ADVANCES IN DRUGS DELIVERY THERAPY FOR DISEASE CONDITIONS

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Introduction

Advances in drug delivery therapy have revolutionized the treatment of various disease conditions by improving drug efficacy, patient compliance, and minimizing side effects. Here are some notable advancements in drug delivery therapy for different disease conditions**.**

The delivery of drugs has changed significantly from the simple basic pill with uncontrolled release to various systems with enhanced bioavailability and very few side effects. The development of targeted drug delivery systems has benefited Alzheimer's disease, Parkinson's disease, cancer, atherosclerosis, myocardial ischemia, asthma, pulmonary tuberculosis, and hyperglycemia.

Chronic conditions, which are also known as non-communicable chronic illnesses, have complex underlying causes. Most often incurable, they need ongoing medical care. Chronic conditions are a significant medical and financial burden on society because they are responsible for 73.4% of all deaths globally in recent years.[(1)]

Targeted therapy aims to treat disease by delivering therapeutic drugs to pathogenic organs or sites of required action at the cellular or molecular level. Targeted drug delivery systems allow doctors to prescribe medications to patients at lower doses by concentrating a drug's active ingredient at the site of a lesion or anatomical target and maintaining the drug in the targeted organ for a longer period of time at an effective concentration. Targeted therapy can aid in the reduction and elimination of drug-related side effects, improving patient compliance and safety. [(2)]

Targeted Treatment of Type 2 Diabetes Mellitus

Four categories can be used to categorise diabetes:

- Type 1 Diabetes
- Type 2 Diabetes
- Gestational Diabetes
- Maturity onset diabetes of the young (MODY)

As a comorbidity, type 2 diabetes is distinguished by reduced levels of inflammation, insulin resistance, inability to tolerate glucose, and a failing insulin secretory response. During the postprandial period, intestinal L-cells secrete glucagon-like peptide 1 (GLP-1), an

insulin-stimulating hormone. GLP-1 stimulates insulin release, delays gastric emptying, decreases food intake, and holds up the uptake of glucose, all of which help to maintain blood glucose homeostasis.GLP-1 is rapidly degraded in vivo by dipeptidyl peptidase-4 (DPP-4) and has a half-life of only two minutes.

Oral Medications: To help manage blood sugar levels, several classes of oral medications are available. Metformin (often prescribed first), sulfonylureas, thiazolidinediones, DPP-4 inhibitors, SGLT-2 inhibitors, and GLP-1 receptor agonists are among them. Medication selection is influenced by factors such as the patient's individual response, potential side effects, and pre-existing medical conditions.

Injectable Medications:

Insulin Therapy: To effectively control their blood sugar levels, some T2DM patients may need insulin therapy. There are many different types of insulin, such as rapid-acting, short-acting, intermediate-acting, and long-acting insulins.

Agonists of the GLP-1 Receptor: These injectable medications stimulate insulin release, slow digestion, and reduce appetite. They can help with blood sugar control and weight management.

Combination therapy: To achieve the best blood sugar control, many patients benefit from taking multiple medications. Combining drugs from various classes can address various aspects of T2DM and have synergistic effects.

Individualised Approaches: Patients react to medications differently, making an individualised approach essential. Healthcare professionals can modify the treatment plan as necessary by routinely monitoring blood sugar levels, A1c levels, and potential side effects.

There are two classes of anti-diabetes medications that target GLP-1 receptor (GLP-1R) signalling: GLP-1R agonists and DPP-4 inhibitors.

- Exenatide, Lixisenatide, Albiglutide, Dulaglutide, and Semaglutide are GLP-1R agonists.
- Sitagliptin, Alogliptin, Linagliptin, Vildagliptin, and Saxagliptin, are DPP-4 inhibitors.

The following are just a few of the many advantages of targeted therapies based on GLP-1R agonists and DPP-4 inhibitors:

- Encourage the release of insulin and have lower risks of hypoglycemia than other diabetes treatments like sulphonylureas.
- Reduce the loss of pancreatic beta cells and postpone the progression of diabetes.
- Offer cardiovascular and renal protection.

