How to Cite:
Hamzy, I. A., Alqhoson, A. I., Aljarbou, A. M., & Alhajri, M. A. (2018). Advancements in macromolecular complexity and their implications for drug delivery systems. *International Journal of Health Sciences*, *2*(S1), 154–169. https://doi.org/10.53730/ijhs.v2nS1.15093

Advancements in macromolecular complexity and their implications for drug delivery systems

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***Abstract*---Background**: Nanomaterials have revolutionized drug delivery systems, offering enhanced efficacy, reduced side effects, and improved patient compliance. Recent advancements in nanomedicine have focused on increasing macromolecular complexity to develop more sophisticated therapeutic options. **Aim**: This review explores the evolution of nanotherapeutics, from simple linear structures to complex branched and hyperbranched architectures and examines their implications for future drug delivery systems. **Methods**: The review discusses various nanocarriers, including liposomes, polymeric nanocarriers, and colloidal suspensions, emphasizing the role of macromolecular complexity in improving drug delivery efficacy. Key chemical techniques for synthesizing these macromolecules, such as controlled radical polymerization and click chemistry, are also analyzed. **Results**: Advances in synthetic polymer chemistry have enabled the development of diverse macromolecular structures that enhance drug loading, stability, and controlled release. Liposomal technology, although highly effective, faces challenges such as drug leakage and immune response, leading to the exploration of synthetic polymers like PLGA and polymeric micelles. These innovations have improved the pharmacokinetic properties of drug delivery systems. **Conclusion**: Increasing macromolecular complexity in drug delivery systems holds significant potential for overcoming physiological barriers, optimizing therapeutic outcomes, and fulfilling the demand for multifunctional nanomedicine. Continued research and

Manuscript submitted: 01 Jan 2018, Manuscript revised: 09 Jan 2018, Accepted for publication: 15 Jan 2018

development in this field will likely lead to more effective and targeted therapies.

***Keywords*---**nanomedicine, drug delivery systems, macromolecular complexity, polymeric nanocarriers, controlled radical polymerization, click chemistry.

Introduction

Nanomaterials have been crucial in increasing medication distribution, simplifying administration regimens, reducing adverse effects, and promoting therapeutic outcomes. Nanomedicine, the application of nanotechnology in medicine, has facilitated the investigation of its usefulness in many clinical issues, with the goal of creating more sophisticated and effective treatment alternatives. In the field of chemistry, this involves integrating various functionalities into nanoscaffolds and developing methods to control the shape and uniformity of macromolecules. This review highlights the expansion of nanotherapeutics from simple linear structures to more complex branched and hyperbranched formations. It also emphasizes the potential of increasing macromolecular complexity to open up new possibilities for nanomedicine applications in the future.

Administering a pharmacological dose of a medication to a specific location with a high level of effectiveness, using a method that ensures patient compliance, is crucial for the successful and safe management of a condition [1]. There is a growing number of deadly diseases, which has made it urgent to find a way to connect the availability of very strong drugs with the negative impact on quality of life caused by traditional therapies [2,3]. The existence of this gap has stimulated innovation and accelerated the development of novel medication delivery methods. It is projected that the U.S. market alone will exceed several hundred billion dollars by 2021 [4]. The task of creating active pharmacological compounds that can successfully navigate physiological obstacles and perform their tasks with optimal effectiveness poses considerable difficulties [5,6]. Macromolecular nanocarriers have the potential to revolutionize therapies [7], offering the scientific community a flexible platform that can adapt as our knowledge of illnesses grows [8,9]. These carriers can be customized for different drug delivery systems and can be adjusted to address the inherent obstacles in therapeutic delivery. Nanomedicine has made remarkable progress over time, transitioning from simple micelle-based formulations created by polymerizing monomers stabilized in solution by surfactants, to advanced technologies that can transport both small and large molecules using conjugation, encapsulation, and combination methods. These technologies can be administered through various routes such as intravenous, localized, oral, pulmonary, transdermal, and transmucosal pathways, and can respond to different stimuli [10,11]. With the rapid advancement of techniques for artificially improving large-scale molecular structures, it is becoming more possible to overcome the constraints of conventional technologies and fulfill the growing need for several functions in a single framework. With the increasing clarity of the conditions for obtaining optimal effectiveness in drug administration [14], a diverse range of

macromolecular architectures has been created. Transporting medications over various biological barriers, such as the skin for topical treatments and the gut-blood barrier for orally delivered pharmaceuticals, continues to be a major difficulty. The advent of branched (miktoarm stars) and hyperbranched (dendrimers) macromolecules [18] has resulted from efforts to address this issue. This document presents a brief summary of the types of materials used in therapeutic formulations, providing a clear guide for the creation of new medical materials.

