

List of Important Papers and their Highlights

1. Intranasal delivery of chitosan decorated PLGA core /shell nanoparticles containing flavonoid to reduce oxidative stress in the treatment of Alzheimer's disease

(Journal Name: Journal of Drug Delivery Science and Technology)

(Impact Factor: 3.981)

Curcumin (Cur), an antioxidant flavonoid has demonstrated high efficiency in attenuating oxidative stress in Alzheimer's disease (AD). Nevertheless, despite of its therapeutic potential, its clinical applications are hindered due to low solubility and low bioavailability and first-pass metabolism. Thus, we fabricated Cur encapsulated chitosan functionalized PLGA core/shell NPs (CH@Cur-PLGA C/S NPs) and administered via intranasal route. Research also include comparative study of PLGA NPs (core) and CH@Cur-PLGA C/S NPs (C/S NPs) to investigate effect of CH coating over PLGA NPs on therapeutic efficacy, cellular uptake and stability. Fabricated NPs were extensively characterized and confirmed Cur encapsulation with 75% of entrapment efficiency and particle size in the range of 200 nm. TEM analysis confirmed uniform coating of CH over PLGA NPs. Release and permeation study demonstrated sustained release and enhanced permeation through nasal mucosa. Cellular uptake mechanism showed caveolae-mediated-enhance endocytosis of NPs. In-vitro BBB-co-culture model exhibited efficient passage for C/SNPs. Antioxidant assay demonstrated significant ROS scavenging activity of C/ SNPs. In-vivo toxicity showed insignificant toxicity. Bio-distribution of C/S NPs was higher in brain following intranasal route. Photo and thermal stability confirmed protection of Cur by C/SNPs. Obtained results demonstrate potential application of C/SNPs for reducing oxidative stress in brain for effective AD treatment.

2. Cationic biopolymer functionalized nanoparticles encapsulating lutein to attenuate oxidative stress in effective treatment of Alzheimer's disease: A non-invasive approach

(Journal Name: Journal of Drug Delivery Science and Technology)

(Impact Factor: 5.875)

Present investigation explores cationic biopolymer core/shell nanoparticles (Chitosan@PLGA C/SNPs) for delivering carotenoids to brain via intranasal route for suppressing oxidative stress in Alzheimer's disease (AD). The prepared C/SNPs exhibited particle size less than 150 nm with more than 80% of entrapment efficiency. Surface morphology confirmed uniform coating of shell (chitosan) over core PLGA NPs and suggested spherical nature and homogenous dispersion of C/SNPs. In-vitro release study demonstrated sustained release of lutein while C/ SNPs permeation enhancement was confirmed by ex-vivo diffusion study. The study also investigated effect of cationic-shell with respect to anionic-core NPs on biocompatibility, cellular uptake, uptake mechanism, reactive oxygen species (ROS) generation, ROS scavenging activity, blood-brain-barrier (BBB) permeation. The cellular uptake revealed enhanced internalization of

nanoparticles via caveolae-mediated endocytosis. In-vitro co-culture model of BBB demonstrated efficient passage for C/SNPs through BBB. Antioxidant assay demonstrated significant ROS scavenging activity of C/SNPs. In-vivo pharmacokinetic and bio-distribution was performed along with in-vivo toxicity and stability. In-vivo toxicity demonstrated absence of any significant toxicity. Photo and thermal stability confirmed protection of lutein by C/SNPs. C/SNPs were highly deposited in brain following intranasal route. The obtained results demonstrate the potential application of cationic C/SNPs for attenuating oxidative stress in brain for effective AD therapy.

3. Intranasal Delivery of Nanotherapeutics/ Nanobiotherapeutics for the Treatment of Alzheimer's Disease: A Proficient Approach

(Journal Name: Critical Reviews in Therapeutic Drug Carrier System)

(Impact Factor: 4.889)

Therapeutics and biotherapeutics-based fabrication of nanoparticles has fascinated scientists since the past two decades and exciting challenges have been surmounted. Particular interest has been paid to the exploitation of functionalized nanocarriers in the treatment of Alzheimer's disease (AD) using nasal route. Development of various material-based nanocarriers is a common approach to obtain advanced drug delivery systems possessing the ability to follow intranasal (IN) route for brain targeting, which would ultimately ameliorate the effect of AD. This review highlights the various pathological theories for AD along with their controversies. This work intends to provide a thorough, up-to-date, and holistic discussion on various pathways for nose-to-brain delivery and different formulation factors impacting on nasal absorption. The various material properties and their engineered nanocarriers as a smart delivery system, including synergistic effect of therapeutic/biotherapeutic agent in IN delivery as well as in AD therapy have been discussed. This review also emphasizes toxicity, especially neurotoxicity concerns pertaining to drug delivery systems.

