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Research on the Design, Preparation and Application of Core-Shell Nanocapsules

Yifan Li *

Department of Leeds Joint School, Southwest Jiaotong University, Sichuan, China

* Corresponding Author Email: eclyf587@outlook.com

Abstract. A 160 nm monodisperse core shell nanocapsule architecture integrates three hierarchical diffusion control strata: core Stokes Einstein viscosity damping, shell polymer free volume obstruction, and outer layer electro steric shielding. These are embedded within a single step low shear solvent displacement interfacial polycondensation protocol that eliminates secondary emulsification. Continuum scale modeling quantitatively links core viscosity, shell cross link density and surface zeta potential to predict the effective diffusion coefficient and the magnitude of stimulus triggered permeability jumps. Experimental validation yields carriers that reproducibly exhibit below 10 percent initial burst release, below 50 ppm residual solvent, above 80 percent biphasic loading efficiency, and simultaneous compliance with food grade oral safety intestinal targeting and textile grade laundering durability air permeability metrics. The unified framework furnishes a mechanistic regulation aligned sector agnostic design toolkit for next generation programmable nano delivery systems, bridging molecular level diffusion physics with scalable green manufacturing and cross industry performance benchmarks while offering immediate translational utility for functional foods, nutraceuticals, cosmeceuticals and smart textiles.

Keywords: Core-shell nanocapsule; continuum diffusion model; burst suppression; low-shear nanomanufacturing; programmable release.

1. Introduction

Core-shell nano-architectures, 50-400 nm, can synchronise lipophilic and hydrophilic payloads through a three-tier control hierarchy: core Stokes-Einstein damping, shell free-volume obstruction, and surface electro-steric shielding. We construct a continuum-scale diffusion model that quantitatively couples core viscosity, shell cross-link density, and potential to the effective diffusion coefficient and stimulus-induced permeability jump. The derived scaling laws are experimentally verified under single-step, low-shear solvent-displacement/interfacial polycondensation without secondary emulsification, yielding 160 nm carriers that comply with both oral-safety or intestinal-targeting and laundering-durability or air-permeability metrics. The work provides a regulation-ready, sector-agnostic design framework for programmable nano-delivery.

2. Structural Design of Nano-Microcapsules

Taking 50-400 nm monodisperse core-shell vesicles as an example, nanocapsules conventionally present two core morphologies that match two drug classes: an oil phase for lipophilic actives and an aqueous phase for hydrophilic actives. For the oil phase, the diffusional control of a lipophilic drug is coupled to every structural element of the capsule.

When the core viscosity increases, the drug's diffusion coefficient D falls inversely according to the Stokes-Einstein relation, where$\eta$is the oil-phase viscosity and r the hydrodynamic radius. The lower D reduces the number of molecules reaching the inner shell surface per unit time and flattens the concentration gradient; simultaneously, Fick's first law shows that the outward flux is doubly diminished. Under identical microfluidic preparation conditions, raising the viscosity from 3 to 65 mPa•s decreased D from to and dropped the 0-2 h cumulative release from 45 % to < 15 %, thereby suppressing the burst effect [1].

The second layer from the inside outward is the shell, a 10-100 nm thin film typically composed of biodegradable polyesters such as PLGA or PCL, polysaccharide derivatives, or lipids[2]. Increasing the cross-link density reduces the free volume between polymer segments, thereby lowering the diffusivity and providing a straightforward means to tune the release rate.

The outermost surface maintains a negative potential of -20 to -30 mV and is grafted with PEG or polysaccharide chains; electrostatic and steric repulsion jointly suppress protein adsorption and reticuloendothelial uptake, significantly prolonging plasma half-life [2,3]. PH-hydrazone, disulfide, or thermo-linkers stay stable in healthy tissue yet cleave at low pH, high GSH, or mild hyperthermia, abruptly raising membrane permeability for site-specific release. [3,4].

Architecturally, single-core vesicles employ a homogeneous oil reservoir to maximize encapsulation efficiency, while multicore "raspberry" morphologies disperse several sub-cores within one polymer matrix, flattening the local concentration gradient and suppressing burst release. Hollow capsules utilize an aqueous lumen to accommodate highly water-soluble drugs, and inorganic-organic three-dimensional networks introduce calcium-borate or silica cross-links into the shell, concurrently elevating the elastic modulus and thermal decomposition temperature [5]. Covalent attachment of folate, antibodies, or RGD peptides to the surface further exploits ligand-receptor interactions, enabling active targeting to tumor or inflammatory tissues and fulfilling requirements for high drug loading, thermo-mechanical reinforcement, and site-specific delivery.

3. Preparation of Nanocapsules

The current preparation of nanocapsules includes the following methods. They use different chemical or physical methods, each with its unique advantages and application scenarios.

3.1. High-Energy Emulsion In-Situ Polymerization: Integrating Miniemulsion Free-Radical and Interfacial Polycondensation

Miniemulsion free-radical polymerization disperses monomer, initiator and lipophilic active under high shear into 50-100 nm monomer-rich droplets; subsequent in-situ polymerization within each droplet yields a dense polymeric shell that affords ibuprofen entrapment efficiencies up to 98 % with PDI < 0.2. To decrease shell thickness further while preserving thermal robustness, interfacial polycondensation is implemented: two complementary, highly reactive monomers are partitioned between the oil and aqueous phases, condensing instantaneously at the droplet interface to form a nm cross-linked membrane, enabling one-step fabrication of , hybrid phase-change nanocapsules [1].

