## TEN BEST PUBLICATIONS
## HIGHLIGHTING IMPORTANT CONTRIBUTIONS

## A. NANOPARTICLE SHAPE BASED SPLEEN TARGETTING

1. **Devarajan PV**., Jindal AB, Patil RR, Mulla F, Gaikwad RV, Samad A. Particle shape: a new design parameter for passive targeting in splenotropic drug delivery. J Pharm Sci.2010;99(6):2576-81. **(Impact Factor: 3.53)**

   *The publication was the first to report role of nanoparticle shape in enabling splenic targetting. The same was confirmed in three animal models namely rodent (rat&mice), rabbit and dog by scintigraphic evaluation wherein asymmetric/irregular Lipomer nanoparticles targetted the spleen. We have captured a video in dog which actually shows high accumulation in the spleen. This paper was cited as cutting-edge research in nanotechnology by the US magazine Scientist.*

2. Patil RR, Gaikwad RV, Samad A, **Devarajan PV**. Role of lipids in enhancing splenic uptake of polymer-lipid (LIPOMER) nanoparticles. J. Biomed. Nanotechnol. 2008; 4(3):359-66. **(Impact factor: 4.52)**

   *This publication was the first to report high spleen targetting by selective Lipomer nanoparticles. This led to the finding of shape related targetting mentioned above. Spleen targetting is very important particularly for spleen resident intracellular infections for instance HIV, tuberculosis, Trypanosomiasis, fungal infections and a host of veterinary infections including zoonotic brucellosis and also theileriosis. Spleen targetting could provide improved therapy of such infections.*

3. Jindal AB, **Devarajan PV**. Asymmetric lipid–polymer particles (LIPOMER) by modified nanoprecipitation: role of non-solvent composition. Int. J. Pharm. 2015;489(1):246-51. **(Impact factor 4.224)**

   *The importance of this publication is the elucidation of why some Lipomer nanoparticles exhibited asymmetric/irregular shape. A scientific explanation was proposed based on Marangoni effect. Moreover this paper presents a simple strategy of modified nanoprecipitation to design asymmetric/irregular nanoparticles. A very innovative approach was employed to explain the same at nanolevel by carrying out experiments at the macro level.*

4. Maithania HV, Mohanty BS, Chaudhari PR, Samad A and **Devarajan PV**., Shape mediated splenotropic delivery of buparvaquone loaded solid lipid nanoparticles. Drug Delivery and Translational Research. 2019: 1-9. **(Impact factor: 3.111)**

   *This publication is important on two counts; i) It demonstrates and confirms shape mediated spleen targetting referred to in the above publications ii) It presents a radical an simple approach called In-Situ nanotechnology to prepare the buparvaquone (BPQ) loaded SLN for targeted spleen delivery. BPQ is a drug used to treat theileriosis a spleen resident infection in cattle. While the SLN enabled efficacy at 1/5$^{th}$ to conventional dose(published), the In situ nanotechnology enabled preparation of BPQ SLN by simple*

*addition of a preconcentrate of BPQ and lipid with stabilizers into Dextrose injection on the farm and shaking to get a ready to inject BPQ SLN. This approach enabled great outreach of the BPQ nanoformulation to the farmer's doorstep. It presents an example of affordable excellence. Interestingly the In-Situ method generated asymmetric BPQ SLN which exhibited splenotropy. The In-Situ Nanotechnology is demonstrated for a number of anticancer drugs and drugs to treat infectious diseases eg: malaria, leishmaniasis and the findings are published.*

## B. SUBLINGUAL BONE TARGETTED NANOFORMULATION

5. Kotak DJ, **Devarajan PV.**, Bone targeted delivery of salmon calcitonin hydroxyapatite nanoparticles for sublingual osteoporosis therapy (SLOT). Nanomedicine: Nanotechnology, Biology and Medicine. 2020; 24:102153. (Impact Factor 6.5)

   *This is an excellent finding which could provide a viable alternative to the injection of Salmon calcitonin (SCT) for osteoporosis. Importantly we demonstrated that although the bioavailability following sublingual administration in rabbits was only ~15%, the bone strength and other efficacy parameters compared with the subcutaneous injection in the ovariectomized rat osteoporosis model. This suggested bone targetting by sublingual delivery of the SCT-HAP nanoparticles and led us to the hypothesis that SCT-HAP nanoparticles were translocated across the sublingual epithelium into the vascular circulation.*

   *We have recently confirmed the same using the imaging flow cytometer and even quantified the intact nanoparticles translocating through porcine sublingual mucosa. Manuscript is in finalization stage*.

