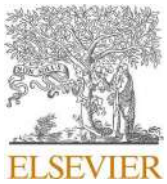
List of Publications

- Rani P, Rahim, J, U, Patra, S, Gupta, R, Gulati M, Kapoor B. Tumor microenvironment-responsive self-assembling polymeric prodrug-based nanomaterials for cancer therapy. Journal of Drug Delivery Science and Technology 2024; 96:105715. Doi: 10.1016/j.jddst.2024.105715
- Rani P, Kapoor B, Gulati M, Gupta R. Nanoscale self-assembling prodrugs of sulfapyridine for treatment of arthritis: Harnessing the dual approach. Medical Hypotheses 2022;165:110896. Doi: 10.1016/j.mehy.2022.110896
- Rani P, Kapoor B, Gulati M, Atanasov AG, Alzahrani Q, Gupta R. Antimicrobial peptides: A plausible approach for COVID-19 treatment. Expert Opinion on Drug Discovery 2022;17(5):473-87. Doi: 10.1080/17460441.2022.2050693
- Isha, Rani P, Gulati M, Rahim, J. U, Kapoor B. Self-assembled peptide-based nanoforms targeting mitochondria for chemotherapy. Journal of Drug Delivery Science and Technology 2024; 99:106006. Doi: 10.1016/j.jddst.2024.106006
- Kaur R, Rani P, Atanasov AG, Alzahrani Q, Gupta R, Kapoor B, Gulati M, Chawla P. Discovery and development of antibacterial agents: Fortuitous and designed. Mini Reviews in Medicinal Chemistry 2022;22(7):984-1029. Doi: 10.2174/1570193X19666211221150119
- Kapoor B, Gulati M, Rani P, Gupta R. Psoriasis: Interplay between dysbiosis and host immune system. Autoimmunity Reviews 2022 Aug 12:103169. Doi: 10.1016/j.autrev.2022.103169
- Kapoor B, Gulati M, Rani P, Kochhar RS, Atanasov AG, Gupta R, Sharma D, Kapoor D. Lycopene: Sojourn from kitchen to an effective therapy in Alzheimer's disease. Biofactors 2023;49(2):208-27. Doi: 10.1002/biof.1910
- Kapoor B, Kochhar RS, Gulati M, Rani P, Gupta R, Singh SK, Machawal L, Thakur A. Triumvirate to treat mucormycosis: Interplay of pH, metal ions and antifungal drugs. Medical Hypotheses 2022;159:110748. Doi: 10.1016/j.mehy.2021.110748
- Kapoor B, Singh A, Gulati M, Singh SK, Rani P, Alzahrani Q, Dua K, Dureja H, Corrie L. Orchestration of obesolytic activity of microbiome: metabiotics at centre stage. Current Drug Metabolism 2022;23(2):90-8. Doi: 10.2174/1389200223666220211095024
- Sharma, P, Kapoor B, Hussain, M. S, Singh, G, Rani, P, Saini, B, Wadhwa, P, Kumar, R. Development and Validation of Reverse-Phase High-Performance Liquid Chromatography Method for Simultaneous Estimation of Doxorubicin and Clotrimazole. ASSAY and Drug Development Technologies 2023; 22:86-96. Doi: 10.1089/adt.2023.057.
- Parveen, S.R, Wadhwa, S, Singh, S.K, Kapoor, B, Rani, P, Vishwas, S. Validated RP-HPLC method for estimation of Chrysin in bulk form and nanostructured lipid carriers for topical application. Nanoscience and Nanotechnology Asia 2023;13:41-48. Doi: 10.2174/2210681213666230227150930.
- Gupta R, Kapoor B, Bandopadhyay, R, Gulati M, Rani P, Kochhar, R.S. Allicin and Probiotics: Double-edged sword for the management of Striae distensae. Medicine in Microecology 2024, 21:100109. Doi: 10.1016/j.medmic.2024.100109.
- Alzahrani QE, Gillis R, Harding SE, Pinto LH, Gulati M, Kapoor B, Rani P, Singh SK, Adams GG. Potential of the triad of fatty acids, polyphenols, and prebiotics from Cucurbita against COVID-19 in diabetic patients: A review. Journal of Reports in Pharmaceutical Sciences 2022;11(1):28-40. Doi: 10.4103/jrptps.JRPTPS_144_21

