International Research Journal of Pharmacy and Pharmacology

VOLUME NO. 13
ISSUE NO. 3
SEPTEMBER - DECEMBER 2025

ENRICHED PUBLICATIONS PVT. LTD

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International Research Journal of Pharmacy and Pharmacology

International Research Journal of Pharmacy and Pharmacology

(Volume No. 13, Issue No. 3, September - December 2025)

Contents

Advancements in Drug Delivery Systems: Revolutionizing Healthcare

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ABSTRACT

Drug delivery systems have undergone significant advancements in recent years, revolutionizing the field of healthcare. Traditional methods such as oral tablets and injectables have limitations in terms of bioavailability and patient compliance. However, controlled release systems provide sustained drug release, improving convenience and reducing side effects. Targeted drug delivery systems deliver medications directly to the site of action, maximizing efficacy while minimizing systemic side effects. Implantable drug delivery systems offer long-term drug administration solutions, particularly beneficial for chronic conditions. Stimuli-responsive and biodegradable drug delivery systems enable precise drug release and eliminate the need for device removal. The future of drug delivery systems holds promise with personalized medicine, 3D-printed systems, smart technology integration, and the use of artificial intelligence for optimization. These advancements will enhance therapeutic outcomes and transform the healthcare landscape.

Keywords: Drug delivery systems, Advancements, Healthcare, Traditional methods, Controlled release

INTRODUCTION

Drug delivery systems have played a pivotal role in modern healthcare, ensuring the safe and effective administration of therapeutic agents. Over the years, significant advancements in drug delivery technology have revolutionized the field, offering enhanced treatment options and improved patient outcomes (Banci L, 1999). From traditional methods to innovative approaches, drug delivery systems have evolved to overcome limitations and address the complex challenges associated with medication administration. Traditionally, pharmaceutical treatments relied on oral tablets, capsules, and injectable formulations. While these methods have served as the foundation of drug delivery, they often exhibit drawbacks such as variable bioavailability, poor patient compliance, and the need for frequent dosing (Johnstone J, 2018). As a result, researchers and scientists have focused on developing more sophisticated drug delivery systems to overcome these limitations and optimize treatment effectiveness. One of the significant breakthroughs in drug delivery systems is the development of controlled release technologies. These systems aim to provide a sustained and controlled release of medications over a prolonged period (Abraham GA, 2003). By utilizing specialized formulations such as hydrogels, microcapsules, and transdermal patches, controlled release systems offer several advantages. They reduce the frequency of dosing, enhance patient convenience, and minimize side effects associated with rapid fluctuations in drug concentrations.

Another area of advancement is targeted drug delivery systems (Heberer T, 2002). These systems have the potential to revolutionize treatment approaches by delivering medications directly to the site of action within the body. Utilizing nanotechnology, nanoparticles, liposomes, or antibodies, targeted drug delivery systems enable precise drug delivery to specific cells, tissues, or organs (Peterjack LR, 2006). This approach significantly enhances therapeutic efficacy while minimizing systemic side effects, making it particularly promising in the treatment of diseases like cancer. Implantable drug delivery systems have also emerged as a significant advancement in the field. These devices are surgically implanted within the body and release medications in a controlled manner. Implants can be designed to deliver medication locally or systemically, depending on the specific therapeutic requirements. This technology has proven invaluable in managing chronic pain, providing hormonal therapy, and addressing conditions that necessitate continuous drug administration (Zhang Y, 2002). Furthermore, stimuli-responsive drug delivery systems have garnered attention for their ability to release medications in response to specific triggers. These triggers can include changes in temperature, pH levels, or enzyme activity. By designing drug delivery systems that respond to such stimuli, precise control over drug release can be achieved, ensuring targeted action at the desired site within the body (WC Li, 2014). This approach holds great promise for the treatment of diseases characterized by abnormal physiological conditions, including inflammation, infection, and tumors. In addition, the development of biodegradable drug delivery systems has gained traction. These systems are designed to degrade or dissolve over time, eliminating the need for device removal (Langford BJ, 2016). By utilizing biocompatible materials that can be metabolized or eliminated from the body, biodegradable drug delivery systems offer several advantages. These include a reduced risk of infection, simplified treatment protocols, and the potential for tissue regeneration. Looking ahead, the field of drug delivery systems continues to evolve rapidly. Exciting areas of future exploration include personalized medicine, where treatment plans are tailored to individual patients based on their genetic makeup and specific needs (FL Mi, 2002). The integration of 3D printing technology allows for the fabrication of customized drug delivery systems, further enhancing treatment outcomes. Additionally, the integration of smart technology and the use of artificial intelligence and machine learning algorithms hold immense potential in realt ime monitoring, feedback, and optimization of drug delivery systems. The advancements in drug delivery systems have transformed the landscape of healthcare, offering improved treatment options, enhanced patient convenience, and targeted therapeutic interventions. From controlled release and targeted delivery systems to implantable and stimuliresponsive platforms, these innovations have paved the way for more effective and personalized approaches to drug administration (Tang YZ, 2007). As researchers continue to explore new frontiers, the integration of cutting-edge technologies and a deeper understanding of patient-specific needs will further revolutionize drug delivery systems, ultimately improving patient outcomes and transforming the way we approach healthcare.

DISCUSSION

Drug delivery systems play a pivotal role in modern healthcare by ensuring the safe and effective administration of therapeutic agents. Over the years, significant advancements in drug delivery technology have revolutionized the field, offering enhanced treatment options and improved patient outcomes. This article explores the various types of drug delivery systems and highlights recent breakthroughs that hold great promise for the future of medicine.

Traditional drug delivery systems

Traditional drug delivery systems primarily include oral tablets, capsules, and injectable formulations. While these methods have served as the foundation of pharmaceutical treatment, they often present limitations such as variable bioavailability, poor patient compliance, and the need for frequent dosing.

Controlled release systems

Controlled release drug delivery systems address the shortcomings of traditional methods by providing a sustained and controlled release of medications. These systems utilize specialized formulations, such as hydrogels, microcapsules, and transdermal patches, to deliver drugs over an extended period. Controlled release systems offer several advantages, including reduced dosing frequency, improved patient convenience, and minimized side effects.

Targeted drug delivery systems

Targeted drug delivery systems aim to deliver medications directly to the site of action, increasing therapeutic efficacy while minimizing systemic side effects. Nanotechnology has played a vital role in developing targeted drug delivery platforms. By utilizing nanoparticles, liposomes, or antibodies, drugs can be precisely delivered to specific cells, t issues, or organs. This approach holds immense potential for treating conditions like cancer, where localized drug delivery is critical.

Implantable drug delivery systems

Implantable drug delivery systems provide a long-term solution for delivering medications. These devices are surgically implanted within the body and release drugs in a controlled manner. Implants can be designed to deliver medication locally or systemically, depending on the desired therapeutic outcome. This technology has proven particularly valuable in chronic pain management, hormonal therapy, and conditions requiring continuous drug administration.

Stimuli-responsive drug delivery systems

Stimuli-responsive drug delivery systems are designed to release medications in response to specific triggers, such as changes in temperature, pH, or enzyme activity. These systems offer precise control over drug release, ensuring targeted action at the desired site. Stimuli-responsive drug delivery systems have shown promise in the treatment of diseases characterized by abnormal physiological conditions, including inflammation, infection, and tumors.