4. Design, optimization and in-vitro study of folic acid conjugated-chitosan functionalized PLGA nanoparticle for delivery of bicalutamide in prostate cancer

(Journal Name: Powder Technology)

(Impact Factor: 5.134)

The present investigation explores the use of folic acid (FA)-conjugated chitosan (CS)-functionalized poly (D,L-lactide-co-glycolide) (PLGA) nanocarriers for treatment of prostate cancer. A folic acid–chitosan conjugate was prepared to coat nanoparticles (NPs). Bicalutamide (BCL)-loaded nanoparticles were prepared using the nanoprecipitation method under a Box–Behnken-RSM design and characterized through MPS, PDI, ZP, SEM, PXRD, DSC, in vitro release, in vitro cytotoxicity, protein adsorption, hemolysis and stability studies. The MPS, ZP, %EE and %DL of the BCL-loaded FA conjugated CS-functionalized PLGA NPs (CPN)

formulation were 206.9 nm, +21.7 mV, 87.11% and 9.37%, respectively. The drug release of the optimized BCL-loaded CPN was found to be $101.27 \pm 1.61\%$ at 120 h. The IC₅₀ value of the optimized coated batch was 80 µg/ml, as compared with a value of 80 µg/ml for the BCL suspension, determined through a cytotoxicity assay. DSC, FTIR and PXRD studies confirmed sufficient drug entrapment along with amorphous behavior of the drug in optimized formulations. Hemolytic studies revealed that the BCL-loaded CPN was stable in blood. The stability data revealed that the CPN was stable in a phosphate buffer (pH 7.4). The CPN was also stable in short term studies carried out according to ICH Q1A (R2) guidelines. It can be concluded from all these studies that FA conjugated CS functionalized PLGA NPs are safe and stable, so may be useful in cancer therapy.

5. Box–Behnken study design for optimization of bicalutamide-loaded nanostructured lipid carrier: stability assessment

(Journal Name: Pharmaceutical Development and Technology)

(Impact Factor: 3.133)

Bicalutamide (BCM) is an anti-androgen drug used to treat prostate cancer. In this study, nanostructured lipid carriers (NLCs) were chosen as a carrier for delivery of BCM using Box–Behnken (BB) design for optimizing various quality attributes such as particle size and entrapment efficiency which is very critical for efficient drug delivery and high therapeutic efficacy. Stability of formulated NLCs was assessed with respect to storage stability, pH stability, hemolysis, protein stability, serum protein stability and accelerated stability. Hot high-pressure homogenizer was utilized for formulation of BCM-loaded NLCs. In BB response surface methodology, total lipid, % liquid lipid and % soya lecithin was selected as independent variable and particle size and %EE as dependent variables. Scanning electron microscopy (SEM) was done for morphological study of NLCs. Differential scanning calorimeter and X-ray diffraction study were used to study crystalline and amorphous behavior. Analysis of design space showed that process was robust with the particle size less than 200nm and EE up to 78%. Results of stability studies showed stability of carrier in various storage conditions and in different pH condition. From all the above study, it can be concluded that NLCs may be suitable carrier for the delivery of BCM with respect to stability and quality attributes.

6. Stimuli responsive and receptor targeted iron oxide based nanoplateforms for multimodal therapy and imaging of cancer: Conjugation chemistry and alternative therapeutic strategies

(Journal Name: Journal of Controlled Release)

(Impact Factor: 9.997)

Cancer being one of the most precarious and second most fatal diseases evokes opportunities for multimodal delivery platforms which will act synergistically for efficient cancer treatment.

Multifunctional iron oxide magnetic nanoparticles (IONPs) are being studied for few decades and still attracting increasing attention for several biomedical applications owing to their multifunctional design and intrinsic magnetic properties that provide a multimodal theranostic platform for cancer therapy, monitoring and diagnosis. The review article aims to provide brief information on various surface chemistries involved in modulating IONPs properties to exhibit potential therapy in cancer treatment. The review addresses structural, magnetic, thermal and optical properties of IONPs which aids in the fabrication of efficient multimodal nanoplatform in cancer therapy. The review discussed the pharmacokinetics of IONPs and attributes influencing them. This review inculcates recent advancements in therapies, focused on tumor-microenvironment-responsive and targeted therapy along with their eminent role in cancer diagnosis. The concept of stimuli-responsive including endogenous, exogenous and dual/ multi stimuli-based delivery platform demonstrated significantly enhanced anticancer therapy. Several therapeutic approaches viz. chemotherapy, radiotherapy, immunotherapy, hyperthermia, gene therapy, sonodynamic therapy, photothermal, photodynamic-based therapy along with biosensing and several toxicity aspects of IONPs have been addressed in this review for effective cancer treatment.

