Title: Advances in polymeric nanoparticles for oral drug delivery: mechanisms, challenges, emerging trends, and preclinical to clinical perspectives

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Abstract: Oral drug delivery remains the most popular method due to its patient compliance, affordability, and ease of use. The effective administration of therapeutic medicines faces physiological challenges such as enzymatic degradation, low permeability, and inadequate bioavailability. Polymeric nanoparticles (NPs) provide targeted distribution, controlled release, and enhanced stability of medications in the gastrointestinal tract, making them a viable solution to overcome these obstacles. Recent advancements have focused on developing new polymers, surface modifications, and stimuli-responsive systems to enhance the performance of NPs. Despite significant advancements, challenges such as large-scale manufacturing, regulatory approval, and long-term safety remain significant obstacles. This review discusses recent advancements in polymeric NPs for oral drug delivery, highlighting challenges and potential future advancements for effective clinical translation. Polymeric NPs significantly enhance oral bioavailability by shielding unstable medications from gastrointestinal conditions and facilitating targeted release. The durability, permeability, and drug loading efficiency of NPs have been improved through innovative techniques, including the use of biodegradable polymers, mucoadhesive coatings, and stimuli-responsive systems. Furthermore, surface alterations targeting intestinal receptors enhance site-specific delivery and absorption, but challenges like scalability limitations, inconsistent performance, toxicity, and regulatory barriers persist. This review critically studies the use of polymeric NPs in oral medication administration, focusing on their physicochemical benefits, gastrointestinal tract interactions, formulation techniques, and clinical translation. Recent advancements, including mucoadhesive systems, targeted strategies, and bioresponsive technologies, are receiving significant attention. Future clinical success in oral drug delivery relies on the development of improved evaluation techniques, enhanced biocompatibility, and increased reproducibility. Research should focus on multifunctional NP systems, nanofabrication technologies, and interdisciplinary cooperation between materials scientists, pharmacologists, and regulatory bodies.

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