

List of ten best papers of the candidate, highlighting the important discoveries:

1. **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 describes comparative data pertaining to generation dependent cancer targeting propensity of Poly(propyleneimine) (PPI) dendrimers. This debut report reports the drug targeting and anticancer 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, cytotoxicity and flow cytometry assay depicted that as the generation of dendrimer increased from fourth to fifth, the only parameter i.e. toxicity is increased exponentially. 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.

2. **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.

3. **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- κ B 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.

4. **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 review 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.

5. **Kesharwani P, Banerjee S, Padhye S, Sarkar FH, Iyer AK. Parenterally administrable nanomicelles of Difluorobenzylidene curcumin difluorinated for treating pancreatic cancers. Colloids Surf. B Biointerfaces, Aug 2015;132:138–45. (Impact factor 5.268)**

Summary: Pancreatic cancer remains one of the most devastating diseases in terms of patient mortality rates for which current treatment options are very limited. 3,4-Difluorobenzylidene curcumin (CDF) is a nontoxic analog of curcumin (CMN) developed in our laboratory, which exhibits extended circulation half-life, while maintaining high anticancer activity and improved pancreas specific accumulation in vivo, compared with CMN. CDF however has poor aqueous solubility and its dose escalation for systemic administration remains challenging. We have engineered self-assembling nano-micelles of amphiphilic styrene-maleic acid copolymer (SMA) with CDF by non-covalent hydrophobic interactions. The SMA-CDF nano-micelles were characterized for size, charge, drug loading, release, serum stability, and in vitro anticancer activity. The SMA-CDF nano-micelles exhibited tunable CDF loading from 5 to 15% with excellent aqueous solubility, stability, favorable hemocompatibility and sustained drug release characteristics. The outcome of cytotoxicity testing of SMA-CDF nano-micelles on MiaPaCa-2 and AsPC-1 pancreatic cancer cell lines revealed pronounced antitumor response due to efficient intracellular trafficking of the drug loaded nano-micelles. Additionally, the nano-micelles are administrable via the systemic route for future in vivo studies and clinical translation. The currently developed SMA based nano-micelles thus portend to be a versatile carrier for dose escalation and targeted delivery of CDF, with enhanced therapeutic margin and safety.

6. **P. Kesharwani*, R. Ma, L. Sang, M. Fatima, A. Sheikh, M.A.S. Abourehab, N. Gupta, Z.-S. Chen, Y. Zhou, Gold nanoparticles and gold nanorods in the landscape of cancer therapy, Mol.**

Cancer 2023 221. 22 (21 June 2023) 1–31. <https://doi.org/10.1186/S12943-023-01798-8>. (Impact factor: 41.444)

Summary: Cancer is a grievous disease whose treatment requires a more efficient, non-invasive therapy, associated with minimal side effects. Gold nanoparticles possessing greatly impressive optical properties have been a forerunner in bioengineered cancer therapy. This theranostic system has gained immense popularity and finds its application in the field of molecular detection, biological imaging, cancer cell targeting, etc. The photothermal property of nanoparticles, especially of gold nanorods, causes absorption of the light incident by the light source, and transforms it into heat, resulting in tumor cell destruction. This review describes the different optical features of gold nanoparticles and summarizes the advance research done for the application of gold nanoparticles and precisely gold nanorods for combating various cancers including breast, lung, colon, oral, prostate, and pancreatic 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: 5.062)**

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. **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 8.3)**

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 $79 \pm 0.001\%$ 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.

9. 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 8.3)

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.

10. 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 9.9).

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 ($+24 \pm 0.12$ 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. subtilis* 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 nanoformulations.