Biodegradable drug delivery systems

Biodegradable drug delivery systems are engineered to degrade or dissolve over time, eliminating the need for device removal. These systems are typically composed of biocompatible materials that are metabolized or eliminated from the body. Biodegradable drug delivery systems offer several advantages, including reduced risk of infection, simplified treatment protocols, and the potential for tissue regeneration.

Future directions

The field of drug delivery systems continues to evolve rapidly, with ongoing research and development focused on improving therapeutic outcomes. Some promising areas of future exploration include personalized medicine, 3D-printed drug delivery systems, and the integration of smart technology for real-time monitoring and feedback. Additionally, the utilization of artificial intelligence and machine learning algorithms may enable the development of predictive models to optimize drug delivery and enhance patient-specific treatment plans.

CONCLUSION

The field of drug delivery systems has witnessed remarkable advancements, leading to significant improvements in healthcare. Traditional methods have been surpassed by innovative approaches that address limitations and challenges associated with medication administration. Controlled release systems offer sustained and controlled drug release, enhancing patient convenience and reducing side effects. Targeted drug delivery systems enable precise delivery of medications to specific sites, maximizing efficacy while minimizing systemic side effects. Implantable drug delivery systems provide long-term solutions for chronic conditions, while stimuli-responsive systems offer precise drug release triggered by specific physiological cues. Biodegradable systems eliminate the need for device removal, simplifying treatment protocols and promoting t issue regeneration. These advancements have already revolutionized healthcare, but the future holds even more promise. Personalized medicine, enabled by tailored treatment plans based on individual genetic profiles, is on the horizon. 3D printing technology allows for the creation of customized drug delivery systems, further optimizing treatment outcomes. The integration of smart technology and artificial intelligence will enhance real-time monitoring, feedback, and optimization of drug delivery systems. In conclusion, the progress made in drug delivery systems has transformed healthcare by offering improved treatment options, enhanced patient convenience, and targeted therapeutic interventions. As research continues to explore new frontiers, the integration of cutting-edge technologies and a deeper understanding of patient-specific needs will revolutionize drug delivery systems further. This ongoing evolution will ultimately improve patient outcomes, redefine the healthcare landscape, and pave the way for a more personalized and effective approach to medication administration.

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Advancements in Pharmaceutical Nanotechnology: Revolutionizing Drug Delivery

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ABSTRACT

Pharmaceutical nanotechnology has emerged as a revolutionary field, offering promising solutions for drug delivery in medicine. By harnessing the unique properties of nanoparticles, this field has paved the way for targeted and controlled delivery of therapeutic agents. This article explores the significant advancements in pharmaceutical nanotechnology, focusing on nanoparticle formulation and design, targeted drug delivery, controlled release systems, enhanced bioavailability, and combination therapy. Nanoparticles can be engineered to encapsulate drugs, protect them from degradation, and enable specific targeting to diseased cells or tissues. Controlled release systems achieve sustained drug release, improving therapeutic outcomes and patient compliance. Nanotechnology enhances the bioavailability of poorly soluble drugs and facilitates drug transport across biological barriers. Furthermore, it enables combination therapy, where multiple drugs are delivered simultaneously for synergistic effects. While challenges remain, such as manufacturing scalability and safety assessments, pharmaceutical nanotechnology holds immense potential to transform drug delivery and shape the future of personalized medicine.

Keywords: Pharmaceutical nanotechnology, Drug delivery, Nanoparticles, Targeted drug delivery, Controlled release systems

INTRODUCTION

Pharmaceutical nanotechnology has emerged as a ground-breaking field that holds immense promise for the development of novel drug delivery systems. The integration of nanotechnology with medicine has revolutionized the pharmaceutical industry, enabling the targeted and controlled delivery of therapeutic agents (Ying JZ, 1987). By harnessing the unique properties of nanoparticles, scientists have unlocked new possibilities for improving drug efficacy, reducing side effects, and enhancing patient outcomes. This article highlights the significant advancements in pharmaceutical nanotechnology and their potential implications for the future of medicine. In traditional drug delivery systems, drugs are administered in a non-specific manner, resulting in suboptimal therapeutic outcomes and potential side effects (Rowan NJ, 2006). However, the advent of pharmaceutical nanotechnology has paved the way for more precise and efficient drug delivery strategies. Nanoparticles, with their nanoscale size and tailored characteristics, offer several advantages for therapeutic applications (Correia DM, 2007). They can encapsulate drugs, protect them from degradation, and deliver them to specific target sites within the body. This targeted approach allows for increased drug concentrations at the desired location, while minimizing exposure to healthy tissues.

The design and formulation of nanoparticles play a pivotal role in pharmaceutical nanotechnology. Various types of nanoparticles, such as liposomes, polymeric nanoparticles, dendrimers, and carbon nanotubes, have been extensively explored for drug delivery applications (Pohleven J, 2007). These nanoparticles can be engineered to encapsulate therapeutic agents, protect them from degradation, and enhance their stability. Surface modifications can be employed to impart specific targeting capabilities, allowing nanoparticles to selectively accumulate in diseased tissues or cells (Li HM, 2007). This precise targeting mechanismholds immense potential for improving the treatment of various diseases, including cancer, cardiovascular disorders, and neurodegenerative conditions. Another significant advancement in pharmaceutical nanotechnology is the development of controlled release systems. Nanoparticles can be designed to release drugs in a controlled and sustained manner, ensuring a prolonged therapeutic effect (Hutchinson J, 2004). This controlled release approach is particularly beneficial for drugs with a narrow therapeutic window or those requiring frequent dosing. By modulating the release kinetics, nanoparticles can optimize drug concentrations at the target site, minimize fluctuations, and enhance patient compliance. Additionally, pharmaceutical nanotechnology has addressed the challenge of poor bioavailability associated with many therapeutic agents (Li WC, 2014). Nanoparticles can enhance the solubility, stability, and permeability of poorly soluble drugs, thus improving their bioavailability. Encapsulation within nanoparticles protects drugs from degradation in the gastrointestinal tract and facilitates their absorption into the bloodstream. Nanocarriers can also aid in the transport of drugs across biological barriers, such as the blood-brain barrier, enabling the delivery of therapeutics to previously inaccessible sites. Combination therapy, involving the simultaneous administration of multiple therapeutic agents, has gained considerable attention in recent years. Nanoparticles offer a versatile platform for combination therapy by enabling the co-encapsulation or conjugation of different drugs within a single carrier system (Heberer T, 2002).

This approach allows for synergistic effects, improved drug interactions, and enhanced therapeutic outcomes. Pharmaceutical nanotechnology has the potential to revolutionize the treatment of complex diseases by enabling personalized combination therapy tailored to individual patient needs (Tien M Lignin, 1999). In conclusion, pharmaceutical nanotechnology has witnessed remarkable advancements, paving the way for a new era of drug delivery and personalized medicine. The ability to engineer nanoparticles with precise control over their properties and functionalities opens up exciting possibilities for targeted drug delivery, controlled release systems, enhanced bioavailability, and combination therapy. While significant progress has been made, there are still challenges to overcome, including scaleup manufacturing, regulatory considerations, and long-term safety assessments (Hartemann P, 2011). Nevertheless, the integration of nanotechnology into the pharmaceutical f ield holds immense potential for improving patient care, optimizing drug therapies, and ultimately transforming the landscape of healthcare.

