Market Opportunities in Nanotechnology Drug Delivery

Cientifica Ltd

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Introduction

Some forecasts have predicted the nanotechnology market to reach close to a trillion dollars by 2015, presenting investors with unique opportunities. However, the market for applications of nanotechnology is complex, multidisciplinary and highly segmented. It is therefore essential to gain an understanding of which market sectors nanotechnology is likely to impact most profoundly in the near term.

That's what we do at Cientifica.

The healthcare market is poised to see some of the earliest benefits of nanotechnology. While early ideas about the impact on nanotechnology on healthcare focussed on fanciful ideas involving small submarines and cancer zapping robots, much of the current advances have been enabled by advances in imaging, control over materials and an increased understanding of how biology works at the nanoscale.

Over the next decade, healthcare will be one of nanotech's highest growth sectors with drug delivery in the vanguard, but to date specific and rational information about markets has been lacking.

Since we now know most (if not all) biological processes occur at the nanoscale, the application of life science principles – studying the causes of biological phenomena at the molecular level – means that medical and biomedical research is increasingly using a bottom-up (rather than the top-down) approach. The low bioavailability resulting from traditional oral and intravenous drug delivery methods and the market forces at work in the pharmaceutical industry, where patents expire after a relatively short period of time unless a novel form of drug delivery is developed that will extend the patent, are two major forces that will fuel the growth of the nanotech drug delivery market. The third factor at play is a combination of improved global health and a correspondingly dramatic increase in the size of the global aging population.

To get to our market forecasts for NDD from 2011 to 2021 we also had to determine the historical market growth for NDD between 2000-2010, which meant wading through a mire of disinformation and speculation (as well as sifting through thousands of publications).

Unusually for this kind of report, we can now segment the market by geographical region and by technology type.

We examined every kind of technology including: solubility & bioavailability, targeted delivery, drug nanocrystals, liposomes, carbon nanotubes, gold nanocarriers, dendrimers, micelles, polymer-based nanocarriers, nanoshells, ceramic nanocarriers, calcium phosphate nanocarriers and many more.

Cientifica's report, Nanotechnology for Drug Delivery 2021, gives a comprehensive analysis and geographic breakdown of the current nanotechnology drug delivery market and its key technologies. It also provides a forecast for the size of total addressable markets and percent share of those key technologies to 2021.

Market Drivers

The aim of drug targeting

The "magic bullet" concept, first theorized by Paul Ehrlich in 1891, represents the first early description of the drug-targeting paradigm. The aim of drug targeting is to deliver drugs to the right place, at the right concentration, for the right period of time. As drug characteristics differ substantially in chemical composition, molecular size, hydrophilicity, and protein binding, the essential characteristics that identify efficacy are highly complex. All of these factors are investigated to bring a new compound to market although only a fraction reaches active clinical use.

Many promising new compounds are compromised by poor physiochemical properties that lead to poor solubility and biodistribution and therefore most of the drug does not interact with the target site. Poor oral absorption (i.e., proteins and peptides), low solubility at physiological pH, insufficient cellular uptake, and rapid drug elimination are impediments for drug development. New drug candidates must provide evidence that they reach the site of action and have an effect. The field of drug delivery designs carriers, excipients, and solubilizers to transport drugs to the site of action.

An answer to poor drug physiochemical properties is to associate the drug with a pharmaceutical carrier [i.e., a drug delivery system (DDS)]. A DDS can enhance a drug's pharmacokinetics and cellular penetration. Moreover, obstacles arising from low drug solubility, degradation, fast clearance rates, nonspecific toxicity, and inability to cross biological barriers may also be addressed by a DDS. To be useful, a DDS is required to be biocompatible with processes in the body as well as with the drug to be delivered. Overall, the challenge of increasing a drug's therapeutic effect, with a concurrent minimisation of side effects, can be optimised through proper design and DDS engineering.

Rapid Market Growth

At present, there are 30 main drug delivery products on the market. The total annual income for all of these is approximately US$33 billion with an annual growth of 15% (based on global product revenue).

Two major drivers are primarily responsible for this increase in the market. First, present advances in diagnostic technology appear to be outpacing advances in new therapeutic agents. Highly detailed information from a patient is becoming available, thus promoting much more specific use of pharmaceuticals. Second, the acceptance of new drug formulations is expensive and slow, taking up to 15 years to obtain accreditation of new drug formulas with no guarantee of success.

Most pharmaceutical research programs involve the search for new pharmaceutical agents as replacements for existing agents. The replacements are justified based upon improved potency, greater specificity, and/or an improved therapeutic index. This type of research involves high risk and high cost. On the other hand, drug delivery and targeting technologies offer the possibility of improving the therapeutic profile of existing drugs with relatively low risk and low cost.

The importance of drug delivery technology to the overall market success of a drug is increasing. Pharmaceutical companies may substantially extend the period of exclusivity (and the competitive edge) of their products that are about to lose patent by delivering them in a novel way. Third party players are excited about the potential cost savings of improved patient compliance and better outcomes. Furthermore, delivery considerations will likely be the key to making biopharmaceuticals and other macromolecular therapeutics derived from the Human Genome Project into workable clinical tools.

