POLYMERIC NANOPARTICLES FOR TARGETED DRUG DELIVERY WITH ENHANCED BIOAVAILABILITY IN HYPERTENSION MANAGEMENT

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ABSTRACT

tihypertensive therapies, although widely used, are often limited by poor aqueous solubility, low bioavailability, extensive first-pass metabolism, frequent dosing requirements, and non-specific distribution, which collectively reduce therapeutic efficacy and patient compliance. This review focuses on the potential of polymeric nanoparticles as advanced drug delivery systems to overcome these limitations and enhance hypertension management. Polymeric nanoparticles, composed of biodegradable and biocompatible polymers such as poly(lactic-co-glycolic acid), chitosan, and polyethylene glycol, offer unique advantages including improved drug stability, enhanced solubility, and controlled as well as sustained drug release. These nanocarriers can be engineered for targeted delivery to specific tissues such as vascular smooth muscle cells and endothelium, thereby increasing therapeutic efficacy while minimizing systemic side effects. Additionally, polymeric nanoparticles facilitate improved drug absorption and can bypass first-pass metabolism, leading to enhanced bioavailability. The review further discusses various classes of antihypertensive drugs incorporated into polymeric nanoparticle systems, including ACE inhibitors, beta-blockers, calcium channel blockers, angiotensin receptor blockers, and diuretics. It also highlights mechanisms of drug release, targeting strategies, and recent advancements in nanoparticle-based formulations. Despite promising outcomes in preclinical studies, challenges such as toxicity, large-scale manufacturing, and regulatory hurdles remain barriers to clinical translation. Overall, polymeric nanoparticles represent a promising approach for improving the efficacy, safety, and patient adherence in hypertension therapy.

Keywords: Hypertension, Polymeric nanoparticles, Targeted drug delivery, Bioavailability, Antihypertensive therapy, Controlled release systems.

INTRODUCTION

1.1 Overview of Hypertension

Hypertension, commonly referred to as high blood pressure, is a chronic cardiovascular disorder characterized by a persistent elevation in arterial blood pressure above normal physiological levels. It is a major risk factor for the development of severe cardiovascular complications, including coronary artery disease, stroke, heart failure, and chronic kidney disease.[1] Hypertension is broadly classified into primary (essential) hypertension, which accounts for the majority of cases and has no identifiable cause, and secondary hypertension, which arises due to underlying conditions such as renal disorders, endocrine abnormalities, or vascular diseases.[2] The pathophysiology of hypertension is complex and involves multiple interconnected mechanisms, including increased peripheral vascular resistance, endothelial dysfunction, overactivation of the renin-angiotensin-aldosterone system (RAAS), sympathetic nervous system dysregulation, and impaired sodium and water balance. Effective management of hypertension is crucial to reduce morbidity and mortality associated with cardiovascular diseases.[3]

1.2 Global Prevalence

Hypertension has emerged as a significant global public health concern, affecting a substantial proportion of the adult population worldwide. The prevalence of hypertension has increased steadily over the past few decades due to factors such as urbanization, sedentary lifestyles, unhealthy dietary habits, obesity, and aging populations.[4] According to global health estimates, more than one billion individuals are affected by hypertension, with a disproportionately higher burden observed in low- and middle-income countries. Alarmingly, a large percentage of individuals with hypertension remain undiagnosed or inadequately controlled, leading to increased risk of complications. The economic burden associated with hypertension is also considerable, encompassing healthcare costs, loss of productivity, and long-term management of associated diseases. These trends highlight the urgent need for improved strategies in prevention, diagnosis, and treatment[5].

1.3 Limitations of Conventional Antihypertensive Therapy

Conventional antihypertensive therapy includes a wide range of pharmacological agents such as diuretics, β-blockers, calcium channel blockers, angiotensin-converting enzyme (ACE) inhibitors, and angiotensin receptor blockers (ARBs). While these medications are effective in lowering blood pressure, they are associated with several limitations.[6] Many antihypertensive drugs exhibit poor water solubility and limited bioavailability, resulting in suboptimal therapeutic

outcomes. Frequent dosing is often required due to short half-lives, which can lead to poor patient adherence. Additionally, non-specific drug distribution may cause systemic side effects such as dizziness, fatigue, electrolyte imbalance, and renal dysfunction. Drug-drug interactions and variability in patient response further complicate treatment regimens. These limitations emphasize the need for innovative drug delivery approaches that can enhance therapeutic efficacy and minimize adverse effects.[7]

