THOUSAND WORDS ABOUT...

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Future Opportunities in the Field of Drug Delivery Research

Joachim Kohn
Rutgers-The State University of New Jersey
BMK Scientific Consulting, Inc. Piscataway, NJ, USA
https://orcid.org/0000-0002-5834-6536
Corresponding author: joachimkohn@gmail.com

Bozena Michniak-Kohn
Department of Pharmaceutical Sciences, Ernest Mario School of Pharmacy, Rutgers University-The State University of New Jersey, NJ, USA
https://orcid.org/0000-0002-3858-158X

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ABSTRACT

Much of the priorities in drug delivery research are focused on targeted drug delivery for cancer therapies and a wide range of controlled drug release systems for commonly used active pharmaceutical ingredients (APIs). In this "thousand words article" we highlight some of the emerging health threats and future opportunities for drug delivery research.

Important emerging health threats include viral pandemics beyond COVID, antibiotic-resistant pathogens, the need for new antifungal therapies, and emerging diseases caused by increasing pollution and climate change. Fundamentally new drugs may be needed. For example, one little known research effort focuses on the development of new antibiotics based on metal-organic frameworks. Finally, new delivery approaches will be needed. This is illustrated by the development of a topical peptide delivery system as a wound dressing for burn patients, combining biotechnology (a new peptide) with polymer science (a new topical delivery system) to address a medical need (burn injury) for which there is currently no effective treatment. Another important trend is the shift in our collective understanding of impact, moving away from "counting papers" to considering the societal benefit of the research including its potential for commercialization. To remain relevant in the coming decade, we need to anticipate and embrace future challenges. This is particularly important for younger scientists.

Important emerging research opportunities are related to a number of new, global health threats, including (but not limited to) viral pandemics beyond COVID, the development of antibiotic-resistant pathogens, the growing number of life-threatening fungal infections, and the health effects of climate change and pollution. To address these challenges, we anticipate significant changes in the way drug delivery research is being conducted.

This article is based on extended literature searches, discussions with numerous biomaterials scientists from the USA and Europe, and the preferential selection of topics relevant to the members of the ORBIS project.

Nanotechnology has greatly contributed to the development of mRNA vaccines and rapid detection kits for the diagnosis of COVID infections [1]. This line of research offers ample room for further innovation and improvement. It is likely that nanotechnology-inspired drug delivery systems will dominate most aspects of drug delivery research in the future [2]. This is an important change from the focus on controlled release formulations and drug-delivery implants that dominated drug delivery research in the past.

The next pandemic could be caused by a virulent and highly transmissible bacterium. Scientists have warned repeatedly of the potential threat of antibiotic resistant pathogens [3, 4]. There is a need to think beyond our current small molecule-based approaches. For example, silver and iodine are exceptionally powerful antimicrobial agents that are difficult to deliver and have therefore not reached their full clinical potential [5, 6]. Another innovative material approach is based on metal-organic frameworks. The work of Jaros et al. [7] has recently demonstrated significant promise and could open a new research direction for the development of metal-organic based antibiotics. One of the promising features of this approach is that these agents show both antibacterial and antiviral activity, in addition to activity against bacteria with multiple drug resistance [8].

Most people are unaware of the serious threat associated with fungal pathogens. According to the US Government Center for Disease Control, the human mortality rate from invasive fungal infections is over 50% [9]. While fungal infections are increasing world-wide, there are only 4 classes of antifungal agents in clinical use: polyenes, azoles, allylamines and echinocandins. Creating a new antifungal agent is much more complicated and time consuming than developing an antibiotic since fungal cells are more similar to mammalian cells than bacterial cells. Therefore, developing innovative delivery platforms for antifungal agents that increase and broaden their activity spectrum is as important as racing to develop new antifungal agents [10]. Another useful strategy is preventing the spread of fungal infections. There are powerful surface coating strategies to prevent fungal attachment and biofilm formation, but only a few laboratories focus on this important global threat. The most innovative approach is the development of intrinsically antifungal polymers as coatings [11]. While 1 billion people currently experience food insecurity, fungi destroy 30% of the global food supply. Thus, intrinsically anti-fungal polymers may also find wide applications as crop-protecting agents in agriculture.

We assume that we will see an accelerated shift away from conventional, small-molecule drugs and towards biological agents such as peptides, proteins, RNA and DNA [12]. These biologics will require new and different drug delivery systems.

Some of the future trends in drug delivery research are illustrated by the development of a peptide-delivery system to treat burn injuries. This research project features the use of engineered peptides as drug candidates (an aspect of biotechnology), the development of electrospun fiber mats as the peptide delivery platform (an aspect of innovative biomaterials) and addresses an important medical need (burn injury progression) for which there is currently no satisfactory treatment.

Burns are categorized by severity. 1st and 2nd degree burns usually heal without complications and without scarring. 3rd degree burns require skin grafts, lead to scarring and result in significant patient morbidity and mortality. Some 2nd degree burns progress to become 3rd degree burns about 48 hours after the actual burn injury [13]. "Burn injury progression" is a major complication, negatively affecting patient outcomes and increasing treatment costs.

Work by Clark et al. identified several fibrinogen-derived peptides, referred to as P12, cP12 and cNP8 [14, 15]. These engineered peptides were shown to reduce burn injury progression when administered by intravenous injection within 24 hours after the burn injury occurred. cNP8 is the most advanced drug candidate since it is resistant to degradation by elastase, an enzyme present in wound sites.

From a clinical perspective, intravenous injection of these peptides is not a viable option. Therefore, to advance this research activity into

clinical use, a suitable delivery system had to be developed. The researchers focused on the development of new, rapidly degradable, biocompatible polymers that could (i) be formulated as a burn wound dressing, (ii) be loaded with hydrophilic, cationic fibrinogen-derived peptides such as P12, cP12 and cNP8, and (iii) release the peptide in a controlled fashion over the course of a few days [16].

