Int.J.Curr.Res.Aca.Rev.2026; 14(7): 134-143

EXCELLENT PUBLISHERS

International Journal of Current Research and Academic Review

ISSN: 2347-3215 (Online) Volume 14 Number 7 (July-2026)

Journal homepage: http://www.ijcrar.com

doi: https://doi.org/10.20546/ijcrar.2026.1407.012

Recent Advances in Nanoparticle-Based Drug Delivery Systems: A Review

Obed Singh* and Mahalaxmi Muskan

College of Pharmacy, Shivalik Campus, Shiniwala, Dehradun, India

**Corresponding author*

Abstract

Nanoparticles, defined broadly as particulate carriers ranging from approximately 1 to 1000 nm, have emerged as a central platform in contemporary drug delivery research. Across the reviewed literature, nanoparticulate systems are reported to improve drug stability, bioavailability, and site-specific delivery while reducing systemic toxicity relative to conventional dosage forms (Kadian, 2018; Mohanraj & Chen, 2006). This review synthesizes findings from five review articles addressing nanoparticle classification, preparation techniques, physicochemical characterization, and therapeutic applications, with particular attention to cancer, brain, gene, oral, and pulmonary delivery. The reviewed sources converge on the primacy of preformed-polymer dispersion methods, such as solvent evaporation, nanoprecipitation, and emulsification-diffusion, as well as polymerization-based and ionic gelation approaches, while differing in the depth of coverage given to novel classes such as dendrimers, quantum dots, and carbon nanotubes (Pal *et al.,* 2011; Nagavarma *et al.,* 2012). Characterization relies throughout on dynamic light scattering, electron microscopy, and zeta-potential analysis, though the underlying studies are not uniformly in agreement—reported effects of particle size on polymer degradation rate, for instance, differ between individual studies cited within the same source. Notable gaps identified include limited comparative data on scale-up feasibility, inconsistent reporting of long-term toxicological outcomes, and underexplored mechanisms of nanoparticle-mediated blood-brain barrier transcytosis. None of the five sources addresses regulatory pathways or clinical-trial evidence in depth; on this basis, this review infers, rather than reports as an explicit finding of the literature, that translational and regulatory validation is likely the next major barrier to clinical adoption.

Article Info

Received: 20 May 2026
Accepted: 28 June 2026
Available Online: 20 July 2026

Keywords

Nanoparticles; drug delivery; polymeric nanoparticles; nanoprecipitation; controlled release; bioavailability; nanomedicine

Introduction

The past two decades have witnessed a marked shift in pharmaceutical formulation science away from conventional micro-scale delivery systems toward nanoscale particulate carriers. Nanoparticles are generally described across the reviewed literature as solid, submicron colloidal carriers, with size ranges reported inconsistently but overlapping substantially: Kadian (2018) restricts the definition to 1–100 nm, whereas Pal *et al.,* (2011), Nagavarma *et al.,* (2012), Mohanraj & Chen (2006), and Nikam *et al.,* (2014) adopt a broader 10–1000 nm range. This discrepancy itself is informative, as it reflects an unresolved terminological ambiguity in the field between strict nanometric definitions and the more permissive usage common in pharmaceutical sciences, where "nanoparticle" is often used interchangeably with "nanosphere" and "nanocapsule" regardless of exact dimension.

Mechanistically, all five sources agree on the same basic rationale for nanoparticulate drug delivery: nanoparticles

protect the incorporated drug from degradation in systemic circulation, restrict its distribution to non-target tissues, and release it at a controlled and sustained rate at the intended site of action (Mohanraj & Chen, 2006; Nikam *et al.,* 2014). This is achieved through a combination of high surface-area-to-mass ratio, tunable surface chemistry, and the capacity to encapsulate, entrap, or surface-conjugate both hydrophilic and hydrophobic therapeutic agents (Kadian, 2018). Nanoparticles are further distinguished from liposomal systems, which offer similar advantages in principle but are limited in practice by low encapsulation efficiency, rapid drug leakage, and poor storage stability; polymeric nanoparticles are presented in each source as the physically and chemically more stable alternative (Mohanraj & Chen, 2006; Nikam *et al.,* 2014).

Collectively, the reviewed articles span more than a decade of publication (2006–2018), allowing this review to trace both the continuity of core preparation principles and the gradual expansion of application domains, from early emphasis on tumor targeting and oral peptide delivery toward more elaborated discussions of brain-targeted and pulmonary systems in the later reviews. The purpose of the present synthesis is not to restate each source individually but to integrate their findings into a unified account of nanoparticle classification, fabrication, characterization, and application, while explicitly identifying points of convergence, divergence, and unresolved gaps.

Types of Nanoparticles

Classification schemes differ somewhat in emphasis across the reviewed sources. Pal *et al.,* (2011) offer the most systematic taxonomy, organizing nanomaterials by dimensionality. One-dimensional nanostructures, such as thin films and monolayers, have long-standing applications in electronics and catalysis. Two-dimensional structures are exemplified by carbon nanotubes (CNTs), hexagonal carbon lattices classified as single-walled or multi-walled, noted for exceptional mechanical strength and current-carrying capacity. Three-dimensional nanostructures include fullerenes, dendrimers, and quantum dots. Fullerenes are hollow, cage-like carbon clusters with pressure-resilient structural properties and potential for encapsulating bioactive agents; dendrimers are highly branched, monodisperse macromolecules with functionalizable surface groups suited to targeted delivery, though their cationic surface charge has been associated with membrane-disruptive toxicity (Pal *et al.,* 2011). Quantum dots are semiconductor nanocrystals (2–10 nm) whose optical tunability supports simultaneous imaging and drug delivery applications.