7. Surface architected black phosphorous nanoconstructs based smart and versatile platform for cancer theranostics

(Journal Name: Coordination Chemistry Reviews)

(Impact Factor: 22.315)

Black Phosphorous has recently gained the attention in the field of 2D nanomaterials owing to its exceptional structure and properties. Specifically, its features like drug loading efficiency, biocompatibility, optical, mechanical, electrical, thermal and phototherapeutic properties contribute to its rising demand as potential alternative to the graphene-based 2D nanomaterials in biomedical applications. Though the BP's outlook appears promising, its practical applicability is highly challenging. In this review we have discussed the different strategies for synthesis of BP and then briefed its unique properties which renders it a potential platform for the biomedical application. We then discuss the importance of heterogeneous doping on improving the stability of BP against chemical degradation and enhancing its photoelectric properties. Meanwhile, BP-based nanoconjugates, stimuli responsive nanoplatforms, therapeutic, imaging and biosensing platforms are the domains of special and comprehensive interest for versatile biomedical applications of BP. The physicochemical interactions at the nano-bio interface like protein corona formation on the surface on nanoparticles due to interaction with the plasma proteins and others play a crucial role in the biological effects of BP. Hence, we have also discussed the recent studies on interactions between Black phosphorus based nanoconstructs with various biological molecules. Further, it is vital to consider the fact that, though biocompatible, BP-nanomaterials can induce inflammatory responses and exhibit toxicity in dose and time dependant manner. Therefore, we have briefed the biodegradation and toxicological aspects of

BP to enlighten the readers about the safety and toxicity of black phosphorous. The future developments of this 2D nanomaterial will not only serve as a boon for oncology, but also functions as a potential nanoplatform for other biomedical applications.

8. Molybdenum-based hetero-nanocomposites for cancer therapy, diagnosis and biosensing application: Current advancement and future breakthroughs

(Journal Name: Journal of Controlled Release)

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In recent years, there have been significant advancements in the nanotechnology for cancer therapy. Even though molybdenum disulphide (MoS₂)-based nanocomposites demonstrated extensive applications in biosensing, bioimaging, phototherapy, the review article focusing on MoS₂ nanocomposite platform has not been accounted for yet. The review summarizes recent strategies on design and fabrication of MoS₂-based nanocomposites and their modulated properties in cancer treatment. The review also discussed several therapeutic strategies (photothermal, photodynamic, immunotherapy, gene therapy and chemotherapy) and their combinations for efficient cancer therapy along with certain case studies. The review also inculcates various diagnostic techniques viz. magnetic resonance imaging, computed tomography, photoacoustic imaging and fluorescence imaging for diagnosis of cancer.

9. Heterogeneous surface architected metal-organic frameworks for cancer therapy, imaging, and biosensing: A state-of-the-art review

(Journal Name: Coordination Chemistry Reviews)

(Impact Factor: 22.315)

With recent progress in inorganic material based nanoplatforms for cancer therapy and imaging, multiple nano vehicles have been developed and evaluated. These recent advancements in material science led to the development of metal organic frameworks (MOFs) and nano MOFs (nMOFs) as the potential and versatile delivery platforms for cancer theranostic. With a vast amount of ongoing research on MOFs, various surface architected MOFs for with variable properties have been developed and tested. The concept of subcellular targeted therapy of cancer has also been employed using MOFs which demonstrated significantly enhanced anticancer therapy. These MOFs have been developed in a way to provide them stimuli-responsive drug release property which can be utilized for externally guided therapy of cancer. Apart from cellular and subcellular targeted platforms and stimuli-responsive platforms, MOFs have also been explored in the field of bioimaging and biosensing. Multiple types of biosensing platforms based on MOFs and nMOFs have been proposed for biosensing of biomolecules related to cancer for sensing and early detection. The bioimaging probes based on MOFs have been employed for multiple diagnostic platforms. The review gives the recent updates for the abovementioned topics along with the toxicity aspects of MOFs for human use. The review overall gives a

detailed overview of research done to date in the field of MOFs based nanoplateforms for cancer theranostics.

10. Two dimensional carbon based nanocomposites as multimodal therapeutic and diagnostic platform: A biomedical and toxicological perspective

(Journal Name: Journal of Controlled Release)

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Graphene based nanocomposites have revolutionized cancer treatment, diagnosis and imaging owing to its good compatibility, elegant flexibility, high surface area, low mass density along with excellent combined additive effect of graphene with other nanomaterials. This review inculcates the type of graphene based nanocomposites and their fabrication techniques to improve its properties as photothermal and theranostic platform. With decades' efforts, many significant breakthroughs in the method of synthesis and characterization in addition to various functionalization options of graphene based nanocomposite have paved a solid foundation for their potential applications in the cancer therapy. This work intends to provide a thorough, up-to-date holistic discussion on correlation of breakthroughs with their biomedical applications and illustrate how to utilize these breakthroughs to address long-standing challenges in the clinical translation of nanomedicines. This review also emphasizes on graphene based nanocomposites based toxicity concerns pertaining to delivery platforms.