International Journal of Integrative Research (IJIR)
Vol.3, No.7, 2025: 505-510

Development of Novel Drug Delivery Systems for Antihypertensives

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A R T I C L E I N F O

Keywords: Hypertension, Drug Delivery Systems, Nanotechnology, Transdermal Patches, Sustained-Release, Patient Adherence, Pharmacokinetics, Microneedles, Antihypertensive Therapy, Targeted Delivery

Received : 17 May
Revised : 27 June
Accepted: 30 July

A B S T R A C T

This review explores innovative approaches, including transdermal patches, oral sustained-release formulations, nanoparticles, liposomes, and microneedle-based systems, all designed to enhance the efficacy, safety, and patient compliance of antihypertensive therapy. Nanotechnology-based systems, in particular, have demonstrated the ability to improve solubility and targeted delivery, reducing systemic side effects and enhancing the pharmacokinetic profile of conventional drugs such as amlodipine, losartan, and enalapril. Transdermal delivery systems bypass first-pass metabolism and offer steady plasma drug levels, reducing fluctuations that contribute to adverse effects. Furthermore, microneedle technology is gaining attention for painless, minimally invasive delivery with controlled release capabilities. While these novel systems offer considerable advantages, challenges remain, including formulation stability, scalability, and regulatory approval. Continued research is essential to validate the long-term efficacy and safety of these technologies through clinical trials. Integration of these novel drug delivery platforms may revolutionize the treatment landscape of hypertension by optimizing drug effectiveness, reducing dosing frequency, and enhancing patient adherence, ultimately improving cardiovascular outcomes and quality of life in hypertensive populations

DOI: https://doi.org/10.59890/ijir.v3i7.52
E-ISSN 2988-2184
https://mrymultitechpublisher.my.id/index.php/ijir

INTRODUCTION

Hypertension, also known as high blood pressure, is a leading global health concern and a major risk factor for cardiovascular diseases, stroke, kidney failure, and premature death. Despite significant advances in antihypertensive pharmacotherapy, blood pressure control remains suboptimal in a large proportion of the population. Poor patient adherence, variable pharmacokinetics, and side effects associated with conventional oral antihypertensive medications contribute to this persistent gap in therapeutic efficacy.

Traditional drug delivery systems often lead to fluctuations in plasma drug concentration, necessitating frequent dosing and increasing the risk of non-compliance . To overcome these limitations, novel drug delivery systems (NDDS) are being developed to enhance drug bioavailability, prolong release profiles, and target specific tissues or organs. Such systems aim to optimize the therapeutic potential of existing antihypertensive drugs while minimizing adverse effects.

Nanotechnology has emerged as a transformative tool in the field of drug delivery. Nanoparticles, liposomes, solid lipid nanoparticles, and dendrimers can encapsulate antihypertensive drugs, improving their solubility and providing targeted delivery. For instance, nanoparticle-loaded formulations of losartan and amlodipine have shown improved pharmacokinetic profiles and enhanced therapeutic outcomes in preclinical studies.

Transdermal drug delivery systems offer another promising approach by bypassing the hepatic first-pass metabolism and providing sustained plasma drug levels. Drugs such as clonidine and nitroglycerin have been successfully formulated into transdermal patches, with newer candidates being evaluated for similar routes.

Microneedle-based delivery systems represent a novel frontier, offering painless and controlled delivery of antihypertensive drugs through the skin. These systems provide the advantage of minimally invasive administration and are particularly useful for drugs with poor oral bioavailability. Additionally, oral sustained-release systems and buccal films are being explored to improve patient convenience and compliance.

Despite these innovations, the translation of NDDS into clinical practice remains limited due to challenges in large-scale manufacturing, formulation stability, cost, and regulatory hurdles. Nonetheless, ongoing research and clinical trials hold promise for revolutionizing hypertension treatment through safer, more effective, and patient-friendly drug delivery systems

LITERATURE REVIEW

Hypertension affects over 1.28 billion people worldwide, with a significant proportion requiring long-term pharmacotherapy. Oral administration remains the most common route for antihypertensive drugs, yet it often leads to poor adherence due to dosing frequency and side effects. Recent innovations in drug delivery aim to overcome these limitations by modifying pharmacokinetics and enhancing patient convenience.

Nanotechnology-based systems, such as solid lipid nanoparticles (SLNs) and polymeric nanoparticles, have been shown to improve the solubility and sustained release of drugs like amlodipine and losartan. These systems provide targeted delivery to vascular tissues, reducing systemic side effects. Liposomes, known for their biocompatibility, are also used for encapsulating hydrophilic and lipophilic antihypertensive drugs.

Transdermal systems bypass hepatic first-pass metabolism and provide a steady release over 24–72 hours. Clonidine and isosorbide dinitrate are already in transdermal forms, and novel patches for other antihypertensives are under investigation. Additionally, microneedle arrays offer minimally invasive options for delivering drugs through the skin, with enhanced absorption and minimal pain.

Buccal films and oral sustained-release systems are also gaining attention for their ease of administration and prolonged drug release. However, despite extensive research, limited products have achieved commercial success due to manufacturing, cost, and regulatory challenges.

