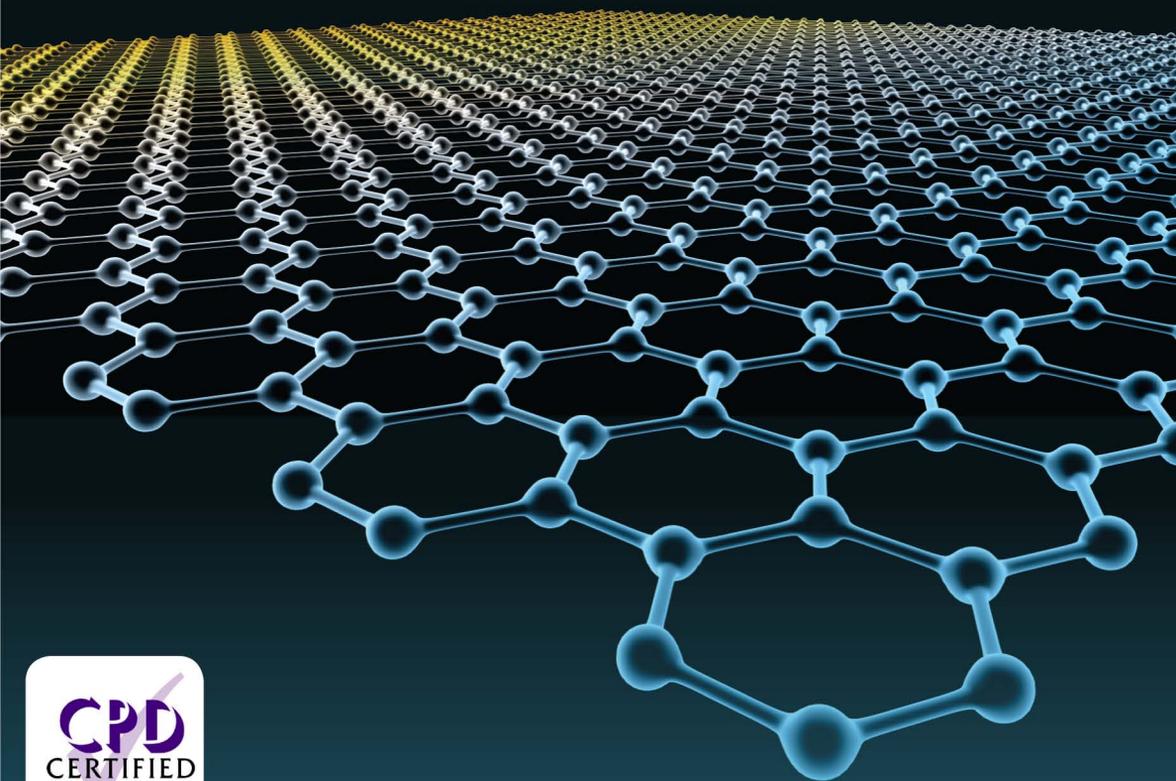


# Nanoconjugate Nanocarriers for Drug Delivery



Editors Raj K. Keservani | Anil K. Sharma

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# **NANOCONJUGATE NANOCARRIERS FOR DRUG DELIVERY**



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# NANOCONJUGATE NANOCARRIERS FOR DRUG DELIVERY

*Edited by*

**Raj K. Keservani, MPharm**  
**Anil K. Sharma, MPharm, PhD**

**AAP** | APPLE  
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*The Present Book Is Dedicated to our Beloved*

*Aashna*

*Anika*

*Atharva*

*and*

*Vihan*



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# LIST OF ABBREVIATIONS

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|                    |  |
|--------------------|--|
| Abs                | antibodies   |
| ACT                | artemisinin-based combination therapy                      |
| AD                 | Alzheimer's disease  |
| ADME               | adsorption, distribution, metabolism, and excretion        |
| AFM                | atomic force microscopy                                    |
| AlPcS              | aluminum phthalocyanines                                   |
| AmB                | amphotericin B   |
| AmB-PLGA-NS        | amphotericin B-loaded PLGA-based nanosphere                |
| apo                | apolipoprotein   |
| Apo b              | apolipoprotein B   |
| APs                | aptamers   |
| ARPES              | angle-resolved photoelectron spectroscopy                  |
| ART                | artemisinin  |
| ASA                | amino salicylic acid                                       |
| AsODN              | antisense oligonucleotides                                 |
| ATD                | anti-tubercular drugs                                      |
| AuCM               | gold-cysteamine  |
| BBB                | blood–brain barrier  |
| BCG                | bacillus Calmette–Guerin                                   |
| BOB                | blood–ocular barrier                                       |
| BPEI               | branched poly-(ethylenimine)                               |
| BPGDD              | biotin-PEG-GNR-DNA/DOX                                     |
| BphEA              | 2-(butylamino)-1-phenyl-1-ethanethiosulfuric acid          |
| BSA-NP             | bovine serum albumin nanoparticle                          |
| CBD                | Centre for Bio-design & Diagnostics                        |
| C-dots             | carbon quantum dots  |
| CD-C <sub>10</sub> | cyclodextrin derivatives grafted with decanoic alkyl chain |
| Ce6                | chlorin e6   |
| CM                 | cerebral malaria   |
| CMC                | critical micelle concentration                             |
| CNT                | carbon nanotube  |
| CP                 | NIR dye (Cy5.5)-labeled-MMP-14 substrate peptide           |

|              |  |
|--------------|--|
| CPT          | camptothecin   |
| CRISPR       | clustered regularly interspaced short palindromic repeats                                |
| CS           | chitosan   |
| CSC          | cancer stem cell   |
| CTLM         | circular transmission line model   |
| CVD          | chemical vapor deposition  |
| DDFR         | dihydrofolate reductase  |
| DDS          | drug delivery system   |
| DHA          | dihydroartemisinin   |
| DHA-SLN      | DHA-loaded solid lipid nanoparticle  |
| DHPS         | dihydropteroate synthase   |
| DI-TSL       | DOX/ICG-loaded temperature sensitive liposomes   |
| DIVEMA       | divinyl ether-maleic anhydride   |
| DLS          | dynamic light scattering   |
| DMF          | N-N dimethyl formamide   |
| DOPC         | dioleoyl phosphatidylcholine   |
| DOPG         | dioleoyl phosphatidylglycerol  |
| DOX          | doxorubicin  |
| DOX@PSS-GNRs | DOX molecules onto the GNRs through PSS  |
