REVIEW ARTICLE

The Miracle of Precision: Innovative Approaches in Drug Delivery for Alzheimer Disease

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Abstract

The therapeutic landscape for cancer is changing as a result of advancements in precision medicine. The cornerstone of precision medicine is technology, which enables molecular profiling, genetic analysis, and the best medication creation for tailoring therapies for specific clients. Notwithstanding certain clinical emerges victorious brought about by precision medicine, toxicities and drug resistance have made it challenging to deploy many prospective medical treatments. The curative landscape for Alzheimer Disease is changing as a result of advancements in precision medicine. Particularly exciting innovations for personalizing treatments for individual patients are those that allow for molecular profiling, genetic analysis, and improved medication formulation. Cornerstone of precision medicine. Notwithstanding certain clinical emerges victorious achieved by precision medicine, toxicities and drug resistance have made it challenging to deploy many prospective treatment options.

Key words: Targeted nanotechnology, nanotoxicity, passive/active targeting, targeted drug delivery, targeting ligands

INTRODUCTION

The skin maintains body temperature, maintains equilibrium of fluids, and acts like the body's first line of defense against dangerous diseases and pesticides. Consequently, having full and the physiological well-being of the human body is contingent on having healthy skin. When wounds heal, a common physiological phenomenon known as scar formation requires the placement of an increase in extracellular matrix (ECM). Patients and their families might go through great distress if it develops after severe burns, surgery, or trauma. Contrarily, scar tissue makes the skin brittle and hardens, which degrades its biomechanical properties. The scar tissue that forms follows a skin injury typically lacks a variety of vital components, including skin glands, dermal papillae, hair follicles, and other supporting structures. On the other hand, excessive fibroblast proliferation and collagen deposition can lead to fibrous tissue that is uncontrolled and out of control. Over the course of a year, type I collagen progressively takes the place of type III collagen during the rebuilding phase.[1]

Scarring is a complicated biological process that is influenced by numerous variables. Atypical scar formation is not solely caused by bacterial infection of skin wounds, inflammation, or disruption of the ECM. This process may result in the production of numerous chemicals, one of which is reactive oxygen species (ROS). Skin flora, or microbiota, can further destroy the regenerable cells required for wound healing and induce oxidative damage.[2] On the flip side, excessive ECM secretion by overly enthusiastic fibroblasts promotes scarring. Keloids and hypertrophic scars are examples of scars that result from abnormal wound healing.[3]

The harm caused sets off physiological reactions that prevent the wound from healing and result in unsuitable scarring. Interleukin (IL)-6, matrix metalloproteinase (MMP), and IL-8 are some instances of proinflammatory cytokines that may be manufactured as a result of chronic inflammatory

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diseases. In a comparable manner, MMPs may change the ECM, which may cause significant scarring.[4]

A difficult task but constrained the process of scar formation is crucial to the healing of dermal wounds. Even though wound healing has been thoroughly studied, there is still much to learn about how to manage and avoid scars, which necessitates more research. A variety of therapies currently available have the potential to improve scar appearance. These kinds of therapies include radiotherapy, laser treatment, compression therapy, silicone gel-formulated band-aids, and topical corticosteroid injections, tapes, plasters, and ointments.[5]

The notion of "scar-free healing" has emerged and attracted a lot of interest as biotechnology advances. This concept's main goal is to promote tissue regeneration rather than entirely prevent scar formation. It first gained popularity as a study of fetal wound healing during gestation.[6] In people who are early to mid-gestational, wounds heal quickly and leave scars, according to research. The concept of scarless healing making a comeback in the wound healing industry is a good thing. The goal of this study's findings is to promote regenerative healing, and the preliminary results appear encouraging.[7]

Nanomaterials have a high specific surface area and small size, which allows them to easily load drugs into their homes. In addition, precise target location targeting is possible with nanomaterials, which translates into more effective drug delivery. They can also prolong the time that a drug announces from its hydrophobic form. These outstanding characteristics make nanomaterials important as treatments for scarring.[8] The results of this study will offer significant new information about how nanotechnology might be applied in the future to medical treatments to heal scars.[9]

Alzheimer's disease (AD) is the most common neurodegenerative disorder and the leading cause of dementia worldwide. First described by Alois Alzheimer in 1906, the disease is characterized by the accumulation of amyloid-β (Aβ) plaques and neurofibrillary tangles, resulting in progressive cognitive decline and memory impairment. Despite decades of research, conventional therapies such as cholinesterase inhibitors and memantine provide only symptomatic relief and do not prevent disease progression.