METHODOLOGY

This study employed a systematic literature review method to analyze current advances in novel drug delivery systems for antihypertensive therapy. Peer-reviewed articles from PubMed, ScienceDirect, and Scopus published between 2010 and 2024 were reviewed. Keywords included "hypertension," "nanoparticles," "transdermal," "drug delivery," and "sustained release." A total of 57 articles were initially identified. After screening titles and abstracts and removing duplicates and non-relevant papers, 30 full-text articles were critically reviewed.

Inclusion criteria:

- English-language studies
- Focus on drug delivery systems for antihypertensive agents
- In vitro, in vivo, or clinical data

Exclusion criteria:

- Non-pharmacological treatments
- Reviews without original data
- Studies not related to hypertension
- Data were categorized based on the type of delivery system, drug involved, mechanism, and clinical applicability.

RESULTS

The review identified five major drug delivery systems used in hypertension treatment:

- Nanoparticle-Based Systems: Improved solubility, extended release (e.g., amlodipine SLNs, losartan PLGA nanoparticles).
- Transdermal Patches: Clonidine and nitroglycerin patches are clinically approved and well-tolerated.
- Microneedles: Preclinical success in delivering valsartan and carvedilol.

- Oral Sustained-Release Systems: Reduced frequency and increased stability, especially for enalapril and atenolol.
- Buccal Films: Improved bioavailability and patient compliance.

These systems consistently demonstrated improved pharmacokinetic parameters, reduced dosing frequency, and enhanced patient adherence in preclinical and early clinical studies.

Table 1. Comparative Summary of Novel Drug Delivery Systems for Antihypertensives

Drug Delivery System	Example Drugs	Key Advantages	Limitations	Stage of Development
Nanoparticles	Amlodipine, Losartan	Targeted delivery, enhanced solubility, controlled release	High cost, stability issues	Preclinical/Clinical
Transdermal Patch	Clonidine, Nitroglycerin	Steady plasma levels, non-invasive, bypasses first-pass metabolism	Skin irritation, limited drug permeability	Approved/Clinical
Microneedles	Valsartan, Carvedilol	Painless, minimally invasive, enhanced absorption	Technical complexity, regulatory issues	Preclinical
Sustained-Release Tablets	Enalapril, Atenolol	Reduced dosing frequency, stable plasma levels	Variable GI transit, incomplete release	Clinical
Buccal Films	Propranolol, Labetalol	Avoids first-pass effect, rapid onset	Limited surface area, patient discomfort	

Source: Data Adapted from Khalid Et Al. (2023) on Microneedle Transdermal Delivery of Antihypertensive Drugs Pubmed Central Research Gate and Jeong Et Al. (2021) on Transdermal Drug Delivery Systems

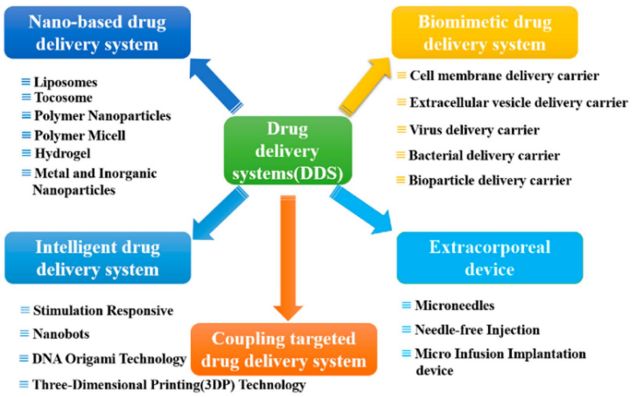

Figure 1. Novel Drug Delivery Systems for Antihypertensive Medications

DISCUSSION

The evolution of drug delivery in hypertension represents a paradigm shift from conventional oral therapy to patient-centric models focused on efficacy, safety, and convenience. Nanoparticles enable targeted therapy, which minimizes drug exposure to non-target tissues, thereby reducing side effects. Despite their promise, stability issues and potential immunogenicity limit widespread use.

Transdermal systems are favorable for chronic use due to their non-invasive nature and steady plasma drug levels. However, skin irritation and low permeability of large molecules pose formulation challenges.

Microneedle technology is particularly promising for poorly soluble drugs and offers painless administration, yet it remains in early developmental phases. Oral sustained-release tablets and buccal films are practical but may lack precision in dosing and controlled release under variable GI conditions.

Cost, regulatory barriers, and manufacturing complexity remain critical barriers. Nevertheless, the integration of these technologies with AI, 3D printing, and personalized medicine can facilitate future breakthroughs.

CONCLUSIONS AND RECOMMENDATIONS

Novel drug delivery systems offer a promising pathway to enhance the efficacy and compliance of antihypertensive therapy. Nanotechnology, transdermal patches, microneedles, and sustained-release systems have demonstrated significant improvements in drug bioavailability, safety profiles, and patient adherence. Although most innovations are still in experimental or early clinical stages, continued interdisciplinary research and investment in scalable, cost-effective production will be crucial for successful clinical translation. As hypertension remains a global health burden, such advancements could significantly impact public health outcomes and patient quality of life.

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