DISCUSSION

Pharmaceutical nanotechnology has emerged as a ground-breaking field that holds immense promise for the development of novel drug delivery systems. The integration of nanotechnology with medicine has revolutionized the pharmaceutical industry, enabling the targeted and controlled delivery of therapeutic agents. By harnessing the unique properties of nanoparticles, scientists have unlocked new possibilities for improving drug efficacy, reducing side effects, and enhancing patient outcomes. This article highlights the significant advancements in pharmaceutical nanotechnology and their potential implications for the future of medicine. Pharmaceutical nanotechnology has witnessed remarkable

advancements in recent years, paving the way for a new era of drug delivery and personalized medicine. The ability to engineer nanoparticles with precise control over their properties and functionalities opens up exciting possibilities for targeted drug delivery, controlled release systems, enhanced bioavailability, and combination therapy. While significant progress has been made, there are still challenges to overcome, including scale-up manufacturing, regulatory considerations, and long-term safety assessments. Nevertheless, the integration of nanotechnology into the pharmaceutical field holds immense potential for improving patient care, optimizing drug therapies, and ultimately transforming the landscape of healthcare.

Nanoparticle formulation and design

The design and formulation of nanoparticles play a pivotal role in pharmaceutical nanotechnology. Various types of nanoparticles, such as liposomes, polymeric nanoparticles, dendrimers, and carbon nanotubes, have been extensively explored for drug delivery applications. These nanoparticles can be engineered to encapsulate therapeutic agents, protect them from degradation, and enhance their stability. Surface modifications can be employed to impart specific targeting capabilities, allowing nanoparticles to selectively accumulate in diseased tissues or cells.

argeted drug delivery

One of the key advantages of pharmaceutical nanotechnology is its ability to achieve targeted drug delivery. Nanoparticles can be functionalized with ligands or antibodies that recognize specific receptors or biomarkers on the surface of diseased cells. This enables the nanoparticles to actively target and deliver therapeutic agents directly to the desired site, minimizing off-target effects and reducing systemic toxicity. Targeted drug delivery holds immense potential for improving the treatment of various diseases, including cancer, cardiovascular disorders, and neurodegenerative conditions.

Controlled release systems

Nanotechnology has enabled the development of controlled release systems that can release therapeutic agents in a controlled and sustained manner. By encapsulating drugs within nanoparticles, researchers can modulate the release kinetics and achieve a prolonged therapeutic effect. This is particularly advantageous for drugs with a narrow therapeutic window or those requiring frequent dosing. Controlled release systems offer improved patient compliance and minimize the fluctuations in drug concentrations, thereby optimizing therapeutic outcomes.

Enhanced bioavailability

Many therapeutic agents suffer from poor bioavailability due to their physicochemical properties or degradation in the gastrointestinal tract. Pharmaceutical nanotechnology provides a solution to this challenge by improving the solubility, stability, and permeability of poorly soluble drugs. Nanoparticles can be designed to encapsulate hydrophobic drugs, allowing them to bypass enzymatic degradation and improve absorption. Additionally, nanocarriers can facilitate the transport of drugs across biological barriers, such as the blood-brain barrier, enabling the delivery of therapeutics to previously inaccessible sites.

Combination therapy

Combination therapy, involving the simultaneous administration of multiple therapeutic agents, has gained considerable attention in recent years. Nanoparticles offer a versatile platform for combination therapy by enabling the co-encapsulation or conjugation of different drugs within a single carrier system. This approach allows for synergistic effects, improved drug interactions, and enhanced therapeutic outcomes. Pharmaceutical nanotechnology has the potential to revolutionize the treatment of complex diseases by enabling personalized combination therapy tailored to individual patient needs.

CONCLUSION

Pharmaceutical nanotechnology has witnessed remarkable advancements in recent years, paving the way for a new era of drug delivery and personalized medicine. The ability to engineer nanoparticles with precise control over their properties and functionalities opens up exciting possibilities for targeted drug delivery, controlled release systems, enhanced bioavailability, and combination therapy. Nanoparticles have proven to be effective carriers for encapsulating and delivering therapeutic agents, enabling precise targeting to diseased cells or tissues while minimizing off-target effects and reducing systemic toxicity. The development of controlled release systems has allowed for sustained drug release, improving therapeutic outcomes and patient compliance. By modulating the release kinetics, nanoparticles provide a prolonged therapeutic effect and minimize fluctuations in drug concentrations. This approach is particularly beneficial for drugs with a narrow therapeutic window or those requiring frequent dosing. Pharmaceutical nanotechnology has also addressed the challenge of poor bioavailability associated with many therapeutic agents. Nanoparticles enhance the solubility, stability, and permeability of poorly soluble drugs, thereby improving their bioavailability. Moreover, nanocarriers facilitate the transport of drugs across biological barriers, such as the blood-brain barrier, enabling the delivery of therapeutics to previously inaccessible sites. Furthermore, combination therapy has gained significant attention in recent years, and nanoparticles offer a versatile platform for its implementation.

Co-encapsulation or conjugation of different drugs within a single carrier system allows for synergistic effects, improved drug interactions, and enhanced therapeutic outcomes. Pharmaceutical nanotechnology has the potential to revolutionize the treatment of complex diseases by enabling personalized combination therapy tailored to individual patient needs. While significant progress has been made in pharmaceutical nanotechnology, there are still challenges to overcome, including scale-up manufacturing, regulatory considerations, and long-term safety assessments. However, with continued research and development, the integration of nanotechnology into the pharmaceutical field holds immense potential for improving patient care, optimizing drug therapies, and ultimately transforming the landscape of healthcare. Pharmaceutical nanotechnology has emerged as a transformative field, revolutionizing drug delivery and opening up new possibilities for targeted, controlled, and efficient therapeutic interventions. The advancements in nanoparticle formulation and design, targeted drug delivery, controlled release systems, enhanced bioavailability, and combination therapy have the potential to significantly impact patient outcomes and improve the treatment of various diseases. The future of pharmaceuticals lies in harnessing the power of nanotechnology to create innovative drug delivery systems that maximize efficacy, minimize side effects, and provide personalized treatments for patients.

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Revolutionizing Healthcare: The Advancements in Drug Delivery Systems

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ABSTRACT

Advancements in drug delivery systems have revolutionized healthcare by enabling targeted and controlled release of pharmaceutical substances within the body. This article explores the recent developments in various drug delivery systems, including injectable systems, transdermal patches, implantable devices, inhalers, and nanotechnology-based carriers. These advancements have improved therapeutic efficacy, reduced side effects, and enhanced patient outcomes. Injectable systems now utilize biodegradable polymers and nano-carriers for sustained drug release, while transdermal patches offer non-invasive administration through the skin. Implantable devices provide precise and prolonged drug release, and inhalers deliver medication directly to the lungs. Nanotechnology-based carriers enhance drug solubility and targeted delivery. The future of drug delivery systems holds promise for personalized and precision medicine, transforming the way medications are administered and improving the quality of life for patients.