In this project the utility of tyrosine-derived polycarbonate [17] electrospun fiber mats was explored. "Ultrafast" and "fast"-eroding polymer compositions were identified that eroded completely in about 24 h and 7 days respectively [16]. Accordingly, the release of the test peptide (P12) from "Ultrafast" fiber mats was controlled by polymer erosion, while the release of P12 from the "fast"-eroding fiber mats was controlled by diffusion of the peptide. A porcine excisional wound model was used to confirm the biocompatibility of these fiber mats in vivo [16]. These results provided the basis for an attempt to develop a clinically useful, new therapy for the treatment of burn injury. These efforts are currently on-going under funding from the US Department of Defense provided to a pharmaceutical company.

Drug delivery research has new challenges and new opportunities. There seems to be a shift away from the traditional macroscopic implants to nanotechnology, a shift away from traditional small molecule drugs to biologics, a shift away from predominantly serving the needs of chronic diseases in affluent countries to looking at emerging global health issues. As a consequence, drug delivery research will continue to be a central discipline in shaping clinical practice in the future.

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Conflict of interest statement

Joachim Kohn is currently a consultant for the Department of Defense funded program on Burn Injury Progression. Bozena Michniak-Kohn has no conflicts to declare.

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Author Contributions

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References

1. Ren H, Jia W, Xie Y, Yu M, Chen Y. Adjuvant physiochemistry and advanced nanotechnology for vaccine development. Chem Soc Rev. 2023 Jul 31;52(15):5172–254.
2. Kassem AA. Nanotechnology Inspired Advanced Engineering Fundamentals for Optimizing Drug Delivery. Curr Drug Targets. 2018;19(15):1839–54.
3. Schito GC, Debbia EA, Marchese A. The evolving threat of antibiotic resistance in Europe: new data from the Alexander Project. J Antimicrob Chemother. 2000 Jul;46 Suppl T1:3–9.
4. Fouladkhah AC, Thompson B, Camp JS. The Threat of Antibiotic Resistance in Changing Climate. Microorganisms [Internet]. 2020 May 16;8(5). Available from: http://dx.doi.org/10.3390/microorganisms8050748
5. Lansdown ABG. Silver in Healthcare: Its Antimicrobial Efficacy and Safety in Use. Royal Society of Chemistry; 2010. 261 p.
6. Sekhon BS. Iodine: A support against infections and emerging as an antibiotic. Journal of Pharmaceutical Education & Research [Internet]. 2012;3(1). Available from: https://search.ebscohost.com/login.aspx?direct=true&profile=ehost&scope=site&authtype=crawler&jrnl=09768173&asa=Y&AN=77554346&h=4GATUigcennnG%2Bt8TexQ6QFzbtUu6W0fGlPImPpsWSTNZMlNKjR%2FVn9z8w9qW4XEoYIcGV%2B4GCPmHve4yJIZAA%3D%3D&crl=c
7. Jaros SW, Król J, Bażanów B, Poradowski D, Chrószcz A, Nesterov DS, et al. Antiviral, Antibacterial, Antifungal, and Cytotoxic Silver(I) BioMOF Assembled from 1,3,5-Triaza-7-Phoshaadamantane and Pyromellitic Acid. Molecules [Internet]. 2020 May 1;25(9). Available from: http://dx.doi.org/10.3390/molecules25092119
8. Jaros SW, Krogul-Sobczak A, Bażanów B, Florek M, Poradowski D, Nesterov DS, et al. Self-assembly and multifaceted bioactivity of a silver(I) quinolinate coordination polymer. Inorg Chem. 2021 Oct 18;60(20):15435–44.
9. Impact of fungal diseases in the United States [Internet]. 2023 [cited 2023 Sep 4]. Available from: https://www.cdc.gov/fungal/cdc-and-fungal/burden.html
10. Jacobs SE, Zagaliotis P, Walsh TJ. Novel antifungal agents in clinical trials. F1000Res. 2021 Jun 28;10:507.
11. Vera-González N, Shukla A. Advances in Biomaterials for the Prevention and Disruption of Candida Biofilms. Front Microbiol. 2020 Sep 17;11:538602.
12. Espiritu MJ, Collier AC, Bingham JP. A 21st-century approach to age-old problems: the ascension of biologics in clinical therapeutics. Drug Discov Today. 2014 Aug;19(8):1109–13.

13. Singer AJ, Hirth D, McClain SA, Crawford L, Lin F, Clark RAF. Validation of a vertical progression porcine burn model. J Burn Care Res. 2011 Nov-Dec;32(6):638–46.
14. Prasad A, Lin F, Clark RAF. Fibronectin-derived Epivi-osamines enhance PDGF-BB-stimulated human dermal fibroblast migration in vitro and granulation tissue formation in vivo. Wound Repair Regen. 2019 Nov;27(6):634–49.
15. Lin F, Prasad A, Weber-Fishkin S, Clark RA. Engineered Fibronectin Peptide Resists Elastase Digestion, Speeds Healing, and Attenuates Scarring in Porcine Burns. J Invest Dermatol. 2020 Jul;140(7):1480–3.
16. Macri LK, Sheihet L, Singer AJ, Kohn J, Clark RAF. Ultrafast and fast bioerodible electrospun fiber mats for topical delivery of a hydrophilic peptide. J Control Release. 2012 Aug 10;161(3):813–20.
17. Jain S, John A, George CE, Johnson RP. Tyrosine-Derived Polymers as Potential Biomaterials: Synthesis Strategies, Properties, and Applications. Biomacromolecules. 2023 Feb 13;24(2):531–65.