Recent advances in genomics, molecular biology, biomarker discovery, neuroimaging, and artificial intelligence have transformed the management of Alzheimer's disease. Precision medicine has emerged as a promising approach that integrates genetic, molecular, and clinical information to enable early diagnosis, patient stratification, and personalized therapeutic interventions. Although precision medicine offers significant potential to improve treatment outcomes, challenges such as disease heterogeneity, drug resistance, limited therapeutic efficacy, and high treatment costs continue to limit its widespread clinical application. This review highlights the recent advances, current challenges, and future prospects of precision medicine in the management of Alzheimer's disease.

NANOPARTICLES (NPS)

Furthermore, to stop scarring altogether, a tiny quantity of dissolved NPs is applied to the wound site using hydrogels and nanotechnology-based scaffolds. Hydrogel and scaffold wound dressings are beneficial at intermediate quantities and advanced stages, on the one hand. Conversely, hyperglycemia leads to the overproduction of ROS in diabetic wounds due to the sophisticated breakdown end products and the chain of electron transport in the mitochondria. Oxidative stress and ongoing inflammation are the results of this. Skin NP collection is located in NPs and scarring.[10]

Figure 1 Illustrates the nanoparticle-based drug delivery approach, demonstrating the targeted transport and controlled release of therapeutic agents at the wound site. This strategy enhances drug bioavailability, reduces oxidative stress and inflammation, and promotes effective tissue regeneration and wound healing (Figure 1).

INDUSTRIAL APPLICATION OF NANOTECHNOLOGY

Food industry

A greater percentage of research has gone into creating instruments to extend food shelf life while improving nutrient absorption in response to consumer demand for and awareness of healthy food alternatives. Recent years have seen the widespread application of nanotechnology as an enabling technology for achieving these goals for the delivery of nutraceuticals and food preservation. NPs have shown a lot of promise and are added to packaging materials to serve as barrier

Figure 1: Approach to use for drug delivery

molecules or antibacterial agents.[11] Studies on strawberries, citrus beverages, asparagus, and poultry meat have been done to examine the preservative effects of packaging that contains silver NPs (AgNPs). Because the labeling prevented pathogens such as yeasts, molds, and *Staphylococcus aureus* from growing, the products had a longer shelf life.[12]

It has been demonstrated that chitosan NPs in particular increase the stability and bioavailability of bioactive food ingredients such as resveratrol and curcumin. Researchers have looked into the possibility of using polymer-based NPs, such as chitosan and poly, to protect and distribute bioactive ingredients, such as antioxidants and vitamin A, in food products.[13] Mica NPs have been studied for usage as food additives and carriers of bioactive compounds due to their large surface area and low toxicity. For instance, silica NPs have been used to transfer nutrients like iron and improve the flavor of food items such as sauces and alcoholic beverages.[14]

There are few and in contradiction reports on the negative effects of ingested agglomerates. However, several studies have reported that the consumption of silver nanoparticles (AgNPs) at appropriate doses does not produce significant adverse effects or toxicity. however, as others have shown, doing so can have disastrous results, such as the accumulation of NPs in organs such as the small intestine, liver, and kidneys. Although this may be concerning, it is crucial to consider whether diet may provide the quantity of AgNPs examined in these studies.[15]

Nanomedicine

Dr. Richard P. Feynman first proposed the application of nanotechnology to medicine in the late 1950s when discussing the development of numerically accurate molecular machines for use in engineering and medicine.

