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Strategies for the enhanced intracellular delivery of nanomaterials

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Highlights

- Targeting specific organelles treat or decrease symptoms of several diseases
- Manipulation of nanomaterials characteristics can improve the intracellular delivery
- Approaches to escape to endocytic route and non-endocytic route as an alternative
- Strategies to reach the target, maintaining the original drug bioavailability

The intracellular delivery of nanomaterials and drugs has been attracting increasing research interest, mainly because of their important effects and functions in several organelles. Targeting specific organelles can help treat or decrease the symptoms of diabetes, cancer, infectious, and autoimmune diseases. Tuning biological and chemical properties enables the creation of functionalized nanomaterials with enhanced intracellular uptake, ability to escape premature lysosome degradation, and to reach a specific target. Here, we provide an update of recent advances in the intracellular delivery mechanisms that could help drugs reach their target more efficiently.

Keywords: nanomaterials; intracellular delivery; drugs; intracellular targets; endosomal escape.
Teaser: This review provides an update of recent advances in intracellular delivery and reports mechanisms that could help drugs reach their target efficiently, resulting in smarter drugs that reach their target still with the original bioavailability**.**

Introduction

Developments in nanomedicine delivery have provided new perspectives of the design and synthesis of efficient nanocarriers and multifunctional nanomaterials. Initially, research focused on nanocarrier biocompatibility and toxicity, whereas second-generation nanomaterials aimed to have an optimized surface, to provide more stability, stealth, and targeting capabilities. The most recent models support the 'smart nanomedicine' idea, improving targeting mechanisms and theranostic abilities [1]. This nanotechnological advance is important because it enables drugs to cross physiological barriers to reach their target sites safely and sustainably [2]. In fact, nanomaterials provide a stable biocompatible environment to encapsulate drugs, promoting their controlled release and efficient absorption [3,4]. They also improve the duration of the therapeutic effects and minimize adverse effects by driving drugs toward the site of action and increasing the concentration of a drug in the area of pathology in a specific way [5,6]. Depending on the accumulation of the delivery system in the tissue, cell, or in a specific subcellular compartment of interest, targeting approaches can be primary, secondary, or tertiary, respectively [7].

Subcellular targeting is vital for efficient, specific treatments and, thus, specific barriers must be overcome. The importance of organelle targeting increases when drugs efficiently treat or decreases symptoms of diseases such as cancer, Alzheimer's, diabetes, infectious and autoimmune diseases [8]. Specifically, the intracellular environment contains compounds, responsible for cell growth, proliferation, differentiation, and death, that are, therefore,