Drug Development & Research©
3 (15) 2023 : 001-005 • Review Article

Drug-carrier interaction modelling for the drug release from nanocarriers

Yanting Li*
College of Pharmacy, Henan University of Chinese Medicine, Zhengzhou 450046, China

AUTHORS' CONTRIBUTION: (A) Study Design · **(B)** Data Collection . **(C)** Statistical Analysis · **(D)** Data Interpretation · **(E)** Manuscript Preparation · **(F)** Literature Search · **(G)** No Fund Collection

ABSTRACT

For the administration and release of medicinal and imaging substances, numerous nanocarriers with different compositions and geometries have been produced. In order to achieve sustained release, many mechanisms like ion pairing and hydrophobic interaction need to be investigated due to the high specific surface areas of nanocarriers. Recently, we created a three-parameter model that takes into account first-order drug release from liposomes and reversible drug-carrier interaction. The analytical problem was solved in closed form. Here, we further investigate the model's capacity to represent the release of bioactive compounds from diverse nanocarriers, including medicines and growth factors. The model may be shown to be capable of mimicking the main types of drug release kinetics through a parameter research. More than 60 sets of experimental data from different drug delivery methods, including nanoparticles, hollow particles, fibers, and hollow fibers, were further fitted using the model. Additionally, bootstrapping is utilised in some circumstances to validate the model and assess the precision of parameter estimation. The model is practical for the design and development of novel drug delivery systems due to its simplicity, universality, and the physical clarity of each model parameter.

Keywords: Nanotechnology; Nanocarriers; Drug delivery; Drug targeting; Drug-carrier interaction

Address for correspondence:

Yanting Li,
College of Pharmacy, Henan University of Chinese Medicine, Zhengzhou 450046, China
E-mail: yanting.li@gmail.com

Word count: 1856 **Tables:** 00 **Figures:** 00 **References:** 10

Received: 01.04.2023, Manuscript No. ijddr-23-13663; **Editor assigned:** 04.04.2023, PreQC No. P-13663; **Reviewed:** 18.04.2023, QC No. Q-13663; **Revised:** 22.04.2023, Manuscript No. R-13663; **Published:** 29.04.2023

INTRODUCTION

For the delivery and regulated release of various treatments, a variety of nanocarriers with varied geometries and material compositions, including liposomes, micelles, nanocapsules, polymeric nanoparticles, solid lipid particles, nanofibers, and hollow nanofibers, have been produced. For instance, the use of nanoparticulate carriers as a mechanism for administering therapeutic and imaging chemicals through various routes of administration, such as intramuscular or subcutaneous injection, oral, and ocular administration, has long been investigated [1]. Liposomes have also made it to clinical applications effectively. Contrary to the lengthy development of Nano particulate delivery methods, the use of fibres for drug delivery has only recently been rigorous examination. In order to regenerate tissue, micro- and Nanofibers that resemble the structural and material properties of extracellular matrix are frequently utilised. When inserted into micro/Nanofibers, bioactive compounds like growth factors and medications can improve the biochemical properties of tissue scaffolds or be employed only as drug carriers [2].

To improve patient compliance and convenience, continuous release must be achieved despite the high surface-to-volume ratio of nanocarriers. Different strategies have been used to improve drug-carrier interaction and drug retention over appropriate time periods, perhaps preventing or altering the burst drug release. As an illustration, carboxyl groups contained in poly (lactide-co-glycolide) acid (PLGA) nanoparticles (NPs) have been complexed with cationic peptides using zinc ions. In order to preserve encapsulated molecules by ionic contact charged additives like amines and heparins may also be incorporated in NPs and nanofibers. However, changes in drug solubility, hydrophobicity, excipient composition, and microstructure can influence drug-carrier interaction and consequent drug release. Drug-carrier interactions are frequently reversible, enabling continuous and/or regulated release of molecules that have been encapsulated. Drug release profiles can be divided into four groups based on the size of the initial burst release and the release kinetics after the burst release: high and low. Although many drug release models have been created, only a small number of them take drug-carrier interactions into account and include all possible drug release characteristics [3].