In contrast, the remaining four sources (Kadian, 2018; Nagavarma *et al.,* 2012; Mohanraj & Chen, 2006; Nikam *et al.,* 2014) adopt a narrower, pharmaceutically oriented classification centered on the distinction between nanospheres and nanocapsules. Nanospheres are matrix systems in which drug is uniformly dispersed throughout a polymeric network, whereas nanocapsules are vesicular systems in which the drug-containing core is enclosed by a distinct polymeric membrane (Nagavarma *et al.,* 2012; Mohanraj & Chen, 2006). This binary classification is functionally significant because it determines drug release kinetics: nanospheres tend to release drug through diffusion and matrix erosion, while nanocapsule release is governed primarily by membrane permeability (Pal *et al.,* 2011).

A further point of convergence across all sources is the classification of nanoparticles by constituent polymer origin, distinguishing natural hydrophilic polymers (chitosan, gelatin, sodium alginate, albumin) from synthetic polymers (polylactides, polyglycolides, poly(lactide-co-glycolide) [PLGA], polycyanoacrylates, polycaprolactone, and related polyesters) (Nagavarma *et al.,* 2012). This polymer-based classification is arguably the most clinically relevant, since polymer selection dictates biodegradability, drug release kinetics, and biocompatibility—criteria repeatedly emphasized in the selection of matrix materials for nanoparticle design (Mohanraj & Chen, 2006; Nikam *et al.,* 2014).

It is worth noting that this divide in classification approach is not merely terminological but tracks a divide in downstream coverage. Dendrimers, quantum dots, and carbon nanotubes, though introduced in structural and mechanistic detail by Pal *et al.,* (2011), are not revisited in any of the five sources' discussions of cancer, brain, gene, oral, or pulmonary delivery (Sections 5.1–5.5 below); the applied literature reviewed here is built almost entirely around polymeric nanospheres and nanocapsules. This asymmetry suggests either that these materials-science nanostructures remain comparatively immature for pharmaceutical application relative to polymeric carriers, or simply that the pharmaceutically oriented reviews in this set were not scoped to cover them—a distinction the source literature itself does not resolve, and which represents a gap in the reviewed evidence rather than a gap in nanoparticle research as a whole.

Preparation Methods

All five reviewed articles converge on a tripartite classification of nanoparticle preparation strategies: (i) dispersion of preformed polymers, (ii) polymerization of monomers, and (iii) ionic gelation or coacervation of hydrophilic polymers, with supercritical fluid technology noted separately as an emerging, solvent-minimizing alternative (Mohanraj & Chen, 2006; Nikam *et al.,* 2014; Nagavarma *et al.,* 2012). Nagavarma *et al.,* (2012) provide the most granular treatment of these categories, extending the polymerization group to include mini-emulsion, micro-emulsion, interfacial, and controlled/living radical polymerization (C/LRP) techniques, none of which are discussed in comparable depth elsewhere.

Dispersion of Preformed Polymers

The solvent (emulsification) evaporation method is described consistently as the earliest and most widely used technique, involving emulsification of a polymer–drug solution in an organic solvent into an aqueous continuous phase, followed by solvent removal via evaporation or reduced pressure, and recovery of nanoparticles by ultracentrifugation (Pal *et al.,* 2011; Mohanraj & Chen, 2006). All sources note that particle size in this method is governed by stirring or homogenization rate, stabilizer type and concentration, and polymer concentration (Nagavarma *et al.,* 2012; Nikam *et al.,* 2014). A double emulsion (w/o/w) modification is uniformly cited as the preferred approach for encapsulating hydrophilic drugs, which the single-emulsion method handles poorly (Kadian, 2018; Pal *et al.,* 2011).

Nanoprecipitation (solvent displacement) is described identically across sources as involving injection of a polymer solution, dissolved in a water-miscible solvent, into an aqueous stabilizer solution, producing instantaneous colloidal particle formation through interfacial solvent diffusion (Nagavarma *et al.,* 2012; Kadian, 2018). This technique is repeatedly noted as being best suited to lipophilic drugs and poorly suited to water-soluble agents, owing to drug partitioning into the aqueous phase during precipitation (Nagavarma *et al.,* 2012).

The emulsification–diffusion method, presented as a modification of solvent evaporation, uses a partially water-miscible solvent pre-saturated with water; dilution with excess water drives solvent diffusion and nanoparticle formation. This method is credited across sources with high encapsulation efficiency (commonly cited as exceeding 70%), reproducibility, and freedom from high-energy homogenization, at the cost of large volumes of process water requiring elimination (Kadian, 2018; Nagavarma *et al.,* 2012).

Salting-out, a related modification, relies on separating a water-miscible solvent from an aqueous phase via a salting-out electrolyte (e.g., magnesium or calcium chloride) rather than by dilution, offering the specific advantage of avoiding elevated temperature—an important consideration for heat-labile and protein-based drugs (Pal *et al.,* 2011; Nagavarma *et al.,* 2012). Dialysis-based nanoparticle formation, described in similar terms across Kadian (2018), Pal *et al.,* (2011), and Nagavarma *et al.,* (2012), exploits progressive solvent exchange across a molecular-weight-cutoff membrane to induce polymer aggregation into narrow-distribution nanoparticles, though the underlying mechanism is acknowledged as incompletely understood (Nagavarma *et al.,* 2012).

