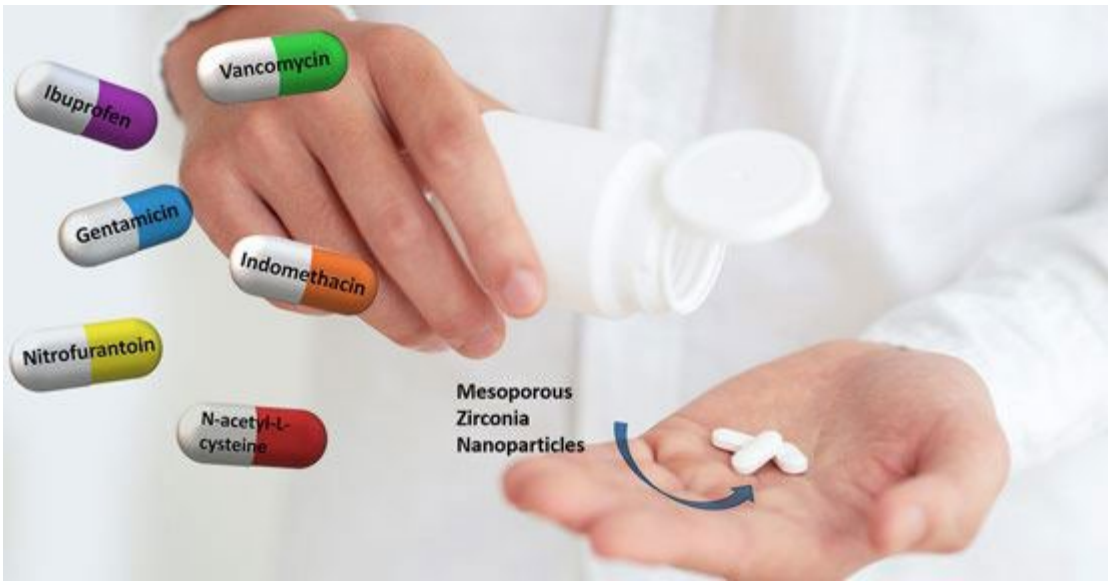
Implen Journal Club | August Issue

Welcome to our August issue of the #Implen #JournalClub in 2021.



Drug delivery systems have been a milestone in medical research in the last twenty years; still representing a key aspect of innovation and evolution in pharmacokinetics and pharmacodynamics. The most common methods to administer drugs include swallowing and injecting. Between them, traditional drugs available now for oral administrations are not always the optimal formulation for achieving systemic absorption. This week's hot-topics: drug discovery issue of Implen's NanoPhotometer® Journal Club features mesoporous zirconia nanoparticles (MZNs), shown

previously to be an ideal candidate for theranostic applications, as a novel drug delivery system to potentially enhance bioavailability due to their high surface area and biocompatibility. Benedetta Leonetti et al. recently published the findings of the investigation on the drug loading, stability, and release efficiencies for MZNs of a wide range of therapeutics including ibuprofen and vancomycin. The NanoPhotometer® was used to detect vancomycin and ibuprofen loading efficiencies, at 280 nm and 265 nm respectively and calculated with the equation Loading content (%) = [initial drug] - [residual drug]/ [MZN] * 100.

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Next, Implen's NanoPhotometer® Journal Club highlights the development and therapeutic potential of novel prodrugs of Cyclic dinucleotides (CDNs), which act as second messengers involved in activation of a pathway that has been shown to have several implications including triggering the immune defense against invading pathogens as well as induction of antitumor immunity. Sensing double-stranded DNA (dsDNA) in cytoplasm is one of the crucial innate immunity mechanisms that protect an organism from pathogens and cell damage. Several sensors of cytosolic dsDNA have been identified, all of which trigger different signaling cascades. Markéta Pimková Polidarová et al. recently described, for the first time in the Journal of Medicinal Chemistry, the synthesis of prodrugs of Cyclic dinucleotides CDNs which were shown to have overall superior activity relative to their parent CDNs as well as rapid and efficient uptake and intracellular metabolism. The NanoPhotometer® N60-Touch was used to measure the concentration of CDNs.