1.4 Role of Polymeric Nanoparticles

Polymeric nanoparticles have gained significant attention as advanced drug delivery systems due to their unique physicochemical properties and versatility. These nanoparticles are typically composed of biodegradable and biocompatible polymers such as poly(lactic-co-glycolic acid) (PLGA), chitosan, and polyethylene glycol (PEG). Polymeric nanoparticles can encapsulate antihypertensive drugs, protecting them from degradation and enhancing their stability.[8] They also allow for controlled and sustained drug release, ensuring prolonged therapeutic effects. Surface modification of these nanoparticles enables active targeting to specific tissues or cells, improving drug accumulation at the desired site while minimizing systemic exposure. Polymeric nanoparticles can enhance drug solubility and bioavailability, particularly for poorly water-soluble drugs. Their ability to be tailored in terms of size, surface charge, and functionalization makes them highly suitable for precision medicine approaches in hypertension management.[9]

1.5 Aim of the Review

The present review aims to provide a comprehensive overview of polymeric nanoparticle-based drug delivery systems for the targeted treatment of hypertension. It focuses on the design, formulation, and functionalization of polymeric nanoparticles, as well as their role in enhancing drug bioavailability and therapeutic efficacy.[10] The review also discusses various antihypertensive drugs incorporated into polymeric nanocarriers, their mechanisms of action, and the outcomes of preclinical and clinical studies. Additionally, challenges related to safety, toxicity, scalability, and regulatory considerations are addressed. By integrating recent advancements and current research trends, this review seeks to highlight the potential of polymeric nanoparticles as a promising strategy for improved hypertension management.[11]

2. PATHOPHYSIOLOGY OF HYPERTENSION

2.1 Primary Hypertension

Primary (essential) hypertension accounts for approximately 90-95% of all hypertension cases and is characterized by elevated blood pressure with no identifiable underlying cause. It is a multifactorial disorder resulting from the complex interplay of genetic predisposition, environmental influences, and lifestyle factors such as high salt intake, obesity, physical inactivity, stress, and excessive alcohol consumption.[12] The pathogenesis of primary hypertension involves multiple physiological abnormalities, including increased peripheral vascular resistance, altered renal sodium handling, and dysregulation of neurohormonal systems. Genetic factors may influence ion transport, vascular tone, and hormonal regulation, thereby predisposing individuals to hypertension. Over time, these changes lead to sustained elevation of blood pressure, which, if left untreated, can contribute to progressive cardiovascular damage.[13]

2.2 Secondary Hypertension

Secondary hypertension arises as a consequence of identifiable underlying conditions and accounts for a smaller proportion of cases compared to primary hypertension. Common causes include renal diseases (such as chronic kidney disease and renal artery stenosis), endocrine disorders (such as hyperaldosteronism, pheochromocytoma, and Cushing's syndrome), and certain medications or substances.[14] Unlike primary hypertension, secondary hypertension often develops rapidly and may be more severe. The pathophysiological mechanisms vary depending on the underlying condition but generally involve alterations in fluid balance, hormonal imbalances, or vascular abnormalities. Early identification and treatment of the underlying cause are crucial, as secondary hypertension can often be controlled or even reversed with appropriate intervention.[15]

2.3 Role of renin-angiotensin-aldosterone system

The renin-angiotensin-aldosterone system (RAAS) plays a central role in the regulation of blood pressure, fluid balance, and electrolyte homeostasis. Activation of this system begins with the release of renin from the juxtaglomerular cells of the kidneys in response to reduced renal perfusion, low sodium levels, or sympathetic stimulation. Renin converts angiotensinogen into angiotensin I, which is subsequently converted into angiotensin II by angiotensin-converting enzyme (ACE).[16] Angiotensin II is a potent vasoconstrictor that increases blood pressure by narrowing blood vessels and stimulating the release of aldosterone from the adrenal glands. Aldosterone promotes sodium and water retention, further increasing blood volume and pressure. Overactivation of the RAAS is a key contributor to hypertension, leading to sustained vasoconstriction, fluid retention, and vascular remodeling. Many antihypertensive drugs, such as ACE inhibitors and angiotensin receptor blockers, specifically target this pathway to control blood pressure.[17]