Polymerization of Monomers

Where dispersion methods use preformed polymer, polymerization-based methods build the polymer matrix in situ around the drug. Emulsion polymerization is the most established of these, though its reliance on toxic organic solvents and surfactants has driven interest toward alternative aqueous-phase mechanisms (Kadian, 2018; Nagavarma *et al.,* 2012). Mini-emulsion and micro-emulsion polymerization are distinguished from conventional emulsion polymerization by their use of a co-stabilizer and high-shear devices (mini-emulsion) or thermodynamically stable, surfactant-rich swollen micelles (micro-emulsion), the latter yielding markedly smaller particle sizes (5–50 nm) at the cost of high surfactant loads requiring subsequent removal (Nagavarma *et al.,* 2012). Interfacial polymerization, involving step-growth reaction of two monomers at the interface of immiscible phases, is highlighted as particularly suited to nanocapsule formation when a small volume of oil is incorporated into the organic phase (Kadian, 2018; Nagavarma *et al.,* 2012).

Ionic Gelation and Coacervation

All five sources describe ionic gelation as a solvent-minimizing technique particularly associated with chitosan nanoparticles, in which the cationic amino groups of chitosan interact electrostatically with an

anionic crosslinker, typically sodium tripolyphosphate, to form coacervate nanoparticles under mild, room-temperature aqueous conditions (Nagavarma *et al.,* 2012; Mohanraj & Chen, 2006). This method is consistently presented as advantageous for protein and peptide encapsulation owing to its avoidance of organic solvents and elevated temperature.

Supercritical Fluid Technology

Supercritical fluid technology, most extensively discussed by Nagavarma *et al.,* (2012) and Mohanraj & Chen (2006), is framed as an environmentally favorable alternative that avoids organic solvent residues entirely. Two principal variants are described: rapid expansion of supercritical solution (RESS), in which a polymer dissolved in supercritical CO2 is expanded through a nozzle to induce nucleation, and rapid expansion of supercritical solution into a liquid solvent (RESOLV), a modification in which expansion into a liquid rather than ambient air suppresses particle growth and yields more consistently nanoscaled products (Nagavarma *et al.,* 2012). Both Mohanraj & Chen (2006) and Nagavarma *et al.,* (2012) note that despite its clean output, the technique remains limited by high equipment cost and specialized infrastructure requirements, which likely explains its comparatively minor role in the remaining three, more application-focused reviews.

Characterization Techniques

Physicochemical characterization is treated with near-identical emphasis across the reviewed literature, converging on particle size and morphology, surface charge, and drug release/loading as the principal evaluative parameters (Pal *et al.,* 2011; Mohanraj & Chen, 2006; Nikam *et al.,* 2014).

Particle Size and Morphology

Dynamic light scattering (DLS), also termed photon correlation spectroscopy (PCS), is uniformly identified as the fastest and most routinely used method for particle size determination, exploiting the Doppler shift induced by Brownian motion of particles under laser illumination (Pal *et al.,* 2011; Mohanraj & Chen, 2006). Because DLS provides an indirect, ensemble-averaged measurement, all sources describe it as requiring verification by electron microscopy. Scanning electron microscopy (SEM) offers direct morphological visualization but requires nanoparticles to be dried, metal-coated, and subjected to vacuum, with the electron beam risking polymer damage (Pal *et al.,* 2011). Transmission electron microscopy (TEM) achieves higher resolution through electron transmission across an ultrathin, stained, or vitrified sample, at the cost of more demanding sample preparation (Pal *et al.,* 2011). Atomic force microscopy (AFM) is presented, uniquely in Pal *et al.,* (2011), as offering the most accurate topographical size data without requiring conductive coating, allowing imaging of unmodified biological and polymeric structures under near-native conditions.

Surface Charge and Hydrophobicity

Zeta potential is consistently used as an indirect measure of surface charge and, by extension, colloidal stability, with a magnitude exceeding approximately ±30 mV generally regarded as indicative of a suspension resistant to aggregation (Nikam *et al.,* 2014; Mohanraj & Chen, 2006). Pal *et al.,* (2011) additionally describes surface hydrophobicity assessment via hydrophobic interaction chromatography, biphasic partitioning, and contact-angle measurement, and notes X-ray photon correlation spectroscopy as a means of identifying specific surface chemical groups—an analytical depth not matched in the other four sources.

Drug Loading and Release

Drug entrapment efficiency is typically determined by separating unentrapped drug from nanoparticles via ultracentrifugation and quantifying the difference between total drug used and drug recovered in the supernatant, most explicitly operationalized by Nikam *et al.,* (2014). Drug release studies commonly employ dialysis bag diffusion, side-by-side diffusion cells, or ultrafiltration/centrifugal ultrafiltration, with dialysis techniques favored for their practicality despite being comparatively slow (Mohanraj & Chen, 2006). Across sources, drug release is understood to proceed via matrix diffusion, polymer erosion or enzymatic degradation, or a combination of both, with the balance between diffusion and erosion rates determining whether release kinetics are diffusion- or degradation-controlled (Nagavarma *et al.,* 2012; Mohanraj & Chen, 2006).

