IJPSR (2010), Vol. 1, Issue 11 **(Review Article)**

INTERNATIONAL JOURNAL OF PHARMACEUTICAL SCIENCES AND RESEARCH

Received on 23 May, 2010; received in revised form 18 August, 2010; accepted 21 September, 2010

NANOMEDICINE: A MAGICAL HOPE FOR THE MEDICAL WORLD

V. Gupta *[1], D. S. Rathore [2] and A. Bhandari [1]

Faculty of Pharmaceutical Sciences, Jodhpur National University [1], Jodhpur (Raj.), India College of Pharmacy [2], Jaipur, (Raj.), India

Keywords:

Nanomedicine,

Nanocrystal technology,

Nanostructures

Correspondence to Author:

Vikas Gupta

Faculty of Pharmaceutical Sciences, Jodhpur National University, Jodhpur (Raj.), India

ABSTRACT

Emerging nanomedicine technologies could dramatically transform medical science as we know it today with their potential to address unmet medical needs and provide targeted therapy. Nanomedicine technologies could find an increasing place in various areas and applications of the healthcare sector including drug delivery, drug discovery and development, diagnostics and medical devices. The advent of nanomedicine and techniques for the early diagnosis of diseases could usher in a new era of superior prophylactic or preventive medicine. By using preventive medicine, treatment for diseases could be initiated even before preliminary symptoms appear. Prophylactic interventions might help postpone or even avoid diseases altogether. Nanomedicine could therefore have a huge impact on people's lives, substantially improving their physical health and quality of life. Nanocrystal technology, for instance, is being used in drug formulation and the new chemical entities screening in the discovery phase of drug development. Quantum dot particles are being applied in high-content drug screening and in the detection of breast cancer cells among others. However, as with other new technologies, nanomedicine also faces its own set of issues. Scalability is one of its biggest technological challenges. While large-scale production makes better economic sense, this is likely to be a complex task, especially when manufacturing three-dimensional nanostructures as compared to stand-alone or two-dimensional layer-shaped nano surfaces. This perceived difficulty is attributed to the fact that manufacturing standards for nano materials and components are yet to evolve. Therefore, there is an urgent need for standardized manufacturing techniques; only then can nanotechnology become ubiquitous in everyday applications. Nanomedicine – Global Developments and Growth Opportunities, part of the Healthcare Vertical Subscription Service, studies the emerging field of nanomedicine and the exciting possibilities it offers. It discusses prospective therapeutic and diagnostic applications of nanomedicine, focusing on path-breaking research developments and trends that have helped bring it to the forefront.

INTRODUCTION: Nanomedicine is the medical application of nanotechnology [1]. The approaches to nanomedicine range from the medical use of nanomaterials, to nanoelectronic biosensors, and even possible future applications of molecular nanotechnology [2]. Current problems for nanomedicine involve understanding the issues related to toxicity and environmental impact of nanoscale materials. Nanomedicine seeks to deliver a valuable set of research tools and clinically helpful devices in the near future [3, 4]. The National Nanotechnology Initiative expects new commercial applications in the pharmaceutical industry that may include advanced drug delivery systems, new therapies, and in vivo imaging [5]. Our aim of this review to discusses prospective therapeutic and diagnostic applications of nanomedicine, focusing on path-breaking research developments and trends that have helped bring it to the forefront.

Nanotechnology and Nanomedicine: Nanomedicine has been defined as ''the monitoring, repair, construction, and control of human biological systems at the molecular level, using engineered nanodevices and nanostructures''. In December 2002 the U.S. National Institutes of Health announced a 4-year program for nanoscience and nanotechnology in medicine [6, 7]. Burgeoning interest in the medical applications of nanotechnology has led to the emergence of a new field called Nanomedicine [6, 8- 15]. Most broadly, nanomedicine is the process of diagnosing, treating, and preventing disease and traumatic injury, of relieving pain, and of preserving and improving human health, using molecular tools and molecular knowledge of the human body [7]. In the relatively near term, over the next 5 years, nanomedicine can address many important medical problems by using nanoscale-structured materials and simple nanodevices that can be manufactured today. This includes the interaction of nanostructured materials with biological systems [10]. For example, there are many nanodevices (e.g., Q-dots, dendrimers) (**Fig. 1-4**) that are widespread and broadly marketed, but have yet to find their way into a wide range of clinical devices.