2.4 Vascular Dysfunction

Vascular dysfunction is a hallmark of hypertension and is primarily characterized by increased vascular resistance and reduced arterial compliance. In hypertensive individuals, structural and functional changes occur in the blood vessels, including thickening of the vascular wall, narrowing of the lumen, and increased stiffness of the arteries.[18] These changes result from chronic exposure to elevated blood pressure and contribute to a vicious cycle of further pressure elevation. Smooth muscle cell proliferation, increased collagen

deposition, and reduced elasticity of the vascular wall are key features of vascular remodeling. Additionally, impaired vasodilation due to reduced nitric oxide availability further exacerbates vascular dysfunction. These alterations not only sustain hypertension but also increase the risk of cardiovascular events such as myocardial infarction and stroke.[19]

2.5 Endothelial Damage

Endothelial dysfunction plays a critical role in the development and progression of hypertension. The endothelium, which lines the inner surface of blood vessels, is responsible for regulating vascular tone by releasing vasodilators such as nitric oxide and vasoconstrictors such as endothelin.[20] In hypertension, the balance between these factors is disrupted, leading to reduced nitric oxide bioavailability and increased oxidative stress. This results in impaired vasodilation, increased vascular tone, and inflammation. Endothelial damage also promotes platelet aggregation, leukocyte adhesion, and the development of atherosclerosis. Factors such as hyperlipidemia, diabetes, smoking, and oxidative stress further aggravate endothelial dysfunction, contributing to the progression of hypertension and its complications.[21]

3. LIMITATIONS OF CONVENTIONAL ANTIHYPERTENSIVE THERAPY

A significant number of antihypertensive drugs, particularly those belonging to classes such as calcium channel blockers and certain angiotensin receptor blockers, exhibit poor aqueous solubility, which limits their dissolution in gastrointestinal fluids. Since drug absorption is highly dependent on its solubility, poorly soluble drugs often demonstrate inconsistent and incomplete absorption profiles.[22] This results in variable therapeutic outcomes and reduced efficacy. Low solubility may necessitate higher doses to achieve the desired pharmacological effect, which can further increase the risk of adverse effects. Formulation challenges associated with poorly soluble drugs also complicate the development of efficient delivery systems, thereby highlighting the need for advanced approaches to enhance solubility and drug performance.[23] Low oral bioavailability is another major limitation of conventional antihypertensive therapy. Many drugs undergo incomplete absorption from the gastrointestinal tract due to poor permeability, instability in the acidic gastric environment, or efflux by transport proteins such as P-glycoprotein. As a result, only a small fraction of the administered dose reaches systemic circulation in an active form. This reduced bioavailability leads to suboptimal therapeutic effects and requires dose escalation, which may increase the likelihood of side effects. Interindividual variability in gastrointestinal physiology further contributes to inconsistent drug absorption and response. Enhancing oral bioavailability remains a key challenge in the effective management of hypertension.[24]

First-pass metabolism significantly affects the pharmacokinetics of many orally administered antihypertensive drugs. After absorption from the gastrointestinal tract, drugs are transported to the liver via the portal circulation, where they undergo extensive metabolic transformation before reaching systemic circulation. This hepatic metabolism can substantially reduce the concentration of active drug available for therapeutic action. In some cases, active metabolites may contribute to the drug's effect, but in many instances, first-pass metabolism leads to reduced efficacy and increased variability in drug response. This phenomenon necessitates higher dosing or frequent administration, which may increase the burden on patients and the risk of toxicity.[25]

Frequent dosing is a common requirement in conventional antihypertensive therapy due to the short half-lives of many drugs. Maintaining optimal blood pressure control often requires multiple daily doses, which can be inconvenient and challenging for patients to adhere to consistently. Irregular dosing or missed doses may lead to fluctuations in plasma drug levels, resulting in inadequate blood pressure control or sudden spikes in blood pressure. This variability increases the risk of cardiovascular complications. Moreover, complex dosing regimens can be particularly problematic for elderly patients or those with comorbid conditions who are already managing multiple medications. Simplifying dosing schedules through sustained-release formulations is therefore an important goal in improving treatment adherence.[26] Side effects associated with conventional antihypertensive drugs can significantly impact patient compliance and overall treatment outcomes. Common adverse effects include dizziness, fatigue, headache, electrolyte imbalances, and gastrointestinal disturbances. Certain drug classes may also cause more serious effects, such as bradycardia with β-blockers, persistent cough with ACE inhibitors, or peripheral edema with calcium channel blockers. Long-term use of these medications may also lead to metabolic disturbances or renal impairment. The occurrence of side effects often leads to dose reduction, switching of medications, or discontinuation of therapy, which can compromise blood pressure control and increase the risk of complications.[27]