Prior to discussing how the augmentation of macromolecular complexity can improve the transportation of active therapeutic substances, it is necessary to provide a concise overview of the basic requirements for creating a nanocarrier for widespread distribution [19–21]. First and foremost, the nanocarriers must be capable of transporting a sufficient amount of a hydrophobic or hydrophilic medicine and maintaining stability while circulating within a physiological medium, with regulated release of the drug. Furthermore, it is imperative that they specifically aim, amass, and disperse the medication at the desired location within anatomical and subcellular compartments. Ultimately, it is imperative that they possess biocompatibility. A drug delivery vehicle primarily has to enhance the solubility of the active pharmacological agent, optimize cellular contacts to increase drug uptake through mechanisms like adsorption or endocytosis, and limit removal or degradation of its contents before reaching the target. In addition, the vehicle must be non-immunogenic and have a synthesis process that is both cost-effective and scalable.

Pharmaceutical Delivery Systems:

Considerable endeavors have been focused on the advancement of highly effective nanodevices, such as liposomes, niosomes, and solid-lipid nanoparticles, for the transportation of medicinal drugs. While liposomes may not be categorized as macromolecular carriers, they have been extensively researched as drug delivery vehicles and have demonstrated significant clinical efficacy. Hence, it is vital to examine their implementation prior to exploring the utilization of macromolecular nanocarriers.

Liposomes:

Liposomes, created by the self-organization of amphiphilic phospholipids, have been extensively studied as vehicles for drug delivery for more than fifty years [22]. These spherical structures, which are stable according to the laws of thermodynamics, can include both water-soluble and water-insoluble medicines. They are widely used in formulations that have been approved for clinical use [23]. Liposomes provide significant benefits in the delivery of several medications that are typically ineffective, by altering their physical and chemical properties, distribution within the body, and decreasing their harmful effects [24]. PEGylation is a process that involves attaching poly(ethylene glycol) (PEG) chains to liposomes. This approach is often employed to provide liposomal nanoparticles stealth qualities, making them typically regarded as harmless and inactive carriers [25]. Nevertheless, it has been found that PEG alone can trigger an immunogenic reaction [26]. In recent times, the emergence of anti-PEG antibodies

has provided a new method to improve the effectiveness of liposomal formulations. This is achieved by guiding liposomes towards certain types of cells [27,28].

Extensive study has been conducted to comprehend the fundamental principles of liposomal drug delivery systems and broaden their range and uses by customization of their manufacturing processes, compositions, and surface changes [29]. The collective scientific endeavors in the advancement of liposomal formulations have led to the creation of numerous novel nanomedicines, a significant portion of which have either received clinical approval or are currently undergoing clinical trials for the treatment of cancer [26,29]. In addition, liposomal technology has been utilized for the treatment of fungal and bacterial diseases, as well as in the field of gene therapy [27,30].

Although liposomes have shown great versatility in terms of their composition, production methods, administration routes, ability to traverse biological barriers, and success in clinical translation, there are still certain fundamental issues that need to be addressed. These challenges encompass a restricted comprehension of the biological characteristics of liposomes and obstacles in the process of creating their structure. The insufficient loading of drug cargo into liposomal formulations, along with drug leakage, leads to a limited amount of the drug reaching the desired target [34]. In addition, the presence of a protein corona on the surface of liposomes, including those that have been PEGylated, can modify the drug-release characteristics in living organisms. To overcome these constraints, such as problems with the consistency of manufacturing, it is necessary to investigate other synthetic polymer platforms. Moreover, it is necessary to conduct a meticulous reevaluation of the presumed lack of toxicity and ability to provoke an immune response, as well as the biological behavior of phospholipids.