Market Drivers For Enhanced Drug Delivery

Traditional chemotherapy treatment relies on the use of high levels of potent chemotherapeutic drugs administered throughout the body. These drugs can lead to dangerous side effects and even death in patients with weakened immune systems or heart conditions. Controlled drug delivery has the ability to revolutionise chemotherapy treatment by spatially and temporally controlling the release of drugs only in the areas where treatment is required. By localising and controlling the drug's release, patients undergoing chemotherapy will be able to receive lower overall doses, which will result in decreased negative side effects and a higher quality of life.

The forces driving the pharmaceutical industry towards novel, more sophisticated drug delivery methods and technologies are compelling. New classes of therapeutic compounds have often been developed for their molecular biological properties at the expense of desirable pharmaceutical properties. Moreover, new drug discovery techniques such as high-throughput screening are generating many new chemical entity (NCE) leads, but without regard for their drug-like characteristics. These new drug candidates often present a multiplicity of delivery challenges, including issues of solubility, *in vivo* stability, poor pharmacokinetics, and undesirable toxicity and side effect profiles, all of which must be dealt with simultaneously in order for the candidate to become a successful therapeutic. These characteristics of the pharmaceuticals industry create a significant opportunity for companies like Insert, which has the means to deliver a wide range of therapeutics that have significant barriers to effective delivery.

Many novel macromolecular therapeutics, such as proteins and peptides, due to their size, complexity and other characteristics, require some form of enhanced delivery in order to be carried through the circulatory system without degradation, across cell membranes and into cells, in addition to dealing with other delivery challenges already discussed.

Traditional drug delivery methods include oral and intravenous routes of administration. These methods are still the most widely used today, yet each has its disadvantages. Oral delivery via tablets or capsules is largely inefficient due to exposure of the pharmaceutical agent to the metabolic processes of the body. Therefore, a larger than necessary dose is often required and the maximum effectiveness of the drug are limited. Traditional intravenous (IV) administration is much more problematic. Specificity for IV injectable drugs is often low, necessitating large amounts of a drug be injected into a patient, creating a high concentration of the drug in the blood stream that could potentially lead to toxic side effects.

Market Growth

'Survival time for all cancer types 40 years ago was just one year, now it is predicted to be nearly six years. This improvement is testament to the improvements in surgery, diagnosis, radiotherapy, and new drugs.'

-Ciarán Devane, - Chief Executive of Macmillan Cancer Support

The healthcare market is poised to see some of the earliest benefits of nanotechnology. Over the next decade, it will be one of nanotech's highest growth sectors. Targeted drug delivery therapies for the treatment of cancer is one of the most commonly cited healthcare benefits of nanotechnologies.

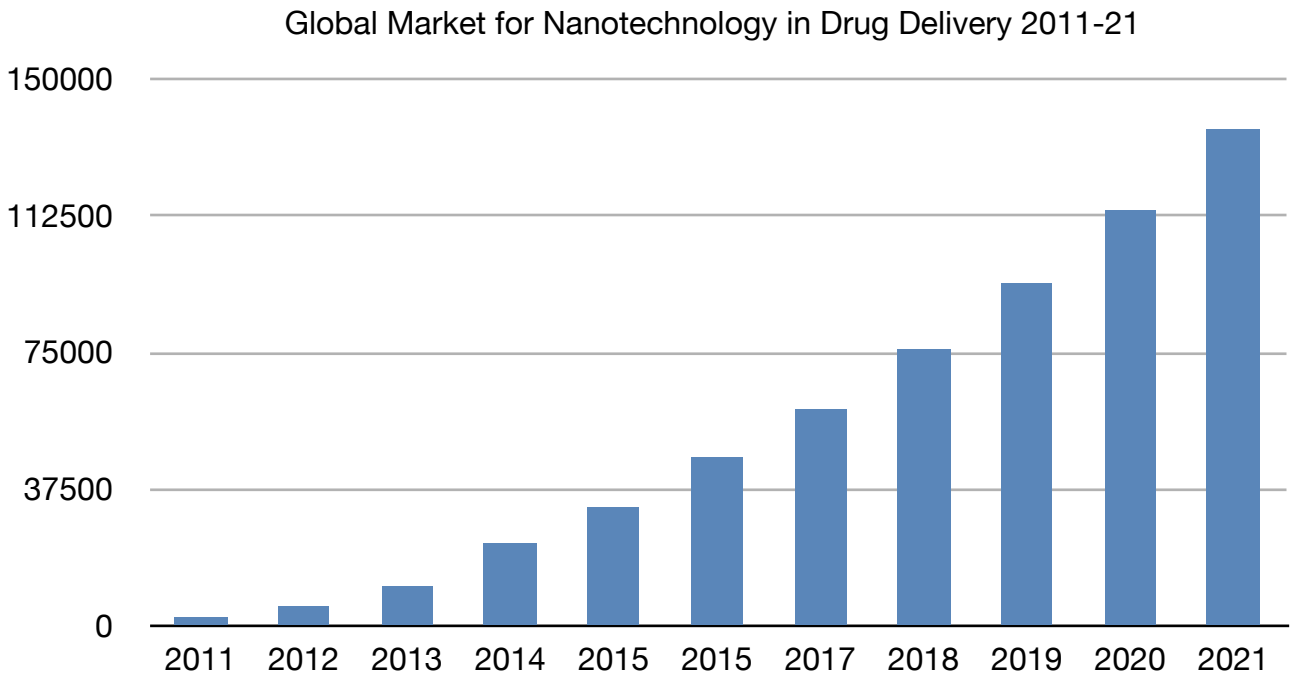
A new study by Macmillan Cancer Support shows a dramatic increase in the median cancer survival times over the past 40 years. Coupling nanotechnology drug delivery (NDD) methods with improvements in diagnostics, we can expect that much more progress will be made in the next 10 years than in the previous 40.

