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Self-nanoemulsifying drug delivery systems (SNEDDS) for treating neglected tropical diseases: affordable and scalable pathways for global health impact

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Nanomaterials present promising avenues for advancing global health, particularly in addressing neglected tropical diseases (NTDs). Affecting over a billion people, NTDs suffer from limited treatment options, often relying on drugs with poor solubility and bioavailability. This challenge is compounded by increasing drug resistance and difficulties in administering treatments effectively. This situation underscores a critical gap in pharmaceutical innovation, influenced more by market forces than by scientific limitations. The prohibitive costs and high failure rates of traditional drug development render standard innovation pathways economically impractical for neglected tropical diseases. Moreover, regulatory frameworks and intellectual property rights often hinder the development of affordable treatments for neglected tropical diseases. Nanotechnology, specifically self-nanoemulsifying drug delivery systems (SNEDDS), offers a scalable solution to overcome solubility and bioavailability barriers. By spontaneously forming emulsions in gastrointestinal fluids, SNEDDS eliminate complex manufacturing needs, as seen with successful clinical examples like ritonavir and cyclosporine. Leveraging these cost-effective, orally compatible platforms allows for the repurposing of existing drugs. Integrating such streamlined nanotechnologies into global health programs is essential to close the therapeutic gap in resource-limited settings.

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The unmet need in neglected tropical diseases

Neglected tropical diseases (NTDs) affect more than one billion people worldwide and remain closely associated with poverty, inadequate sanitation, and insufficient healthcare infrastructure.[1] Despite their global burden, the therapeutic arsenal against most NTDs is extremely limited.[2] Current treatments rely on small molecules developed decades ago, often characterized by poor solubility, limited bioavailability, and suboptimal pharmacokinetic and pharmacodynamic profiles. These pharmacological shortcomings are further aggravated by the emergence of drug resistance and the challenge of administering treatments in regions that lack cold-chain infrastructure or advanced manufacturing capacity.

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This persistent therapeutic gap represents one of the most evident failures of modern pharmaceutical innovation. Although scientific capacity in medicinal chemistry, molecular biology, and computational modeling has advanced significantly, the translation of this knowledge into new antiparasitic drugs remains slow.[3] The cause of this stagnation is not scientific inability but structural inequality within the global research and development (R&D) system, which continues to be driven primarily by market incentives rather than by public health priorities.

Market failures and structural barriers to innovation

Commercial R&D is guided by profit expectations. Diseases that predominantly affect impoverished populations rarely attract sufficient investment. As a result, NTDs such as schistosomiasis, Chagas disease, and visceral leishmaniasis remain chronically underserved.[4] The cost of bringing a single new medicine to market often exceeds 800 million US dollars when considering development failures and capital expenditures.[5,6] Under these circumstances, the traditional innovation pathway

becomes economically unfeasible for conditions that do not promise financial return. In addition, regulatory frameworks are designed mainly for high-income markets and high-value products, imposing long and costly approval processes that discourage smaller or publicly funded initiatives. Intellectual property mechanisms, originally intended to promote innovation, may also restrict access when patents and exclusivity clauses limit generic competition or affordable production.

In response to these structural barriers, several countries have established regulatory frameworks aimed at stimulating research and development for rare and neglected conditions by offsetting commercial risk. These include the United States Orphan Drug Act (1983), which provides tax credits, user fee waivers, and market exclusivity; the European Union Regulation (EC) no. 141/2000 on orphan medicinal products, which harmonizes incentives across member states; and national initiatives in low- and middle-income regions, such as Taiwan's Rare Disease Prevention and Medicine Law, India's National Policy for Treatment of Rare Diseases (NPTRD, 2021), and Brazil's regulatory pathways coordinated by ANVISA for rare and neglected diseases. Collectively, these policies reflect a growing global recognition that targeted regulatory incentives are essential to partially correct market failures and stimulate innovation in areas where conventional profit-driven models remain insufficient.

This scenario and interconnected barriers perpetuate a paradox: although science can generate effective new treatments, such as the use of innovative peptide biomolecules[7] or novel delivery systems,[8,9] the global economic structure prevents their development and distribution to those who need them most. Overcoming this challenge requires rethinking the current drug development model, moving beyond market-driven solutions toward collaborative, open, and mission-oriented approaches that prioritize equity and access.[10,11]

To face this problem, public–private partnerships (PPPs) such as the Drugs for Neglected Diseases initiative (DNDi) and other product development partnerships (PDPs) have shown that coordinated funding and shared intellectual frameworks can accelerate progress. However, the scale of the problem demands broader and more systemic change, particularly in discovering and formulating drugs that can be produced, distributed, and administered efficiently in low-resource settings. Within this context, nanomaterials have emerged as a technological alternative capable of improving pharmacological performance, reducing dosage frequency, and enabling oral delivery of poorly soluble compounds.[12–17]