Keywords: Drug delivery systems, Advancements, Targeted drug release, Injectable systems, Transdermal patches

INTRODUCTION

In the ever-evolving field of healthcare, the development of efficient drug delivery systems plays a vital role in improving patient outcomes. Traditional approaches to medication administration have often relied on systemic delivery methods, resulting in suboptimal therapeutic efficacy and undesirable side effects (Hartemann P, 2011). However, recent advancements in drug delivery systems have paved the way for more targeted, controlled, and personalized approaches to drug delivery. These innovative drug delivery systems have the potential to revolutionize healthcare by enhancing the efficacy of medications, minimizing adverse effects, and improving patient compliance (Paul M, 2016). They enable precise dosing, sustained release, and localized delivery of pharmaceutical substances, ensuring that therapeutic agents reach their intended targets with optimal efficiency. Various types of drug delivery systems have emerged as groundbreaking solutions in recent years. Injectable drug delivery systems, for instance, have undergone significant improvements (Errico ME, 2002). Biodegradable polymers and nano-carriers now enable sustained and controlled release of drugs, reducing the frequency of administration and enhancing patient compliance. Moreover, the integration of smart injectable systems with sensors and feedback mechanisms allows for precise dosing and real-time monitoring, leading to personalized medicine tailored to individual patient needs. Transdermal drug delivery systems have also witnessed remarkable progress (Banci L, 1999). These systems utilize patches or gels to deliver drugs through the skin and into the bloodstream. Recent advancements have enhanced their permeation capabilities, allowing for the delivery of a wider range of drugs (Downing M,

2018). Additionally, the development of microneedle arrays and skin-penetrating nanoparticles has improved drug absorption, ensuring precise and controlled release. Implantable drug delivery systems have gained traction as well, offering sustained and controlled release of drugs over an extended period. These devices, often made of biocompatible materials, are directly implanted into the body to target specific tissues or organs (Abraham GA, 2003). Recent breakthroughs include the use of microfluidic technologies for precise control of drug release rates and the development of remotely controlled devices for personalized therapy adjustments. Inhalable drug delivery systems have proven particularly effective for respiratory conditions. These systems provide a direct route to the lungs, ensuring targeted delivery of medications (Heberer T, 2002). Recent advancements have led to the development of dry powder inhalers and nebulizers with improved drug dispersion and connectivity options for realt ime monitoring of patient response. Furthermore, the integration of nanotechnology in drug delivery systems has opened up new frontiers. Nanoparticles and nanocarriers can be engineered to encapsulate drugs, enhancing their solubility, stability, and targeted delivery to specific tissues (Peterjack LR, 2006). Surface modifications enable the attachment of ligands for targeted drug release, increasing therapeutic efficacy while minimizing off-target effects. The potential of nanotechnology in personalized medicine and combination therapy holds great promise for the future. The continuous advancements in drug delivery systems are reshaping the landscape of healthcare (Chu CC, 2002).

These innovative technologies are improving patient outcomes, revolutionizing medication administration, and paving the way for personalized, efficient, and patientcentric treatment modalities. As researchers and scientists push the boundaries of drug delivery, we anticipate a future where precision medicine becomes the norm, leading to better therapeutic outcomes and improved quality of life for patients worldwide (WC Li, 2014).

MATERIAL AND METHODS

Injectable drug delivery systems

Injectable drug delivery systems have been extensively used for decades, but recent advancements have brought about significant improvements. Biodegradable polymers and nano-carriers now enable precise and sustained drug release, reducing the frequency of administration and enhancing patient compliance. The emergence of smart injectable systems, equipped with sensors and feedback mechanisms, ensures precise dosing and real-time monitoring, leading to personalized medicine.

Transdermal drug delivery systems

Transdermal drug delivery systems offer a non-invasive approach to medication administration. These systems employ patches or gels that deliver drugs through the skin and into the bloodstream. Recent advancements have enhanced the permeation capabilities of transdermal systems, allowing for the delivery of a broader range of drugs. Furthermore, the development of microneedle arrays and skin-penetrating nanoparticles has improved drug absorption, enabling precise and controlled release.

Implantable drug delivery systems

Implantable drug delivery systems are designed to provide sustained and controlled release of drugs over an extended period. These devices, often made of biocompatible materials, are implanted directly

into the body, ensuring targeted drug delivery to specific tissues or organs. Recent breakthroughs in implantable systems include the use of microfluidic technologies, which enable precise control of drug release rates and the development of remotely controlled devices for personalized therapy adjustments.

Inhalable drug delivery systems

Inhalable drug delivery systems offer a direct route to the lungs, making them particularly effective for treating respiratory conditions. Advancements in this field have resulted in the development of dry powder inhalers and nebulizers with improved drug dispersion and targeted delivery. Furthermore, the integration of smart sensors and connectivity options allows for real-time monitoring of patient response and adjustments to the treatment plan.

Nanotechnology-based drug delivery systems

Nanotechnology has opened up new horizons in drug delivery systems. Nanoparticles and nanocarriers can be engineered to encapsulate drugs, enhancing their solubility, stability, and targeted delivery to specific t issues. Additionally, surface modifications can enable the attachment of ligands for targeted drug release, increasing therapeutic efficacy while minimizing off-target effects. The potential of nanotechnology in personalized medicine and combination therapy holds great promise for the future.

DISCUSSION

In the ever-evolving field of healthcare, the development of efficient drug delivery systems plays a vital role in improving patient outcomes. Over the years, significant advancements have been made in this domain, enabling targeted and controlled release of pharmaceutical substances within the body. These innovative drug delivery systems are revolutionizing the way medications are administered, enhancing therapeutic efficacy, reducing side effects, and ultimately transforming the landscape of healthcare. The continuous advancements in drug delivery systems are reshaping the landscape of healthcare. These innovative technologies are not only improving patient outcomes but also revolutionizing the way medications are administered. From injectable systems to transdermal patches, implantable devices, inhalers, and nanotechnology-based carriers, each development brings us closer to personalized, efficient, and patient-centric treatment modalities. As researchers and scientists continue to push the boundaries of drug delivery, we can anticipate a future where precision medicine becomes the norm, paving the way for better therapeutic outcomes and improved quality of life for patients worldwide.

CONCLUSION

The advancements in drug delivery systems are transforming the healthcare landscape by revolutionizing the way medications are administered and improving patient outcomes. These innovative technologies have addressed the limitations of traditional systemic delivery methods, offering targeted, controlled, and personalized approaches to drug administration. Injectable drug delivery systems have evolved with the use of biodegradable polymers and nano-carriers, enabling sustained and controlled release of drugs. This reduces the frequency of administration and enhances patient compliance. The integration of smart injectable systems with sensors and feedback mechanisms allows for precise dosing and real-time monitoring, facilitating personalized medicine. Transdermal drug delivery systems have seen significant progress, enhancing their permeation capabilities and

enabling the delivery of a wider range of drugs. Microneedle arrays and skin-penetrating nanoparticles have improved drug absorption, ensuring precise and controlled release. Implantable drug delivery systems provide sustained and targeted drug release, enhancing therapeutic efficacy. Microfluidic technologies allow for precise control of drug release rates, and remotely controlled devices offer personalized therapy adjustments. Inhalable drug delivery systems have proven effective for respiratory conditions, ensuring targeted delivery to the lungs. Advances in dry powder inhalers and nebulizers have improved drug dispersion, while smart sensors and connectivity options allow for real-time monitoring of patient response. The integration of nanotechnology in drug delivery systems has expanded possibilities. Nanoparticles and nanocarriers enhance drug solubility, stability, and targeted delivery to specific tissues. Surface modifications enable targeted drug release, increasing therapeutic efficacy and minimizing off-target effects. The future of drug delivery systems holds promise for personalized and precision medicine, where medications are tailored to individual patient needs. These advancements are transforming healthcare, improving therapeutic outcomes, and enhancing the quality of life for patients worldwide. As researchers continue to push the boundaries of drug delivery, we can anticipate a future where precision medicine becomes the norm, revolutionizing healthcare practices and benefiting patients in profound ways.