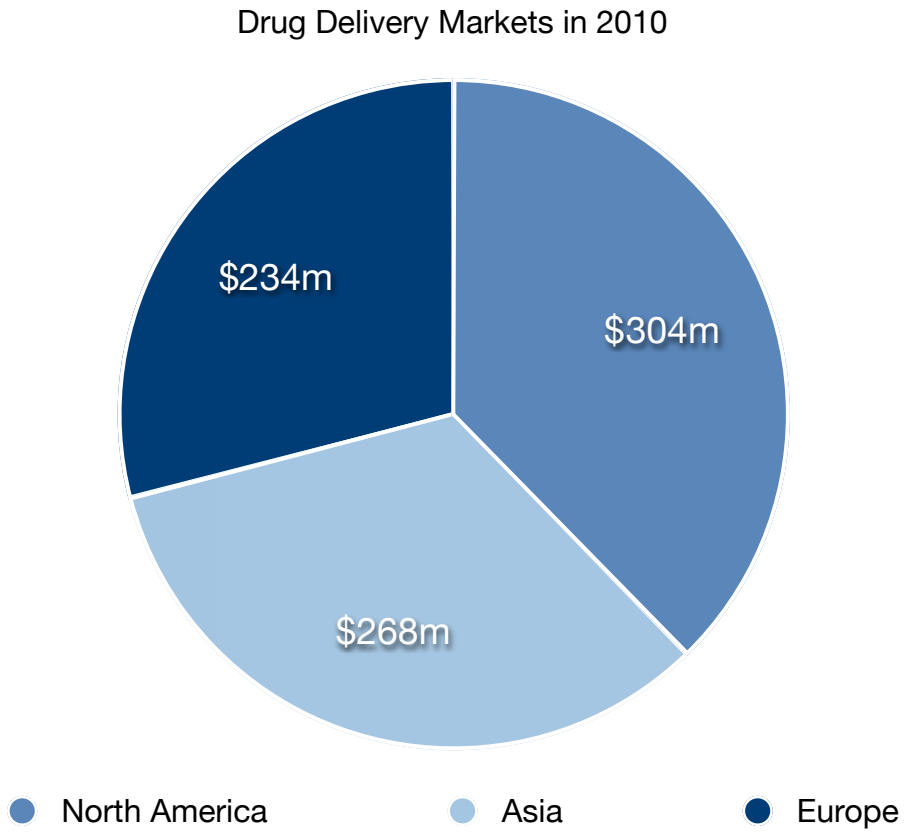
Although nanotechnology is revolutionising the diagnosis and treatment of a number of cancers, it is only six years since the first nanoparticulate drug delivery product for the treatment of breast cancer, Abraxane, was launched by Abraxis Oncology, a division of American Pharmaceutical Partners, Inc. The initial announcement saw the company's share prices rise by 50% and required the Food and Drug Administration (FDA) to create a new class of therapeutic products. But this was only the opening shot in the war against cancer, and there are now hundreds of new nanotech based treatments under development ranging from reformulation of existing drugs to enhance their effectiveness to radical new "magic bullet" therapies.

There are two different approaches to Nanotechnology in Drug Delivery making drug crystals smaller to increase solubility and bioavailability, or using some form of nanocarrier to deliver them in a more effective manner.

We forecast the total market size in 2021 to be US$ 136Bn,with a 60/40 split in favour of drug nanocrystals although developing new delivery mechanisms may allow more value to be created for companies and entrepreneurs.

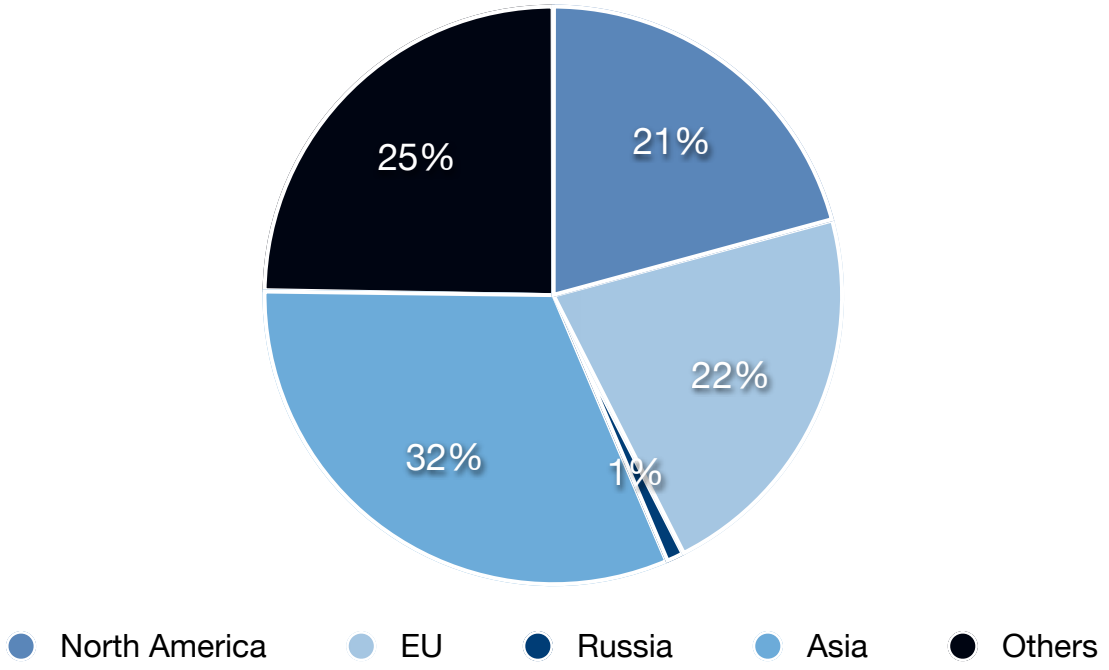
Global Markets For Nanotechnology Drug Delivery