4. POLYMERIC NANOPARTICLES IN DRUG DELIVERY

Polymeric nanoparticles are nanoscale drug delivery systems, typically ranging from 10 to 1000 nm in size, composed of natural or synthetic polymers designed to encapsulate, adsorb, or conjugate therapeutic agents. These nanocarriers can exist in different structural forms, such as nanospheres (matrix systems in which the drug is uniformly dispersed) or nanocapsules (reservoir systems in which the drug is confined within a core surrounded by a polymeric shell). Owing to their small size and modifiable surface properties, polymeric nanoparticles can effectively interact with biological systems,

cross physiological barriers, and deliver drugs in a controlled and targeted manner. In the context of hypertension management, these systems offer significant potential for improving the pharmacokinetic and pharmacodynamic profiles of antihypertensive drugs.[28] A wide variety of polymers are utilized in the formulation of polymeric nanoparticles, depending on the desired drug delivery characteristics, biocompatibility, and degradation profile. These polymers can be broadly classified into biodegradable and non-biodegradable categories, with further subdivision into synthetic and natural polymers. The choice of polymer significantly influences key properties such as drug loading capacity, release kinetics, stability, and targeting ability. Polymers may also be chemically modified or combined to create copolymers with tailored functionalities. The versatility of polymer selection enables the design of nanoparticles suited for specific therapeutic applications, including sustained release, targeted delivery, and improved bioavailability.[29]

Biodegradable polymers are widely preferred in drug delivery applications due to their ability to degrade into non-toxic byproducts that can be safely eliminated from the body. Common examples include poly(lactic acid) (PLA), poly(glycolic acid) (PGA), poly(lactic-co-glycolic acid) (PLGA), and polycaprolactone (PCL). These polymers undergo hydrolytic or enzymatic degradation, allowing for controlled and sustained release of the encapsulated drug. The degradation rate can be modulated by altering the polymer composition, molecular weight, and crystallinity. In hypertension management, biodegradable polymeric nanoparticles enable prolonged drug release, reducing dosing frequency and improving patient compliance. Additionally, their established safety profiles and regulatory acceptance make them highly suitable for clinical applications.[30] Synthetic polymers are extensively used in the fabrication of polymeric nanoparticles due to their well-defined chemical structure, reproducibility, and tunable properties. Examples include PLGA, polyethylene glycol (PEG), polyvinyl alcohol (PVA), and polyacrylic acid.[31] These polymers can be engineered to achieve specific characteristics such as controlled degradation rates, enhanced drug loading, and improved stability. PEGylation, for instance, is commonly employed to increase the circulation time of nanoparticles by reducing recognition and clearance by the immune system. Synthetic polymers also allow for precise control over particle size, surface charge, and functionalization, making them highly suitable for targeted drug delivery. However, careful consideration must be given to potential toxicity and long-term accumulation, particularly for non-biodegradable synthetic materials.[32]

Natural polymers, derived from biological sources, have gained considerable attention due to their inherent biocompatibility, biodegradability, and minimal toxicity. Common natural polymers used in nanoparticle formulation include chitosan, alginate, gelatin, dextran, and starch. These polymers often possess functional groups that facilitate drug binding and surface modification, enabling targeted delivery and enhanced mucoadhesion. For example, chitosan exhibits excellent mucoadhesive properties and can enhance drug absorption across mucosal surfaces. Natural polymers are particularly advantageous for oral and transdermal drug delivery systems due to their compatibility with biological tissues. However, variability in source material, potential for microbial contamination, and limited mechanical strength may pose challenges in their large-scale application.[33] Polymeric nanoparticles offer numerous advantages over conventional drug delivery systems, making them highly attractive for the treatment of hypertension. These advantages include improved drug solubility and stability, particularly for poorly water-soluble drugs, and enhanced bioavailability through better absorption and protection from degradation. They enable controlled and sustained drug release, maintaining consistent therapeutic levels and reducing dosing frequency. Surface modification allows for targeted delivery to specific tissues or cells, thereby increasing therapeutic efficacy and minimizing systemic side effects. Additionally, polymeric nanoparticles can bypass biological barriers, such as the gastrointestinal mucosa, and improve intracellular drug delivery. Their versatility, tunability, and ability to incorporate a wide range of drugs make them a promising platform for advanced antihypertensive therapy.[34]