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Understanding Adverse Drug Reactions: Safeguarding Patient Health

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A B S T R A C T

Adverse Drug Reactions (ADRs) are unintended and potentially harmful effects that arise from medication use. Despite the numerous benefits of modern medicine, ADRs pose significant challenges to patient safety and treatment efficacy. This article provides an overview of Adverse Drug Reactions, encompassing their types, risk factors, and prevention strategies. ADRs can manifest in various forms, ranging from mild discomfort to lifethreatening conditions. The types of ADRs include Type A (Augmented), Type B (Bizarre), Type C (Chronic), Type D (Delayed), and Type E (End-of-use) reactions, each with distinct characteristics. While ADRs can affect anyone, certain factors, such as age, genetics, pre-existing conditions, polypharmacy, and allergies, heighten susceptibility. Prevention and management of ADRs require a collaborative approach between healthcare professionals and patients, encompassing accurate medical history, proper prescription, patient education, regular monitoring, and reporting ADRs to relevant regulatory agencies. Although it may not be possible to eliminate ADRs entirely, fostering a better understanding of their nature and adopting proactive measures will help enhance patient safety and optimize treatment outcomes.

Keywords: Adverse Drug Reactions (ADRs), Medication side effects, Drug safety, Drug-induced toxicity, Pharmacovigilance

INTRODUCTION

Modern medicine has revolutionized healthcare, providing an extensive array of medications to treat a wide range of illnesses and conditions (Ying JZ et al., 1987). These medications have undoubtedly improved patient outcomes and quality of life. However, alongside their benefits, drugs carry inherent risks. Adverse Drug Reactions (ADRs) represent a critical concern in contemporary healthcare, posing challenges to patient safety and optimal treatment strategies (Sullivan R et al., 2006). Understanding ADRs, their diverse manifestations, underlying risk factors, and appropriate prevention and management measures is crucial for safeguarding patient health and ensuring the efficacy of medical interventions (Barros L et al., 2007). Adverse Drug Reactions encompass any unintended and harmful effects resulting from the use of medications. They can manifest as mild inconveniences or serious, life-threatening conditions. While some ADRs are predictable and dose dependent (Type A reactions), others are unpredictable and unrelated to the drug's pharmacological action (Type B reactions) (Pohleven J et al., 2007). Prolonged drug use may lead to chronic reactions (Type C), while delayed reactions (Type D) and end-of-use reactions (Type E) can occur even after drug cessation. Recognizing the different types of ADRs is paramount for healthcare professionals to differentiate between normal drug effects and potential adverse outcomes. The impact of ADRs is not uniform across all patient populations. Certain

factors, such as age, genetics, pre-existing medical conditions, polypharmacy, and allergies, increase the susceptibility of individuals to adverse drug effects (Tang YZ et al., 2007). These risk factors emphasize the need for tailored and vigilant approaches in prescribing and monitoring medications for each patient, particularly those with heightened vulnerability. This article aims to shed light on the multifaceted nature of Adverse Drug Reactions, addressing their various types, risk factors, and implications (Patrick DM et al., 2004). Furthermore, it explores the importance of preventive measures, including patient education, regular monitoring, and reporting systems, to mitigate the occurrence of ADRs and enhance patient safety (Li WC 2014). By fostering a comprehensive understanding of ADRs, healthcare professionals and patients can collaboratively work together to ensure that medications are administered safely and effectively, thereby optimizing treatment outcomes and improving overall healthcare quality (Heberer T 2002).

MATERIAL AND METHODS

Modern medicine has significantly improved our ability to treat and manage various health conditions, saving countless lives and improving the quality of life for millions. However, like all medical interventions, drugs are not without risks (Banci L et al., 1999). Adverse Drug Reactions (ADRs) are an unfortunate but inevitable aspect of healthcare. Understanding these reactions is vital in ensuring patient safety, maximizing treatment benefits, and minimizing potential harm. This article aims to shed light on Adverse Drug Reactions, their types, risk factors, and how healthcare professionals and patients can work together to minimize their impact (Deblonde T et al., 2011).

What are adverse drug reactions?

Adverse Drug Reactions, commonly referred to as ADRs, are any harmful, unintended, and undesired effects that occur as a result of medication use. These reactions can manifest in various ways, ranging from mild discomfort to severe, life-threatening conditions. ADRs can emerge shortly after drug initiation or after prolonged use, and they may affect anyone, irrespective of age or health status.

Types of adverse drug reactions

Type A (Augmented) reactions: Type A reactions are the most common and result from the pharmacological action of a drug. They are usually dose-dependent and predictable. Examples include nausea, vomiting, dizziness, and allergic reactions like rashes.

Type B (Bizarre) reactions: Type B reactions are less common and unpredictable. They are unrelated to the drug's pharmacological action and may be influenced by individual factors such as genetics or immune response. Anaphylaxis, drug-induced liver injury, and drug-induced aplastic anemia are examples of Type B reactions.

Type C (Chronic) reactions: Type C reactions are associated with prolonged drug use and may develop over time. Longterm use of certain medications can lead to issues such as drug tolerance, dependence, and metabolic effects.

Type D (Delayed) reactions: Type D reactions occur long after the drug has been discontinued. An example is the development of cancer following exposure to certain medications or treatments.

Type E (End-of-use) reactions: Type E reactions happen when a drug is abruptly discontinued or withdrawn, leading to withdrawal symptoms or a rebound effect.

Risk factors for adverse drug reactions

While ADRs can occur in anyone, certain factors may increase the likelihood of their development. These risk factors include:

Age: The elderly and children are more susceptible to ADRs due to differences in drug metabolism and organ function.

Genetics: Genetic variations can influence drug metabolism, making some individuals more prone to adverse reactions.

Pre-existing conditions: Patients with certain medical conditions may be at a higher risk of experiencing ADRs due to potential drug interactions or altered physiological responses.

Polypharmacy: Taking multiple medications simultaneously increases the risk of drug interactions and adverse effects.

Allergies: Individuals with known drug allergies have a heightened risk of experiencing adverse reactions when exposed to those specific medications.

Prevention and management

Minimizing the occurrence of ADRs requires a collaborative effort between healthcare professionals and patients:

Accurate medical history: Healthcare providers must obtain a comprehensive medical history, including known allergies and previous ADRs, before prescribing any medication.

Proper prescription: Healthcare professionals should carefully select medications based on the patient's condition, medical history, and potential drug interactions.

Patient education: Patients should be educated about their medications, including possible side effects and what to do in case of adverse reactions.

Regular monitoring: Regular follow-ups and monitoring can help identify any early signs of ADRs, enabling timely intervention.

Reporting ADRs: Patients and healthcare providers should report any suspected adverse reactions to relevant regulatory agencies, which contributes to drug safety databases and ongoing surveillance.

