceutical Sciences*, vol. 2, no. 1, pp. 01–20, 2012. 18
4. Estevinho BN, Rocha F, Santos L, Alves A. Microencapsulation with chitosan by spray drying for industry applications - A review,” *Trends in Food Science and Technology*, vol. 31, no. 2, pp. 138–155, 2013.
5. Gouin S. Microencapsulation: industrial appraisal of existing technologies and trends,” *Trends in Food Science Technology*, vol. 15, no. 7-8, pp. 330–347, 2004.
6. Desai KGH, Park HJ. Recent developments in microencapsulation of food ingredients,” *Drying Technology*, vol. 3937, no. 23, pp. 1361–1394, 2005.
7. Okafor, Nnamdi. (2024). Microencapsulation Techniques in HIV Pediatric Formulations: Advances and Future Outlook. *Advances in Pharmacological and Pharmaceutical Sciences*. 2024. 10.1155/2024/5081655.
8. G. Ma. Microencapsulation of protein drugs for drug delivery: strategy, preparation, and applications. *J. Control. Release*, 193 (2014), pp. 324–340
9. Filipa Paulo, Lúcia Santos, Design of experiments for microencapsulation applications: A review, *Materials Science and Engineering: C*, Volume 77, 2017, Pages 1327-1340,
10. Sukardi, Sukardi & Asmara, S.N.L. & Setyawan, Hendrix & Pranowo, Dodyk. (2023). Optimization of coating materials on microencapsulation of red galangal (*Alpinia purpurata*, K. Schum) rhizome essential oil with freeze dry method. *Food Research*. 7. 53-60. 10.26656/fr.2017.7(5).033.
11. D.D. Frey, F. Engelhardt, E.M. Greitzer A role for “one-factor-at-a-time” experimentation in parameter design *Res. Eng. Des.*, 14 (2003), pp. 65-74
12. A.A. Kharia, A.K. Singhai. Screening of most effective variables for development of gastroretentive mucoadhesive nanoparticles by Taguchi design *ISRN Nanomaterials*, 2013 (2013)
13. K.M. Bower Design of Experiments (DOE) Retrieved September 16, 2016, from
14. D. Christolear Design of Experiments (DOE) Tutorial Retrieved September 16, 2016, from
15. Atmane Madene, Muriel Jacquot, Joël Scher, Stéphane Desobry Flavour encapsulation and controlled release - a review. *Int. J. Food Sci. Technol.*, 41 (1) (2006), pp. 1-21
16. F. Salaün Microencapsulation technology for smart textile coatings. *Active Coatings for Smart Textiles*, Elsevier Inc (2016), pp. 179-220, [10.1016/B978-0-08-100263-6.00009-5](https://doi.org/10.1016/B978-0-08-100263-6.00009-5)
17. Joseph A. Bakan. Microencapsulation using coacervation/phase separation techniques *Controlled Release Technologies: Methods, Theory, and Applications* (2019), pp. 83-105, [10.1201/9780429287428-4](https://doi.org/10.1201/9780429287428-4)
18. M.K.A. Iqbal, M Shuaib - Indo Am, J. Pharm Iqbal, and undefined 2015‘An exquisite technology of pharmaceutical science: nanotechnology *Indo American Journal of Pharmaceutical Research*, 5 (2015), pp. 3528-3540
19. Sapana P. Ahirrao, S Gide Paraag, B. Shrivastav, Pankaj Sharma *RESEARCH AND REVIEWS : JOURNAL OF PHARMACEUTICS AND NANOTECHNOLOGY Ionotropic Gelation : A Promising Cross Linking Technique for Hydrogels*, 2 (1) (2014), pp. 1-6

20. Munmaya Mishra Overview of encapsulation and controlled release. Handbook of Encapsulation and Controlled Release (2015), [10.1201/b19038-3](https://doi.org/10.1201/b19038-3)
21. Rukkumani Rajagopalan, Jatinder V. Yakhmi Nanotechnological Approaches toward Cancer Chemotherapy. Nanostructures for Cancer Therapy (2017),
22. Kashappa Goud H. Desai. Chitosan nanoparticles prepared by ionotropic gelation: an overview of recent advances Crit. Rev. Ther. Drug Carrier Syst., 33 (2) (2016), pp. 107-158,
23. Subhashis Debnath, R. Suresh Kumar, M. Niranjana Babu. Ionotropic gelation - a novel method to prepare chitosan nanoparticles. Res. J. Pharm. Technol., 4 (4) (2011), pp. 492-495
24. Sergio Freitas, Hans P. Merkle, Bruno Gander. Microencapsulation by solvent extraction/evaporation: reviewing the state of the art of microsphere preparation process technology. J. Contr. Release, 102 (2) (2005), pp. 313-332,
25. Amit Singh, Garima Garg, P.K. Sharma. Nanospheres: a novel approach for targeted drug delivery system. Int. J. Pharmaceut. Sci. Rev. Res., 5 (3) (2010), pp. 84-88
26. Cristina Prieto. Supercritical Fluid Extraction of Emulsions to Nanoencapsulate Liquid Lipophilic Bioactive Compounds. Process Development and Scale-Up.' (2017), p. 282
27. Soon Hong Soh, Lai, Yeng Lee. Microencapsulation and nanoencapsulation using supercritical fluid (SCF) technique Pharmaceutics, 11 (1) (2019),
28. Sumio Sakka. Sol-gel process and applications. Handbook of Advanced Ceramics: Materials, Applications, Processing, and Properties (second ed.), Elsevier Inc (2013), pp. 883-910,
29. Kavitha Pathakoti, Manjunath Manubolu, Huey Min Hwang. Nanotechnology applications for environmental industry Handbook of Nanomaterials for Industrial Applications, Elsevier (2018), pp. 894-907, [10.1016/B978-0-12-813351-4.00050-X](https://doi.org/10.1016/B978-0-12-813351-4.00050-X)
30. Mingyuan Li, Chunyang Du, Na Guo, Yuou Teng, Xin Meng, Hua Sun, Shuangshuang Li, Yu Peng, Hervé Galons. Composition design and medical application of liposomes. Eur. J. Med. Chem., 164 (February) (2019), pp. 640-653,
31. Abolfazl Akbarzadeh, Rogaie Rezaei-Sadabady, Soodabeh Davaran, Sang Woo Joo, Nosratollah Zarghami, Younes Hanifehpour, Mohammad Samiei, Mohammad Kouhi, Kazem Nejati-Koshki Liposome: classification, preparation, and applications Nanoscale Res. Lett., 8 (1) (2013),
32. Loureiro MV, Aguiar A, Santos RGD, Bordado JC, Pinho I, Marques AC. Design of Experiment for Optimizing Microencapsulation by the Solvent Evaporation Technique. Polymers (Basel). 2023 Dec 29;16(1):111.
33. Hülya KAFTELEN-ODABAŞI, Evaluation of morphological, structural, thermal, electrical, and chemical composition properties of graphene oxide, and reduced graphene oxide obtained by sequential reduction methods, Carbon Trends, Volume 17, 2024, 100429,