The relationship between particle size and polymer degradation rate is one point on which the underlying evidence, as presented within the reviewed sources, is not fully consistent. Mohanraj & Chen (2006) note that the degradation rate of PLGA was found to increase with increasing particle size in vitro, an effect attributed to slower outward diffusion of acidic degradation products

from larger particles, which in turn accelerates autocatalytic polymer breakdown. The same source, however, also reports that a separate investigation using PLGA particles of varying size found no substantial difference in degradation rate across size ranges. Neither Kadian (2018), Pal *et al.,* (2011), Nagavarma *et al.,* (2012), nor Nikam *et al.,* (2014) engage with this discrepancy, and none of the five sources attempts to reconcile it. This unresolved disagreement, even though it is documented within a single review, is a clear illustration of a broader pattern in the collective literature: mechanistic claims about nanoparticle behavior are frequently stated with more confidence than the underlying primary evidence, taken as a whole, actually supports.

Applications in Drug Delivery

The application scope of the reviewed literature is broad but unevenly distributed: Kadian (2018) offers the most systematic route-by-route treatment (oral, transdermal, parenteral, pulmonary, ocular, intranasal), while Mohanraj & Chen (2006) and Nikam *et al.,* (2014) concentrate more heavily on tumor targeting, brain delivery, and gene delivery mechanisms.

Cancer Therapy

Tumor targeting is presented as one of the most extensively validated applications of nanoparticulate delivery. The underlying rationale is twofold: nanoparticles concentrate drug at tumor sites via the enhanced permeability and retention effect or through ligand-mediated active targeting, while simultaneously reducing exposure of healthy tissue by restricting biodistribution (Mohanraj & Chen, 2006; Nikam *et al.,* 2014). Both sources cite doxorubicin incorporated into poly(isohexylcyanoacrylate) nanospheres as producing higher hepatic, splenic, and pulmonary drug concentrations than free doxorubicin in murine models, illustrating the pronounced hepatic and splenic tropism of conventional (uncoated) nanoparticles via the mononuclear phagocyte system (MPS) (Mohanraj & Chen, 2006).

This MPS tropism is presented as a double-edged property: advantageous for treating MPS-resident malignancies such as hepatocarcinoma and leukemia, but an obstacle to reaching tumors outside MPS-rich organs unless nanoparticles are further engineered as long-circulating, PEGylated ("stealth") carriers (Mohanraj & Chen, 2006). Kadian (2018) extends this discussion with more recent examples, citing etoposide and paclitaxel-loaded lipid nanocapsules showing four- to forty-fold higher efficiency than free drug solution in cell culture, iron oxide nanoparticles enabling combined magnetic and photothermal tumor ablation, gold nanoparticle bioconjugates for low-cytotoxicity targeted therapy, and silk fibroin-derived curcumin nanoparticles for sustained breast cancer therapy—applications entirely absent from the earlier Mohanraj & Chen (2006) and Pal *et al.,* (2011) reviews, reflecting the field's evolution over the intervening decade.

Nanoparticles have also been proposed as a means of reversing multidrug resistance (MDR), a major limitation of conventional chemotherapy arising from P-glycoprotein-mediated efflux of anticancer agents. Because P-glycoprotein is thought to recognize drug primarily when localized in the plasma membrane rather than in the cytoplasm or lysosomes, nanoparticle-mediated endocytic delivery may bypass this resistance mechanism (Mohanraj & Chen, 2006)—a mechanistic argument not addressed in the other four sources.

Brain-Targeted Delivery

The blood-brain barrier (BBB) is uniformly identified as the principal obstacle to central nervous system drug delivery, owing to tight endothelial junctions, enzymatic activity, and active efflux transport (Kadian, 2018; Mohanraj & Chen, 2006; Nikam *et al.,* 2014). Polysorbate 80-coated poly(butylcyanoacrylate) nanoparticles are cited across three sources as capable of ferrying otherwise non-transportable agents, including the hexapeptide dalargin and doxorubicin, across the BBB, though Mohanraj & Chen (2006) and Nikam *et al.,* (2014) both note practical shortcomings including desorption of the polysorbate coating, rapid nanoparticle degradation, and toxicity at high polysorbate concentrations. Receptor-mediated strategies are also discussed, including transferrin-receptor-binding antibodies (OX26) and lactoferrin, with lactoferrin reported to achieve brain uptake twice that of OX26 and native transferrin in vivo (Mohanraj & Chen, 2006; Nikam *et al.,* 2014).

Kadian (2018) adds a complementary account of apolipoprotein E-functionalized nanoparticles, which enhance BBB transit via low-density lipoprotein receptor binding, and peptidomimetic-antibody-functionalized pegylated immunonanoparticles capable of parenchymal drug delivery without disrupting BBB integrity—mechanisms not discussed in the earlier reviews.

Gene Delivery

Nanoparticle-mediated gene delivery is discussed principally by Mohanraj & Chen (2006) and Nikam *et al.,* (2014), which describe polynucleotide vaccines as capable of eliciting both humoral and cell-mediated immunity by enabling intracellular antigen expression, in contrast to extracellular protein-based vaccines. A key advantage cited is the rapid endo-lysosomal escape of nanoparticle-encapsulated plasmid DNA into the cytoplasmic compartment, which is associated with sustained gene expression (Mohanraj & Chen, 2006). Proposed applications include PLGA nanoparticles carrying osteogenic genes (e.g., bone morphogenic protein) to facilitate bone healing. Notably, gene delivery receives minimal or no treatment in Kadian (2018), Pal *et al.,* (2011), and Nagavarma *et al.,* (2012), representing an area of applications coverage that is unevenly distributed across the reviewed literature.

