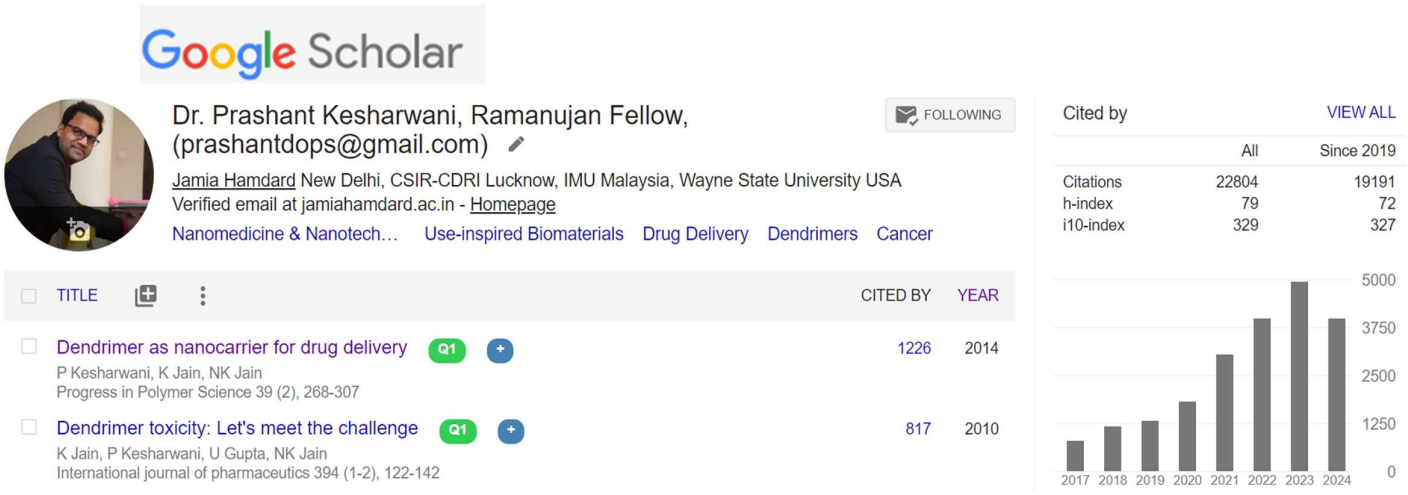
LIST OF TEN BEST PAPERS OF THE CANDIDATE, HIGHLIGHTING THE IMPORTANT DISCOVERIES (Dr. Prashant Kesharwani):



1. N. Parveen, A. Sheikh, N. Molugulu, S. Annadurai, S. Wahab, P. Kesharwani*, Drug permeation enhancement, efficacy, and safety assessment of azelaic acid loaded SNEDDS hydrogel to overcome the treatment barriers of atopic dermatitis, Environ. Res. 236 (Nov 2023) 116850. https://doi.org/10.1016/J.ENVRES.2023.116850. (Impact factor 7.7)

Summary: Atopic dermatitis is one of the most widespread chronic inflammatory skin conditions that can occur at any age, though the prevalence is highest in children. The purpose of the current study was to prepare and optimize the azelaic acid (AzA) loaded SNEDDS using Pseudo ternary phase diagram, which was subsequently incorporated into the Carbopol 940 hydrogel for the treatment of atopic dermatitis. The composition was evaluated for size, entrapment efficiency, in vitro, ex vivo, and in vivo studies. The polydispersity index of the optimized preparation was found to be less than 0.5, and the size of the distributed globules was found to be 151.20 ± 3.67 nm. The SNEDDS hydrogel was characterized for pH, viscosity, spreadability, and texture analysis. When compared to the marketed formulation, SNEDDS hydrogel was found to have a higher rate of permeation through the rat skin. In addition, a skin irritation test carried out on experimental animals showed that the SNEDDS formulation did not exhibit any erythematous symptoms after a 24-h exposure. In conclusion, the topical delivery of AzA through the skin using SNEDDS hydrogel could prove to be an effective approach for the treatment of atopic dermatitis.