We are seeing some huge growth potential too, but not spread evenly. The combination of social need coupled with willingness to pay will see the introduction of highly targeted therapies in some areas being much quicker than in others. Asia is the world region that will achieve the leading TAM in 2021 42,641 US$ Million Dollars (31%,) and the highest value of CAGR (2011, 2021): 32.5%.

Geographical Distribition of Nanotechnology Drug Delivery Market in 2021



Among the Asian countries studied, P. R. China is the country that will achieve the leading TAM in 2021: 18,594 US$ Million Dollars (43%,) and the highest value of CAGR (2011, 2021): 14.2%.

The current market for drug delivery is evenly split between North America (304 US$ Million Dollars), (30%), Asia (268 US$ Million Dollars), (26%); and the EU (27), (234 US$ Million Dollars), (23%);

Market Analysis By Key Technologies

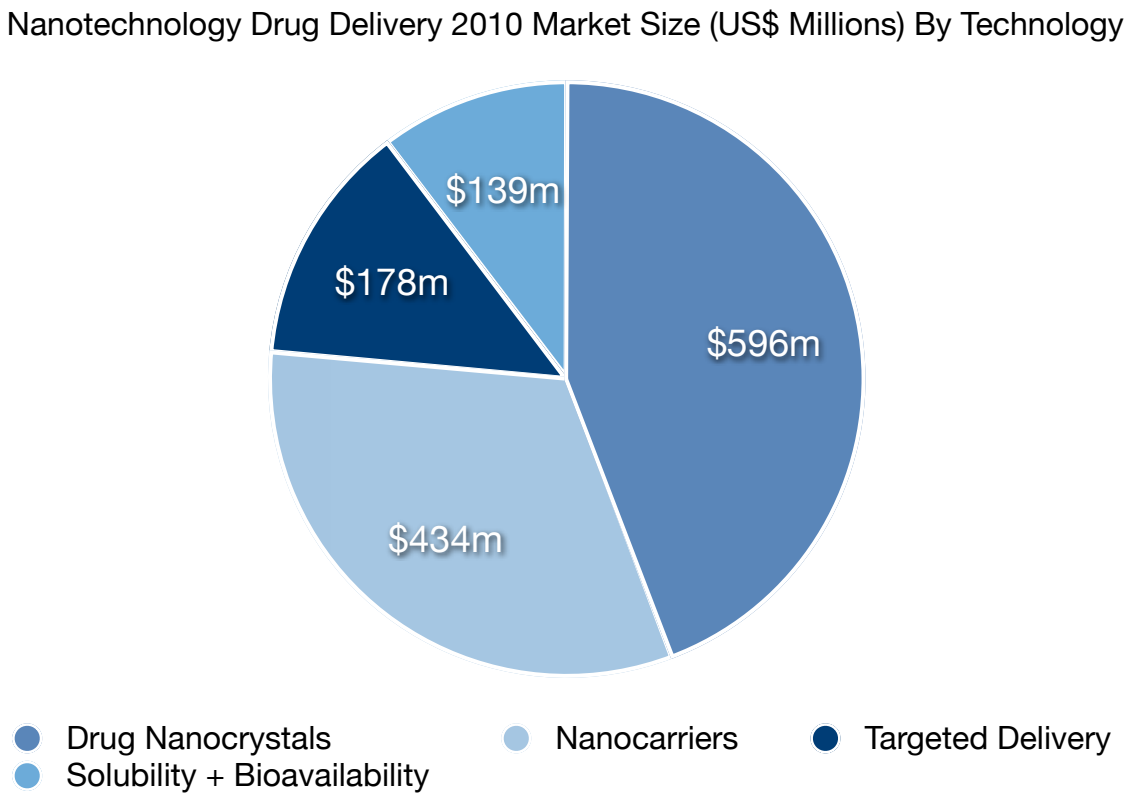
An analysis of the Total Addressable Market (TAM) in 2010, for nanotechnology in drug delivery (NDD), all key technologies studied shows the following values in 2010 (by descending order):