DISCUSSION

Adverse Drug Reactions remain a significant challenge in modern healthcare. While we cannot

completely eliminate ADRs, understanding their types, risk factors, and appropriate management strategies can significantly improve patient safety. Healthcare professionals and patients must work hand in hand to strike a delicate balance between maximizing treatment benefits and minimizing the potential harm associated with medications. By remaining vigilant and proactive, we can ensure safer and more effective medication use, ultimately safeguarding the health and well-being of patients.

CONCLUSION

Adverse Drug Reactions (ADRs) are an inherent part of modern medicine, posing a significant challenge to patient safety and treatment efficacy. While medical interventions have brought about remarkable advancements, understanding and addressing the potential risks associated with drug use is imperative. This article has provided an insightful overview of ADRs, encompassing their types, risk factors, and preventive strategies. The diverse manifestations of ADRs, ranging from mild to severe, demand a proactive and vigilant approach from healthcare professionals. Type A, B, C, D, and E reactions each carry distinct characteristics, underscoring the importance of accurate diagnosis and appropriate management. Equally significant are the risk factors that predispose certain individuals to ADRs. Age, genetics, medical history, polypharmacy, and allergies must all be carefully considered during the prescribing process. Furthermore, fostering patient education and open communication plays a crucial role in mitigating potential harm. Encouraging patients to be actively involved in their treatment plan empowers them to recognize and report any adverse effects promptly. Preventive measures such as regular monitoring and early intervention can contribute to early detection and management of ADRs, minimizing their impact on patients' well-being. Furthermore, the active participation of healthcare professionals in reporting ADRs to regulatory agencies helps create a robust pharmacovigilance system, ensuring that drug safety is continually monitored and improved. In conclusion, while Adverse Drug Reactions cannot be entirely eliminated, a comprehensive understanding of their nature, combined with diligent efforts from both healthcare providers and patients, can significantly enhance patient safety and improve treatment outcomes. By prioritizing the wellbeing of patients and advocating for a culture of safety, the medical community can work towards achieving a more secure and effective healthcare system for the benefit of all.

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Peptide nucleic acid: Current perspectives and application for future therapeutics

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ABSTRACT

Peptide nucleic acid (PNA) is a deoxyribonucleic acid (DNA) mimic based on a polyamide backbone first synthesized and reported by Peter Nielsen in 1991. PNA shows remarkable hybridization properties and has many exciting applications. It is chemically and biologicaly stable and can readily conjugate with peptides and other useful molecules. The search for new chemical modification of the PNA is a very active field of research and new structures are continuosly proposed. Conjugation of an oligonucleotide to some peptides that can move through the cell membrane would facilitate the passage of this conjugate across for delivery into the cell's cytosol. Oligonucleotides can also be conjugated to lipids to yield derivatives with lipophilic properties that are capable to pass across the cell membrane. Thus, PNA can have multiple roles to perform in molecular biology, antigene therapy, molecular diagnostics and nanobiotechnology.

Key words: Peptide nucleic acid, oligonucleotide, electroporation, ribonucleic acid, polyamide

INTRODUCTION

PNA contain nucleobases with a peptide-like backbone, making them resistant to both proteases and nucleases, and giving PNA/DNA complexes enhanced stability compared to DNA/DNA complexes due to the lack of negatively charged phosphodiester bonds (Figure 1). PNAs can form a triplex structure with DNA by strand invasion, inducing DNA repair, and thereby stimulating recombination of short donor DNA fragments near the PNA's binding site. It has been previously shown that bis-PNA-194 (IVS2-194), which targets a polypurine site in the second intronic sequence of the human β-globin gene, can stimulate site-specific gene modification when co-introduced with a short, single-stranded donor DNA encoding the desired modification (Chin et al., 2008). PNAs do not readily cross the cell membrane, so special delivery methods are needed. Thus the PNAs are polyamidic oligonucleotide analogues which have been described for the first time almost twenty years ago and were immediately found to be excellent tools in binding DNA and RNA for diagnostics and gene regulation (Rogers et al., 2002).

Their use as therapeutic agents have been proposed since early studies and recent advancements in cellular delivery systems and in the so called anti-gene strategy make them good candidates for drug development. Thesearch for new chemical modification of PNAs is a very active field of research and new structures are continuously proposed. This review focuses on the modification of the PNA backbone, and their possible use in medicinal chemistry with an update of this topics in view of emerging new trends and opening of new possibilities In particular two classes of structurally biased PNAs have been described in recent studies I) PNAs with acyclic structures and their helical preference, which is

regulated by stereochemistry and ii) cyclic PNAs with pre-organized structures, whose performances depend both on stereochemistry and on conformational constraints. The properties of these compounds in terms of affinity for nucleic acids, and several examples of their use in cellular or animal systems are presented, with exciting new fields of research such as microRNA targeting and gene repair, delivery mechanisms and use in nano-biotechnology (Eriksson and Nielsen, 1996).

PNA application in neuro-degenerative and musculo-skeletal disorders

Nanoparticles have the potential to deliver new drug

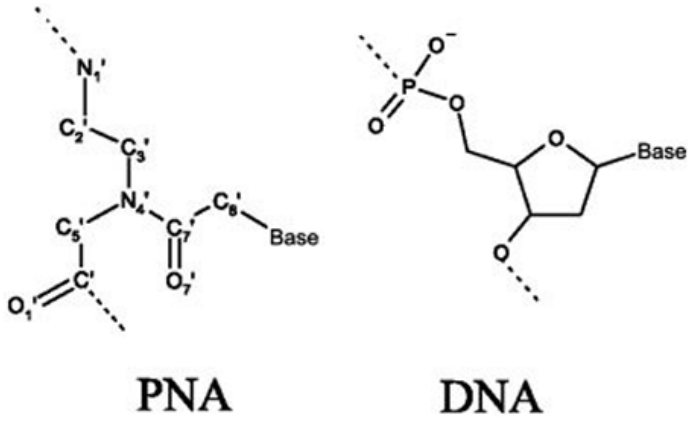

Figure 1: Structure of Peptide nucleic acid and Deoxyribonucleic acid

molecules across the blood brain barrier and are biodegradable in nature. The physicochemical properties of the NPs at different surfactant concentrations, stabilizers, and amyloid-affinity agents could influence the transport mechanism and have potential for usage in AD (Soppimath et al., 2001, Roney et al., 2005). Alzheimer's disease (AD) is a neurodegenerative disease associated with increased expression of amyloid precursor protein (APP) and the deposition of its proteolytic cleavage products, the amyloid-β peptides, Aβ1–40 and Aβ1–42. In this regard, the peptide nucleic acids have been shown to block the expression of proteins at transcriptional and translational levels. In this study, a sense and an antisense PNA specifically targeted to APP to inhibit the transcription and translation of APP by complementary binding to DNA or RNA, respectively were used. Using Western blotting techniques, APP showed a drastic decrease (50% and 90% reduction, in two separate experiments, as compared with saline control) with the injection of sense APP mRNA levels were higher at the same time point after injection of APP sense PNA, most probably because of a compensatory mechanism in response to the drop of APP that might have occurred at an earlier time point (0–1 h) and was reflected in a drop at the protein level at 1 hour. The injection of antisense PNA showed about 70% decrease in APP as estimated by Western blotting. Unmodified PNA can be used in vivo to reduce the levels of APP, which plays an important role in the development of AD (Boules et al., 2004).