## C. SAFE AMPHOTERICIN B NANOFORMULATION BY ALTERING THE AGGREGATED STATE

6. Das S, **Devarajan PV.,** Enhancing safety and efficacy by altering the toxic aggregated state of Amphotericin B in lipidic nanoformulations. Molecular Pharmaceutics. 2020; 23;17(6):2186-95. (Impact Factor 4.321)

   *Amphotericin B (AmB) is a drug of choice for leishmaniasis and gained importance during the pandemic for treating COVID related mucormycosis. A major challenge with AmB is the severe and sometimes fatal renal toxicity, attributed to the aggregated state. We reported an AmB nanoformulation developed using scientific principles to ensure that AmB is in the safe superaggregated/ monomeric form. We have demonstrated enhanced efficacy and safety in vitro in amastigotes. Considering the raw materials used are affordable this is an important development of an affordable AmB nanoformulation with great outreach.*

## D. NANOMEDICINE FOR INFECTIOUS DISEASES

7. Dawre SS, Pathak S, Sharma S., and **Devarajan PV.**, Enhanced Antimalalarial Activity of A Prolonged Release In Situ Gel of Arteether−Lumefantrine In A Murine Model, European Journal of Pharm. Biopharm. 2018;123:95-107. **(Impact factor 4.491)**

*This publication presents for the first time single dose therapy for malaria. Considering that one of the reasons for incomplete cure in malaria is patient non compliance due to severe drug side effects, this finding represents an exciting development. High efficacy at low dose without recrudescence is demonstrated in the Peter's 4 day suppressive test and the clinical simulation model of P. berghei in mice. The technology is licensed to industry and is under active development.*

8. Bachhav SS, Dighe VD, and **Devarajan PV.**, Exploring Peyer's Patch Uptake as a Strategy for Targeted Lung Delivery of Polymeric Rifampicin Nanoparticles, Mol. Pharm. 2018; 15 (10):4434-4445. **(Impact factor 4.556)**

   *The importance of this publication is demonstration of lung targetting by oral administration. The same was achieved by facilitating lymph mediated nanoparticle absorption. Pulmonary delivery or direct lung delivery permits administration of only small drug doses. In contrast the approach we proposed through Peyer's patches permits high oral dose administration and proposes a practical approach for tuberculosis which requires high doses and prolonged therapy. While Peyers patch uptake is reported, exploiting the same for lung delivery is proposed by our group by including in the nanoparticles a mucoadhesive polymer Gantrez. This has important implications for lung targetting by oral delivery for treatment of Covid-19 using drugs like favipiravir, ivermectin etc.*

## E. IN-SITU NANOTECHNOLOGY FOR CANCER

9. John R, Dalal B, Shankarkumar A, Devarajan PV. Innovative Betulin Nanosuspension exhibits enhanced anticancer activity in a Triple Negative Breast Cancer Cell Line and Zebrafish angiogenesis model. International Journal of Pharmaceutics. 2021; 22:120511. (Impact factor: 5.871)

   *This publication reports a nanosuspension of a natural anticancer agent prepared using the revolutionary In-Situ nanotechnology mentioned in Reference 4 above. In-Situ Nanotechnology in an unbelievably simple technology for preparation of nanosuspension/ nanoparticles. It bypasses the technological and stability challenges of conventional nanotechnology. It needs no specialised or high cost infrastructure and is prepared and used immediately on-site, and hence overcomes stability challenges. A monophasic preconcentrate of drug, and stabilizers in a pharmaceutically accepted solvent is added to an aqueous medium to enable spontaneous and instantaneous generation of drug nanosuspension which can be administered orally. Importantly prepared by this simple In-Situ nanotechnology, betulin nanosuspension showed excellent enhancement in anticancer activity in the resistant triple negative breast cancer cell line when evaluated by various studies including the zebrafish angiogenesis model. This confirms and validates the application of this novel technological approach in nanomedicine.*

10. Joshi HA, Patwardhan RS, Sharma D, Sandur SK, Devarajan PV., Pre-clinical Evaluation of An Innovative Oral Nano-formulation of Baicalein for Modulation of Radiation Responses. International Journal of Pharmaceutics. 2020; 24:120181. (Impact factor: 5.871)

    *This publication reports solid lipid nanoparticles of a natural anticancer agent prepared using the revolutionary In-Situ nanotechnology mentioned in Reference 4 & 9 above as a*

*radioprotective agent. The nano-formulation revealed superior efficacy and also served as a radio sensitizer for lung cancer cells to effect improved therapy. The importance of this study is exploiting the In-Situ nanotechnology effectively to develop an efficacious nano-formulation of a drug with limited stability, which would create huge challenges through conventional nanotechnology.*

While innovation is a hall mark of all the above publications, I wish to highlight that our mantra is synergising innovation with affordable excellence, and also integration of science with technology to develop relevant interventions with high social outreach. The in situ nanotechnology is already demonstrated and licensed to industry.