There has been an attempt to increase the efficiency of traditional and conventional medications because it is now thought that most of them have low bioavailability and water solubility, which initially limits their absorption and retention within biological systems.[15]

It is possible to encapsulate both hydrophilic and hydrophobic drugs in liposomes, which initially helps to reduce the toxicity associated with anticancer drugs. More precisely, as demonstrated by Doxil™ (liposomal doxorubicin), which has received Food and Drug Administration approval for the treatment of ovarian cancer and Kaposi sarcoma, delivery systems made possible by NPs are well-established for the treatment of diseases.[14] Owing to their association with the cells of mammals and their physicochemical properties that can be altered (including size, shape, optical, magnetic, and electronic characteristics), NPs have also become popular in internal organ and tissue medical and diagnostic photography.[11] Among the most common worries are:

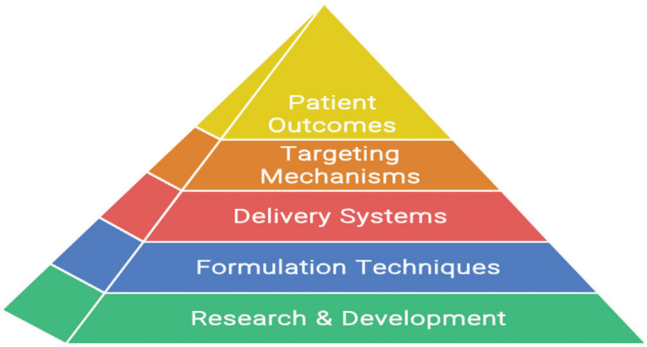


Figure 2: Miraculous drug delivery approach

- Size and shape: The iron/silica NPs' size and shape need to be carefully controlled to enhance their effectiveness and minimize any potential harm
- Surface functionalization: The surface of the NPs can be customized with a variety of moieties, such as polymers, antibodies, or small molecules, to target specific cells or tissues.

This kind of medication delivery system has several benefits

Nanosponges (NSs) aid in concealment the taste of pharmaceuticals, particularly those that must be taken orally or by buccal route. Because the different ingredients used in the formulation are encapsulated within the NSs, there can be a reduction in their side effects. They stay stable at temperatures that reach as much as 300°C and a pH range of 1–11. Increased compatibility is observed with a wide range of solvents and the electorate. They can be easily commercialized, considering that the process of scaling them up is simple. The NS can encapsulate drug moieties with properties that are lipophilic or hydrophilic. The medication that is encapsulated in NSs is protected from first-pass metabolism since they are made using crosslinkers and other components.[12] Figure 2 Illustrates the miraculous drug delivery approach, highlighting the targeted delivery and controlled release of therapeutic agents to improve treatment efficacy while minimizing systemic side effects. This approach enhances drug bioavailability, site-specific action, and therapeutic outcomes through advanced nanotechnology-based delivery systems (Figure 2).

TECHNIQUE USED TO PREPARE NPs

Solvent technique

Appropriate solvents were used in the procedure, including the polar aprotic solvents dimethylformamide and dimethyl sulfoxide. After that, the polymer was added and thoroughly mixed in. Adding the above-mentioned crosslinkers and polymers in an 8:2 ratio is an ideal blend. After the previously indicated mixing, the combination was allowed

to react for 48 h at a temperature between 10°C and the solvent's reflux temperature. The solution was allowed to cool to room temperature once the reaction was finished. The product was extracted from the above-cooled solution by adding an excessive amount of bi-distilled water, which was then recovered using vacuum filtering. Techniques for the preparation of nanoparticles.[14]

Melt technique

The crosslinker and polymer melt together during the melting process. Each component has been finely homogenized. The acquired item was repeatedly washed in a suitable liquid to collect NSs.

A bubble electrospinning

The basic components of a typical and traditional electrospinning arrangement are a syringe, a grounded collector, a high-voltage power supply, and a syringe pump, according to various literature. Still, the primary impediment to their wider application is the amount of nanofibers they generate.

Targeting and formulating NPs

Changes to the drug's formulation or molecular structure can affect the drug's kinetics and biodistribution. In the past, formulas have been developed to increase a drug's bioavailability or facilitate its dissolution. NP formulations have the power to significantly modify a wide range of other medical aspects, such as toxicity, absorption, distribution, metabolism, and excretion, in addition to pharmacokinetics.