Drug Nanocrystals (596 US$ Million Dollars),

Total Nanocarriers (434 US$ Million Dollars),

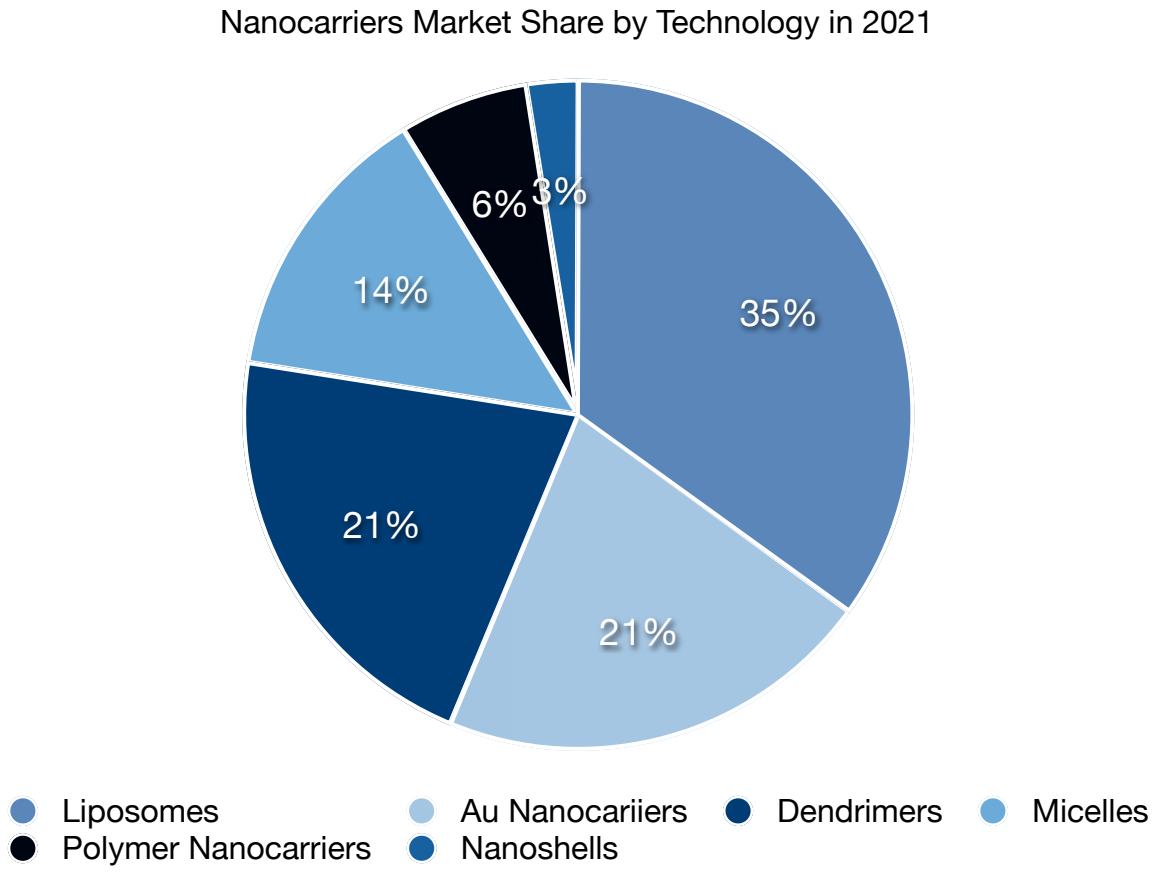
Targeted Delivery (178 US$ Million Dollars),

Solubility + Bioavailability (139 US$ Million Dollars),



Among all key technologies studied, drug nanocrystals (nanosized drugs) are the key technology that will achieve the leading TAM in 2021: 81,921 US$ Million Dollars (46%).

Among all nanocarriers studied, liposomes are the nanocarriers that will achieve the leading TAM in 2021: 15,313 US$ Million Dollars (28%). However, gold nanoparticles are the key technology with the highest value of CAGR (2011, 2021): 53.8%.



Nanocarriers as a Whole...

An analysis of the TAM in 2010, for NDD, nanocarriers as a whole shows the top 5 nanocarriers TAM values in 2010 as follows (by descending order):