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Next, Implen's NanoPhotometer® Journal explores a novel membrane-lipid therapeutic strategy using membrane active agents (MAAs) in the treatment of Alzheimer's disease. Recent studies indicate that Amyloid-β (Aβ) plaques may be the result as opposed to the cause of neurotoxicity, with Aβ peptides actually being responsible for initiating a cascade leading to neural system failure, neurodegeneration, and cognitive decline. Xingyuan Zou et al. recently published, in the journal of ACS Chemical Neuroscience, the effect of curcumin and homotaurine representing two different types of membrane-active inhibitors on Aβ aggregates. Both curcumin and homotaurine were found to significantly reduce the number of small Aβ aggregates as was confirmed by the decrease of the β-sheet signal using the UV–Vis spectroscopy. Based on their results, it has been shown that membrane active drugs may be as efficient as peptide targeting drugs in inhibiting amyloid aggregation. The NanoPhotometer® NP80 was used to perform full wave scans (200-900 nm) in which Thioflavin T (ThT), the "gold standard" for the detection of Aβ, showed absorption around 410 nm in the presence of β-sheets indicating the formation of Aβ aggregates.

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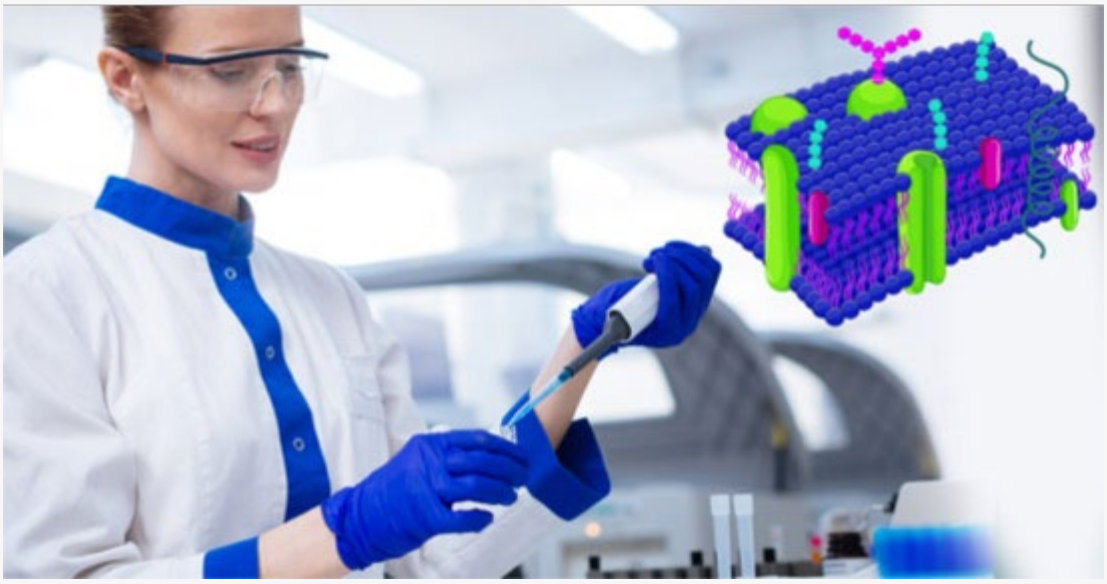