Emerging nanotechnological strategies for neglected diseases

Nanotechnology offers a versatile set of tools to overcome the intrinsic limitations of classical drug molecules. By employing this innovative approach, we aim to not only reduce therapy development costs but also shorten the development timeline, specifically targeting regulatory approvals.[9,18,19] Manipulating matter at the nanometer scale makes it possible to modify solubility, stability, tissue distribution, and controlled release profiles. These features are especially valuable in antiparasitic therapy, where drugs must act in complex host–parasite environments. Over the past decade, various nanoplatforms have been explored for NTDs, including polymeric nanoparticles, lipidic nanoparticles, and inorganic nanoparticles.[14,20,21]

Some of these approaches aim to discover new chemical entities with improved selectivity, while others focus on reformulating existing drugs to enhance pharmacokinetic properties and reduce toxicity.[15] The second strategy, pharmaceutical repurposing through advanced formulation, provides a pragmatic shortcut that avoids the high costs of *de novo* drug discovery. Nanocarrier-based reformulation can increase bioavailability, prolong circulation time, and improve drug accumulation at target sites. For neglected diseases, in which affordability and scalability are crucial, the goal is to identify materials and manufacturing methods that enhance pharmacological efficacy without significantly increasing production costs or regulatory complexity.

Within this scenario, one of the most promising directions is the development of self-nanoemulsifying drug delivery systems (SNEDDS).[22] This platform combines technological simplicity with great potential to improve oral bioavailability. The following sections discuss the rationale behind SNEDDS, their mechanisms of action, and their translational opportunities for NTD treatment.

SNEDDS: a cost-effective and scalable platform for oral delivery

Self-nanoemulsifying drug delivery systems (SNEDDS) are technologically simple yet highly efficient formulations designed to enhance the oral bioavailability of poorly water-soluble drugs. These systems are composed of a mixture of oils, surfactants, and co-surfactants that spontaneously form fine oil-in-water emulsions when exposed to gastrointestinal fluids under mild agitation. This spontaneous emulsification process occurs without the need for high-energy input, complex equipment, or sophisticated manufacturing facilities, making SNEDDS a practical and low-cost alternative for large-scale production.[22–24]

While most nanoplatforms like polymeric, solid-lipid, and micellar systems offer unique advantages, self-nanoemulsifying drug delivery systems (SNEDDS) are prioritized for neglected tropical diseases (NTDs) due to their superior balance of cost-effectiveness and scalability.[15,17,20] Unlike many nanoparticle-based approaches that require complex, high-energy manufacturing, or sophisticated equipment, SNEDDS form spontaneously upon contact with gastrointestinal fluids, making them highly suitable for large-scale production in resource-limited settings. From a regulatory standpoint, SNEDDS often utilize well-established, food-grade excipients,[25] which can simplify safety evaluations compared to novel synthetic polymers.

The SNEDDS technology involves the intentional production of nano-sized lipid droplets, less than 500 nm in diameter, when in contact with the gastrointestinal fluids, with lipophilic drugs entrapped inside the core of these nanostructures. This strategy allows the insoluble, entrapped drugs to cross the hydrophilic mucus layer and reach the mucosa for absorption, or at least to disperse within the mucous acellular layer to access target parasite structures. Without nanoencapsulation, most administered drugs are excreted in feces without effectively penetrating the mucous barrier, significantly reducing their contact with the targeted parasitic cells. In contrast, the nanodroplets created by SNEDDS technology act as true nanocarriers, efficiently delivering therapeutic agents directly to the desired regions.[16,17]

Regarding these absorption mechanisms, SNEDDS facilitate drug permeation across intestinal mucous and mucosal barriers through several interrelated processes. Upon dispersion in gastrointestinal fluids, SNEDDS form nano-sized oil-in-water emulsions, which significantly increase the interfacial surface area for drug diffusion and enable intimate contact with the intestinal epithelium. The supersaturated state creates a high thermodynamic activity of the drug, enhancing the concentration gradient across the intestinal membrane and promoting passive diffusion.[22,26]

Additionally, lipid and surfactant components in SNEDDS modulate membrane fluidity and inhibit efflux transporters such as P-glycoprotein (P-gp), thereby reducing drug efflux and improving transcellular uptake. Some surfactants may also transiently open tight junctions, facilitating paracellular transport. Furthermore, the formation of mixed micelles with bile salts and lipid digestion products enhances drug solubilization and promotes lymphatic transport, bypassing first-pass metabolism. Collectively, these mechanisms—enhanced solubilization, supersaturation-driven flux, membrane interaction, and efflux inhibition—work synergistically to overcome mucosal barriers and significantly improve oral drug absorption.[26]