| DPPA         | dipalmitoyl phosphatidic acid  |
| DPPC         | 1,2-dipalmitoyl-sn-glycero-3-phosphocholine  |
| DPPC         | dipalmitoyl phosphatidylcholine  |
| DPPE         | dipalmitoyl phosphatidylethanolamine   |
| DPPS         | dipalmitoyl phosphoserine  |
| DSPE-PEG2000 | 1,2-distearoyl-sn-glycero-3-glycero-3-phosphoethanolamine-N-[(polyethylene glycol)-2000] |
| DSPE-PEG2000 | 1,2-distearoyl-sn-glycero-3-phosphoethanolamine-N-[methoxy(polyethylene glycol)-2000]    |
| dsRNA        | double-stranded RNA  |
| DT-DTPA      | dithiolated diethylenetriamine pentaacetic acid  |
| DTPA         | diethylenetriaminepentaacetic dianhydride  |
| DV           | dengue virus   |
| EGF          | epidermal growth factor  |
| EGFR         | epidermal growth factor receptor   |
| EMA          | European Medicines Agency  |
| EOEOVE-ODVE  | poly[2-(2-ethoxy) ethoxyethyl vinyl ether-block-octadecyl vinyl ether]                   |
| EPR          | enhanced permeability and retention  |

|                        |   |
|------------------------|---|
| f-CNT                  | functional CNT  |
| FA                     | folic acid  |
| FA-ICG//RAPA-TSL       | RAPA-loaded and folate-conjugated ICG TSL             |
| FCC                    | face-centered cubic                                   |
| FRET                   | fluorescence resonance energy transfer                |
| FTIR                   | Fourier-transform infrared spectroscopy               |
| G <sup>-</sup>         | Gram-negative species                                 |
| G <sup>+</sup>         | Gram-positive bacteria                                |
| GCSCs                  | gastric cancer stem cells                             |
| Gd                     | gadolinium  |
| GD                     | gramicidin  |
| Gd-nanoLE              | Gd-containing lipidenanoemulsion                      |
| GDS                    | gene delivery system                                  |
| GFN                    | graphene nanoparticle                                 |
| GFP                    | green fluorescent protein                             |
| GI                     | gastrointestinal                                      |
| GL-COO- $\beta$ -CD/CA | graphene- $\beta$ -cyclodextrin/chlorhexidine acetate |
| GNCgs                  | gold nanocages  |
| GNP                    | gold nanoparticle                                     |
| GNPs/AuNPs             | gold nanoparticles                                    |
| GNR                    | gold nanorods   |
| GO                     | graphene oxide  |
| GQD                    | graphene quantum dot                                  |
| GrO                    | reduced graphene oxide                                |
| GSH                    | glutathione   |
| HA                     | hyaluronic acid                                       |
| HbF                    | fetal hemoglobin                                      |
| HBsAg                  | hepatitis B surface antigen                           |
| HGNS                   | hollow gold nanosphere                                |
| His-co-Phe             | poly(histidine)-co-phenylalanine-b-PEG                |
| hMSC                   | human mesenchymal stem cell                           |
| HNE                    | human neutrophil elastase                             |
| HPMA                   | N-(2-hydroxypropyl) methacrylamide                    |
| HSPC                   | hydrogenated L- $\alpha$ -phosphatidylcholine         |
| HUVEC                  | human umbilical vein endothelial cells                |
| ICG                    | indocyanine green                                     |
| IFN $\gamma$           | interferon $\gamma$                                   |
| INH                    | isoniazid   |