2. U. Rehman, A. Sheikh, A. Alsayari, S. Wahab, P. Kesharwani*. Hesperidin-loaded cubogel as a novel therapeutic armamentarium for full-thickness wound healing. Colloids and Surfaces B: Biointerfaces. Volume 234, February 2024, 113728 https://doi.org/10.1016/j.colsurfb.2023.113728 (Impact factor 5.4)

Summary: Wounds are a physical manifestation of injury to the skin causing it to rupture or tear. The process of wound healing naturally restores skin integrity while minimizing the extent of the damage. Hesperidin (HPN) is a natural polyphenolic flavonoid and is effective in treating wounds due to its ability to reduce inflammation and stimulate angiogenesis. However, its use is limited by its poor physicochemical attributes such as poor solubility in water. Recently, nanoparticles, particularly Cubosomes, are found to be promising candidates for advancing wound-healing therapies, owing to their unique properties. The present study was conducted to develop a hydrogel system based on Cubosomes encapsulating HPN (HPN-Cubogel), with the potential to mitigate full-thickness wounds. The therapeutic efficacy of the formulation assessed in the animal model showed that the HPN-Cubogel formulation group exhibited a wound closure rate of 98.96 ± 1.50% after 14 days post-wounding

compared to 89.12 ± 2.6% in the control group suggesting superior wound contraction activity. Collagen synthesis was superior in the formulation compared to the control group, as determined through MT staining. In summary, the HPN-Cubogel formulation was found to be the most effective in enhancing full-thickness wound healing.

3. Fatima M, Almalki WH, Khan T, Sahebkar A, Kesharwani P*. Harnessing the Power of Stimuli-Responsive Nanoparticles as an Effective Therapeutic Drug Delivery System. Volume36, Issue24. June 13, 2024. 2312939. https://doi.org/10.1002/adma.202312939 (Impact factor 27.4)

Summary: The quest for effective and reliable methods of delivering medications, with the aim of improving delivery of therapeutic agent to the intended location, has presented a demanding yet captivating field in biomedical research. The concept of smart drug delivery systems is an evolving therapeutic approach, serving as a model for directing drugs to specific targets or sites. These systems have been developed to specifically target and regulate the administration of therapeutic substances in a diverse array of chronic conditions, including periodontitis, diabetes, cardiac diseases, inflammatory bowel diseases, rheumatoid arthritis, and different cancers. Nevertheless, numerous comprehensive clinical trials are still required to ascertain both the immediate and enduring impacts of such nanosystems on human subjects. This research delves into the benefits of different drug delivery vehicles, aiming to enhance comprehension of their applicability in addressing present medical requirements. Additionally, it touches upon the current applications of these stimuli-reactive nanosystems in biomedicine and outlines future development prospects.

4. S.A. Hazari, A. Sheikh, M.A.S. Abourehab, A.S. Tulbah, P. Kesharwani*, Self-assembled Gallic acid loaded lecithin-chitosan hybrid nanostructured gel as a potential tool against imiquimod-induced psoriasis, Environ. Res. 234 (Oct 2023) 116562. https://doi.org/10.1016/J.ENVRES.2023.116562. (Impact factor 7.7)

Summary: Increased thickness of the skin and hyperproliferation of keratinocyte cell is the main obstacle in the treatment of psoriasis. Gallic Acid (GA) has shown efficacious results against the hyperproliferation of keratinocytes while lipid-polymer loaded hybrid nanoparticles (LPHNs) have an edge over lipidic and polymeric nanoparticles considering drug loading, controlled release, stability, and retention. The LPHNs were optimized using Box-Behnken method and was further characterized by FTIR, DSC and Zetasizer. The optimized preparation demonstrated a size of 170.5 ± 0.087 nm and a PDI of 0.19 ± 0.0015, respectively. The confocal study has suggested that the hybrid nanosystem enhanced the drug penetration into the deeper layer with a higher drug release of 79 ± 0.001% as compared to the gallic acid-loaded gel. In addition, the formulation significantly reduced PASI score and splenomegaly without causing any serious irritation. The morphological study of the spleen suggested that the prepared formulation has well controlled the disease compared to the marketed formulation while maintaining a normal level of immune cells after treatment. Hence GALPHN could be accepted as one of the excellent vehicles for the topical conveyance of GA (gallic acid) due to enhanced penetration, and good retention, along with fewer side effects and higher efficacy of the GALPHN gel against imiquimod (IMQ) induced psoriasis.

5. Mahor A, Prajapati SK, Verma A, Gupta R, Iyer AK, Kesharwani P*. Moxifloxacin loaded gelatin nanoparticles for ocular delivery: Formulation and in-vitro, in-vivo evaluation. J Colloid Interface Sci. Dec 2016;483:132-8. (Impact factor 9.4).