Oral Delivery

Oral delivery is treated most extensively by Kadian (2018), Mohanraj & Chen (2006), and Nikam *et al.,* (2014), all of which identify the gastrointestinal epithelial barrier, proteolytic degradation (pepsin, trypsin, chymotrypsin, brush-border endopeptidases), and mucus-layer exclusion as the principal obstacles to peptide and protein absorption. Nanoparticles are proposed to overcome these barriers via transcytosis and intracellular uptake through epithelial cells and Peyer's patch M-cells, with ligand-functionalized systems (e.g., lectin-conjugated, vitamin B12-conjugated) enhancing receptor-mediated uptake (Kadian, 2018; Mohanraj & Chen, 2006). Insulin-loaded nanoparticles are cited by both Mohanraj & Chen (2006) and Nikam *et al.,* (2014) as preserving insulin bioactivity and producing sustained blood glucose reduction in diabetic rats for up to fourteen days post-oral administration—one of the few instances in the reviewed literature where an efficacy claim is reported with a specific, quantifiable outcome measure rather than in general terms. Kadian (2018) additionally discusses the neonatal Fc receptor as a novel oral-delivery target and cites vitamin B12–dextran nanoparticle conjugates as viable oral insulin carriers, representing more recent mechanistic elaboration than found in the earlier sources.

Pulmonary Delivery

Pulmonary delivery is addressed almost exclusively by Kadian (2018), which notes that direct lung delivery reduces systemic toxicity, exploits high vascularization for rapid absorption, and circumvents first-pass hepatic metabolism, while acknowledging that mass median aerodynamic diameter remains a critical constraint on deposition efficiency. Cited examples include PLGA nanoparticles of antitubercular drugs improving bioavailability and reducing dosing frequency, solid lipid nanoparticles of amikacin reducing nephrotoxicity via microsprayer delivery, and paclitaxel-loaded nanoparticles improving lung chemotherapy efficacy.

This application area is essentially unaddressed in Pal *et al.,* (2011), Nagavarma *et al.,* (2012), and Nikam *et al.,* (2014), and is mentioned only implicitly by Mohanraj & Chen (2006) in the context of general route flexibility—constituting one of the clearer coverage gaps among the reviewed sources.

Taken together, these five application domains illustrate that the therapeutic promise of nanoparticles is not confined to a single route or disease area but recurs across markedly different physiological barriers—the tumor microenvironment, the blood-brain barrier, the intestinal epithelium, and the pulmonary epithelium alike. The advantages and limitations that make this possible, several of which have already been touched on route by route above, are consolidated more systematically in the two sections that follow.

Advantages

Despite differences in scope, the reviewed literature converges on a consistent set of advantages attributed to nanoparticulate drug delivery systems:

- Enhanced bioavailability through increased surface area, promoting faster dissolution and absorption (Nagavarma *et al.,* 2012; Nikam *et al.,* 2014).
- Controlled and sustained drug release, achieved by modulating polymer composition and matrix erosion characteristics (Mohanraj & Chen, 2006).
- Protection of labile drugs, proteins, and nucleic acids from enzymatic and hydrolytic degradation in systemic or gastrointestinal environments (Kadian, 2018).
- Site-specific targeting via passive accumulation (enhanced permeability and retention) or active targeting through surface-conjugated ligands and antibodies (Nikam *et al.,* 2014).
- Versatility across administration routes, including oral, parenteral, transdermal, pulmonary, ocular, and intranasal delivery (Kadian, 2018).

- Reduced dosing frequency and lower effective doses, translating to decreased systemic toxicity (Pal *et al.,* 2011).
- Compatibility with combined diagnostic and therapeutic (theranostic) functions, particularly for quantum dots and magnetic nanoparticles (Pal *et al.,* 2011; Kadian, 2018).

Limitations

The reviewed sources are similarly consistent in identifying the practical and translational limitations of nanoparticle-based delivery, though the depth of discussion varies.

- ✓ Aggregation tendency: the same high surface-area-to-mass ratio that confers therapeutic advantage also predisposes nanoparticles to particle–particle aggregation, complicating handling in both liquid and dry forms (Mohanraj & Chen, 2006; Nikam *et al.,* 2014).
- ✓ Burst release and limited drug loading: small particle size and large surface area frequently result in weakly bound surface drug being released rapidly ("burst release"), undermining sustained-release objectives (Mohanraj & Chen, 2006).
- ✓ Scale-up constraints: several preparation methods, including salting-out and emulsification-diffusion, require extensive washing or large process-water volumes that complicate industrial-scale manufacture (Nagavarma *et al.,* 2012).
- ✓ Residual solvent and toxicity concerns: organic solvents such as dichloromethane, though partially superseded by ethyl acetate for toxicological reasons, may persist in the final product (Nagavarma *et al.,* 2012).
- ✓ Mononuclear phagocyte system (MPS) clearance: conventional, non-PEGylated nanoparticles are rapidly opsonized and cleared by hepatic and splenic macrophages, limiting circulation time and access to tumors outside MPS-rich tissue (Mohanraj & Chen, 2006).
- ✓ Health and safety uncertainty: inhaled ultrafine nanoparticles have been associated with pulmonary inflammation and tumorigenesis in animal models, and dermal penetration depth appears inversely related to particle size, raising occupational and environmental safety questions that remain incompletely characterized (Pal *et al.,* 2011).
- ✓ Mechanistic uncertainty: the mechanism underlying dialysis-based nanoparticle formation, for example, is explicitly acknowledged as "not fully understood at present" (Nagavarma *et al.,* 2012), illustrating that even well-established preparation techniques retain unresolved theoretical gaps; the size-dependent degradation discrepancy discussed in Section 4.3 is a further example of this pattern.