|              |   |
|--------------|---|
| iRGD         | internalized RGD                            |
| iRGD-ICG-LPs | iRGD-modified ICG liposomes                 |
| IT           | itraconazole                                |
| ITO          | indium tin oxide                            |
| IUV          | unilamellar vesicles                        |
| IV           | intravenous                                 |
| KET          | ketoconazole                                |
| LCST         | lower critical solution temperature         |
| LDC          | lipid drug conjugate                        |
| LDH          | lactate dehydrogenase                       |
| LET          | linear energy transfer                      |
| LP           | lipid peroxidation                          |
| LSPR         | localized surface plasmon resonance         |
| LUV          | large unilamellar vesicles                  |
| MCT          | medium-chain triglyceride                   |
| MDA          | malondialdehyde                             |
| MDR          | multidrug resistance                        |
| MDR-TB       | multidrug-resistant TB                      |
| miRNA        | micro-RNA                                   |
| MLV          | multilamellar vesicles                      |
| MMP          | matrix-metalloproteinases                   |
| MMP-2        | matrix metalloproteinase-2                  |
| MMP-14       | matrix metalloproteinase-14                 |
| MPEG-SS-PLA  | redox-responsive PEG-b-poly (lactic acid)   |
| MPS          | mononuclear phagocyte system                |
| MRC          | Medical Research Council                    |
| MRI          | magnetic resonance imaging                  |
| MSN          | mesoporous silica                           |
| MSOT         | multispectral optoacoustic tomography       |
| MSP-119      | merozoite surface protein-119               |
| MVV          | multivesicular vesicles                     |
| MWCN         | multiple-walled carbon nanotube             |
| NCs          | nanoconjugates                              |
| NECT         | eflornithine/nifurtimox combination therapy |
| NGO          | nanoscale GO                                |
| NIR          | near-infrared                               |
| NLC          | nanostructured lipid carrier                |
| NPs          | nanoparticles                               |

|                  |   |
|------------------|---|
| NRF              | National Research Foundation  |
| NSCLC            | non-small-cell lung carcinoma   |
| NSs              | nanosystems   |
| NTD              | neglected tropical disease  |
| OASIS            | Organic and Sustainable Industry Standards  |
| ODN              | oligonucleotides  |
| p(OEGMA-co-MEMA) | poly(oligo(ethylene oxide) methacrylate-co-2-(2-methoxyethoxy)ethyl methacrylate) |
| P-gp             | P-glycoprotein  |
| PAA              | poly(acrylic acid)  |
| PAA              | polyamidoamines   |
| PbAE             | poly( $\beta$ -amino esters)  |
| PBS              | phosphate-buffered saline   |
| PC               | cyclophosphamide  |
| PC               | phosphatidylcholine   |
| PC-12            | pheochromocytoma-derived  |
| PC-Chol-SSG      | SSG-loaded PC-cholesterol liposomes   |
| PC-SA-SSG        | SSG-loaded phosphatidylcholine stearylamine liposomes                             |
| PCL              | PEG-b-polycaprolactone  |
| PCL-SSPEEP       | copolymer of PCL and poly (ethylethylene phosphate)                               |
| PCMX             | parachlorometaxylenol   |
| PD               | Parkinson's disease   |
| pDNA             | plasmid DNA   |
| PDT              | photodynamic therapy  |
| PEG              | polyethylene glycol   |
| PEG-b-PBD        | PEG-b-poly (butadiene)  |
| PEG-b-PLA        | poly(ethylene glycol) with poly(lactic acid)                                      |
| PEG-b-PPO-b-PEG  | polyethylene glycol-b-polypropylene oxide-b-polyethylene glycol                   |
| PEI              | polyethylenimine  |
| PEO-b-PMABC      | poly(ethyleneoxide)-b-poly {N-methacryloyl-N-(t-butyloxycarbonyl)cystamine}       |
| PEO-PbAE         | PEO-modified PbAE   |
| PERL             | polyunsaturated ER-targeting liposome   |
| PF-DNA           | proton-fueled DNA   |
| PGA              | poly(glutamic acid)   |