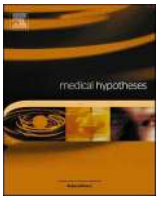
Medical Hypotheses 165 (2022) 110896



Contents lists available at ScienceDirect

Medical Hypotheses

journal homepage: www.elsevier.com/locate/mehy



Nanoscale self-assembling prodrugs of sulfapyridine for treatment of arthritis: Harnessing the dual approach

Pooja Rani, Bhupinder Kapoor *, Monica Gulati, Reena Gupta

School of Pharmaceutical Sciences, Lovely Professional University, Phagwara, India

ARTICLE INFO

Keywords:
Sulfapyridine
Nanoparticles
Self-assembling structures
Rheumatoid arthritis
Inflammation

ABSTRACT

Rheumatoid arthritis is a chronic, autoimmune, inflammatory joint disease, affecting mainly joints of hands, wrists, and knees. Although a number of potent drugs are available for the treatment of arthritis, the management of this life-long disease becomes challenging because of their poor bioavailability, frequent administration, toxicity, instability and limitations related to their formulation development. Self-assembling nanoparticles are the emerging class of therapeutic drug delivery systems that have been explored in past few years for the treatment of various diseases. Intra-articular administration of these systems prolongs the retention of drug in the target site by virtue of their size as well as two-steps release of the entrapped drugs (disassembly and then lysis of prodrug to release the active drug) and provide a sustained action which is desirable in this condition. Based on the prior reports, it is hypothesized that self-assembly delivery systems of sulfapyridine will provide an effective and sustained treatment of rheumatoid arthritis. Promoieties including saturated, unsaturated fatty acids and amino acids are proposed.

Background

Rheumatoid arthritis (RA), the most common form of inflammatory arthritis, is a chronic, systemic, autoimmune disorder characterized by persistent synovitis, production of auto-antibodies to immunoglobulin G (rheumatoid factor and anti-citrullinated protein antibody), destruction of cartilage and bone, and progressive disability [1–3]. In severe cases, there is a risk of development of extra-articular manifestations including keratitis, pulmonary granulomas (rheumatoid nodules), pericarditis/pleuritis, small vessel vasculitis, and other non-specific extra-articular symptoms, ultimately leading to early death [2]. The global prevalence of RA is approximately 1–2%, and the risk in women is 3 times higher than that in men, which is attributed to the involvement of sex hormones in the pathogenesis of the disease [4,5]. The incidence and prevalence of RA has been increasing over the past 20 years, thereby increasing the economic burden of the disease [6].

Although the exact cause of RA still remains unknown, it is believed that a combination of genetic and environmental factors, as well as other auto-immune initiating agents are implicated [7,8]. T cells, B cells and the orchestrated interaction of pro-inflammatory cytokines play key roles in the pathogenesis of the disease. Tumor necrosis factor-α (TNF- α) and interleukin-6 (IL-6) are mainly involved in this process. IL-1 and IL-17 may also play, albeit, less important role in the disease process [9].

Treat-to-target approach, based on tight monitoring of disease activity and change of management if a treatment target is not reached, has been adopted by American College of Rheumatology, European League against Rheumatism, Asia Pacific League of Associations for Rheumatology for the management of RA [10]. The goal of this strategy is disease remission or low disease activity, normalizing the physical function of joints in early stages, maximizing the physical function in established disease, and to prevent the progression of the disease [11]. In the past 30 years, therapeutic resources available for the treatment of RA have grown tremendously. Pharmacotherapy for RA generally involves nonsteroidal anti-inflammatory drugs (NSAIDs) for pain management, with selective use of low-dose oral or intra-articular glucocorticoids, and initiation of a disease modifying anti-rheumatic drugs (DMARDs) that delay the progression of the disease [12]. The available DMARDs are subdivided into conventional synthetic DMARDs (methotrexate, sulfasalazine, chloroquine, hydroxychloroquine and gold salts), targeted synthetic DMARDs (Janus kinase inhibitors like baricitinib, tofacitinib), and biologic DMARDs i.e. TNF-α inhibitors (adalimumab, certolizumab, etanercept, golimumab and infliximab), IL-6 receptor inhibitors (tocilizumab and sarilumab), IL-6 inhibitors (clazakizumab, olokizumab and sirukumab), B cell depleting antibodies,

* Corresponding author.
E-mail address: bhupipharma@gmail.com (B. Kapoor).