Summary: The current research focuses on developing positively charged gelatin nanoparticles loaded with moxifloxacin for its effective ocular delivery and controlled release in corneal eye layer. We selected type A gelatin because of its biodegradable and non-toxic nature as the polymer of choice for fabricating the nanoparticles by a modified two step desolvation technique. The produced nanoparticles were positively charged (+24 ± 0.12 mV) with a narrow particle size of 175 ± 1.11 nm as measured by dynamic light scattering (DLS). The in-vitro drug release from the nanoformulations exhibited a burst effect in the first hour followed by a controlled release of the drug for the subsequent 12 h. The

Korsmeyer-Peppas model showed better linearity and the formulations displayed non-Fickian drug release pattern. The optimized formulation was assessed for its utility as an anti-bacterial agent and its effectiveness was tested on the corneal eye surface of rabbits. The in-vivo tolerance tests revealed that the drug loaded nano-formulations was non-irritant to the ocular tissues indicating its safety. The in-vivo anti-bacterial activity of the nanosuspension was more effective against S. aureus than the commercially market product, MoxiGram®. Microbiological efficacy assessed against B. subtilus using cup-plate method suggested that our fabricated nanosuspension possess better anti-microbial activity as compared to the commercial agent, MoxiGram® revealing promising potentials for the currently developed gelatin based nanoformualtions.

6. Kesharwani P*, Choudhury H, Meher JG, Pandey M, Gorain B. Dendrimer-entrapped gold nanoparticles as promising nanocarriers for anticancer therapeutics and imaging. Progress in Materials Science, June 2019:103:484-508 (IMPACT FACTOR: 48.580).
Summary: Theranostic nanotherapeutic strategy has been widely emphasized now a day to develop next-generation nanomedicine. Dendrimer-entrapped gold nanoparticles (DE-Au-NP) have acquired emerging application in therapeutic, imaging as well as in theranostics sciences. DE-Au-NP decorated with a specific ligand for cancer cells could deliver contrast agents at target sites for imaging as well as chemotherapeutics for anticancer activity. Entrapped Au in DE-Au-NP complex could serve as an excellent contrast agent for CT imaging with better signal intensity to identify initial stages of cancer, whereas its photothermal effect can kill cancerous cells effectively. Although, reported nonspecific binding of DE-Au-NP due to free amine groups and associated toxicities of dendrimer complex could be minimized through PEGylation or acetylation of such surface amines. Recent research on gene delivery also revealed DE-Au-NP as an active tool to deliver plasmids to cancer cells to express/suppress particular protein(s) to combat against cancer.

7. P. Kesharwani*, A. Sheikh, M.A.S. Abourehab, R. Salve, V. Gajbhiye, A combinatorial delivery of survivin targeted siRNA using cancer selective nanoparticles for triple negative breast cancer therapy, J. Drug Deliv. Sci. Technol. 80 (February 2023) 104164. https://doi.org/10.1016/J.JDDST.2023.104164. (Impact factor: 4.5)
Summary: Triple-negative breast cancer (TNBC) is one major type of cancer for which there has been no effective therapy to date. An important reason for it being the lack of expression of important receptors such as estrogen, progesterone and human epidermal growth factor receptor-2 (HER-2). There is no FDA approved targeted treatment available till date leading to high rate of proliferation and multi-drug resistance. Here, we developed doxorubicin (Dox) (chemotherapeutic) and lycopene (LCP) (chemo-protective) loaded polyamidoamine (PAMAM) dendrimer as an extensive anti-survivin siRNA nanocarrier (DLP/siRNA). The developed dendriplex was characterized by FTIR, DSC, NMR, Zetasizer and AFM. In vitro study depicted an elevated apoptosis rate and tumor cell uptake rate for this formulated dendriplex. Additionally, the gel retardation technique confirmed the siRNA-protecting ability of dendrimer from nuclease. Most importantly, the silencing of survivin siRNA as observed in the cancer cell population with the combined effect of chemotherapeutic and chemo-protective agents inhibited the cancer cell stemness and suppressed the tumor growth without causing cardiac toxicity in the TNBC xenograft model. Altogether, this combinatorial approach of gene delivery and chemotherapy with an application of chemo-protective effect suggests an enhanced therapeutic efficacy in the treatment of triple-negative breast cancer.