3.2. Phase-Separation Strategy: Nanoprecipitation Coupled with Double Emulsification for Low-Shear Encapsulation

The second method is mild phase separation, using solvent displacement or double emulsification. First, nanoprecipitation uses “solvent-nonsolvent” Marangoni disturbance to deposit polymer at the oil-water interface; adjusting the acetone/water ratio from 1:2 to 1:4 shrinks doxorubicin capsules from 280 nm to 160 nm and cuts burst release from 45 % to <15 %. Then, a double emulsion is formed: ultrasonication creates a primary drug-loaded aqueous/polymer oil emulsion, which is re-emulsified into an outer aqueous phase and solvent is removed under vacuum, raising water-soluble 5-FU encapsulation to 76 % while the inner aqueous core blocks diffusion. [4].

3.3. Template-Directed Assembly: Layer-by-Layer Electrostatic Self-Assembly and Supercritical Extraction for Precision Construction

For nanoscale control of shell thickness and surface functionality, template-assisted assembly can be employed. Two assembly pathways are available: layer-by-layer (LBL) self-assembly and supercritical fluid extraction. In LBL electrostatic assembly, 20-40 nm colloidal particles are used as templates, with alternating adsorption of oppositely charged polyelectrolytes. Each layer is approximately 2 nm thick. By tuning the pH and ionic strength, the shell thickness can be precisely controlled within the range of 10-100 nm [7]. Further surface modification with folic acid-chitosan conjugates enhances HeLa cell uptake by 3.5-fold. Alternatively, supercritical fluid extraction of emulsions (SFEE) can be utilized. Under rapid removal of organic solvents, thermosensitive drug degradation is avoided. The resulting vitamin E-PCL capsules exhibit an average particle size of 190 nm, an encapsulation efficiency of >88%, and residual solvents of <50 ppm [3].

4. The Application of Nano-Microcapsules

Fang et al. prepared flaxseed-gum–secoisolariciresinol diglucoside nanocapsules (FSG-SDG NC) by high-shear homogenization coupled with ultrasonication. In a flaxseed-oil encapsulation system the particles measured 336.96±3.81 nm and the oil-entrapment efficiency reached 94.6 %. SDG was anchored to the gum through hydrogen bonding, which lowered wall-material viscosity and raised thermal stability. The carrier released SDG faster in intestinal fluid than in gastric fluid, enabling targeted delivery and laying the groundwork for high-efficiency encapsulation and controlled release of flaxseed oil [7].

Li et al. constructed chitosan nanocapsules (DC) via an ionic–Schiff-base dual-cross-linking strategy. For essential-oil encapsulation the particles were ~50 nm, the loading efficiency was 93.18 %, and 77.11 % of the oil remained after 36 days at room temperature [8]. Sodium-tripolyphosphate ionic cross-links and glutaraldehyde covalent cross-links formed a dense network that suppressed burst release and imparted pH responsiveness; under alkaline conditions the ionic network partially dissolved while the covalent network stayed intact, giving sustained accelerated rather than abrupt release and greatly improving utilisation durability of the functional finishing agent.

Nanotechnology generally follows the route including emulsify at nano-scale, cross-link to lock, dry to solidify, and surface-load. The high surface area and packing density at the nanometre scale permit precise release, while green electrostatic strategies replace conventional adhesives to meet safety, breathability and wash-fastness requirements across fields.

In food applications, oral safety and bioavailability dominate. Edible wall materials are chosen, freeze-drying is used, particle size is kept near 200 nm, and oxidative stability plus gut-microbiota response are the key indices. While, in textile applications, hand-feel and laundering fastness are paramount. Fibre-affine chitosan is selected, dual cross-linking reinforces mechanical strength, plasma pre-treatment is employed, and washing residue, retained air-permeability and aroma release serve as the main metrics.

5. Future expectation

Over the next decade, nanocapsules will iterate along four main lines: smaller particle size, narrower size distribution, smarter shell layers, and greener manufacturing. First, microfluidic-instantaneous nanoprecipitation coupling technology can complete mixing within 1 ms, reducing the average particle size to below 20 nm while controlling the PDI at around 0.05, providing an invisible carrier for intravenous injection [9]. Second, adaptive shell layers will become a research focus: by introducing cleavable hydrazone or disulfide bonds, nanocapsules can disintegrate within 30 s in the tumor’s mildly acidic or high-GSH environment, achieving zero-order and pulsatile biphasic conjugation release, which has extended the drug exposure window by four times in colorectal cancer models [10]. Third, continuous and green processes will accelerate industrialization: supercriticalextraction of emulsions (SFEE) has been verified in kilogram-scale reactors, with an encapsulation efficiency of >88% and residual solvent <50 ppm, meeting the injectable-grade standards of FDA, and is expected to complete Phase III clinical scale-up before 2028 [9]. Finally, artificial intelligence-high-throughput platforms are being used for reverse design: machine learning predicts the shell material composition and release curve, allowing the screening of formulations within 24 h and shortening the development cycle by 70%, laying the foundation for personalized drug delivery [11]. With the integration of these technologies, nanocapsules are expected to upgrade from carriers to drug robots, delivering greater clinical value in the fields of oncology, metabolism, and rare diseases.

6. Conclusion

This study elucidates the quantitative law of the synergistic suppression of burst by nuclear viscosity-shell crosslinking-surface potential and demonstrates that a single-step low-shear process can enable 160 nm carriers to simultaneously meet the criteria of <10% burst release, <50 ppm solvent, >80% biphasic loading, and cross-industry safety/durability thresholds. This finding bridges the long-standing gap between drug delivery-level performance and large-scale compliant production, providing an immediately transferable nano-encapsulation paradigm for the food and textile industries. Future work needs to further integrate in-situ SAXS online control with kilogram-scale continuous flow reactors and develop near-infrared responsive degradable hybrid shells to achieve precise spatiotemporal release in vivo/in situ and minimize carbon footprint.

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