Conversely, hydrogels have the ability to control the rate of exchange with tissues or cells via the microenvironment. As a result, combining hydrogels and nanofibers as carriers can produce a superior wound dressing material that enables controlled drug release. To produce bioactive, injectable matrices for skin regeneration, silk nanofiber hydrogels were filled with the hydrophobic medication AC. By dispersing in hydrogels composed of water-based silk nanofibers, AC preserves its biological activities, which control vascularization and the inflammatory reaction and promote scarless wound healing.[11]

Inhibitors of kinase

Nanomedicine has primarily focused on the delivery of small-molecule therapeutics, such as paclitaxel and doxorubicin, to tumors by wrapping them in these drugs. More precisely, creating nanocarriers that enhance localization has been the main goal. There is a pressing need to increase the number of targeted medications, and precision medicine can play a significant role in this endeavor. In the subsections that follow, we address some of the most important limitations on precision pharmaceuticals and pair each limit with a suitable delivery option. It is important to remember that even with the best drug delivery system, monotherapies rarely result in long-term benefit for treating cancer. Because cancer almost always returns or develops resistance over time, effective treatment combinations are required. Toxicities that restrict the number of some side effects can be so severe that patients cannot receive treatment at effective doses.[10]

IMPORTANT FEATURES FOR DRUG DELIVERY WITH NP

Size of particles

Particle size also affects drug release. Due to their higher surface area to volume ratio, smaller particles will have the majority of the medication bound to them closest to the particle surface. As a result, the medication releases more quickly. The encapsulation of more medication per particle and a slower release, however, is made possible by the bigger particles' larger cores. As a result, adjusting the particle size offers the opportunity to modify the rates at which medications are released.

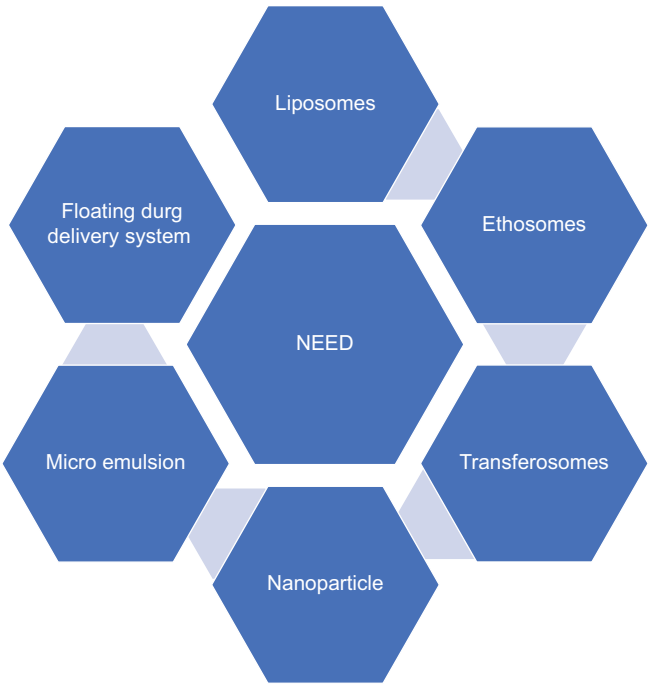
Furthermore, during the processes of transportation, storage, and dispersal, smaller particles are more likely to aggregate. The degradation of polymers can also be significantly influenced by particle size.[12] For instance, it was found that the rate at which poly lactic-co-glycolic acid (PLGA) degraded was correlated with the size of the particles formed from this polymer. It has been suggested that the breakdown products of PLGA, which more easily diffuse over shorter distances when in the form of smaller NPs, are what initiate this process.

Features of the surface of an NP

When a medication is connected with conventional carriers, its biological distribution profile alters because the drug is largely carried to organs that are a part of the mononuclear phagocyte system (MPS), which includes the lungs, bone marrow, liver, and spleen. The human immune system recognizes the intravenous-injected NPs, and phagocytes take them out of the bloodstream. The amount of blood constituents that adhere to this surface depends on the hydrophobicity and size of the NPs. As such, hydrophobicity affects how NPs behave *in vivo*. Actually, once surface non-modified NPs (conventional NPs) enter the circulation, the MPS rapidly neutralize and extensively clear them.