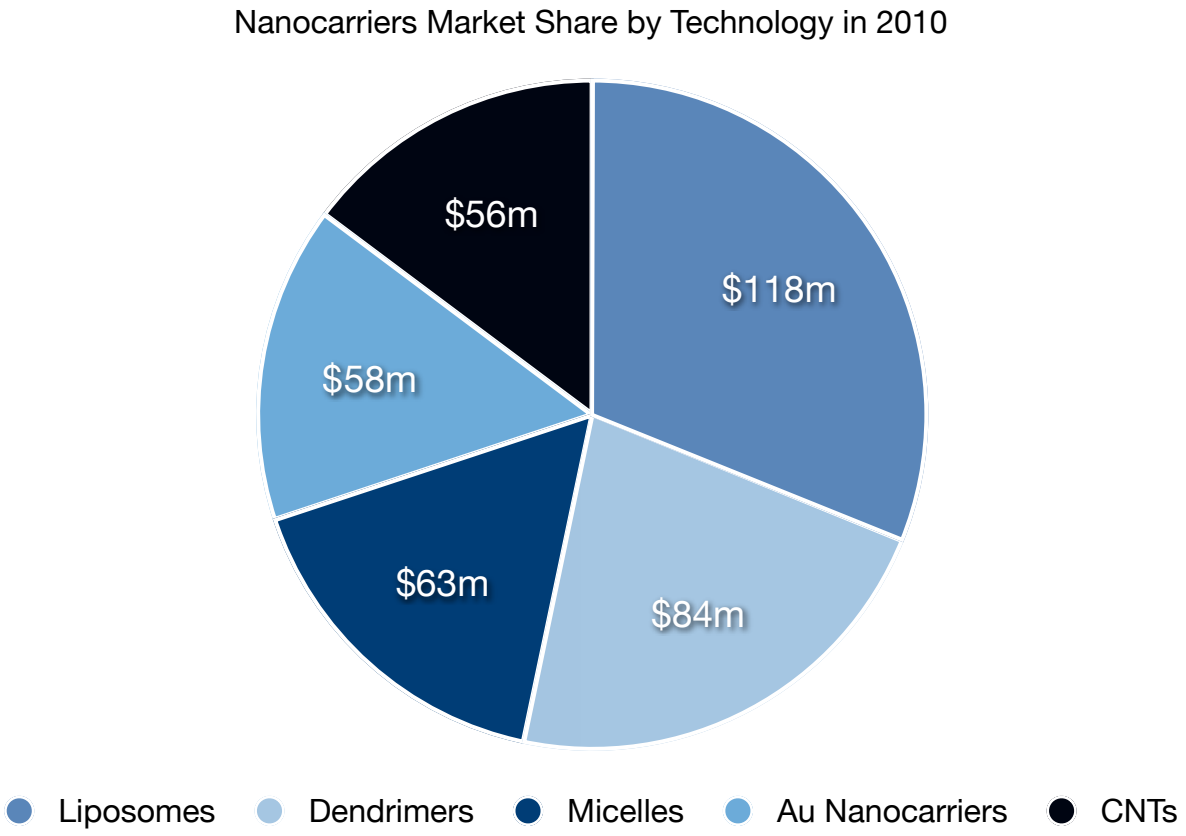
Liposomes (118 US$ Million Dollars), (28%);

Dendrimers (84 US$ Million Dollars), (19%);

Micelles (63 US$ Million Dollars), (15%);

Gold Nanocarriers (56 US$ Million Dollars), (13%);

CNTs (56 US$ Million Dollars), (13%).



Nanocarriers Versus Drug Nanocrystals...

Regarding total nanocarriers versus drug nanocrystals, drug nanocrystals show a higher TAM value in 2010, when compared with total nanocarriers:

Drug Nanocrystals (596 US$ Million Dollars), (58%);

Total Nanocarriers (434 US$ Million Dollars), (42%).

Key Nanotechnologies For Drug Delivery

Nanopharmaceuticals

Nanopharmaceuticals consist of ultra-small particles measured in nanometers. These particles can be designed to target diseased tissues, to control the release of therapeutic concentrations over a prolonged period of time, and to enable alternative routes of administration.

The emerging field of nanopharmaceuticals has the potential to transform drug therapy and become one of the most important advancements in technology over the next decade. Intelligently engineered drugs that utilize nanotechnology have the potential for much improved properties, including efficacy and safety.

Nanotechnology-derived drug delivery systems

The therapeutic advantages of this technology are becoming apparent and it is predicted it will soon be associated with every route of drug administration. The advantages over current treatment modalities include lower drug toxicities, improved bioavailability, reduced economic costs of treatment, and increased patient adherence to treatment. The medical management of malignancies has already been greatly impacted by nanotechnology, but soon other medical specialties will utilize these novel forms of drug delivery to achieve optimal treatment success. Additionally, innovative research and development of more therapeutically effective carriers will continue including improved forms of polymer–drug conjugates, liposomes, dendrimers, micelles, polymeric vesicles and nanocapsules. Finally, implantable drug delivery systems will open up many more opportunities for nanotechnology utilization. Optimized drug release from implantable delivery systems is preferable to intravenous administration. The extended duration of action, reduced frequency of redosing, and improved patient acceptance, are all positive attributes of implantable drug delivery systems.

Nanoparticle biotechnology

This is the next generation of the technological revolution in drug delivery. Specifically, this technology has vast medical and pharmacological potential because, combined with gene therapy, it can target a host of medical conditions.

Advances in nanotechnology that enable drugs to be delivered in ways that preserve their efficacy and to precise therapeutic targets are creating a host of opportunities for drug developers. A variety of nanostructures are being investigated as functional drug carriers for a wide range of therapies, most notably cardiovascular medicine, autoimmune diseases, and cancer. While the concept of nanoparticles in drug delivery is not new, the number of research programs and active drug development projects has escalated as funding for nanotechnology developers has increased. The result is the emergence of a host of novel nanotechnologies tailored to meet the physicochemical requirements of drug developers. Nanoparticles have already improved the availability and efficacy of some drugs and the capabilities that evolving technologies possess will lead to a dramatic increase in the number of therapies delivered via nanoparticles

Case Study

Researchers from IBM Research and the Institute of Bioengineering and Nanotechnology recently made an exciting discovery in nanomedicine. Their discovery, published online in Nature on 3 April 2011 demonstrated that: bacteria and infectious diseases like Methicillin-resistant Staphylococcus aureus (known as MRSA) Biodegradable nanostructures are physically attracted to infected cells like a magnet attracts iron filings, allowing them to selectively eradicate hard to treat bacteria without destroying healthy cells in the surroundings.