|           |  |
|-----------|--|
| PG-b-PCL  | poly(glycidol-block- $\epsilon$ -caprolactone)               |
| PIT       | phase inversion temperature                                  |
| PLA       | poly(dl-lactide)   |
| PLA       | polylactides   |
| PLG       | poly(lactideco-glycolide)                                    |
| PLGA      | poly(d,l-lactide-co-glycolide)                               |
| PLL       | poly-L-lysine  |
| PM-MTH    | mithramycin encapsulated in polymeric micelles               |
| PMA       | poly(methacrylic acid)                                       |
| PMMA      | PZQ in poly(methyl methacrylate)                             |
| pNIPAAm   | poly(N-isopropylacrylamide)                                  |
| PNP       | polymeric nanoparticle                                       |
| PNP       | RSV-encapsulated lipid nanoparticle                          |
| PPa       | pyropheophorbide-a   |
| PPEI-EI   | poly(propionylethyleneimine-coethyleneimine)                 |
| PPI       | polypropylenimine  |
| PQP       | piperaquine  |
| pri-miRNA | primary miRNA  |
| PSs       | photosensitizers   |
| PSS       | poly(sodium 4-styrene sulfonate)                             |
| pTAT      | polypeptide derived from the transactivator of transcription |
| PTT       | photothermal therapy   |
| PTX       | paclitaxel   |
| PVA       | poly(vinyl alcohol)  |
| PVA       | polyvinyl acrylonitrile                                      |
| PVA-R     | polyvinyl alcohol conjugated hydrophobic anchors             |
| PVK       | poly-N-vinyl carbazole                                       |
| PVP       | poly(vinylpyrrolidone)                                       |
| PZA       | pyrazinamide   |
| PZQ       | praziquantel   |
| QD        | quantum dots   |
| QN        | quinine  |
| RAPA      | anti-angiogenesis agent rapamycin                            |
| rb        | Bohr's radius  |
| RBCs      | red blood cells  |
| RCPN      | Research Center for Pharmaceutical Nanotechnology            |
| RGD       | arginine-glycine-aspartate                                   |

|           |   |
|-----------|---|
| RGD-GNR   | RGD peptides-conjugated GNRs                                |
| rGO       | reduced graphene oxide                                      |
| rGO-GNRVe | rGO-loaded ultrasmall plasmonic GNR vesicles                |
| RIF       | rifampicin  |
| RISC      | RNA-induced silencing complex                               |
| RNA       | ribonucleic acid  |
| RNAi      | RNA interference  |
| ROS       | reactive oxygen species                                     |
| RSV       | resveratrol   |
| SA        | stearylamine  |
| SC        | stratum corneum   |
| SDBS      | sodium dodecyl benzene sulfonate                            |
| SDS       | sodium dodecyl sulfate                                      |
| SDS-PAGE  | sodium dodecyl sulphate polyacryl amide gel electrophoresis |
| SEM       | scanning electron microscope/microscopy                     |
| shRNA     | short hairpin RNA   |
| siRNA     | small interfering RNA                                       |
| SLN       | solid lipid nanoparticle                                    |
| SPIONs    | superparamagnetic iron oxide nanoparticles                  |
| SPN       | solid lipid nanoparticle                                    |
| SPR       | surface plasmon resonance                                   |
| SRD       | sustained release system                                    |
| SRN       | stimuli-responsive nanocarrier                              |
| ssDNA     | single-stranded DNA   |
| SSG       | sodium stibogluconate                                       |
| ssLips    | submicron-sized liposomes                                   |
| STEM      | scanning electron transmission microscopy                   |
| STM       | scanning tunneling microscope                               |
| STS       | scanning tunneling spectroscopy                             |
| SUV       | small unilamellar vesicles                                  |
| SWCN      | single-walled carbon nanotube                               |
| SWCNT     | single-wall carbon nanotubes                                |
| TAT       | transactivator of transcription                             |
| TCPS      | tissue culture polystyrene substrates                       |
| TEM       | transmission electron microscope/microscopy                 |
| TGA       | thermogravimetric analysis                                  |
| THF       | tetrahydrofuran   |