These limitations are not evenly distributed across the reviewed sources—several, such as MPS clearance and burst release, are treated in mechanistic depth only by Mohanraj & Chen (2006)—but none of the five reviews proposes that they have been fully resolved. The following section considers where the field appears to be heading in response.

Future Perspectives

Synthesizing the forward-looking statements across the five reviews, several converging research priorities emerge. First, there is a shared call for continued refinement of surface engineering strategies—PEGylation, ligand conjugation, and stimuli-responsive coatings—to prolong circulation time and improve active targeting precision beyond passive accumulation (Mohanraj & Chen, 2006; Nikam *et al.,* 2014). Second, several sources highlight the need for "smart" or bioresponsive delivery systems capable of triggered release in response to local physiological cues, alongside architecturally biomimetic polymers and virus-like intracellular delivery systems (Nagavarma *et al.,* 2012).

Third, environmentally and physiologically benign manufacturing routes are identified as a priority, particularly the expansion of supercritical fluid and controlled/living radical polymerization techniques, which reduce reliance on toxic organic solvents and surfactants (Nagavarma *et al.,* 2012). Fourth, greater mechanistic clarity regarding nanoparticle transport across the blood-brain barrier and intestinal epithelium is warranted, given that several receptor-mediated transcytosis pathways (transferrin, lactoferrin, apolipoprotein E, neonatal Fc receptor) remain only partially characterized despite promising early data (Kadian, 2018; Mohanraj & Chen, 2006). It should be noted that these four priorities are inferred from the collective direction of the reviewed literature rather than stated as an explicit research agenda by any single source. Finally, none of the five reviewed articles provides substantial discussion of regulatory pathways, batch-to-batch reproducibility standards, or long-term clinical safety data, despite each acknowledging, at least implicitly, that translation from bench to bedside remains incomplete.

Table.1 Comparative Summary

Reference	Journal / Year	Primary Focus	Nanoparticle Size Range Cited	Distinctive Contribution
Kadian, 2018	Asian J Pharm Clin Res, 2018	Route-specific therapeutic applications	1–100 nm	Most comprehensive route-by-route (oral, transdermal, parenteral, pulmonary, ocular, intranasal) application coverage; recent nanomaterial examples (gold, iron oxide, silk fibroin)
Pal *et al.*, 2011	J Applied Pharm Science, 2011	Classification and characterization	10–1000 nm (particles); 1–100 nm (general nanotech)	Dimensionality-based classification (1D/2D/3D); most detailed AFM/SEM/TEM and surface-hydrophobicity methodology; health-risk discussion
Nagavarma *et al.*, 2012	Asian J Pharm Clin Res, 2012	Preparation technique taxonomy	10–1000 nm	Most granular treatment of polymerization sub-types (mini-, micro-emulsion, interfacial, C/LRP) and supercritical fluid methods (RESS, RESOLV)
Mohanraj & Chen, 2006	Trop J Pharm Res, 2006	Formulation science and applications	10–1000 nm	Earliest and most detailed treatment of MPS clearance, long-circulating "stealth" particles, and multidrug-resistance reversal
Nikam *et al.*, 2014	Int J Res Dev Pharm L Sci, 2014	Overview / applications synthesis	10–1000 nm	Concise entrapment-efficiency formula; brief coverage of antimicrobial nanotechnology and cell-repair nanorobot concepts

Table.2 Comparison of Nanoparticle Preparation Methods

Method	Category	Key Advantage(s)	Key Limitation(s)	Cited By
Solvent evaporation	Preformed polymer dispersion	Widely established; suitable for thermolabile drugs; narrow size distribution achievable	Poor entrapment of hydrophilic drugs; possible residual solvent	All five sources
Double emulsion & evaporation	Preformed polymer dispersion	Enables hydrophilic drug encapsulation	Sensitive to stabilizer/polymer concentration and aqueous phase volume	Kadian, 2018; Pal *et al.,* 2011; Mohanraj & Chen, 2006
Nanoprecipitation	Preformed polymer dispersion	Simple, rapid; good for poorly soluble drugs; easy size control	Limited to water-miscible solvents; not efficient for water-soluble drugs	Nagavarma *et al.,* 2012; Kadian, 2018; Pal *et al.,* 2011
Emulsification–diffusion	Preformed polymer dispersion	High encapsulation efficiency (>70%); no homogenization needed; scalable	Large water volumes to remove; possible drug leakage during emulsification	Kadian, 2018; Nagavarma *et al.,* 2012
Salting-out	Preformed polymer dispersion	No heating required; minimizes protein stress	Limited to lipophilic drugs; extensive washing steps	Kadian, 2018; Pal *et al.,* 2011; Nagavarma *et al.,* 2012
Dialysis	Preformed polymer dispersion	Simple, effective; narrow size distribution	Mechanism not fully understood; solvent choice affects morphology	Kadian, 2018; Pal *et al.,* 2011; Nagavarma *et al.,* 2012
Supercritical fluid (RESS/RESOLV)	Preformed polymer / solvent-free	Environmentally safe; solvent-free, high-purity product	Expensive, specialized equipment; RESS prone to microscale rather than nanoscale product	Nagavarma *et al.,* 2012; Mohanraj & Chen, 2006; Kadian, 2018
Emulsion / mini- / micro-emulsion polymerization	Monomer polymerization	Fast, scalable (emulsion); smaller/more uniform particles (micro-emulsion)	Requires toxic solvents/surfactants/initiators; non-biodegradable products in some cases	All five sources (varying detail)
Interfacial polymerization	Monomer polymerization	Well-established; suited to nanocapsule formation	Organic solvent serves as monomer vehicle, requiring careful removal	Kadian, 2018; Nagavarma *et al.,* 2012
Ionic gelation / coacervation	Hydrophilic polymer	Mild, aqueous, room-temperature conditions; ideal	Limited mainly to natural polyelectrolytes (e.g.,	All five sources