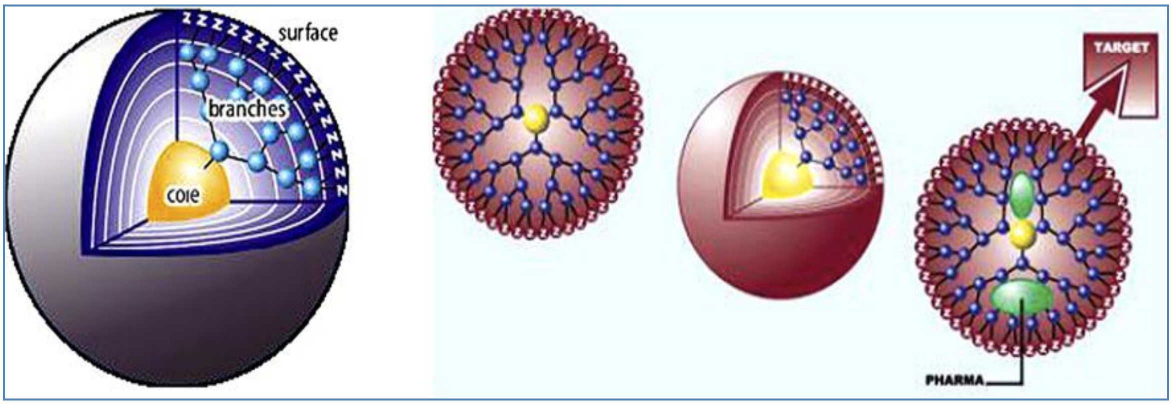

FIG. 1: STRUCTURE OF DENDRITIC DRUG-DELIVERY VEHICLES

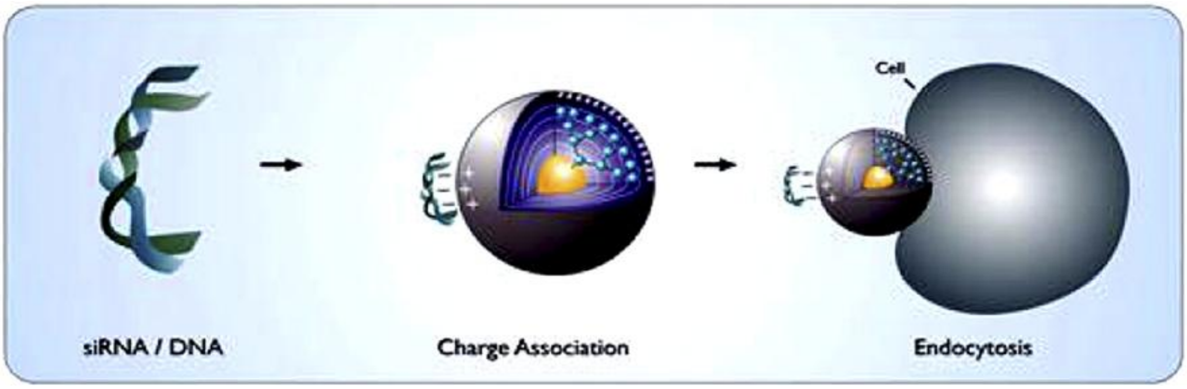

FIG. 2: DENDRITIC NANOTECHNOLOGIES' VEHICLE FOR DRUG DELIVERY/GENE SILENCING. PROMISING NANOPARTICLES: RESEARCHERS ARE WORKING TO CONVERT DENDRIMERS LIKE THESE INTO USEFUL DRUG-DELIVERY TOOLS. DENDRIMERS ARE ALREADY USED WIDELY IN THE LABORATORY. QIAGEN'S SUPERFECT DNA TRANSFECTION REAGENT IS A DENDRIMER WHOSE POSITIVELY CHARGED SURFACE BINDS THE NUCLEIC ACID'S NEGATIVELY CHARGED PHOSPHATE BACKBONE. SIRNA, SILENCING RNA