https://doi.org/10.1016/j.mehy.2022.110896
Received 13 January 2022; Received in revised form 8 June 2022; Accepted 15 June 2022
Available online 18 June 2022

Journal of Drug Delivery Science and Technology 96 (2024) 105715

Contents lists available at ScienceDirect

Journal of Drug Delivery Science and Technology

journal homepage: www.elsevier.com/locate/jddst

Review article

Tumor microenvironment-responsive self-assembling polymeric prodrug-based nanomaterials for cancer therapy

Pooja Rani [a], Junaid Ur Rahim [b], Samiksha Patra [a], Reena Gupta [a], Monica Gulati [a,c], Bhupinder Kapoor [a,*]

[a] School of Pharmaceutical Sciences, Lovely Professional University, Phagwara, Punjab, India
[b] Department of Radiology and Biomedical Imaging, University of California San Francisco, San Francisco, CA, 94143, USA
[c] Faculty of Health, Australian Research Centre in Complementary and Integrative Medicine, University of Technology Sydney, NSW, 2007, Australia

ARTICLE INFO

Keywords:
Cancer
Prodrugs
Self-assembled nanoparticles
Tumor targeting
Endogenous-responsive

ABSTRACT

Prodrug approach, involving the chemical modification of an active moiety, is one of the clinically proven strategies to overcome the unfavorable physicochemical and biopharmaceutical properties of potential therapeutic compounds. Despite many success stories, a number of small-molecule prodrugs face challenges in their druggability properties, thus limiting their clinical applications. Self-assembling prodrugs represent an emerging nanotherapeutic approach that possess the advantages of both prodrug design and nanotechnology. The self-assembling/formulating property of these prodrugs in aqueous media, by virtue of their amphiphilic character, constructs a wide variety of supramolecular nanostructures with numerous intrinsic advantages viz., high drug loading, minimal premature release, and improved pharmacodynamic and pharmacokinetic properties. Moreover, selection of suitable linker between the drug and promoiety, that selectively undergo cleavage at the target site, increases the selectivity of the delivery system, while decreasing the risk of off-targets effects. Although, majority of the self-assembling prodrug-based delivery systems have been developed for chemotherapeutic agents, a few examples of molecules belonging to other pharmacological classes can be found in the literature. In this review, we have comprehensively summarized the various self-assembling polymeric prodrugs of chemotherapeutic agents that have been developed for mono- and combination therapy. Responsiveness of linkers to the various endogenous stimuli of tumor microenvironment such as acidic pH, reactive oxygen species (ROS), redox, enzymes, and hypoxia is used to categorize these studies. This review is expected to be a unique document which along with providing the information hitherto available on this industrially relevant area, will provide guidance for the rational design of effective prodrug nanoassemblies that have clinical translational potential.

1. Introduction

The efficient delivery of drugs to their target site plays a key role in the treatment of various diseases. However, targeted delivery is still considered a major challenge due to the unfavorable physicochemical, pharmacokinetic and biopharmaceutical properties of drug molecules [1]. Chemical modification of drugs i.e., the prodrug approach is one of the most extensively explored strategy to overcome these challenges. The term 'prodrug', coined by Adrian Albert in 1958 [2], relates to the bio-reversible inert derivatives of drug molecules that undergo biotransformation *i.e., in vivo* chemical and/or enzymatic conversion to liberate the pharmacologically active moiety [3]. Among the 249 new chemical entities approved by US Food and Drug Administration (US FDA) during 2008–2017, 31 *i.e.,* 12.4 % were prodrugs [4]. Almost every year, at least two prodrugs were approved by US FDA, except for year 2016 and 2012, in which no and only one prodrug was approved respectively [5]. Despite their immense potential, the limited clinical applications of this strategy are attributed to various drawbacks such as hepatic metabolism, premature activation, short plasma residence time and extensive renal clearance [6,7].

Novel drug delivery system is another excellent strategy to improve pharmacokinetic properties of various drugs with diverse physiochemical properties [8,9]. Among the various delivery systems explored, drug nanocarriers have been utilized in different forms like e.

* Corresponding author.
E-mail address: Bhupipharma@gmail.com (B. Kapoor).

https://doi.org/10.1016/j.jddst.2024.105715
Received 31 January 2024; Received in revised form 15 April 2024; Accepted 23 April 2024
Available online 27 April 2024