The release of drugs from polymeric nanoparticles occurs through several mechanisms, primarily including diffusion, polymer degradation, erosion, and swelling. In diffusion-controlled systems, the drug gradually diffuses from the nanoparticle matrix into the surrounding environment. In degradation-controlled systems, the polymer matrix undergoes hydrolytic or enzymatic breakdown, releasing the encapsulated drug over time.[35] Erosion mechanisms involve the gradual dissolution of the polymer surface, while swelling-controlled release occurs when the polymer absorbs water, expands, and facilitates drug diffusion. The release profile can be precisely tailored by modifying polymer composition, molecular weight, particle size, and environmental conditions such as pH and temperature. In advanced systems, stimuli-responsive mechanisms may also be incorporated, allowing drug release in response to specific physiological triggers. These controlled release strategies are essential for maintaining optimal drug concentrations and improving therapeutic outcomes in hypertension management.[36]

Sr. No.	Polymer	Type	Drug Loaded	Advantage	Reference
1	PLGA (Poly(lactic-co-glycolic acid))	Synthetic biodegradable	Amlodipine	Controlled release, high biocompatibility, FDA-approved polymer	37
2	PLA (Poly(lactic acid))	Synthetic biodegradable	Nifedipine	Sustained release, good stability	38
3	PCL (Polycaprolactone)	Synthetic biodegradable	Losartan	Slow degradation, prolonged drug release	39
4	PEG (Polyethylene glycol)	Synthetic	Enalapril	Increased circulation time, reduced immune clearance	40
5	PVA (Polyvinyl alcohol)	Synthetic	Atenolol	Stabilizer, improved nanoparticle formation	41
6	Polyacrylic acid	Synthetic	Captopril	pH-responsive release, enhanced solubility	42
7	Chitosan	Natural biodegradable	Amlodipine	Mucoadhesive, improved intestinal absorption	43
8	Alginate	Natural biodegradable	Propranolol	Biocompatible, controlled drug release	44
9	Gelatin	Natural biodegradable	Nifedipine	Biodegradable, good drug encapsulation	45
10.	Dextran	Natural biodegradable	Losartan	Improved stability, reduced toxicity	46
11.	Starch	Natural biodegradable	Hydrochlorothiazide	Biocompatible, cost-effective	47
12.	Hyaluronic acid	Natural biodegradable	Telmisartan	Targeted delivery, enhanced cellular uptake	48
13.	Eudragit	Synthetic	Metoprolol	pH-dependent release, improved oral delivery	49
14.	Poloxamer	Synthetic	Carvedilol	Enhanced solubility, improved drug dispersion	50
15.	Polyethyleneimine (PEI)	Synthetic	Lisinopril	High drug loading, efficient cellular uptake	51
16.	Albumin	Natural biodegradable	Amlodipine	Biocompatibility, prolonged circulation	52
17.	Silk fibroin	Natural biodegradable	Nifedipine	Controlled release, mechanical strength	53
18.	Pullulan	Natural biodegradable	Losartan	Water solubility, biocompatibility	54
19.	Poly(ethylene oxide)	Synthetic	Valsartan	Improved stability and drug dispersion	55
20.	Cyclodextrin	Natural derivative	Telmisartan	Enhanced solubility and inclusion complex formation	56

Table 1:Polymers used in polymeric nanoparticles for antihypertensive drug delivery

5. POLYMERIC NANOPARTICLES FOR ANTIHYPERTENSIVE DRUGS

Angiotensin-converting enzyme (ACE) inhibitors, such as captopril, enalapril, and lisinopril, are widely used in the management of hypertension due to their ability to inhibit the conversion of angiotensin I to angiotensin II, thereby reducing vasoconstriction and aldosterone secretion. However, many ACE inhibitors exhibit limitations such as short half-life, poor stability, and low oral bioavailability.[57] Polymeric nanoparticles have been explored to overcome these challenges by enhancing drug stability and enabling sustained release. Encapsulation of ACE inhibitors within biodegradable polymers such as PLGA or chitosan protects the drug from degradation and allows controlled release over an extended period. This not only reduces dosing frequency but also improves therapeutic efficacy. Additionally, targeted delivery using functionalized nanoparticles can enhance drug accumulation at vascular sites, further improving blood pressure control while minimizing systemic side effects.[58]