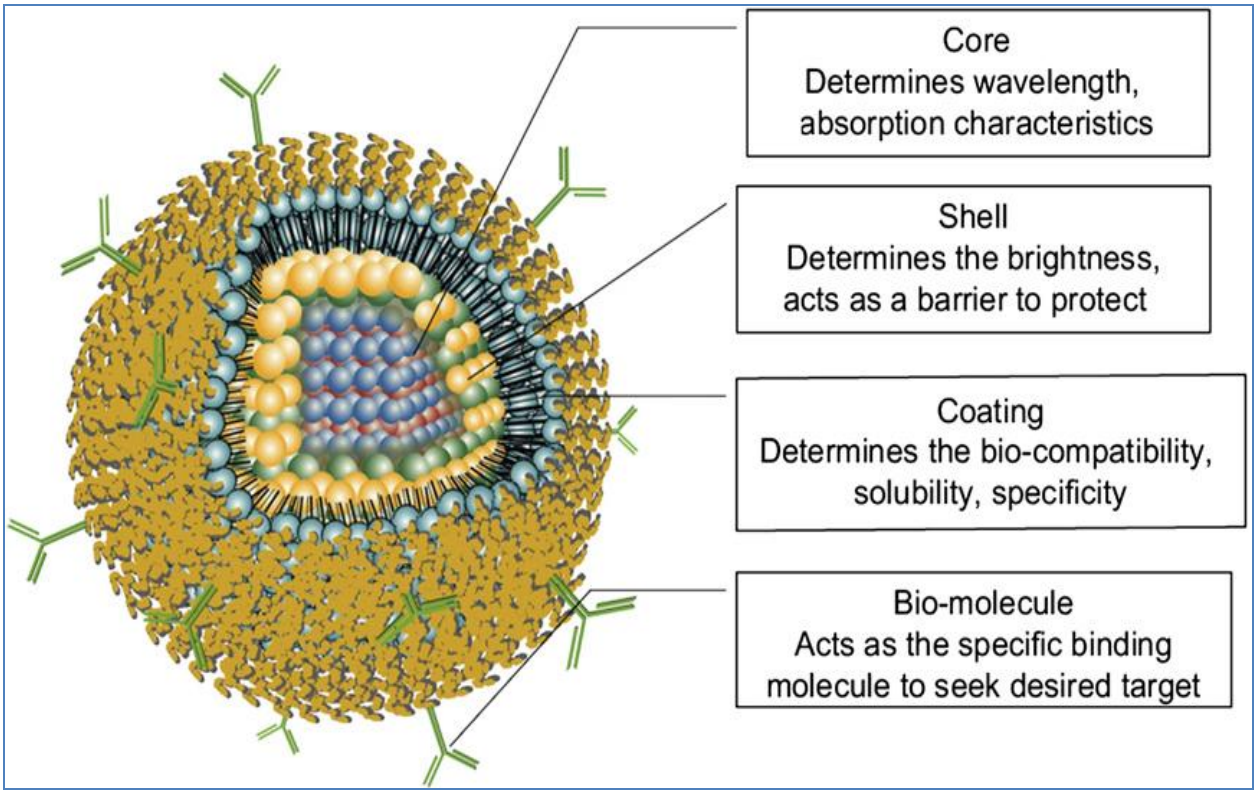

FIG. 3: STRUCTURE AND APPLICATIONS OF Q-DOTS

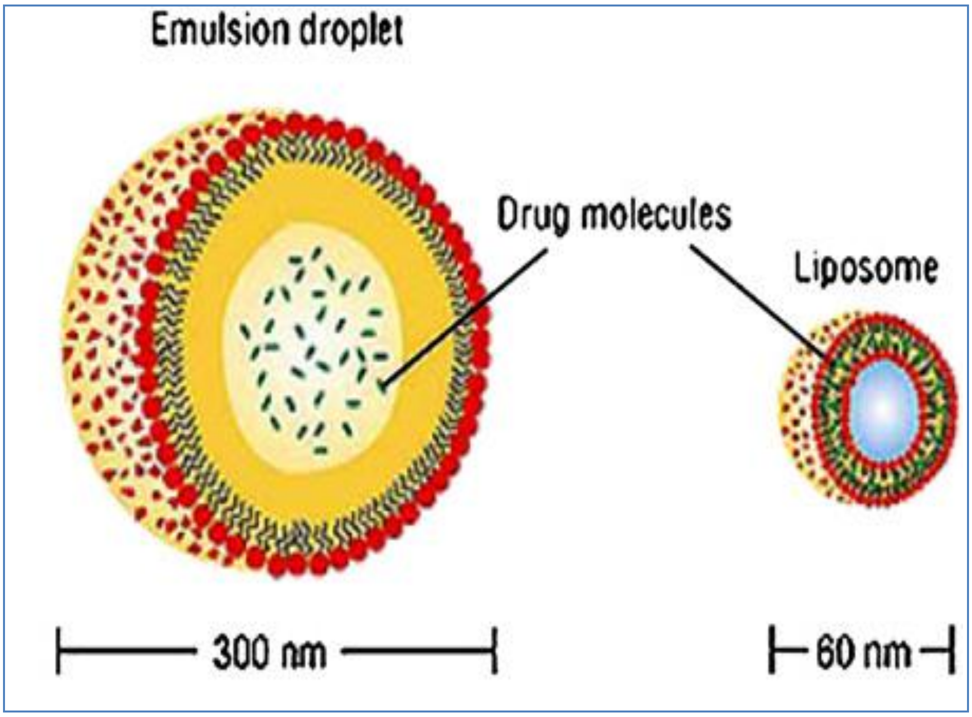

FIG. 4: Q-DOTS FOR DRUG DELIVERY

Nanomaterials and Nano devices:

Nanopores: one of the simplest medical nanomaterials is a surface perforated with holes, or nanopores. In 1997 Desai and Ferrari created what could be considered one of the earliest therapeutically useful nonmedical devices [16], employing bulk micromachining to fabricate tiny cell-containing chambers within single crystalline silicon wafers.

Artificial Binding Sites and Molecular Imprinting: Another early goal of nanomedicine is to study how biological molecular receptors work, and then to build artificial binding sites on a made-to-order basis to achieve specific medical results. Molecular imprinting [17-18] is an existing technique in which a cocktail of functionalized monomers interacts reversibly with a target molecule using only non-covalent forces. The complex is then cross-linked and polymerized in a casting procedure, leaving behind a polymer with recognition sites complementary to the target molecule in both shape and functionality.

Quantum Dots and Nanocrystals: Quantum dot" nanocrystals have none of these shortcomings. These dots are tiny particles measuring only a few nanometers across, about the same size as a protein molecule or a short sequence of DNA [19]. Quantum dots are useful for studying genes, proteins and drug targets in single cells, tissue specimens, and living animals [20]. Quantum dots are being investigated as chemical sensors [21], for cancer cell detection [19], gene expression studies [22], gene mapping and DNA microarray analysis [23]. Immunocytochemical probes [24], intracellular organelle markers [25], live cell labeling [26-27].