	crosslinking	for proteins/peptides	chitosan)	

Table.3 Summary of Nanoparticle Applications in Drug Delivery

Application Domain	Mechanism / Rationale	Representative Example(s)	Primary Source(s)
Cancer therapy	Enhanced permeability and retention effect; active ligand targeting; MPS-mediated accumulation	Doxorubicin-loaded poly(isohexylcyanoacrylate) nanospheres; paclitaxel/etoposide lipid nanocapsules; iron oxide magnetic-photothermal particles; gold nanoparticle bioconjugates	Mohanraj & Chen, 2006; Kadian, 2018; Nikam *et al.,* 2014
Brain delivery	Receptor-mediated transcytosis across the blood-brain barrier; surfactant-coated carrier uptake	Polysorbate 80-coated poly(butylcyanoacrylate) nanoparticles; transferrin/lactoferrin-targeted carriers; apolipoprotein E-functionalized nanoparticles	Kadian, 2018; Mohanraj & Chen, 2006; Nikam *et al.,* 2014
Gene delivery	Endo-lysosomal escape enabling sustained cytoplasmic/nuclear gene expression	PLGA nanoparticles encoding bone morphogenic protein; polynucleotide vaccine carriers	Mohanraj & Chen, 2006; Nikam *et al.,* 2014
Oral delivery	Transcytosis via enterocytes and M-cells; protection from gastric/enzymatic degradation	Insulin-loaded nanoparticles (sustained glycemic reduction in diabetic rats); lectin- and vitamin B12-conjugated carriers	Kadian, 2018; Mohanraj & Chen, 2006; Nikam *et al.,* 2014
Pulmonary delivery	High vascularization and surface area; avoidance of first-pass metabolism	PLGA antitubercular nanoparticles; solid lipid amikacin nanoparticles; paclitaxel nanoparticles for lung cancer	Kadian, 2018
Ocular / transdermal / intranasal delivery	Mucoadhesion and reservoir effect; nose-to-brain olfactory transport	Chitosan brimonidine and rivastigmine nanoparticles; solid lipid vitamin A carriers	Kadian, 2018

This represents perhaps the most consequential gap in the collective literature: while preparation science and preclinical proof-of-concept data are extensively documented, the clinical, regulatory, and manufacturing-scale evidence needed to fully validate nanoparticulate therapeutics is comparatively underdeveloped across all five sources.

Conclusion

Taken together, the five reviewed articles present a coherent and cumulative picture of nanoparticle-based drug delivery as a mature yet still-evolving field. There is strong consensus regarding core preparation methods (solvent evaporation, nanoprecipitation, emulsification-diffusion, salting-out, dialysis, polymerization, and ionic gelation), characterization approaches (dynamic light scattering, electron microscopy, zeta potential), and the fundamental advantages of nanoparticulate carriers over conventional and liposomal delivery systems. Differences among the sources are primarily differences of emphasis and chronology rather than contradiction: earlier reviews (Mohanraj & Chen, 2006; Pal *et al.,* 2011) focus more heavily on classification and characterization fundamentals, while the more recent reviews (Kadian, 2018) incorporate a broader range of route-specific applications and more recently reported nanomaterial classes such as gold and iron oxide nanoparticles. Persistent gaps—particularly around scale-up feasibility, long-term toxicology, and regulatory translation—suggest that future research and future reviews should place greater emphasis on the clinical and manufacturing dimensions of nanoparticle-based therapeutics, rather than solely on preparation chemistry and preclinical efficacy.

References

Aksungur P, Demirbilek M, Denkbas EB, Vandervoort J, Ludwig A, Unlu N. Development and characterization of cyclosporine A loaded nanoparticles for ocular drug delivery. J Control Release. 2011; 151: 286-294.

Bibby DC, Talmadge JE, Dalal MK, Kurz SG, Chytil KM, Barry SE, *et al.,* Pharmacokinetics and biodistribution of RGD-targeted doxorubicin-loaded nanoparticles in

tumor-bearing mice. Int J Pharm. 2005; 293: 281-290.

Calvo P, Remunan-Lopez C, Vila-Jato JL, Alonso MJ. Novel hydrophilic chitosan-polyethylene oxide nanoparticles as protein carriers. J Appl Polym Sci. 1997; 63: 125-132.

