



# An Overview on recent Applications of Nanotechnology in Medical & Health Sciences

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## Abstract

Extensive research on various scientific resources had led to finding new solutions too many problems. One of those sources which has transformed itself into the most valuable resource which would be helpful in treating any kind of heinous disorder in the coming future is Nanotechnology. Nanotechnology and its varied applications have thrown light on treatment for brain tumors and other kinds of cancers, Coronary heart diseases and HIV virus. This sector has also paved way for replacing immunotherapy in near future for decimation of cancer cells and various Neurodegenerative diseases. Fluorescence imaging by nanopobes was also introduced which comparatively more effective than MRI scanning. This review article would mainly focus on the major applications of Nanotechnology which have been recently developed that makes us understand its enormous importance in near future.

## Keywords

Nanoparticles; Cancer; HIV; Quantum dots; Nanoprobe; Gold NPs.

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## INTRODUCTION

### 1.1 Nanotechnology

Nanotechnology is simply stated as an understanding and control of matter at dimensions between approximately 1 and 100 nanometers, where unique phenomena enable novel applications.<sup>1</sup> Encompassing nanoscale science, engineering, and technology, which involves imaging, measuring, modelling, and manipulating matter at this length scale. Nanomedicine is considered to be one of the most vital applications of Nanotechnology.<sup>2</sup> The term nanotechnology was coined by Norio Taniguchi

who described it as the processing, separation, consolidation and deformation of materials by one atom or one molecule.<sup>3</sup> The birth of cluster science and invention of the scanning tunneling microscope (STM) were the two milestones in development of NT which further lead to discovery of fullerenes in 1986 and carbon nanotubes (CNTs).<sup>4</sup>

### 1.2 Nanomedicine

According European Technology Platform on Nanomedicine (ETPN) nanomedicine can be defined as the application of nanotechnology to health. It exploits the improved and often novel physical,

chemical, and biological properties of materials at the nanometric scale.<sup>5</sup> Nanomedicine has potential impact on the prevention, early and reliable diagnosis and treatment of diseases.<sup>6</sup> There are varied types of NP platforms which vary in size, shape, compositions, and functionalities.<sup>7</sup> Liposomes were the first NP platform which were initially described as a model for cell membranes. Albumin-bound NPs (nab) are being used as one of the endogenous albumin pathways to carry hydrophobic molecules into the bloodstream.<sup>8</sup> Polymeric NPs are biocompatible and biodegradable polymers which are extensively being used as therapeutic carriers.<sup>9</sup> Dendrimers are another type of NPs which are made from synthetic or natural elements including amino acids, sugars, and nucleotides.<sup>10</sup> There are many metallic NPs such as gold NPs which provide varied optical and chemical properties, biocompatibility and surface modification.<sup>11</sup>

There are various biomedical applications of Nanotechnology such as it is being used extensively as biosensors.<sup>12</sup> They are also used in pathogen detection and separation along with cell detection and separation (Detection and capturing of circulating tumor cells).<sup>13</sup> NPs are also used in target imaging.<sup>14</sup> These nanomaterials are also used extensively as delivery vehicles for many such as siRNA, hydrophobic compounds and delivering agents to sub cellular organelles.<sup>15</sup>

### 1.3 Protein NPs

Protein NPs are considered to be a biodegradable carrier which would help in incorporating drugs.<sup>16</sup> These NPs provide metabolized covalent attachment of drugs and ligands.<sup>17</sup> These NPs are easily amenable for surface modification.<sup>18</sup> They can also be utilized for pulmonary delivery of protein therapeutics.<sup>19</sup> These are most commonly used for oral delivery systems.

Protein NPs are considered to be the most efficient colloidal drug carrier systems which primarily effect the drug targeting system with the help of modified protein NPs by reducing drug toxicity. Prevention of enzymatic degradation by these NPs was considered to be a vital merit for these NPs. This type of NPs are already being extensively used as pharmaceutical carriers in various cancer therapies. Parenteral, peroral and ocular types of administration were conducted using PNPs in order to deliver large and small biological molecules.

### 1.4 Oral Gene Delivery System

There are several advantages of oral route of administration such as it is easy to use and very much safe for the patient, self-administration by patient is

possible through oral route of drug intake and it is also economically very cheap when compared with other types of administration.<sup>20</sup> The major challenge of this type of drug administration is to overcome the acidic pH of gastric juice and presence of digestive enzymes which limits the potential of therapeutic agents.