Drug delivery polymers:

Natural polymers, although not the main topic of this review which examines the development of structural complexity in synthetic macromolecular nanocarriers, have been effectively used in clinical contexts and hence deserve a brief mention [35]. Proteins and polysaccharides that exist naturally have been thoroughly studied as nanoparticles for drug delivery because of their intrinsic characteristics, including biocompatibility, degradability, and the ease with which their surfaces can be modified [36]. Albumin and gelatin are the most extensively researched protein-based nanoparticles. Albumin, a protein that is highly soluble and stable in water, has many binding sites and reactive functional groups on its surface. Because of these properties, it is an appealing choice for delivering drugs, as stated in reference [37]. Abraxane is a commercially available medication used for treating cancer. It is a formulation of paclitaxel that is coupled to albumin and exists in the form of nanoparticles. It has a strong ability to dissolve in water and builds up in tumors by utilizing mechanisms such as the increased permeability and retention (EPR) effect and the albumin transport pathway [38]. Utilizing nanocarriers based on natural polymers presents significant benefits, and it is necessary to expand their range and create nanomaterials with many functions. As the amount of data on protein-based nanocarriers increases, we can expect the

development of more effective and intelligent nanotechnologies for delivering drugs.

Synthetic polymers play a critical role in the efficient delivery of various small molecules, proteins, and nucleic acids. To do this, it is essential to manipulate the properties of polymer-based nanostructures [1,9,11,39]. Considerable endeavors have been undertaken to enhance the specificity [40], bioavailability, toxicity reduction, and favorable pharmacokinetics [41] of supramolecular assemblies of linear amphiphilic polymers and polymer conjugates. The continued investigation into the relationship between the composition of polymers, surface qualities, and biological interactions remains a driving force behind the advancement of novel and enhanced technologies [42–44].

The field of macromolecule-based drug delivery has undergone substantial advancements, starting from its first stages with basic and easily obtainable materials, to the present cutting-edge designs that utilize the wide range of linear, branched, hyperbranched, and hybrid structures that are currently accessible [45–54]. The advancement of chemical technology has been significant in enhancing the overall composition and characteristics of these polymers. Extensive research has focused on the development of effective techniques for polymer synthesis, such as living anionic polymerization, controlled free-radical polymerization (e.g., atom transfer radical polymerization (ATRP) and reversible addition–fragmentation chain transfer (RAFT)), ring-opening polymerization (ROP), and ring-opening metathesis polymerization (ROMP) [55–57]. RAFT, one of the controlled free-radical polymerization processes, is becoming increasingly popular for producing amphiphilic block copolymers with narrow polydispersities.

These copolymers have the ability to encapsulate chemotherapeutics within their core by self-assembly. An ABC-type tri-block copolymer, specifically poly (ethylene glycol)-b-poly (2,4,6-trimethoxybenzylidene-1,1,1-tris (hydroxymethyl) ethane methacrylate)-b-poly(acrylic acid), was synthesized. This was achieved by using PEG-cyanopentanoic acid dithionaphthalenoate as the RAFT agent, followed by the sequential addition of 2,4,6-trimethoxybenzylidene-1,1,1-tris (hydroxymethyl) ethane methacrylate and acrylic acid monomers [58]. Upon undergoing self-assembly in an aqueous environment, these polymeric vesicles exhibited a high degree of effectiveness in loading and releasing doxorubicin hydrochloride into cells, with the release being dependent on the pH level. The synthesis of complex architectures is best achieved by combining various approaches. Miktoarm polymers have been synthesized using sequential ring-opening polymerization (ROP) of various monomers or a combination of ROP with controlled radical polymerization. An instance of ring opening was performed on 2,2-bis (hydroxymethyl) propionic acid, which was then combined with PEG and an amine-functionalized alkoxy amine. This was followed by sequential ring opening polymerization of L- and D-lactides. The purpose of this process was to manufacture amphiphilic ABC miktoarm polymers, as described in reference [59]. The resultant polymers, poly (ethylene glycol)–poly (D-lactide)–poly (L-lactide), have two polymeric arms that can interact in a stereoselective manner. When placed in water, these miktoarm polymers created micelles that were stable and had a low critical micelle concentration (CMC). These micelles were highly effective in encapsulating and slowly releasing paclitaxel.

