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Smart drug delivery system – overcoming swallowing barriers in dementia-affected seniors

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Abstract

In patients with Alzheimer's disease (AD), dysphagia - a condition affecting most individuals with moderate-to-severe dementia - novel drug delivery systems (NDDS), including orally disintegrating tablets, transdermal patches, and intranasal sprays, offer a promising approach to improving medication adherence. These delivery modalities enhance compliance, provide more stable drug exposure, reduce swallowing-related complications such as aspiration pneumonia, and facilitate integration with non-pharmacological interventions by eliminating the need for oral swallowing. However, their implementation faces several challenges, including skin sensitivity associated with transdermal systems, nasal irritation with intranasal formulations, regulatory hurdles related to advanced nanocarrier technologies, and the need for supportive health policies and caregiver education to ensure equitable and effective use across diverse care settings.

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Editorial

Medication adherence represents a major challenge for patients with Alzheimer's disease (AD) who experience swallowing difficulties (Dysphagia). Dysphagia affects up to 84 - 93% of individuals with moderate-to-severe AD and is associated with underdosing, poor adherence, and serious complications such as aspiration pneumonia (1,2).

Among community-dwelling adults aged over 70 years, the prevalence of dementia has been reported to be as high as 86.6% and is frequently accompanied by frailty and functional dependence. In hospitalized patients with dementia, rates of dysphagia are even higher - reaching up to 75% among those referred for swallowing evaluation- substantially increasing the risk of aspiration pneumonia (3).

In AD, dysphagia arises from both disease-related neuropathology and age-associated physiological changes, leading to reduced intake of solid and liquid foods and contributing to malnutrition and dehydration. These factors indirectly compromise adherence to orally administered medications, including cholinesterase inhibitors. In geriatric practice, the cumulative impact of these challenges substantially increases caregiver burden and daily care complexity (3-5).

Pharmacotherapy for older adults with dementia and dysphagia is being reshaped by the development of novel drug delivery systems (NDDS). This editorial builds on earlier sections by examining underlying mechanisms, comparative effectiveness, implementation considerations, and economic implications. Collectively, these advances aim to enhance patient safety, support caregiver sustainability, and maintain stable therapeutic drug exposure (6-8).

For patients with dementia who are unable to swallow solid dosage forms, orally disintegrating tablets (ODTs) and films dissolve rapidly on the tongue, facilitating administration. Transdermal systems, such as rivastigmine patches, provide more consistent plasma drug concentrations, reduce gastrointestinal adverse effects, and improve overall tolerability. In addition, recent studies have demonstrated the feasibility of intranasal delivery for mild cognitive impairment, enabling agents such as insulin to reach the brain directly while bypassing the blood-brain barrier (9,10).

Superdisintegrants such as crospovidone are commonly used in orally disintegrating tablets (ODTs), which typically disintegrate within 30 seconds through mechanisms such as wicking or effervescence. Transdermal patches deliver drugs across the stratum corneum via passive diffusion, generally over a 24-hour period, using matrix or reservoir designs to achieve near zero-order release. Intranasal formulations bypass hepatic first-pass metabolism and blood–brain barrier efflux mechanisms by exploiting olfactory pathways for direct nose-to-brain delivery. In addition, lipophilic Alzheimer's medications, such as memantine, can be rendered more soluble through nanocarrier systems including liposomes and polymeric micelles (11-13).

By eliminating the need for swallowing, rivastigmine transdermal patches improve treatment adherence, while their smoother pharmacokinetic profiles reduce the incidence of adverse effects. In patients with treatment-resistant dementia, orally disintegrating olanzapine has demonstrated clinical utility owing to its rapid dissolution without the need for water. Emerging platforms such as hydrogels and nanocarrier-based systems are designed to target Alzheimer's pathology while accommodating the specific needs of patients with dysphagia. Collectively, these NDDS facilitate integration with non-pharmacological dementia care strategies and may reduce hospitalization risk (8,14).

Clinical tools such as bedside swallowing screening can assist clinicians in selecting appropriate NDDS. Caregiver education emphasizes proper patch application techniques to minimize skin irritation and correct storage of ODTs to prevent moisture-related degradation. Evidence suggests that pneumonia incidence can be reduced by approximately 40% when multidisciplinary teams combine NDDS with texture-modified diets and structured swallowing therapy. Educational workshops can further tailor these approaches to local cholinesterase inhibitor prescribing protocols (5,15).

Health economic models support reimbursement policies for geriatric-specific formulations by demonstrating gains in quality-adjusted life years (QALYs). As reflected in European geriatric medicine directives that prioritize swallow-friendly dosage forms, global population aging necessitates corresponding policy adaptations. Moreover, the availability of cost-effective generic ODT formulations can promote equity in dementia care, particularly in resource-limited settings (5,16).

Consistent dosing of cognitive enhancers can be achieved through novel drug delivery systems (NDDS), which may act synergistically with non-

pharmacological interventions such as reminiscence therapy. In mild dementia, stable pharmacokinetic profiles support spaced retrieval training and may enhance memory consolidation. Looking ahead, hybrid approaches that integrate NDDS with AI-driven geriatric care tools - such as orally disintegrating tablets embedded with adherence-monitoring sensors - represent a promising direction for individualized care (17).

Emerging orally disintegrating films (ODFs) containing donepezil show particular promise for cognitive rehabilitation, with studies demonstrating more than 85% drug release within minutes. Advances in precision intranasal delivery devices are also facilitating targeted treatment of neuroinflammation. From a health economics perspective, NDDS are increasingly favored because of their potential to reduce complications and the downstream burden of caregiver training. Regulatory pressure for geriatric-specific formulations is likely to further shape elder care policy in the coming years (18).

Despite these advantages, important limitations remain. Transdermal patches are poorly tolerated in approximately 10 - 15% of frail older adults because of skin sensitivity, although this can be mitigated through site-rotation schedules. Similarly, up to 20% of patients using intranasal formulations report nasal tolerability issues, which may be alleviated with mucoadhesive gel formulations. Although U.S. Food and Drug Administration (FDA) fast-track designations can accelerate approval, regulatory challenges related to nanocarrier-based systems continue to delay clinical translation. Long-term efficacy and safety across diverse dementia phenotypes must therefore be established through well-designed longitudinal studies (3,13).

While innovative drug delivery systems address many caregiver concerns related to medication adherence in Alzheimer's disease, they also introduce new challenges - particularly in frail elderly populations and in patients with dysphagia - making implementation more nuanced. Despite fast-track regulatory pathways, nanocarrier platforms remain limited by potential immunogenicity, manufacturing scalability constraints, and regulatory complexity, even as they improve the solubility of lipophilic agents such as memantine. Moreover, formulation-related dose modifications carry the risk of altering pharmacokinetic profiles, potentially leading to variability in exposure or reduced therapeutic efficacy. Robust longitudinal studies across multiple Alzheimer's disease phenotypes are therefore still required to define their long-term clinical value (19,20).

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Author contributions

Kamyar Khoshnevisan conducted the literature review and contributed to study conceptualization. The manuscript was written, critically revised, and submitted by Maryam Chehrehgosha. Both authors reviewed and approved the final version of the manuscript and agree to its publication in the Jorjani Biomedicine Journal.

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Not applicable

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