Drug discovery continues with highlighting the therapeutic potential of membrane active agents (MAAs). An important study in understanding membrane-based drug effects to aid in designing novel drugs for various diseases in which the drugs need to interact with or cross through cell membranes and reach certain intracellular targets was recently published in Membranes by Md Ashrafuzzaman of King Saud University; wherein it was shown the antimicrobial peptide gramicidin s (GS) enhances the potency of the chemotherapeutics thiocolchicoside (TCC) and taxol by enhancing adsorption and pore formation in the membrane. The newly patented direct detection method (DDM), which allows for the use of UV-absorption to detect molecules directly at their target site, was utilized to detect the quantitative membrane adsorption of CD molecules without and with the effects of GS. GS effects are found to be consistent with a large number of MAAs suggesting the effects of other agents of this type may also regulate the effects of drugs on the cell membrane. The NanoPhotometer® was used with the direct detection method to perform wavescans for the detection of MAA having specific wavelengths (λDNA= 260, λcolchicine= 243 nm, λtaxol= 227 nm). The resulting absorbance spectra were used to quantify the concentration of MAAs. These concentrations were used to calculate the molarities of both of the lipid-bound and lipid-unbound MAAs.

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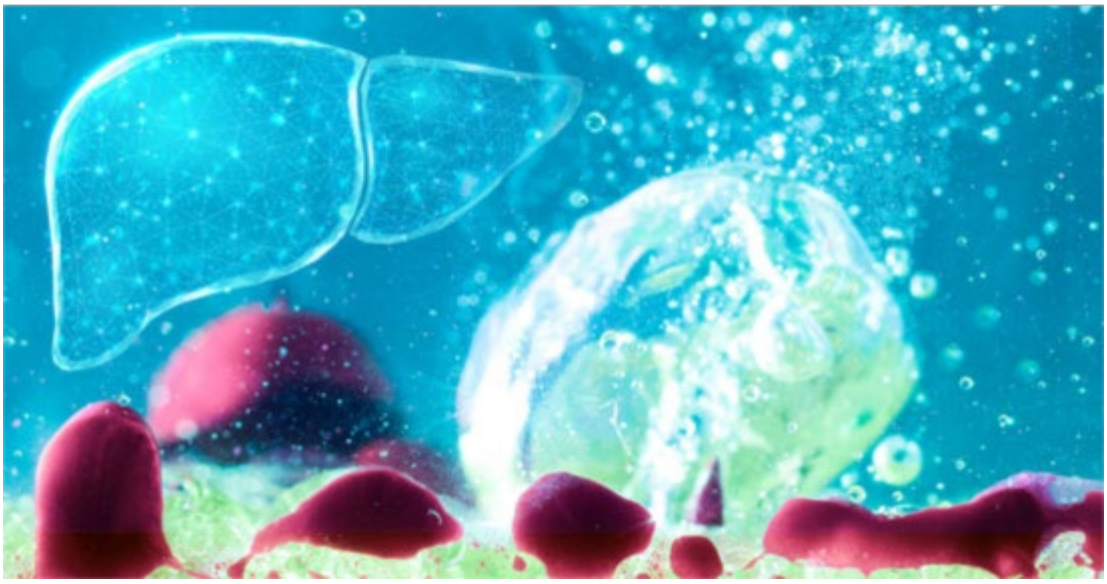

The final article covers the promising antitumor agent EPS364, a Novel Deep-Sea Bacterial Exopolysaccharide, for the treatment of liver cancer. Liver cancer tumors have proven to be highly chemotherapy-resistant tumors with most chemotherapy regimens being severely limited by the underlying liver disease. Given the inferior prognosis, new treatments for liver cancer are urgently needed. Researchers have been exploring the diverse and novel marine ecosystems for the possibility to discover and develop new therapeutic agents with unique mechanisms. In the past few decades, small-molecule compounds from marine organisms have been widely studied for drug use. In this work, Wang et al. purified EPS364, a promising antitumor agent for pharmacotherapy, from a deep-sea cold seep of the South China Sea. EPS364 exhibited a significant antitumor activity inhibiting cancer cell growth and adhesion via targeting the FGF19-FGFR4 signaling pathway, which is an effective cancer target, suggesting that EPS364 is a promising antitumor agent for pharmacotherapy. The NanoPhotometer® was used to detect the UV spectrum of EPS364 from 200–800 nm. The purified EPS364 had no obvious absorption at 260 or 280 nm, indicating the absence of nucleic acids and proteins in EPS364, suggesting that EPS364 is a pure polysaccharide.

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