|                            |   |
|----------------------------|---|
| THSTI                      | Translational Health Science & Technology Institute |
| TME                        | tumor microenvironment                              |
| TNBC                       | triple-negative breast cancer                       |
| TPGS                       | polyethylene glycol-succinate                       |
| Trp                        | l-tryptophan  |
| TSL                        | thermal sensitive liposome                          |
| TZB                        | trastuzumab   |
| TZB-GNP- <sup>111</sup> In | <sup>111</sup> In-labeled TZB-modified GNP          |
| US FDA                     | United States Food and Drug Administration          |
| UV                         | ultraviolet   |
| VL                         | visceral leishmaniasis                              |
| WHO                        | World Health Organization                           |
| XRD                        | X-ray diffraction                                   |

# PREFACE

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The association of medicine and mankind is age old. There has been a constant evolution in treatment strategies aimed at curing the variety of ailments. Academicians as well researchers from industry have yielded many viable formulations that are being used as drug carriers. However, the conventional dosage forms suffer from a few pitfalls, such as non-specific drug delivery, dose dumping, poor patient compliance, toxicities linked with higher doses, etc. The past several decades have witnessed an emergence of nanotechnology-based products. Nanotechnology has been observed to uplift the level of sophistication through a variety of ways. Its uses embrace material science, engineering, medical, dentistry, drug delivery, etc.

In light of the drug delivery context, the present book is an attempt to provide the requisite information to its readers. The content of this book has been written by highly skilled, experienced, and renowned scientists and researchers from all over the world. They provide updated knowledge and drug delivery information to readers, researchers, academicians, scientists, and industrialists around the globe.

*Nanoconjugate Nanocarriers for Drug Delivery* comprises 16 chapters divided into 4 sections that present an introduction of nanocarriers, physicochemical features, and generalized and specific applications dealing with drug delivery in particular. The materials used as well as formulation and characterization have been discussed in detail. The nanocarriers covered are nanoparticles, vesicular carriers, carriers having carbon as core constituent, dispersed systems, etc.

## SECTION I: INTRODUCTION TO NANOCARRIERS

**Chapter 1**, written by *B. A. Aderibigbe*, provides an overview of different nanobiomaterials used for delivery of drug molecules. The nanobiomaterials are further classified as polymeric, metallic, and derived from carbon. The author has summarized the nanobiomaterials with their striking features.

**Chapter 2**, written by *M. Pilar Vinardell* and *colleagues*, describes to what extent the surfactants are essential for preparation of numerous drug delivery systems. The chapter begins with a brief preamble of nanotechnology followed by classification of surfactants. The discussion of different polymeric and lipidic nanoparticles is provided in ensuing sections. In addition, the chapter covers delivery systems meant via various routes of application containing surfactants. Interestingly, there is mention of utility of surfactant-based nanocarriers in cancer chemotherapy.

The details of general principles and methods of preparation of smart nanoconjugates have been presented in **Chapter 3**, written by *Subham Banerjee* and *Jonathan Pillai*. The authors have reviewed various therapeutic applications of such stimuli-responsive systems in brief. Finally, the authors conclude with mentioning future perspectives on the therapeutic uses of smart polymeric nanocarriers.

**Chapter 4**, written by *Ayuob Aghanejad* and *colleagues*, gives an exhaustive description of gold nanoparticles, beginning with introduction going across various synthesis methods and applications in different fields. Further, smart gold nanoparticulates are mentioned with relevance to cancer and gene delivery.

## SECTION II: VESICLE-BASED DRUG CARRIERS

Different aspects of drug delivery via vesicular nanocarriers are described in **Chapter 5**, written by *Sanja Petrović* and *colleagues*. The authors have given an overview of the delivery systems that represent multifunction carriers of active substances for controlled, delayed, and targeted drug substance delivery, with a special review of the vesicular drug carriers. The liposomes have been the key formulations with an elaborated discussion.

**Chapter 6**, written by *Preethi Naik* and *Mangal S. Nagarsenker*, deals with issues related to biological systems in particular. The authors have strived to provide information about different attempts for improving intracellular delivery of siRNA, with special focus on excipient-driven liposomal nanocarrier systems, clinical relevance of siRNA delivery vehicles, and the toxicity concerns associated with such carrier systems. In addition, the toxicity and clinical perspectives of liposomal delivery for siRNA have been discussed.