These nanostructures also prevent the bacteria from developing drug resistance by actually breaking through the bacterial cell wall and membrane, thereby inducing the lyses of these cells. This mode of attack approach is fundamentally different from the traditional antibiotics approach. MRSA is just one (among several) types of dangerous bacteria that is commonly found on the skin and easily contracted in places like gymnasiums, schools and hospitals where people are in close contact. In 2005, MRSA was responsible for nearly 95,000 serious infections, and associated with almost 19,000 hospital stay-related deaths in the United States – the main reason why MRSA is designated as a hospital bacterium. The challenge with infections like MRSA has two aspects

i.Drug resistance occurs because microorganisms are able to evolve to a new form effectively resistant to antibiotics. This happens because current treatments leave their cell wall and membrane largely undamaged.

ii.The high doses of antibiotics required to kill such an infection destroy both contaminated cells, as well as healthy red blood cells, in other words it is indiscriminate. The human body's immune system protects us from harmful substances (both inside and out). However, due to several reasons, many of today's conventional antibiotics:

- Are rejected by the body;
- Demonstrate a limited success rate in treating drug-resistant bacteria.

Once these polymers come into contact with water in or on the body, they self assemble into a new polymer structure that is designed to target bacteria membranes based on electrostatic interaction and break through their cell membranes and walls (inducing lyses). From the physical point of view, this action prevents bacteria from developing resistance to these nanoparticles due to the lyses. The electric charge naturally found in cells is important because the new polymer structures are attracted only to the infected areas – combating bacteria - while preserving the healthy red blood cells the body needs to transport oxygen throughout the body. The antimicrobial polymers created by IBM Research and the Institute of Bioengineering and Nanotechnology were tested against clinical microbial samples by The State Key Laboratory for Diagnosis and Treatment of Infectious Diseases and College of Medicine and Zhejiang University in China.

In the case that this technology is commercially manufactured, these biodegradable nanostructures:

- Can be injected directly into the body;
- Can be applied topically to the skin, treating skin infections through consumer products like deodorant, soap, hand sanitizer, table wipes and preservatives;
- Can be used to help heal wounds, tuberculosis and lung infections.

Selected Companies Active in Nanotechnology Drug Delivery

Company	URL
CytImmune Sciences, Inc.	http://www.cytimmune.com/
Cytokine PharmaSciences, Inc.	http://www.cytokinepharmasciences.com/
Debiopharm Group	http://www.debio.com/
Debiotech SA	http://www.debiotech.com/
Delpor, Inc.	http://www.delpor.com/
Digilab, Inc.	http://www.digilabglobal.com/
Druggability Technologies	http://drgtco.com/
Elan Corporation, plc	http://www.elan.com/
Enzon Pharmaceuticals, Inc.	http://enzon.com/
F. Hoffmann-La Roche Ltd	http://www.roche.com/
FEI Company	http://www.fei.com/
Flamel Technologies SA	http://www.flamel.com/
Flexible Medical Systems	http://www.flexmedsys.com/
FLUIDINOVA, ENGENHARIA DE FLUIDOS, SA	http://www.fluidinova.com/
Gamma Medica, Inc.	http://www.gammamedica.com/
Genencor	http://www.genencor.com/
Genetic Immunity, Inc	http://www.geneticimmunity.com/
GENOMIC VISION	http://www.genomicvision.com/
Gilead	http://www.gilead.com/
GlaxoSmithKline	http://www.gsk.com/
Intas Biopharmaceuticals Ltd.	http://www.intasbiopharma.co.in/
Intertek Cantox	http://www.cantox.com/
Intezyne, Inc	http://www.intezyne.com/
IOTA NanoSolutions Ltd.	http://www.iotanano.com/
Izon Science Ltd	http://www.izon.com/
Kiadis Pharma	http://www.kiadis.com/
Kuecept Ltd	http://www.kuecept.com/

Company	URL
Labopharm Inc.	http://www.labopharm.com/
Lena Nanoceutics Ltd	http://www.lenanano.com/
Leonardo Biosystems, Inc.	http://www.leonardobiosystems.com/
Life Technologies	http://www.lifetechnologies.com/
LiPlasome Pharma ApS	http://www.liplasome.com/
Lypro Biosciences	http://www.lyprobio.com/
Makefield Therapeutics, Inc.	http://www.makefieldtherapeutics.com/
Malvern Instruments Ltd	http://www.malvern.com/
Medical Nanotechnologies, Inc.	http://www.nanomedinc.com/
Merck & Co., Inc.	http://www.merck.com/
Merck Serono	http://www.merckserono.com/
Merck Sharp & Dohme Corp.	http://www.merck.com/
Midatech Ltd	http://www.midatechgroup.com/
MonoSol Rx	http://www.monosolrx.com/
NanGenex Inc.	http://www.nangenex.com/
Nano Interface Technology, Inc	http://www.nanointerfacetech.com/
Nano S Biotechnology	http://www.nano-s.com/
NanoBio® Corporation	http://www.nanobio.com/
NanoBioMagnetics, Inc	http://www.nanobmi.com/
Nanobiotix	http://www.nanobiotix.com/
NanoCarrier Co. Ltd.	http://www.nanocarrier.co.jp/
Nanoco Group PLC	http://www.nanocotechnologies.com/
Nanocopoeia, Inc.	http://www.nanocopoeia.com/
NanoForm Therapeutics	http://www.nanoformtherapeutics.com/
NanoInk, Inc.	http://nanoink.net/
NanoMaterials Technology Pte Ltd	http://www.nanomt.com/
NanoMedica, Inc.	http://www.nanomedica.com/
NanoMedical Systems, Inc.	http://www.nanomedsys.com/
NANOMOL TECHNOLOGIES SA	http://www.nanomol-tech.com/