Chiannilkulchai N, Ammoury N, Caillou B, Devissaguet JP, Couvreur P. Hepatic tissue distribution of doxorubicin-loaded nanoparticles after i.v. administration in reticulosarcoma M5076 metastasis-bearing mice. Cancer Chemother Pharmacol. 1990; 26: 122-126.

Damge C, Michel C, Aprahamian M, Couvreur P, Devissaguet JP. Nanocapsules as carriers for oral peptide delivery. J Control Release. 1990; 13: 233-239.

Desai MP, Labhasetwar V, Walter E, Levy RJ, Amidon GL. The mechanism of uptake of biodegradable microparticles in Caco-2 cells is size dependent. Pharm Res. 1997; 14: 1568-1573.

Dunne M, Corrigan OI, Ramtoola Z. Influence of particle size and dissolution conditions on the degradation properties of polylactide-co-glycolide particles. Biomaterials. 2000; 21: 1659-1668.

Espinosa A, Di Corato R, Kolosnjaj-Tabi J, Flaud P, Pellegrino T, Wilhelm C. Duality of iron oxide nanoparticles in cancer therapy: amplification of heating efficiency by magnetic hyperthermia and photothermal bimodal treatment. ACS Nano. 2016; 10: 2436-2446.

Fazil M, Md S, Haque S, Kumar M, Baboota S. Development and evaluation of rivastigmine loaded chitosan nanoparticles for brain targeting. Eur J Pharm Sci. 2012; 47: 6-15.

Fessi H, Puisieux F, Devissaguet JP, Ammoury N, Benita S. Nanocapsule formation by interfacial deposition following solvent displacement. Int J Pharm. 1989; 55: R1-R4.

Gupta V, Aseh A, Rios CN, Aggarwal BB, Mathur AB. Fabrication and characterization of silk fibroin-derived curcumin nanoparticles for cancer therapy. Int J Nanomedicine. 2009; 4: 115-122.

Ji B, Maeda J, Higuchi M, Inoue K, Akita H, Harashima H, *et al.,* Pharmacokinetics and brain uptake of lactoferrin in rats. Life Sci. 2006; 78: 851-855.

Kadian R. Nanoparticles: a promising drug delivery approach. Asian J Pharm Clin Res. 2018; 11(1): 30-35.

Kreuter J, Ramge P, Petrov V, Hamm S, Gelperina SE, Engelhardt B, *et al.,* Direct evidence that polysorbate-80-coated poly (butylcyanoacrylate) nanoparticles deliver drugs to the CNS via specific mechanisms requiring prior binding of drug to the nanoparticles. Pharm Res. 2003; 20: 409-416.

Kreuter J. Nanoparticles. In: Kreuter J, editor. Colloidal drug delivery systems. New York: Marcel Dekker; 1994. p. 219-342.

Lacoeuille F, Garcion E, Benoit JP, Lamprecht A. Lipid nanocapsules for intracellular drug delivery of anticancer drugs. J Nanosci Nanotechnol. 2007; 7: 4612-4617.

Mohanraj VJ, Chen Y. Nanoparticles - a review. Trop J Pharm Res. 2006; 5(1): 561-573.

Nagavarma BVN, Yadav HKS, Ayaz A, Vasudha LS, Shivakumar HG. Different techniques for preparation of polymeric nanoparticles - a review. Asian J Pharm Clin Res. 2012; 5(Suppl 3): 16-23.

Nikam AP, Ratnaparkhiand MP, Chaudhari SP. Nanoparticles - an overview. Int J Res Dev Pharm Life Sci. 2014; 3(5): 1121-1127.

Pal SL, Jana U, Manna PK, Mohanta GP, Manavalan R. Nanoparticle: an overview of preparation and characterization. J Appl Pharm Sci. 2011; 1(6): 228-234.

Pandey R, Khuller GK. Subcutaneous nanoparticle-based antitubercular chemotherapy in an experimental model. J Antimicrob Chemother. 2004; 54: 266-268.

Panyam J, Dali MM, Sahoo SK, Ma W, Chakravarthi SS, Amidon GL, *et al.,* Polymer degradation and in vitro release of a model protein from poly(D,L-lactide-co-glycolide) nano- and microparticles. J Control Release. 2003; 92: 173-187.

Sharma A, Sharma S, Khuller GK. Lectin-functionalized poly (lactide-co-glycolide) nanoparticles as oral/aerosolized antitubercular drug carriers for treatment of tuberculosis. J Antimicrob Chemother. 2004; 54: 761-766.

Varshosaz J, Ghaffari S, Mirshojaei SF, Jafarian A, Atyabi F, Kobarfard F, *et al.,* Biodistribution of amikacin solid lipid nanoparticles after pulmonary delivery. Biomed Res Int. 2013; 2013: 136859.

Verdun C, Brasseur F, Vranckx H, Couvreur P, Roland M. Tissue distribution of doxorubicin associated with polyhexylcyanoacrylate nanoparticles. Cancer Chemother Pharmacol. 1990; 26: 13-18.

How to cite this article:

Obed Singh and Mahalaxmi Muskan. 2026. Recent Advances in Nanoparticle-Based Drug Delivery Systems: A Review. *Int.J.Curr.Res.Aca.Rev.* 14(76), 134-143. doi: https://doi.org/10.20546/ijcrar.2026.1407.012