The emergence of 'click' chemistry, which includes alkyne–azide cycloaddition, Diels–Alder reaction, thiol-ene addition [60], and other coupling techniques including thiol-ene Michael addition [61], has significantly broadened the range of macromolecular structures that can be obtained. The alkyne-azide cycloaddition is a widely studied click reaction used for modifying and synthesizing macromolecules [62]. The Diels–Alder [4 + 2] cycloaddition reaction has been used to create several types of large molecules. Its ability to reverse under certain temperatures makes it a useful tool for developing nanocarriers that can break down and release drugs. This was discussed in a study referenced as [63].

The utilization of cycloaddition processes to change small-molecule inhibitors has been extensive [64,65]. The researchers used a combination of Huisgen alkyne–azide cycloaddition and reversible Diels–Alder adduct formation between furan and maleimide to create dendrimers. These dendrimers were designed to undergo retro-Diels–Alder disassembly, which would release a surface-functionalized anti-inflammatory drug (lipoic acid) within the temperature range found in the body (37–42 °C) [66]. Thiol-ene coupling is a very adaptable reaction that may be carried out under many conditions. It has been employed to synthesis dendrimers using a divergent approach, beginning with a 2,4,6-triallyloxy-1,3,5-triazine core and reacting it with 1-thioglycerol. The reaction, which does not require a solvent, starts with 2,2-dimethoxy-2-phenylacetophenone. The growth process continues by creating terminal alkene groups on the surface using 4-pentenoic anhydride. This procedure is then repeated [67]. Methods that do not require the use of metal catalysts are very attractive for the development of nanocarriers for drug delivery. The process of thiol-ene addition was used to modify a PEG-peptide telodendrimer by introducing carboxylic groups. These groups were then used to chemically bond cisplatin [68]. This study found that the linear-dendritic block copolymer may effectively administer both cisplatin and encapsulated paclitaxel in different quantities as combination medicines.

The versatility of the chemical methods is essential for altering the self-assembly characteristics of macromolecular materials. This allows for the optimization of their loading and release properties, while simultaneously preserving their structural integrity and circulation. This is achieved by adjusting the critical micelle concentration (CMC). The diverse array of structures achievable using simple and scalable synthetic methods is tackling the job of producing precisely defined constructions that incorporate a harmonious blend of functions and can effectively carry out many predetermined duties in a collaborative manner [69].

Polymeric nanocarriers are being used to address key challenges in drug administration, such as assuring the appropriate dosage of the active chemical, protecting it from the in vivo environment, and releasing it gradually at the desired location without causing systemic toxicity. Much prior research have focused on describing the transport and release mechanisms of these nanocarriers [70,71]. More precisely, in polymeric nanoparticle and drug conjugate-based systems, the release of the drug is usually controlled by the diffusion of the drug from its storage area, the erosion of the polymeric nanocarrier, or the degradation of the bonds between the carrier and the drug. Therefore, in the case of polymeric nanocarriers, the release of drugs can be

controlled either by diffusion or by activating the polymer matrix using solvents, local chemistry, or external variables like pH or temperature [72,73]. The structure and shape of the polymeric nanocarrier are anticipated to have a substantial impact on the rate at which the drug is released and its pharmacokinetic characteristics [74,75].

