



Implen Journal Club | July Issue

Welcome to our July issue of the #Implen #JournalClub in 2022.

Novel Drug Delivery Edition

The image is a promotional graphic for the July issue. It features a central molecular model with grey, blue, and red spheres. To the left, a circular inset shows a surgical suture being held by forceps. To the right, another circular inset shows a line graph with two curves. The IMPLEN logo is in the top right corner. A red banner at the top left reads 'July | Novel Drug Delivery'. Below the molecular model, the title 'Synthesis of a novel monofilament bioabsorbable suture for biomedical applications' is displayed in bold black text. Underneath the title, the authors' names are listed in red: Kara M. de la Harpe, Thashree Marimuthu, Pierre P. D. Kondiah, Pradeep Kumar, Philemon Ubanako, and Yahya E. Choonara. In the bottom right corner, there is an image of the NanoPhotometer instrument.

In this kick-off issue of this month's Implen NanoPhotometer® Journal Club: novel drug delivery issue, we are exploring the topic of biopolymers which have inimitable potential to revolutionize the biomedical field. Harpe et. al. recently reported in the Journal of Biomedical Materials Research, a novel bioabsorbable suture material consisting of natural biopolymers capable of localized drug delivery was fabricated and coated with a lipid-drug layer for sustained, localized drug release of dexamethasone (DEX). This release profile is suitable for the prevention of IRI after microvascular surgery where immediate, yet sustained anti-inflammatory action is needed,

as well as no-reflow, where extended protection is required. The results reported in this study provide information on a novel, monofilament, absorbable, drug-eluting bioabsorbable suture that, if it reaches the clinical market, can drastically improve microvascular surgery outcomes and decrease the severity and occurrence of IRI and no-reflow after microvascular anastomosis.

The NanoPhotometer® was used in this study to calculate the amount of drug released from the lipid-drug coated bioabsorbable sutures by measuring the absorbance of the solution at $\lambda = 241$. A calibration curve for DEX was constructed by measuring the absorbance of standard solutions with known DEX concentrations. The linear regression equation of the calibration curve in this study was $y = 0.0575x - 0.0299$ ($R^2 = 0.9983$).

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Microneedle Aptamer-Based Sensors for Continuous, Real-Time Therapeutic Drug Monitoring

Yao Wu, Farshad Tehrani, Hazhir Teymourian, John Mack, Alexander Shaver, Maria Reynoso, Jonathan Kavner, Nickey Huang, Allison Furmidge, Andrés Duvvuri, Yuhang Nie, Lori M. Laffel, Francis J. Doyle III, Mary-Elizabeth Patti, Eyal Dassau, Joseph Wang,* and Netzahualcōyotl Arroyo-Currás

In the second issue, we are discussing advancements in the development of wearable and autonomous sensing technologies enabling continuous, real-time monitoring of clinically relevant therapeutics, metabolites, and biomarkers, enabling the ability to continuously monitor the concentration of specific molecules in the body. Wu et al. recently demonstrated in the *Journal of Analytical Chemistry*, the first use of aptamer based microneedle sensor arrays. This platform achieves molecular recognition based on affinity interactions, vastly expanding the scope of molecules that can be sensed. Such technologies could be used to, for example, achieve highly precise and personalized drug therapy via real-time monitoring of patient specific pharmacokinetics, pharmacodynamics, and toxicology, which could dramatically transform the way we study, understand, diagnose, and treat diseases.

All aptamer solutions were diluted to a final concentration of 200 nM prior to electrode functionalization, which was measured via UV-vis spectroscopy employing an Implen NanoPhotometer® NP80.

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An Oral 3D Printed PLGA-Tocopherol PEG Succinate Nanocomposite Hydrogel for High-Dose Methotrexate Delivery in Maintenance Chemotherapy

Pierre P. D. Kondiah, Thankhoe A. Rants'o, Sifiso S. Makhathini, Siphso Mdanda and Yahya E. Choonara

Next, we are covering an improvement in delivery of high-dose methotrexate (MTX), one of the chemotherapeutic agents used to treat a variety of cancers. The combination of toxicity and poor bioavailability of MTX led to the development recently published in the journal of biomedicines by Kondiah et. al. of a novel drug delivery system of a 3D-printed hydrogel-based tablet with methotrexate-loaded nanoparticles for oral delivery with improved bioavailability for MTX that has the potential to overcome the chemotherapeutic challenges that are experienced with conventional therapies. This study demonstrated the effective encapsulation of PLGA-TPGS polymeric nanoparticles into alginate-gelatine hydrogel provides a good insight for future applications in controlled drug release systems.

The NanoPhotometer® NP80 was used in this study for in vitro drug release studies of MTX from the methotrexate-loaded TPGS and PLGA nanoparticles in conditions simulating the stomach and intestines by analyzing the UV absorption of MTX at 303 nm. The NP80 was utilized to determine the maximum wavelength of an MTX and then plot the calibration curve to determine the release profile.

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Peptides vs. Polymers: Searching for the Most Efficient Delivery System for Mitochondrial Gene Therapy

Rúben Faria, Milan Paul, Swati Biswas, Eric Vivès, Prisca Boisguérin, Ângela Sousa and Diana Costa

In the final issue, we are discussing the emerging valuable and promising therapeutic tool of mitochondrial gene therapy for mitochondrial diseases originating from mtDNA mutations. Faria et. al. reported in the journal of pharmaceuticals their work in which they explored the ability of novel polymer- and peptide-based systems for mitochondrial targeting, gene delivery, and protein expression, performing a comparison between them to reveal the most adequate system for mitochondrial gene therapy, leading them to synthesize a novel mitochondria-targeting polymer (polyethylenimine–dequalinium) to load and complex a mitochondrial-gene-based plasmid. This report is a significant contribution to the implementation of mitochondrial gene therapy, instigating further research on the development of peptide-based delivery systems towards clinical translation.

The NanoPhotometer® was used in this work to quantify mRNA.

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