Targeted Treatment of CKD

A chronic kidney disease is characterised by abnormalities in kidney structure or function lasting longer than three months and having an impact on health. High incidence and mortality rates as well as low awareness levels are linked to CKD. Additionally, strategies to stop the growth or worsening of CKD are currently being implemented insufficiently. Current CKD treatments only slow the disease's progression, and the cost of care can be prohibitive for patients. Glomerular cells are particularly damaged as CKD progresses, along with endothelium cells, podocytes, macrophages, and tubular epithelial cells. Extensive research is being done on novel therapies for the treatment of CKD, some of which include:

- Gary et al. recently demonstrated that carboxymethyl-terminated poly (20-200nm) modified nanoparticles can more efficiently deliver medications to the kidney for the treatment of glomerular kidney disease, allowing for an accumulation of a higher concentration of medication in diseased glomeruli.
- Bruni et al. began with four-arm star-shaped polymers to create new drug-loaded ultra-small colloidal nanocarriers with a tunable size range of 5-30 nm. These incredibly tiny colloidal nanocarriers can reduce albumin permeability and repair podocyte damage in in vitro drug models.
- Tripathy et al. found that transdermal microneedles can specifically target the folate receptors on renal epithelial cells in vitro.
- Li et al. created a system to deliver Celastrol (CEL) specifically to interstitial myofibroblasts using PEGylated liposomes (CREKA-Lip), which have a strong affinity for the fibronectin-binding pentapeptide Cys-Arg-Glu-Lys-Ala (CREKA). In mice with unilateral ureteral obstruction, CREKA-Lip accumulates in the fibrotic kidneys after systemic administration. It is more effective than free CEL at treating renal fibrosis, injury, and inflammation while being less toxic to other major organs.[4]

Targeted Treatment of COPD

A chronic respiratory condition known as chronic obstructive pulmonary disease (COPD) is characterised by breathing problems, restricted airflow, and other symptoms that get worse over time. The third leading cause of death in the world, chronic obstructive

pulmonary disease (COPD), affects over 250 million people. Only now are COPD therapeutic methods able to lessen symptoms. The use of targeted therapies as essential adjuvant therapies may provide COPD patients with new treatment options. Targeted therapies that are administered through the lungs have a number of advantages over treatments that are administered orally, including quicker absorption rates, concentrated metabolic enzyme distribution throughout the lung, and slower rates of active ingredient degradation.

According to studies, drug delivery systems that generate more particles with a diameter of between 1.0 and 3.0 m cause more of the drug to settle in the alveoli and bronchioles, improving therapeutic effects. The diameter of the drug delivery particles has a significant impact on how the drug is deposited in the respiratory system.[5]

The severity of the condition, the patient's symptoms, and their general health are all taken into consideration when treating chronic obstructive pulmonary disease (COPD).The purpose of treatment is to stop exacerbations, improve lung function, lessen symptoms, and improve the patient's quality of life. Here are some essential elements of a targeted COPD treatment:

Smoking Cessation: Giving up smoking is the most crucial step in managing COPD. Quitting smoking significantly slows the disease's progression and eases symptoms.

Bronchodilators: By relaxing the airway muscles and enhancing airflow, short-acting bronchodilators (such as short-acting beta-agonists and anticholinergics) quickly relieve acute symptoms.

Inhaled Corticosteroids: Patients who experience frequent exacerbations and signs of inflammation may benefit from using inhaled corticosteroids (ICS) in addition to bronchodilators. They aid in lowering mucus production and airway inflammation.

Combination Therapy: Inhalers that contain both bronchodilators and corticosteroids may be helpful for some patients. These drugs can effectively treat all symptoms and lessen the need for multiple inhalers.