Colloidal suspensions. Extensive research has been conducted on colloidal nanocarriers that undergo degradation mechanisms for the purpose of medication delivery. Linear polylactide and poly(lactide-co-glycolide) (PLGA) are commercially accessible synthetic polymers that undergo degradation through hydrolysis of ester bonds. These polymers are widely employed in many applications [76,77]. The biodegradability and biocompatibility of the matrix make this technology promising for regulating the drug release profile and reducing toxicity. Although there has been progress in developing microparticle formulations of these polymers, achieving substantial success at the nanoscale remains elusive. Various novel polymers with functional groups that can undergo similar degradation processes through hydrolysis, either on the surface or throughout the material, have been created using highly effective techniques. Some of these methods are: ring-opening polymerization (ROP) for poly(caprolactone), poly(anhydrides), poly(phosphazenes), and poly(phosphoesters); anionic polymerization for poly(cyanoacrylates); and transesterification of orthoesters with diols for poly(orthoesters). The clinical application of PLGA-based formulations for drug delivery has been hindered by several challenges, including difficulties in reproducing and scaling up polymer synthesis, variations in nanoencapsulation techniques, potential toxicity resulting from the premature and excessive release of therapeutic cargo, and interactions between the polymer and the encapsulated drug. Recent advancements in synthetic biodegradable polymers have demonstrated potential in tackling these difficulties, with certain polymers currently undergoing clinical research [78–83]. Among these polymers is Poly(orthoester) IV, which can be manufactured with precise control over its drug release and erosion rates. Clinical trials have assessed the effectiveness of injectable formulations of semi-solid poly(orthoester), which are created by combining diketene acetal with either triethylene glycol or 1,10-decanediol [78]. Poly(alkyl cyanoacrylates) production has the capacity for expansion, and BioAlliance Pharma (France) has focused on nanotechnology based on poly(hexyl cyanoacrylate) for doxorubicin (Doxorubicin Transdrug) [84]. The bulk erosion characteristics of PLGA nanocarriers have been extensively investigated, and the ensuing non-toxic byproducts (such as lactic acid and glycolic acid) are removed by the body's metabolism [85–87]. Nevertheless, a more comprehensive understanding is needed regarding the biological destiny of degradation products derived from novel polymeric structures.

Polymeric micelles. Amphiphilic block copolymers. The deliberate manipulation of different polymer blocks in the process of polymer synthesis has resulted in the creation of linear amphiphilic block copolymers. These large molecules have the ability to spontaneously arrange themselves into different structures, such as micelles, based on the surrounding environment. Pharmaceutical medicines, which generally have low solubility in water, can be effectively enclosed within polymeric micelles that have a hydrophobic core. These micelles also include a hydrophilic corona that allows them to interact with the biological environment.

This artificial polymer platform tackles the main difficulties that were previously identified for liposomes [86–88]. The choice of hydrophobic blocks (to optimize drug solubility) and hydrophilic blocks (for improved stealth and circulation) is made to strike a balance between the conflicting requirements of drug loading capacity and controlled/sustained release at a specific gastrointestinal region, in order to achieve maximum bioavailability through oral delivery [89]. The CMC, or critical micelle concentration, is a crucial factor in the process of micelle formation. It refers to the concentration at which the polymeric chains come together to reduce the system's free energy. The critical micelle concentration (CMC) is directly related to the stability of the self-assembled structures. A high CMC suggests that the structures will disassemble when diluted in biological fluids [90]. The progress made in controlled radical polymerization techniques and click chemistry has increased the range of complex macromolecules that can be produced and has enabled the customization of their self-assembly into more precisely defined forms. For example, the use of RAFT polymerization has enabled the creation of block copolymers with highly accurate block lengths. These block lengths can have an impact on the critical micelle concentration (CMC) of the resulting micelles, which is a vital element in determining the durability of nanocarriers loaded with drugs [91]. Although there is a wide range of amphiphilic block copolymer designs at the disposal of chemical engineers, a significant portion of drug delivery research has primarily utilized amphiphilic diblock (AB) and triblock (ABA) polymers. Polyethylene glycol (PEG) is frequently utilized as the hydrophilic block in these systems because of its strong attraction to water and lack of toxicity [88]. Amphiphilic block copolymers have made significant advancements in dissolving lipophilic medicines. However, there are still issues with the long-term stability, length of sustained release, and low bioavailability of these medications.