Medication release

When drugs are released from uniformly distributed nanospheres, matrix erosion or diffusion takes place. If drug diffusion is greater than matrix erosion, diffusion is a key



Flow Chart 1: Need for a miraculous approach

factor in regulating the release process. The drug's weak binding to the relatively large size of the NPs and inadequate adsorption surface are the main causes of the rapid initial release, commonly referred to as the "burst."

Nanotechnology's place in drug delivery and therapeutics

It is anticipated that pharmaceutical sciences, medical technology, and a wide range of other fields will be significantly impacted by the quickly evolving field of nanotechnology, which has made it possible to control and manipulate molecular structures.

Cellular organelles, including mitochondria, lysosomes, and the endoplasmic reticulum, play crucial roles in the pathogenesis of Alzheimer's disease by regulating energy metabolism, protein homeostasis, and neuronal survival.

Flow Chart 1 summarizes the need for a miraculous drug delivery approach by outlining the limitations of conventional drug delivery systems and the advantages of advanced targeted delivery strategies. It highlights how innovative drug delivery systems can improve therapeutic efficacy, enhance bioavailability, and reduce adverse effects.

NPs in therapeutics against infectious diseases

These NP combinations are less expensive, more stable for long-term storage, and resistant to extreme processing conditions such as high pH and temperature without becoming inactive than traditional antibiotics. The sections that follow provide an explanation of a number of significant metal and metal oxide NPs used in medical products.[5]

Silver

It has long been known that silver ions and silver-based products have a wide variety of antibacterial qualities. Among other things, silver is utilized in nitrates, metals, and sulfadiazine. Silver's antibacterial action can be increased by lowering particle size to the nanometer range. Rai and his students discussed the mechanisms of action and antibacterial potential of metallic silver and compounds based on silver.[17]

Gold

Many investigations on the antibacterial properties of gold NPs in combination with antibiotics have been carried out. The scientific name for an *Escherichia coli* strain that is resistant to erythromycin is *Streptococcus pyogenes*. It was feasible to determine whether a panel of bacteria was drug-resistant or drug-susceptible to silver NPs in the solution using luciferase assays. The minimum bactericidal concentration and minimum inhibitory concentration (MIC) values of the bacteria were found to be between 30 and 100 mm, respectively.

Zinc oxide and magnesium oxide

Enterotoxigenic *E. coli* is one of the food-borne pathogens that zinc oxide NPs are sensitive to due to their antibacterial properties. *Botrytis cinerea* and *Penicillium expansum*, two harmful postharvest fungi, were the subject of a study by Lili and colleagues investigating the antifungal activity of zinc oxide NPs.[10,18]

Oxide of titanium

Nonetheless, titanium oxide (TiO_2) NPs have photo-catalytic antibacterial activity. TiO_2 is a semiconductor photocatalyst that is frequently utilized. Free radical oxides and peroxides, which have strong antibacterial activity and broad reactivity against a variety of pathogenic microbes, are produced by photo-catalytic TiO_2.[16]

Oxide of Aluminum

It is commonly known that aluminum dioxide (Al_2O_3) NPs barely hinder the growth of microorganisms; however, they only rupture cell membranes when absorbed in large quantities. Sadiq noted the presence of *S. aureus*, *Pseudomonas aeruginosa*, *E. coli*, and *Candida albicans.* When the concentration of alumina NPs was increased to more than 1000 g/mL, the inhibitory effect on *E. coli* was

no longer significant. The interactions between the surface charges of the particles and the cells may have produced this effect. Al_2O_3 combined with silver demonstrates enhanced antibacterial properties, similar to TiO_2 NPs.[10]