8. Kesharwani P, Jain K, Jain NK. Dendrimer as nanocarrier for drug delivery. Prog Polym Sci, Feb 2014;39:268-307. (IMPACT FACTOR 29.190)
Summary: Dendrimers are novel three dimensional, hyperbranched globular nanopolymeric architectures. Attractive features like nanoscopic size, narrow polydispersity index, excellent control over molecular structure, availability of multiple functional groups at the periphery and cavities in the interior distinguish them amongst the available polymers. Applications of dendrimers in a large variety

of fields have been explored. Drug delivery scientists are especially enthusiastic about possible utility of dendrimers as drug delivery tool. Terminal functionalities provide a platform for conjugation of the drug and targeting moieties. In addition, these peripheral functional groups can be employed to tailor-make the properties of dendrimers, enhancing their versatility. The present research highlights the contribution of dendrimers in the field of nanotechnology with intent to aid the researchers in exploring dendrimers in the field of drug delivery.

9. Kesharwani P, Banerjee S, Padhye S, Sarkar FH, Iyer AK. Hyaluronic acid engineered nanomicelles loaded with 3, 4-difluorobenzylidene curcumin for targeted killing of CD44+ stem-like pancreatic cancer cells. Biomacromolecules, Aug 2015;16:3042–53. (Impact factor 6.988)

Summary: Cancer stem-like cells (CSLCs) play a pivotal role in acquiring multidrug resistant (MDR) phenotypes. It has been established those pancreatic cancers overexpressing CD44 receptors (a target of hyaluronic acid; HA) is one of the major contributors for causing MDR. Therefore, targeted killing of CD44 expressing tumor cells using HA based active targeting strategies may be beneficial for eradicating MDR-pancreatic cancers. Here, we report the synthesis of a new HA conjugate of copoly(styrene maleic acid) (HA-SMA) that could be engineered to form nanomicelles with a potent anticancer agent, 3,4-difluorobenzylidene curcumin (CDF). The anticancer activity of CDF loaded nanomicelles against MiaPaCa-2 and AsPC-1 human pancreatic cancer cells revealed dose-dependent cell killing. Results of cellular internalization further confirmed better uptake of HA engineered nanomicelles in triple-marker positive (CD44+/CD133+/EpCAM+) pancreatic CSLCs compared with triple-marker negative (CD44-/CD133-/EpCAM-) counterparts. More importantly, HA-SMA-CDF exhibited superior anticancer response toward CD44+ pancreatic CSLCs. Results further confirmed that triple-marker positive cells treated with HA-SMA-CDF caused significant reduction in CD44 expression and marked inhibition of NF-κB that in-turn can mitigate their proliferative and invasive behavior. Conclusively, these results suggest that the newly developed CD44 targeted nanomicelles may have great implications in treating pancreatic cancers including the more aggressive pancreatic CSLCs.

10. Kesharwani P, Tekade RK, Jain NK. Generation dependent cancer targeting potential of poly(propyleneimine) dendrimer. Biomaterials. July 2014;35(21):5539-48. (Impact factor 15).

Summary: Dendrimer-mediated delivery of bioactive is a successful and widely explored concept. This paper desribes comparative data pertaining to generation dependent cancer targeting propensity of Poly(propyleneimine) (PPI) dendrimers. This debut report reportsthe drug targeting and antciancer potential of different dendrimer generations. PPI dendrimers of different generations (3.0G, 4.0G and 5.0G) were synthesized and loaded with Melphalan. Results from loading, hemolysis, hematologic, cytotoxicty and flow cytometry assay depicted that as the generation of dendrimer increased from fourth to fifth, the only parameter i.e. toxicty is increased exponentionally. However, others parameters, i.e. loading, sustained release behavior, and targeting efficacy increased negligibly. Kaplan–Meier survival curves clearly depicted comparable therapeutic potential of PPI4M with PPI5M. In vivo investigations in Balb/c mice again favored 4.0G PPI dendrimer to be preferable nanocarrier for anticancer drug delivery owing to analogous anticancer potential. The outcomes of the investigation evidently project 4.0G PPI dendrimer over 3.0G and 5.0G dendrimer in respect of its drug delivery benefit as well as superior biocompatibility. Thus, much against the common belief, 4.0G PPI dendrimers may be considered to be optimum in respect of drug delivery precluding the use of much more toxic 5.0G PPI dendrimer, which offers no benefit over 4.0G.