Extended release. The liberation of cargo from a polymeric assembly is significantly impacted by the critical micelle concentration (CMC), which impacts the overall stability of the structure in the biological environment, as well as the strength of the binding between drug molecules in the core. Both aspects rely on the structure of the amphiphile [92]. A lower CMC (Critical Micelle Concentration) is preferable for achieving continuous release. An effective method to accomplish this is by augmenting the hydrophobic composition of the copolymer [93]. Nevertheless, the utilization of innovative polymeric combinations in diblock (poly(ethylene glycol)-b-poly(valerolactone), poly(phosphazenes)-b-poly(N-isopropylacrylamide)) and triblock (polylactide-b-poly(ethyleneoxide)-b-polylactide) copolymers has also effectively decreased CMCs [94,95]. For instance, the critical micelle concentration (CMC) of self-assembled structures formed from a diblock copolymer created by ring-opening polymerization (ROP) of valerolactone triggered by polyethylene glycol (PEG) can be adjusted by altering the molecular weight of the poly(valerolactone) segment [94]. Enhancing the contacts between the drug molecule and the hydrophobic core allows for the engineering of a slow drug release from a micelle [83,95]. Micelles formed from copolymers consisting of identical hydrophilic segments (PEG) but varying hydrophobic portions of comparable chain length, namely poly(caprolactone) (PEG-b-PCL) and poly(L-lactide) (PEG-b-PLLA), demonstrated distinct capacities for loading drugs. A study utilizing quercetin [96] observed that the loading capacity of micelles formed from PEG-b-PLLA polymer was superior to that of micelles formed from PEG-b-PCL

polymer. The drug exhibited the highest level of engagement with the PLLA core through hydrophobic interactions, whereas in the PCL-based copolymer, the drug mostly interacted through hydrogen bonding.

Utilizing responsive micelles to enhance bioavailability. Advances in drug delivery have necessitated the use of different methods and optimal dosages to ensure maximum effectiveness. This has led to the development of "smart polymers" by manipulating their composition [Ref. 97]. These large molecules have the ability to detect changes in the biological environment and react to different physical and chemical stimuli, such as pH, temperature, ultrasound, and ionic strength. They do this by changing their physical and chemical characteristics [98,99]. pH-responsive systems provide chances to optimize absorption at specific locations in the gastrointestinal tract or in inflamed and malignant tissues, where the pH levels differ from the surrounding tissue. Several copolymers including a pH-responsive block have been developed to improve medication bioavailability using this approach. As an example, ATRP was used to prepare block copolymers with different lengths of hydrophobic fragments, specifically poly(ethylene glycol)-b-poly(alkyl acrylate-co-methacrylic acid), by employing PEG as a hydrophilic macroinitiator. The inclusion of pendant carboxyl (COOH) groups in these polymers led to aggregation that was dependent on pH, allowing for adjustable critical aggregation behavior through the modification of the hydrophobic chain length [100]. The release of drugs from these water-based assemblies can also be controlled by pH, with greater release occurring when the medium changes from strongly acidic to basic. The utilization of pendant acidic groups to generate pH-responsive polymers has been widely employed for the purpose of controlled release of encapsulated cargo. For instance, researchers created micelles that react to changes in pH levels in the gastrointestinal tract by combining acrylic acid with poly(ethylene glycol)-b-(4-(2-vinylbenzyloxy)-N,N-(diethylnicotinamide)) [101].

Additionally, a versatile micelle system with varying sensitivity to pH in different environments was developed using a mixture of two block copolymers: poly(L-histidine)-b-poly(ethylene glycol) and poly(L-lactide)-b-poly(ethylene glycol)-b-polyhistidine [102]. Poloxamers are block copolymers that include a hydrophobic center segment and two hydrophilic segments at the ends. They are very responsive to temperature changes, allowing for the adjustment of their critical micelle concentration (CMC) based on temperature. This, in turn, modifies the release kinetics of the micelle [103]. Temperature-sensitive micelles have been created using block copolymers such poly(N-isopropylacrylamide) (PNIPAM)-b-poly(styrene) and PNIPAM-b-polycaprolactone. These systems maintain stability at normal body temperatures but quickly release their contents when exposed to heat [104]. Researchers have created polymers that contain segments responsive to changes in the ionic strength of a solution and ultrasound. Additionally, they have designed polymeric nanocarriers with photo-sensitive groups that break apart when exposed to specific wavelengths of light, therefore releasing the enclosed cargo. Click chemistry, in combination with controlled radical polymerization techniques, will persist in producing polymer nanocarriers with intricate structures and advanced functionalities. This will enhance the ability to regulate the release kinetics, pharmacokinetics, and bioavailability of these materials.