Beta-adrenergic blockers, including propranolol, atenolol, and metoprolol, are commonly prescribed antihypertensive agents that reduce blood pressure by decreasing heart rate and cardiac output. Despite their effectiveness, these drugs may suffer from issues such as variable bioavailability, frequent dosing requirements, and systemic side effects. Polymeric nanoparticle-based formulations have been developed to improve their pharmacokinetic profiles.[59] By encapsulating beta blockers within polymeric matrices, sustained and controlled drug release can be achieved, leading to prolonged therapeutic action and reduced dosing frequency. Furthermore, nanoparticle systems can enhance drug solubility and absorption, particularly for drugs with poor aqueous solubility. Surface modification of nanoparticles may also enable targeted delivery to cardiac tissues, improving efficacy and reducing unwanted effects on non-target organs.[60] Calcium channel blockers (CCBs), such as amlodipine and nifedipine, are widely used to manage hypertension by inhibiting calcium ion influx into vascular smooth muscle cells, resulting in vasodilation. However, these drugs often exhibit poor water solubility, extensive first-pass metabolism, and fluctuating plasma concentrations. Polymeric nanoparticles offer a promising strategy to address these limitations by enhancing solubility and protecting the drug from metabolic degradation. Nanoparticle-based delivery systems can provide sustained drug release, maintaining consistent plasma levels and improving blood pressure control. Additionally, targeted delivery of CCBs to vascular tissues can enhance therapeutic outcomes while reducing systemic side effects such as edema and hypotension. These advantages make polymeric nanoparticles an attractive platform for improving the performance of calcium channel blockers.[61]

6. MECHANISM OF TARGETED DELIVERY AND BIOAVAILABILITY ENHANCEMENT

One of the primary mechanisms by which polymeric nanoparticles enhance drug delivery is by protecting encapsulated drugs from physical, chemical, and enzymatic degradation. Many antihypertensive drugs are susceptible to degradation in the gastrointestinal tract due to acidic pH and enzymatic activity. Polymeric nanoparticles act as protective carriers by encapsulating the drug within a polymer matrix or core-shell structure, thereby shielding it from harsh environmental conditions. This protection preserves the structural integrity and pharmacological activity of the drug until it reaches the desired site of action. Additionally, protection from premature degradation leads to improved stability during storage and administration, ensuring consistent therapeutic performance.[62]

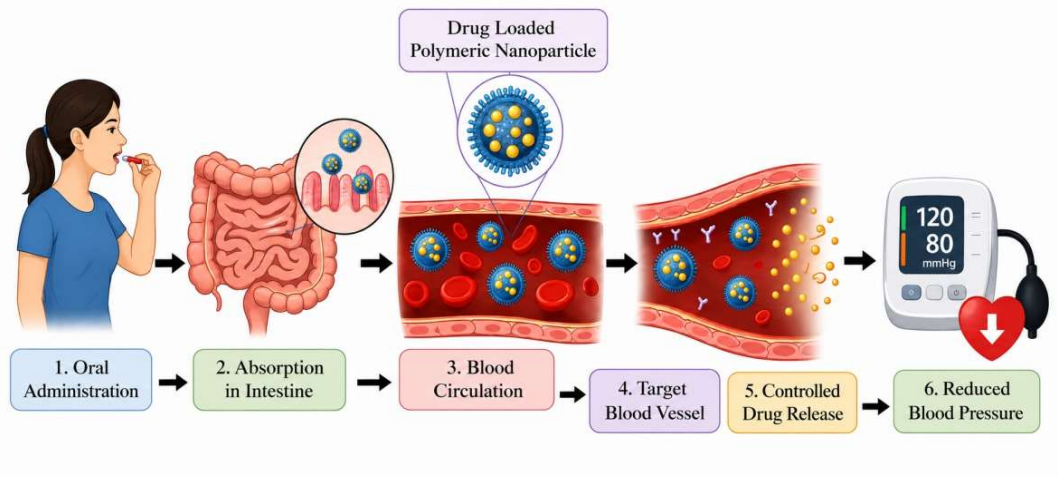

Figure 1. Mechanism of polymeric nanoparticle based targeted drug delivery in hypertension