Fullerenes and Nanotubes: Soluble derivatives of fullerenes such as C_{60} have shown great utility as pharmaceutical agents. These derivatives, many already in clinical trials (www.csixty.com), have good biocompatibility and low toxicity even at relatively high dosages. Fullerene compounds may serve as antiviral agents (most notably against HIV [28], where they have also been investigated computationally [29-30]), antibacterial agents (*E. coli* [31], *Streptococcus* [32], *Mycobacterium tuberculosis* [33] etc.), photodynamic antitumor [34- 35] and anti-cancer [36] therapies, antioxidants and anti-apoptosis agents which may include treatments for amyotrophic lateral sclerosis (ALS or Lou Gehrig's disease) [37] and Parkinson's disease. Single-walled [38-39] and multi-walled [40-42] carbon nanotubes are being investigated as biosensors, for example to detect glucose [41-43] ethanol [43] hydrogen peroxide [40] selected proteins such as immunoglobulins [39] and as an electrochemical DNA hybridization biosensor [38].

Nanoshells and Magnetic Nanoprobes: Halas and West at Rice University in Houston have developed a platform for nanoscale drug delivery called the nanoshell [44-45]. Unlike carbon fullerenes, the slightly larger nanoshells are dielectric-metal nanospheres with a core of silica and a gold coating, whose optical resonance is a function of the relative size of the constituent layers. An alternative approach pursued by Triton BioSystems (www.tritonbiosystems.com) is to bond iron nanoparticles and monoclonal antibodies into nanobioprobes about 40 nanometers long. The chemically inert probes are injected and circulate inside the body, whereupon the antibodies selectively bind to tumor cell membranes. Once the tumor (whether visible or micrometastases) is covered with bioprobes after several hours, a magnetic field generated from a portable alternating magnetic field machine (similar to a miniaturized MRI machine) heats the iron particles to more than 170 degrees, killing the tumor cells in a few seconds [46].

Targeted Nanoparticles and Smart Drugs: Multisegment gold/nickel nanorods are being explored by Leong's group at Johns Hopkins School of Medicine [47] as tissue-targeted carriers for gene delivery into cells that "can simultaneously bind compacted DNA plasmids and targeting ligands in a spatially defined manner" and allow "precise control of composition, size and multifunctionality of the gene-delivery system." Targeted radioimmunotherapeutic agents [48] include the FDA-approved "cancer smart bombs" that deliver tumorkilling radioactive yttrium (Zevalin) or iodine (Bexxar) attached to a lymphoma-targeted (anti-CD20) antibody [49].

Dendrimers and Dendrimer-Based Devices: Dendrimers [50] represent yet another nanostructured material that may soon find its way into medical therapeutics [51]. Starburst dendrimers are tree-shaped synthetic molecules with a regular branching structure emanating outward from a core that form nanometer by nanometer, with the number of synthetic steps or "generations" dictating the exact size of the particles, typically a few nanometers in spheroidal diameter.

Radio-Controlled Biomolecules: While there are already many examples of nanocrystals attached to biological systems for biosensing purposes, the same nanoparticles are now being investigated as a means for directly controlling biological processes. Jacobson and colleagues [52] have attached tiny radio-frequency antennas 1.4 nanometer gold nanocrystals of less than 100 atoms—to DNA. When a 1 GHz radio-frequency magnetic field is transmitted into the tiny antennas, alternating eddy currents induced in the nanocrystals produce highly localized inductive heating, causing the double stranded DNA to separate into two strands in a matter of seconds in a fully reversible dehybridization process that leaves neighboring molecules untouched.

CONCLUSION: Nanoscience is the study of microscopic machines, each with the ability to perform functions on the cellular level, the molecular level, or even the atomic level. Nanoscience creates these tiny machines with the goal of performing functions that would seem almost miraculous with standard procedures. Nanomachines have the potential to perform delicate surgery, cure previously unstoppable diseases, convert toxic waste into harmless and useful materials, and build nearly anything imaginable from basic materials. If it reaches its full potential, nanoscience may change the world in fantastic and wonderful ways.

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