Conclusion

The evolution of drug delivery systems, driven by advancements in nanotechnology and macromolecular chemistry, has led to significant improvements in therapeutic efficacy and patient outcomes. The shift from simple linear structures to more complex branched and hyperbranched architectures has opened new avenues for enhancing drug delivery. These advancements have allowed for more precise control over drug loading, stability, and release, enabling the development of nanocarriers that can effectively navigate the body's physiological barriers. Liposomal technology, while successful in many clinical applications, presents challenges such as drug leakage and immune responses, prompting further exploration into synthetic polymer-based nanocarriers. The integration of advanced chemical techniques, such as controlled radical polymerization and click chemistry, has facilitated the creation of a wide array of macromolecular structures, each tailored to specific therapeutic needs. Polymeric nanocarriers, including PLGA and polymeric micelles, have emerged as promising alternatives, offering enhanced stability, biocompatibility, and targeted drug release. The continued refinement of these nanocarriers, coupled with a deeper understanding of their interactions within biological systems, is essential for overcoming current limitations and unlocking the full potential of nanomedicine. As research progresses, the increasing complexity of macromolecular architectures will likely play a pivotal role in the development of next-generation drug delivery systems. These systems will not only improve therapeutic outcomes but also pave the way for personalized and precision medicine, where treatments are tailored to the specific needs of individual patients. Ultimately, the advancements in macromolecular complexity will contribute to the realization of more effective, safer, and patient-friendly therapeutic options.

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التطورات في تعقيد الجزيئات الكبيرة وتداعياتها على أنظمة توصيل الدواء

الملخص:
الخلفية: أحدثت المواد النانوية ثورة في أنظمة توصيل الدواء، حيث قدمت فعالية محسنة، وتقليل الآثار الجانبية، وزيادة التزام المرضى. تركزت التطورات الأخيرة في الطب النانوي على زيادة تعقيد الجزيئات الكبيرة لتطوير خيارات علاجية أكثر تطوراً.
الهدف: يستعرض هذا البحث تطور العلاجات النانوية، بدءاً من البنى الخطية البسيطة وصولاً إلى الهياكل المتفرعة والمعقدة للغاية، ويدرس تداعياتها على أنظمة توصيل الدواء في المستقبل.
الطرق: يناقش البحث أنواعًا مختلفة من النواقل النانوية، بما في ذلك الجسيمات الدهنية، والنواقل البوليمرية، والمعلقات الغروانية، مع التركيز على دور تعقيد الجزيئات الكبيرة في تحسين فعالية توصيل الدواء. كما يتم تحليل التقنيات الكيميائية الرئيسية لتخليق هذه الجزيئات الكبيرة، مثل البلمرة الجذرية المضبوطة وكيمياء النقر.
النتائج: مكنت التطورات في كيمياء البوليمرات الاصطناعية من تطوير هياكل جزيئية كبيرة متنوعة تعزز من تحميل الدواء، والثبات، والتحرير المتحكم فيه. على الرغم من فعالية تكنولوجيا الجسيمات الدهنية، إلا أنها تواجه تحديات مثل تسرب الدواء والاستجابة المناعية، مما أدى إلى استكشاف البوليمرات الاصطناعية مثل PLGA والمسيلات البوليمرية. لقد حسنت هذه الابتكارات من خصائص الحركة الدوائية لأنظمة توصيل الدواء.
الاستنتاج: يحمل تعقيد الجزيئات الكبيرة المتزايد في أنظمة توصيل الدواء إمكانيات كبيرة للتغلب على الحواجز الفسيولوجية، وتحسين النتائج العلاجية، وتلبية الطلب على الطب النانوي متعدد الوظائف. من المرجح أن يؤدي استمرار البحث والتطوير في هذا المجال إلى علاجات أكثر فعالية واستهدافًا.
الكلمات المفتاحية: الطب النانوي، أنظمة توصيل الدواء، تعقيد الجزيئات الكبيرة، النواقل البوليمرية، البلمرة الجذرية المضبوطة، كيمياء النقر.