Recently, we created a straightforward, three-parameter model that takes into account the first-order release of lipophilic medicines from liposomes and the reversible drug-carrier interaction, providing a closed-form analytical solution. Here, the model is applied to examine drug release

from several different nanocarriers, such as fibers, hollow fibers, polymeric nanocapsules, NPs, and liposomes. The study is focused on examining the effects of carrier properties (such as pore size, hydrophobicity) and composition (such as molecular weight, copolymer composition, additives) as well as external stimuli (such as pH, temperature) on the release kinetics of pharmaceuticals [4]. Our objective is to demonstrate the potential role of carrier composition and properties in the regulation of drug-carrier interaction and diffusion-driven release. In order to accomplish this, a methodical parameter research is conducted to show how each model parameter affects release kinetics. More than 60 sets of release data from diverse delivery mechanisms are then fitted to the model. Finally, bootstrapping statistical analysis is used to validate the model in a few specific scenarios [5].

The release kinetics of the drug from the host, which has been studied for a number of model systems, is a crucial aspect of liposome-based drug delivery. A small ion exchange column approach has recently been used in experimental studies of the transfer of temoporfin between two different types of liposomes (i.e., from donor liposomes to acceptor liposomes). The column distinguishes between donor and acceptor liposomes, enabling the observation of the drug transfer's temporal dependency. It has been noted that the transfer often exhibits what appears to be a single exponential function, first-order behaviour. Given the intricacy of the system, this is impressive because different physical pathways allow the drug molecules to go from the donor liposome to the acceptor liposome [6].

Actually, there are two systems that typically operate in tandem. Drugs are transferred via the first mechanism when two liposomes collide. In this instance, there is little to no exposure to the aqueous phase as the drug molecules travel directly from one liposome to another. The second mechanism deals with drug transfer by aqueous phase diffusion. We see that the transfer of lipids and cholesterol between vesicles, as well as the transfer of fatty acids between vesicles and fatty acid binding proteins, has all been explained, among other things, by the collision process. The transport of lipids was found to be consistent with the diffusion mechanism as well. Both mechanisms have been proposed in some instances to be involved in the movement of lipids between vesicles, the movement of lipophilic medicines from oil-in-water emulsions to cells, and the movement of plasma proteins to lipid vesicles. In our previous experimental work, where we looked at the kinetics of temoporfin transport from donor to acceptor liposomes, we discovered that the transfer was dominated by collisions above a certain concentration (corresponding to a liposome-to-liposome distance of about 200 nm for our particular system); for smaller concentrations, diffusion was more common [7].

DISCUSSION

This work describes the production of new biodegradable HMW drug carriers and conjugates as well as their physicochemical and preliminary biological properties. HMW polymer systems are linear pHPMA copolymers grafted onto third- and fourth-generation bis-MPA dendrimers, resulting in water-soluble polymers having star-like structures. Because the ester bonds in the bis-MPA dendrimer core of HMW star polymers are hydrolytically unstable, they are made to slowly degrade in the presence of living things. The pH of physiological settings, which is 7.4, is the optimal pH for this hydrolysis. By creating new biodegradable structures of the star pHPMA-DOX conjugates with well-defined architecture and proper control of molecular weight (with preservation of low polydispersity), we focused on enhancing the characteristics of biodegradable HMW drug delivery systems. Additionally, we sought to create polymer structures that effectively accumulated in solid tumors, were expelled from the body after the drug load was removed, and were then destroyed under physiological settings [8].