Fundamentals of nanotechnology-based drug design methodologies

Biocompatible NPs and nanorods are examples of materials at the nanoscale that is used in "nanomedicine" for a range of purposes in living organisms, including perception, actuation, diagnosis, and delivery. This research approach uses the science of nanotechnology to treat and prevent a variety of illnesses. Pharmaceuticals with very low solubility face several challenges in the delivery of biopharmaceuticals: Low oral bioaccessibility, decreased capacity to permeate the outer membrane, increased need for intravenous infusion, and harmful side effects that appear before the traditional immunization process.[9]

Miraculous reaction to drug delivery

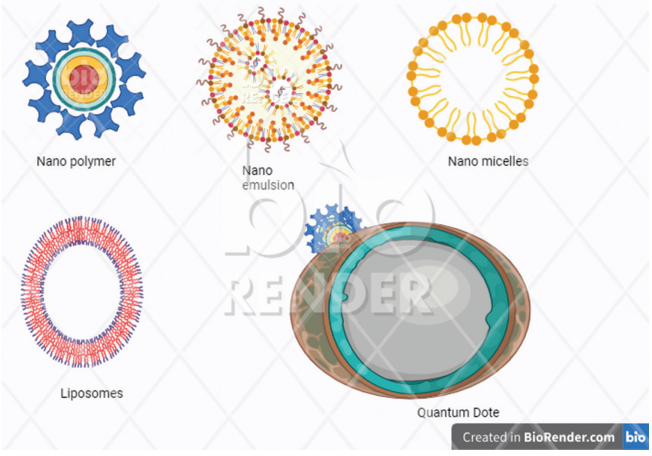
It becomes clear that the family genuinely believes God can intervene and completely recover their mother's health. They sincerely think that God will answer their prayers and faith, and they often tell the tale of an uncle who made a full recovery even though "the doctors had said there was no hope."

Consequently, a physician does not have to base treatment decisions on the expectation of divine intervention when death is imminent.[8]

TOOLS AND PROCESSES

Strains of bacteria and their instruments

Kanon Pharma invented the fluoroquinolone moxifloxacin (MF).



Creation of MF in complex form with cyclodextrin (CD) derivatives

CD and MF solutions were combined to create MF-CD complexes. Cyclophosphamide, methotrexate, and fluorouracil were kept at 1 mg/mL, and the MF: CD torus molar ratio was kept at 1:1. The complexes were continuously mixed for an hour at 37°C during the incubation process. After that, the samples were frozen for 72 h at 60°C using a thermostatic freeze-dryer.

Unintentional scattering of light

Dynamic light scattering (DLS) was used with the nano to ascertain the potential of the sample. The device consisted of a thermostatic cell (25°C) and a 4 W He-Ne laser (633 nm). We used the Correlator System K70 and Software, 7.12, to evaluate the data. Three measurements were made, and the data were presented with standard deviations.

Examination of NP following

The solution was diluted to obtain Particle's = 107–109 particles/ml using Milli Q-purified water. An analysis of NP tracking was carried out using the t LM10-HS apparatus (nanoparticle tracking analysis). Three measurements were made, and standard deviations were provided for the outcomes.[11]

Benefits of a drug delivery

The result of ongoing cooperation between our teams for advanced drug delivery and the Chalmers University of Technology teams under the direction of Fredrik and Elinr is a publication in the American Chemical Society's Nanotechnology in 2022. The researchers employed surface-sensitive fluorescence microscopy to look at individual ionizable lipid-containing lipid nanoparticles as they interacted with a synthetic membrane that mimicked the environment of the endosomal membrane.[10,16,19,20]

CONCLUSION

We think that the novel strategy put forth will help upcoming scholars comprehend the whole. We use both fundamental microbiological methods and sophisticated physical-chemical techniques to show the antibacterial activity and ultrastructural morphology of two *E. coli* strains over the course of 7 days. Unlike drug delivery systems (DDS) based on CDs, MF loses its antibacterial efficacy at concentrations near MIC values. The idea that the medication in DDS may have an antimicrobial effect is intriguing. For example, the observed prolonged antibacterial action may necessitate a reduction in the dosage or administration frequency of

antibiotics. The technique may be applied to comprehensive *in vitro* investigations on various pharmaceutical products and innovative drug formulations, especially those that exhibit prolonged drug release.

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