PDE-4 Inhibitors: PDE-4 inhibitors are oral medicines that aid in reducing airway inflammation and enhancing lung function. Patients with more severe COPD and chronic bronchitis may want to consider them.

Oxygen Therapy: To increase oxygen saturation and reduce shortness of breath, supplemental oxygen therapy may be prescribed in cases of severe COPD and low blood oxygen levels.

Pulmonary Rehabilitation: Programmes for enhancing breathing, wellness, and overall quality of life in COPD patients include exercise training, education, and support.

Vaccinations: To lower the risk of respiratory infections that can exacerbate the symptoms of COPD, it is advised to receive annual influenza vaccinations and periodic pneumococcal vaccinations.

Management of Exacerbations: An acute worsening of symptoms and lung function is referred to as an exacerbation. They might need to take antibiotics, oral corticosteroids, and more bronchodilators. For managing exacerbations, patients should have a plan of action.

The potential drugs targeting COPD and their mechanisms

Drug name	Method of preparation	Size
Liposomal dry powders of N-acetylcysteine (SD-NAC-Lip)	Reverse phase evaporation	100 nm
Budesonide and Colchicine liposomes	Thin layer film hydration method	100 nm
Chitosan or hyaluronan-coated liposomes of curcumin	Sonication and stirring	90~130 nm
Small Unilamellar Liposomes, Pluronic F127surface modified liposomes and PEG 2000PE-surface modified liposomes of beclomethasone dipropionate	Micelle-to-vesicle transition method	40~65 nm
Codelivery system using core-shell type lipid-polymer nanoparticles (LPNs)	Solvent displacement method	123 ± 31 nm
PEGylated dextran-coated superparamagnetic iron oxide nanoparticles	_	82.7~133.7 nm
Chitosan nanoparticles of budesonide	Ionotropic gelation technique	363~543 nm
Polymeric Nanoparticles of miRNA	Oil-in-water single emulsion solvent evaporation method	244.80 ± 4.4 nm
atRA formulated into solid lipid nanoparticles	Emulsification-ultrasonication method	177.3nm ± 29.23 nm
Mucoadhesive solid lipid microparticles	Ethanolic precipitation technique and ultraturrax homogenization	3.5~4.0 μm
Chitosan-genipin nanohydrogel	Reverse microemulsion method	30~100 nm
siRNA-loaded, lipidoid-modified PLGA hybrid nanoparticles	Double emulsion solvent evaporation method	200~260 nm

Targeted Treatment of CAHD

Coronary Atherosclerotic Heart Disease (CAHD) is a medical condition where there is a buildup of plaque (atherosclerosis) in the arteries that supply blood to the heart muscle. The term "coronary" refers to the blood vessels of the heart, and "atherosclerotic" denotes the presence of atherosclerosis, a condition in which cholesterol, fats, calcium, and other materials build up in the walls of the arteries and form plaques. Annual increases in coronary heart disease incidence and mortality rates across the globe have a significant financial impact.

Coronary atherosclerosis is primarily brought on by lipid buildup and macrophage infiltration in the arterial wall, both of which result in chronic inflammation. Inflammation is therefore one of the key areas that need to be treated in order to treat coronary heart disease. CAHD patients do not currently have access to any specific anti-inflammatory drugs, so drug therapy for the condition focuses primarily on lowering risk factors and giving antithrombotic therapy.[6]

- A monoclonal anti-IL-1 antibody called canakinumab has the ability to reduce IL-1-mediated inflammatory reactions. Additionally, IL-1 can stimulate the production of endogenous platelet-derived growth factor (PDGF) and the proliferation of smooth muscle cells by activating downstream IL-6 receptor transduction pathways.
- Tocilizumab, an IL-6 inhibitor, can halt this inflammatory cascade and delay the onset of atherosclerosis.
- Tozizumab can significantly enhance endothelial function in high-risk rheumatoid arthritis while lowering IL-6 activity, even in the presence of high levels of total cholesterol and low-density lipoprotein.

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