Company	URL
Nanoquantum Sciences, Inc.	http://www.nanoquantum.com/
NanoSight Ltd.	http://www.nanosight.com/
Nanosphere, Inc.	http://www.nanosphere.us/
nanoTechnology Systems Pty Ltd	http://www.nanotechsys.com.au/
Nanotherapeutics, Inc.	http://www.nanotherapeutics.com/
Nanotrope Inc.	http://www.nanotrope.com/
NanoVector, Inc.	http://www.nanovectorinc.com/
Nemucore Medical Innovations	http://www.nemucore.com/
NexImmune, Inc.	http://www.neximmune.com/
NLAB Drug Delivery	http://www.nlabdrugdelivery.com/
nLife Therapeutics, S.L.	http://www.n-life.es/
Novartis Institutes for Biomedical Research (NIBR)	http://www.novartis.com/careers/careers-research-development/novartis-institutes-biomedical-research.shtml
Novartis Pharmaceuticals	http://www.novartis.com/
Novavax, Inc.	http://www.novavax.com/
NUCRYST Pharmaceuticals Corp.	http://www.nucryst.com/
Oxford Nanopore Technologies	http://www.nanoporetech.com/
Oz Biosciences	http://www.ozbiosciences.com/
PAR Pharmaceutical, Inc.	http://www.strativapharma.com/
Particle Sciences, Inc.	http://www.particlesciences.com/
Pfizer	http://www.pfizer.com/
PharmaIN	http://www.pharmain.com/
PharmaNova Inc	http://www.pharmanovaco.com/
Pharmidex	http://pharmidex.co.uk/
Phoenix S&T	http://www.phoenix-st.com/
PI (Physik Instrumente) L.P.	http://www.pi-usa.us/
PolyMicrospheres, Division of Vasmo, Inc.	http://www.polymicrospheres.com/
pSivida	http://www.psivida.com/
QIAGEN	http://www.qiagen.com/

Company	URL
QuantuMDx Group	http://www.quantumdx.com/
Quest PharmaTech Inc.	http://www.questpharmatech.com/
RevaNanoSystem	http://www.revananosystem.com/
Richman Chemical	http://www.richmanchemical.com/
SDG INC.	http://sdgpharma.com/
Selecta Biosciences, Inc.	http://www.selectabio.com/
Sigma-Tau Pharmaceuticals, Inc.	http://www.sigmatau.com/
SkyePharma PLC	http://www.skyepharma.com/
SoluBest Ltd.	http://www.solubest.com/
Spectrum Pharmaceuticals, Inc.	http://www.spectrumpharm.com/
Spherics, Inc.	http://www.spherics.com/
TetraLogic Pharmaceuticals, Inc.	http://www.tetralogicpharma.com/
The Dow Chemical Company ("Dow")	http://www.dow.com/
to-BBB technologies BV	http://www.tobbb.com/
Vindico Pharmacuticals	http://vindicopharma.com/
VYOME Biosciences	http://www.vyome.in/

About Cientifica

Cientifica is distinct from all other companies providing consulting and information services. It combines knowledge and expertise in both the science and business of emerging technologies, with nearly 20 years' experience in the field of science and research, and nearly 10 years' providing information on the business and science of emerging technologies. Cientifica employees are all highly experienced technical project managers and familiar not only with the commercialization of technology but also with the technology transfer of science from the laboratory to the marketplace.

Cientifica's numerous reports on commercial aspects of nanotechnology and other emerging technologies are well known for cutting through the hype and getting to the root of the issues. In the same way, Cientifica uses its experience in the reality of commercializing technologies and its wide network of international science and technology practitioners to provide down-to-earth and practical advice to companies, academics and governments.

Cientifica also provides advice to clients who are considering investment in emerging technology companies.

Through this experience Cientifica has a deep understanding of the drivers and associated risks associated with investment and management of cutting-edge technology projects.

Cientifica has worked in a wide variety of markets and with a diverse portfolio of clients, from oil and gas and biotechnical to automotive in both public and private sectors, providing technology advice on all aspects of the realities of emerging technologies.

For More Information

Nanotechnology for Drug Delivery 2021, gives a comprehensive analysis and geographic breakdown of the current nanotechnology drug delivery market and its key technologies. It also provides a forecast for the size of total addressable markets and percent share of those key technologies to 2021.

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