The ability of the sensor system to detect normal, wild-type human DNA sequences, and those sequences containing a single base mutation is of tremendous biological importance. Specifically, experiments were conducted with a PNA probe complementary to a region of the gene encoding the microtubule associated protein tau. The probe sequence covers a known point mutation implicated in a dominant neurodegenerative dementia known as frontotemporal dementia with parkinsonism linked to

chromosome 17 (FTDP-17), which has clinical and molecular similarities to Alzheimer's disease. By using an appropriate PNA probe, the conjugated polymer poly [(9,9-bis(6′-N,N,N-trimethylammoniumhexylbromide) fluorene)-co-phenylene] and S1 nuclease, unambiguous FRET signaling is achieved for the wildtype DNA and not the mutant sequence harboring the SNP. Distance relationships in the CP/PNA assay are also discussed to highlight constraints and demonstrate improvements within the system (Brent et al., 2005). Alternatively, peptide nucleic acid (PNA) probes can be used for diagnosis of AD instead of DNA probes or as complementary probes to DNA. They exactly mimic DNA probes are therefore one of the most powerful tools for molecular biology and medical diagnostic analysis. PNA can bind to complementary strand of DNA and RNA sequences with high affinity and high specificity. PNA-based FISH analyses are used for quantitative telomere analysis using fluorescent-labeled PNA probes (Egholm et al., 1993; Giesen et al., 1998) Labeling analysis reveals human telomeric repeat sequences and also can accurately estimate telomere lengths. PNA can also form a triplex with the target double-stranded DNA (Pellestor and Paulasova, 2004). Other studies demonstrate the usefulness of PNA in Amyotrophic lateral sclerosis. Novel antisense peptide nucleic acid constructs targeting p75NTR as a potential therapeutic strategy for amyotrophic lateral sclerosis (ALS) have been designed, synthesized and evaluated against phosphorothioate oligonucleotide sequences (PS-ODN). An 11-mer antisense PNA directed at the initiation codon dose-dependently inhibited p75NTR expression and death signalling by nerve growth factor in Schwann cell cultures. Inhibition of p75NTR production was not detected in cultures treated with the nonsense PNA or antisense PNA directed at the 3′terminus sequence. The 19-mer PS-ODN sequences also failed to confer any activity against p75NTR but, unlike the PNA sequences, were toxic in vitro at comparable doses (Irwin et al., 2003).

PNA can also be useful for possible therapeutics of musculo-skeletal disorders like the Duchenne muscular dystrophy (DMD). DMD is the most common and severe form of muscular dystrophy, arising from mutations in the dystrophin gene that preclude the synthesis of functional protein. Antisense oligonucleotides (AOs) have been shown to induce specific exon skipping and thereby restore the reading frame and expression of functional dystrophin. In this report, investigation was done on the effects of peptide nucleic acid (PNA) oligonucleotides and PNAs conjugated with peptides including TAT, muscle-specific peptide (MSP), adenoassociated virus 6 (AAV6) functional domain (AAV6), and AAV8 functional domain (AAV8), on exon skipping in vitro and in vivo. Efficient skipping of targeted exon 23 was achieved in cultured mdx myoblasts with PNA and PNA–peptide conjugates. Furthermore, single intramuscular injections of PNA and all PNA–peptide conjugates resulted in significant numbers of dystrophin-positive fibers in the injected tibialis anterior (TA) muscles of mdx mice, with no apparent local toxicity. Similar effects of exon skipping and dystrophin expression were obtained in mice of all ages. PNA and PNA-AAV6, PNA-AAV8 conjugates induced dystrophin expression in a dose-dependent manner. The results demonstrate that PNAs have a higher efficiency of exon skipping than 2′O methyl phosphorothioate AOs do, and have a potential use in AO chemistry for antisense therapy of DMD (Haifang et al., 2008).

Soluble N-ethymaleimide sensitive factor attachment protein receptor (SNARE) analogous PNA hybrid i.e the transmembrane domain was based on the native peptide sequence. Where as the SNARE identifying motif was replaced by PNA oligomers. PNA oligomers form stable and well-defined double-stranded nucleobase recognition complexes. The PNA recognition motif resembles the double-stranded DNA already used in a SNARE analogue. Nevertheless, PNA oligomers offer the advantage of the sequence dependent formation of antiparallel as well as parallel duplexes with high thermal stability,

sequence selectivity, and noncharged backbone, and protease resistance (Lygina et al., 2011).

PNA as an Anti-sense Oligonucleotide

During the past decade, many biotechnology companies have showed an interest in antisense oligonucleotides for the treatment and prevention of disease. Anti-sense oligonucleotides are synthetic molecules that resemble pieces of single stranded DNA and incorporate any and/or all of the four bases. These oligonucleotides can then be used to either inhibit or promote gene expression by binding directly to target DNA or RNA.

Thus a particular sequence of antisense oligonucleotide could be designed specifically around a known mRNA transcript and then allowed to bind with that mRNA in order to control the production of a specific protein. Also, a plethora of information about any gene could be obtained by synthesizing a vast library of complementary oligonucleotide sequences. This is because of the hydrogen bonding that exists between the 6 complementary base pairs; it can provide necessary information for the design of an oligonucleotide which will target any gene with a known sequence. Greater control over binding specificity could be obtained as a result of targeting a defective gene with such oligonucleotides which in turn would give birth to a new strategy of drug design. Anti-sense RNA can be described as a naturally occurring phenomenon in which the cell transcribes a strand of RNA which is complementary to a specific segment of mRNA. These antisense RNA strands hybridized to the mRNA thereby inhibiting gene expression. In order to keep these antisense RNA strands in check, certain enzymes have important key roles in the regulatory process of these antisense RNA strands. It has been shown that studying a small portion of any gene can reveal its sequencing information thus providing scientists with the anti-sense sequence. The inhibition of gene expression through a natural process is already known for anti-sense RNA strands. However, a similar natural system involving anti-sense DNA is unknown at this time. In theory, the inhibition of a single gene target could be accomplished through the use of an oligomer 15 nucleotide bases in length that binds complementary to the mRNA strand in question (Gaglione et al., 2011).

Cellular delivery of anti-sense peptide nucleic acid by electroporation

In 1978, Zamecnik and Stephenson discovered a new class of therapeutic agents called anti-sense oligonucleotides which specifically targeted mRNA. In their research, Zamecnik and Stephenson successfully showed that anti-sense could be used to inhibit viral replication using an anti-sense phosphodiester oligodeoxynucleotide (ODN), they observed that it bound to the mRNA strands of the Rous sarcoma virus which in turn inhibited replication. Earlier studies into the mode of this type of inhibition prove that the binding between the mRNA strands and the ODN's follow the antisense mechanism. These studies used two types of ODN's, control ODN's, which were sequences that were not complementary for the target mRNA and complementary ODN's (Joergensen et al., 2011).

PNA may give the molecule several advantages over oligonucleotide- type compounds. Most important is the very high biological (and chemical) stability as well as easy access to a wide range of chemical modifications in a medicinal chemistry context. However, despite these apparent advantages, biological applications of

Table 1: Luciferase activity in PC 12 cells exposed to electrotransfer of PNA at different concentrations using the cuvette system.