The P1 TT end groups were reacted with an excess of ethylene diamine to produce the polymer precursor P2, which has hydrazide groups that are Boc-protected. The excess was employed to introduce primary end-chain amino groups and prevent crosslinking of the polymer precursor. Copolymer P2's (F = 1.3) functionality was comparable to that of P1's. The P2 copolymer's molecular weight and polydispersity did not alter following reaction. Due to their FRP preparation, polymers P1 and P2 had slightly larger dispersities. By performing controlled radical RAFT polymerization in tert-butyl alcohol, the semitelechelic polymer precursor P3 with a restricted molecular weight distribution was created. The synthesis of almost monodisperse PHPMA precursors using the RAFT polymerization process using a dithiobenzoate-based chain-transfer agent was effective and the yields were equivalent to those attained using the free radical polymerization method. By reducing the dithiobenzoate end groups of copolymer P3 with NaBH4, thiol groups were created that were then used to introduce amino groups in situ by reacting with AEMI•TFA. The copolymer P3 was projected to be highly beneficial and effective in the synthesis of HMW star polymers due to its low dispersity (1.1) and the functionality of the amino end groups (0.9), which is near to unity [9].

The semitelechelic copolymer P2, which was made via FRP, had a functionality that was much higher than 1, indicating the presence of telechelic copolymers with amino groups on both polymer chain ends. For this reason, after grafting polymer P2 to the dendrimers core, a negligible number of cross-linked structures were also discovered. A star copolymer precursor with low dispersity was created because the functionality of copolymer P3, produced by RAFT polymerization, was close to unity, which reduced the likelihood of crosslinking reactions during the production of the star copolymer [10].

CONCLUSION

We tested a straightforward, three-parameter model's capacity to accurately represent the release of bioactive chemicals from diverse nanocarriers. The model specifically takes into account reversible drug-carrier interaction and provides a closed-form analytical answer. The dependency of

release kinetics on each model parameter was demonstrated by a parameter analysis. Notably, the model is consistent with 60 sets of release data that represent a broad range of release kinetics. Our comprehension of the underlying principles of sustained release in diverse delivery systems may be improved by the model. This model offers a helpful tool for the design and synthesis of new nanostructured delivery vesicles, such as NPs, nanocapsules, Nanofibers, and hollow Nanofibers, despite its limits.

ACKNOWLEDGMENT

None

CONFLICT OF INTEREST

None

REFERENCES

1. **Ramezankhani R, Torabi S.** Two Decades of Global Progress in Authorized Advanced Therapy Medicinal Products: An Emerging Revolution in Therapeutic Strategies. *Front Cell Dev Biol*. 2020;8:547-653.
2. **Hwang YG, Lee JW, Park KH, et al.** Allogeneic keratinocyte for intractable chronic diabetic foot ulcers: A prospective observational study. *Int Wound J*. 2019;16:486-491.
3. **Hosseini Mansoub N.** The role of keratinocyte function on the defected diabetic wound healing. *Int J Burns Trauma*. 2021;15:430-441.
4. **You HJ, Han SK, Lee JW, et al.** Treatment of diabetic foot ulcers using cultured allogeneic keratinocytes-a pilot study. *Wound Repair Regen*. 2012;20:491-9.
5. **Alharbi Z, Piatkowski A, Dembinski R, et al.** Treatment of burns in the first 24 hours: simple and practical guide by answering 10 questions in a step-by-step form. *World J Emerg Surg*. 2012;7:13.
6. **Herndon DN, Barrow RE, Rutan RL et al.** A comparison of conservative versus early excision: therapies in severely burned patients. *Ann Surg*. 1989;209:547-53.
7. **Pereira C, Murphy K, Herndon D, et al.** Outcome measures in burn care. Is mortality dead? *Burns* 2004;30:761-71.
8. **Gallico GG3rd, O'Connor NE, Compton CC, et al.** Permanent coverage of large burn wounds with autologous cultured human epithelium. *N Engl J Med*. 1984;311:448-51.
9. **Gallico GG3rd, O'Connor NE.** Cultured epithelium as a skin substitute. *Clin Plast Surg*. 1985;12:149-57.
10. **Wood FM, Kolybaba ML, Allen P, et al.** The use of cultured epithelial autograft in the treatment of major burn wounds: eleven years of clinical experience. *Burns.* 2006;32:538-44.