7. SAFETY AND TOXICITY OF POLYMERIC NANOPARTICLES

Biocompatibility is a critical parameter in the design and application of polymeric nanoparticles for antihypertensive drug delivery. It refers to the ability of the nanoparticle system to interact with biological tissues without eliciting adverse immune or inflammatory responses. Polymers such as poly(lactic-co-glycolic acid) (PLGA), polyethylene glycol (PEG), chitosan, and alginate are widely used due to their well-established safety profiles. The physicochemical properties of nanoparticles, including size, surface charge, hydrophobicity, and surface functionalization, significantly influence their interaction with cells and biological fluids. Properly engineered nanoparticles can evade immune detection, minimize protein adsorption, and exhibit prolonged circulation. However, inappropriate surface characteristics may trigger immune responses, complement activation, or rapid clearance. Therefore, careful optimization and thorough biological evaluation are essential to ensure safe clinical application.63 Biodegradability is another essential feature of polymeric nanoparticles, particularly for long-term therapeutic applications such as hypertension management. Biodegradable polymers degrade into non-toxic metabolites that can be easily eliminated from the body through natural physiological processes. For example, PLGA degrades into lactic acid and glycolic acid, which enter normal metabolic pathways. Controlled degradation of the polymer matrix allows for sustained drug release while preventing long-term accumulation of the carrier in tissues. The rate of biodegradation can be tailored by modifying polymer composition, molecular weight, and crystallinity. This property ensures that the nanoparticle system remains safe over prolonged use, reducing the risk of chronic toxicity and making biodegradable polymers highly suitable for clinical applications.[64]

8. CURRENT RESEARCH AND CLINICAL APPLICATIONS

Recent research in the field of polymeric nanoparticles for antihypertensive drug delivery has shown significant progress in improving drug solubility, stability, and therapeutic efficacy. Numerous preclinical studies have demonstrated that encapsulating antihypertensive drugs within polymeric nanocarriers enhances their pharmacokinetic profiles by enabling sustained release and improved bioavailability. For instance, nanoparticle formulations of drugs such as losartan, amlodipine, and captopril have shown prolonged antihypertensive effects and reduced dosing frequency in experimental models. Advances in surface modification techniques have also enabled targeted delivery to vascular tissues, improving drug localization and minimizing systemic side effects. Additionally, research is increasingly focusing on multifunctional nanoparticles that combine targeting, controlled release, and stimuli-responsive properties, thereby offering more precise and efficient hypertension management.[65] Various nano-antihypertensive formulations have been developed using polymeric nanoparticles to address the limitations of conventional drug delivery systems. These formulations include drug-loaded nanoparticles, nanocapsules, and polymeric micelles designed to improve solubility and enhance drug absorption. For example, PLGA-based nanoparticles have been widely used for delivering poorly soluble drugs such as nifedipine and valsartan, resulting in improved dissolution and bioavailability. Chitosan-based nanoparticles have been explored for oral delivery due to their mucoadhesive properties and ability to enhance intestinal permeability. PEGylated nanoparticles have demonstrated prolonged circulation time and reduced immune clearance, contributing to improved therapeutic outcomes. These formulations are also being designed to provide controlled and sustained drug release, ensuring stable blood pressure control over extended periods. The development of such nanoformulations represents a significant advancement in antihypertensive therapy.[66]

CONCLUSION

Polymeric nanoparticles represent a highly promising and innovative approach for improving the management of hypertension by addressing the limitations associated with conventional antihypertensive therapies. Their unique physicochemical properties enable enhanced drug solubility, stability, and controlled release, leading to improved bioavailability and sustained therapeutic effects. By facilitating targeted drug delivery to specific vascular sites, these nanocarriers minimize systemic side effects and enhance treatment efficacy. Additionally, the ability of polymeric nanoparticles to bypass biological barriers and reduce first-pass metabolism further contributes to their superior pharmacokinetic performance.Despite these significant advantages, the clinical translation of polymeric nanoparticle-based systems remains limited due to challenges such as potential toxicity, large-scale manufacturing, regulatory concerns, and long-term safety evaluation. Nevertheless, ongoing research and advancements in nanotechnology continue to expand their potential in hypertension therapy. Future studies focusing on optimizing formulation strategies, ensuring safety, and conducting robust clinical trials are essential to fully realize their therapeutic

benefits. Overall, polymeric nanoparticles hold great potential to revolutionize antihypertensive drug delivery and improve patient outcomes in the long term.

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