Clinical translation and lessons from other therapeutic areas

While no SNEDDS-based product for neglected diseases has yet reached the market, experience from other therapeutic fields provides valuable insight into the feasibility of this technology. For instance, the self-microemulsifying system used in ritonavir (Norvir®) was a landmark example of how emulsification approaches can overcome severe solubility barriers in antiviral therapy. The commercial success of Norvir®, formulated as a liquid SMEDDS in soft gelatin capsules, demonstrated that such systems could significantly enhance the oral bioavailability of hydrophobic drugs like ritonavir, which is crucial for effective HIV treatment.[27,28]

Another clinically validated case is cyclosporine, a highly insoluble immunosuppressant drug commercialized as Sandimmune® and later as Neoral®. Both products rely on nanoemulsion technology, but Neoral® offers more consistent droplet sizes (100–250 nm), leading to improved and more predictable absorption. These examples show that self-nanoemulsifying technologies can enhance dissolution, reduce inter-patient variability, and ensure reliable bioavailability for drugs with poor aqueous solubility. Such improvements are critical for chronic conditions that require precise plasma concentration control, such as immunosuppression following organ transplantation.[28]

These successful clinical experiences underscore the potential of SNEDDS as a robust, adaptable, and cost-effective formulation platform. They also demonstrate that the technical and regulatory challenges associated with these delivery systems can be overcome when industrial-scale production and safety validation are well structured. Translating this success to the field of neglected diseases depends primarily on adapting existing formulations to therapeutic compounds with similar biopharmaceutical limitations.

Following the potential of SNEDDS, one critical advantage of this kind of formulation is their nature as anhydrous products. The absence of water in the pre-concentrate significantly enhances long-term stability by minimizing drug hydrolysis and preventing the chemical degradation often seen in aqueous systems. This anhydrous state also inherently reduces the risk of microbiological contamination, a vital factor for ensuring safety and extending shelf life in tropical regions where high humidity and temperature are prevalent. From an industrial perspective, the water-free composition simplifies scale-up and manufacturing processes, as it eliminates the need for complex stabilization techniques required for water-containing emulsions. By reducing the reliance on cold-chain logistics and specialized storage, the anhydrous nature of SNEDDS directly addresses the logistical and quality control challenges of resource-poor settings, making them a more viable candidate for sustainable global health interventions.

Challenges and opportunities for implementation in neglected tropical diseases

Despite encouraging progress, several challenges must be addressed to ensure successful implementation of SNEDDS in neglected disease treatment. One of the main issues is the selection of excipients that are both affordable and compatible with large-scale production in endemic countries. While many SNEDDS employ food-grade materials such as lecithin, chitosan, and proteins,[29–31] the availability and cost of pharmaceutical-grade surfactants can still be limiting factors. Establishing regional production chains and technology-transfer programs may help overcome these barriers, promoting local capacity building.

Another important challenge involves regulatory harmonization. Although the use of well-known excipients simplifies safety evaluation, regulatory agencies often require additional studies to assess long-term stability, *in vivo* bioequivalence, and potential interactions between formulation components.

Aligning these requirements across regions can accelerate clinical translation. Furthermore, interdisciplinary collaboration between chemists, pharmacologists, and clinicians is essential to identify the most suitable candidate drugs for reformulation.[18,19]

On the other hand, several opportunities strengthen the case for adopting SNEDDS and similar nanotechnologies in neglected disease programs. These systems are compatible with oral administration, the preferred route in mass drug administration campaigns, and they can be developed at a relatively low cost compared to other nanocarrier systems. Advances in computational modeling and artificial intelligence may further support formulation design, enabling the prediction of optimal compositions, droplet size distribution, and drug-loading efficiency based on molecular descriptors. Such tools can significantly reduce experimental workload and development time, accelerating the path from laboratory to field application.

Concluding perspectives

The strategic application of nanotechnology provides an opportunity to bridge the long-standing gap between scientific innovation and global health needs. Among the available platforms, SNEDDS stand out as an affordable and scalable solution capable of improving oral delivery of poorly soluble drugs, many of which are critical for treating neglected tropical diseases. Their combination of simplicity, regulatory familiarity, and high biopharmaceutical performance makes them particularly suitable for use in low- and middle-income countries, where resources and infrastructure are limited.

Moving forward, integrating SNEDDS and other nanomaterial-based strategies into neglected disease programs will require coordinated efforts among academia, industry, and public-health institutions. This integration must focus on both innovation and accessibility, ensuring that technological advances translate into tangible benefits for the populations most affected by these diseases.

Harnessing such cost-effective nanotechnologies could redefine how we approach drug delivery for neglected diseases, transforming affordability from a barrier into an enabler of equitable healthcare. By leveraging established materials, simplified production methods, and interdisciplinary collaboration, nanomedicine may finally help close the therapeutic gap that has persisted for decades, paving the way toward more inclusive and sustainable global health solutions.

Conflicts of interest

There are no conflicts of interest to declare.

Data availability

No primary data were generated or analysed in this perspective review article. All references and sources cited are publicly available and accessible through relevant publications and databases.

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