No.	Treatment	Relative light units (RLU)	% Change
1	No PNA	393	
2	PNA (0.5μM)	2229	467.1
3	PNA (1.0 μM)	4392	1017.5
4	PNA (1.5 μM)	5487	1296.1
5	PNA (2.0 μM)	6223	1483.4

PNA molecules are limited by their inherently poor cellular uptake, being a relatively hydrophilic molecule that does not readily cross cell membranes (Wittung et al., 1995). Although several delivery methods have been described to enhance cellular uptake in vitro, including microinjection (Hanvey et al., 1992), electroporation (Karras et al., 2001), incorporation into liposomes (Wittung et al., 1994; Shiraishi et al., 2008), and conjugation to cell penetrating peptides (Koppelhus and Nielsen, 2003; Bendifallah et al., 2006) or receptor targeted ligands (Basu and Wickstrom, 1997; Zhang et al., 2001), and several studies have demonstrated in vivo effects in animal models of PNA conjugates (Sazani et al., 2002; Ivanova et al., 2008), a major challenge still exists in finding effective and easy in vivo delivery methods of PNA to be able to reach clinical trials and eventually clinical use.

Electroporation is a simple, transitory, and straightforward method for delivery of molecules, which may aid or substitute transfer, mediating modifications of the PNAs such as conjugation to delivery peptides or receptor-specific ligands. A study conducted by this author demonstrated that a 15-oligomer PNA which was introduced into PC 12 cells by electroporation showed increase in luciferase activity in a concentration gradient manner with maximal effect at 2M (Table 1). Thus, electrotransfer may eliminate some of the problems (such as endosomal entrapment) encountered by exploiting other transport mechanisms across the membrane (Koppelhus and Nielsen, 2003; Lundin et al., 2006).

By focused delivery, using electrotransfer, the target cells can be selectively exposed to the molecules, and cells in other tissues may remain unaffected. Further, electroporation is widely used for in vivo gene electrotransfer, and it has become an acknowledged method in clinical use for enhancing delivery of chemotherapeutics. Currently, electroporators for clinical use are approved and have been proven efficient with few side effects in several clinical studies (Gothelf et al., 2003; Marty et al., 2006; Mir et al., 2006; Daud et al., 2008). Thus, the necessary technical set up for future electrotransfer of PNA in a clinical setting is ready once potential drug candidates have been identified.

Peptide nucleic acid and nano-biotechnology

The development of advanced biological sensors could impact significantly the areas of genomics, proteomics, biomedical diagnostics, and drug discovery. While both silicon nanowires (SiNWs) and nanotubes (NTs) have been used previously for detecting biological species,there has been a focus on SiNWs, since the electrical properties and sensitivity of SiNWs can be tuned reproducibly by controlling dopant concentration and NW diameter (Zhang, 2011). The modification of silicon oxide surfaces also has been well studied, and this information can be exploited for tailoring SiNW surfaces with biological

or chemical receptors. Recent reports suggest the use of SiNWs for realtime, labelfree detection of DNA and DNA mismatches. It has been shown that SiNW sensors functionalized with peptide nucleic acid (PNA) receptors and can distinguish wild-type from the CF508 mutation site in the cystic fibrosis transmembrane receptor (CFTR) gene. The p-type SiNWs used in these studies were synthesized using a gold nanocluster catalyzed chemical vapor deposition (CVD) approach described previously. SiNWs were assembled into sensor devices consisting of electrically addressable NWs with PNA surface receptors, where the receptors were linked to the NW surface using intervening avidin protein layer, and a microfluidic sample delivery structure (Hahm and Lieber, 2004). PNA was chosen as a recognition sequence in our studies, since it is known to bind to DNA with much greater affinity and stability than corresponding DNA recognition sequences, and has shown binding without either WT or MU DNA exhibited no substantial change in conductance (Cattani-scholz et al., 2010).

The nanowires incorporated into the PNA have tremendous futuristic potential in genomics, proteomics and drug discovery. One strategic way of introducing these SiNW with PNA would be through electroporation into blood cells and culturing these stable transfected cells under optimal conditions and injecting them into patients for therapeutic and diagnostic purpose. I presume this will happen in the decades to come.

Peptide-Based Strategy for Ex Vivo and In Vivo Oligonucleotide Delivery

Cellular uptake of therapeutic oligonucleotides and subsequent intracellular trafficking to their target sites represents the major technical hurdle for the biological effectiveness of these potential drugs. Accordingly, laboratories worldwide focus on the development of suitable delivery systems. Among the different available non-viral systems like cationic polymers, cationic liposomes and polymeric nanoparticles, cell-penetrating peptides (CPPs) represent an attractive concept to bypass the problem of poor membrane permeability of these charged macromolecules. Most cationic CPPs bind to cell-associated glycosaminoglycans and are internalized by endocytosis, although the detailed mechanisms involved remain controversial. Sequestration and degradation in endocytic vesicles severely limits the efficiency of cytoplasmic and/or nuclear delivery of CPP-conjugated material. Re-routing the splicing machinery by using steric-block ON (oligonucleotide) analogues, such as PNAs (peptide nucleic acids) or PMOs (phosphorodiamidate morpholino oligomers), has consequently been inefficient when ONs are conjugated with standard CPPs such as Tat (transactivator of transcription), R(9) (nona-arginine), K(8) (octalysine) or penetratin in the absence of endosomolytic agents (Laufer and Restle, 2008). The identification of new nucleic acid-based therapeutic molecules such as short interfering RNA (siRNA) and PNA analogues has provided new perspectives for therapeutic targeting of specific genes responsible for various pathological disorders. However, the inappropriate cellular uptake of nucleic acids together with the low permeability of the cell membrane to negatively charged molecules remain major obstacles to their clinical development. Numerous non-viral strategies have been proposed to improve the delivery of synthetic short oligonucleotides both in cultured cells and in vivo Cell-penetrating

peptides constitute very promising tools for noninvasive cellular uptake of oligonucleotides and analogs. Recent research studies demonstrate a noncovalent strategy based on short amphiphatic peptides (MPG8/PEP3) that have been successfully applied ex vivo and in vivo for the delivery of therapeutic siRNA and PNA molecules. PEP3 and MPG8 form stable nanoparticles with PNA analogues and siRNA, respectively, and promote their efficient cellular uptake, independently of the endosomal

pathway, into a wide variety of cell lines, including primary and suspension lines, without any associated cytotoxicity (Scherf et al., 2000). These studies describe convenient protocols for the use of MPG-8 or PEP-3-nanoparticle technologies for PNA and siRNA delivery into adherent and suspension cell lines as well as in vivo into cancer mouse models (Crombez et al., 2011).

CONCLUSION

The high affinity and sequence selectivity of PNA can be used in therapeutic and diagnostic applications based on hybridization nucleic acid strands such as DNA/RNA microarrays, polymerase chain reaction and fluorescent in situ hybridization techniques. Thus it can be suggested based on the current research status on PNA that it has multifaceted role to play in various fields of medical science and biotechnology. Novel applications of the PNA based on novel delivery systems will throw new vistas open in the future.

ACKNOWLEDGEMENT

The author wishes to thank Mrs.Nidhi Tyagi, MSc for her help in the preparation of this manuscript.

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