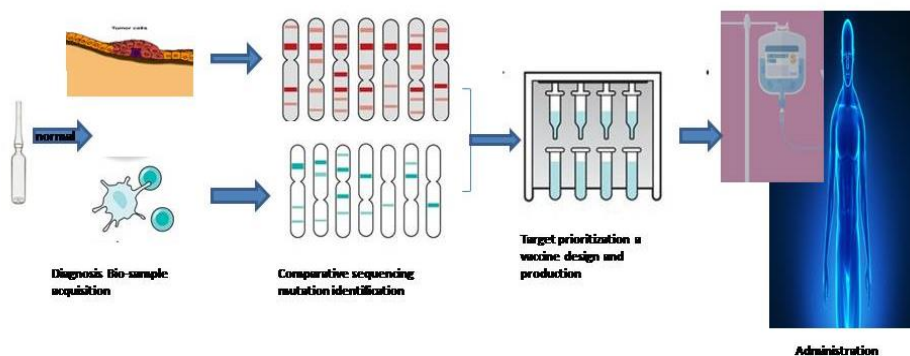
Oral gene delivery systems are said to be one of the most efficient gene delivery systems which have enhanced the efficacy of delivery of proteins, peptides, nucleic acids to the target tissues.<sup>21</sup> There have also been many obstacles in this type of oral gene delivery systems such as poor efficiency of delivering the DNA to the target cells and poor bioavailability of macromolecules.<sup>22</sup> These systems are generally used in transporting proteins, peptides and desired nucleic acids to the target tissues in an efficient way.<sup>23</sup> Oral way of administration is comparatively very easy and safe than that of other routes of administration.<sup>20</sup> This route of administration is also very much economical as it is very cheap. There has been varied range of applications related to oral gene delivery systems. One of the most important and widely used applications of this type of delivery system is gene therapy for various parts of our body such as intestine. Intestinal epithelium is said to show large cellular surface area which is useful for transduction with a therapeutically useful gene.<sup>24</sup> Gene vaccines are also one of the most widely used application of oral gene delivery systems whose concept was derived from a theory which briefed about vaccination with naked DNA.<sup>25</sup>

### 1.5 Vaccination and Immunotherapy

Vaccines activates the immune system for intercept and therapy of infection and other diseases which may harmful to human healthcare.<sup>26</sup> Cancer vaccine have been actively followed and studied for decades with many successful vaccines that are in market. However prophylactic cancer vaccines so far have been potent only for virus related cancers, such as human papillomavirus produce cervical cancer. provenge (stipuleucel-T), the only U.S food and drug administration approved therapeutic cancer vaccine to date, has only had modest clinical effect for therapy of prostate cancer. Compared to other immunotherapies, such as notable clinical efficacy. One of the key drawback to the development of an efficacy cancer vaccine is the difficulty in antigen selection. Traditionally, cancer vaccine are selected to target tumor associated antigens (TAAs) as they are overexpressed in cancer and it is universal targets among patients of the same malignancy. Nonetheless, TAAs can potentially initiate central

and peripheral resistance leading to less vaccination efficacy or autoimmunity against normal tissue, in which TAAs are also present in that tissue. One of the

study proved that nanomedicine approach would act as an alternative treatment option to induce the autophagy in cancer therapy<sup>26</sup>.



**Fig1:** The overall genomic configuration of malignant cells, potentially favouring the emergence of immunogenic tumour neoantigens, as well as specific mutations that compromise the ability of the immune system to recognize or eradicate the disease have been associated with differential sensitivity to immunotherapy in preclinical and clinical settings.

### Nanoprobes & their applications

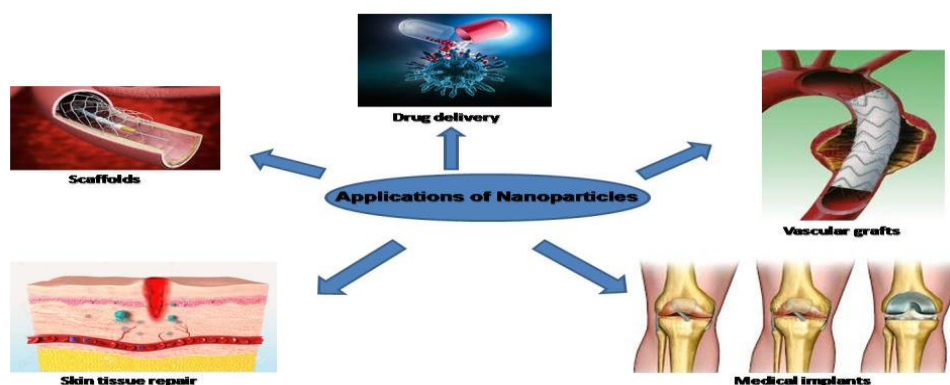
The repeated appearance of tumour on the same organ site is the major reason for failure of treatment in patients with abnormal tissue that do not contain cyst<sup>27</sup>. Tumour targeted surgical operation. Fluorescence represents method of presenting, reduction of volume of tumour in decrease in number of cells and to become better in surgical operation. Cutting or removal of part of body or organ is the most used technique and it is easily curable. But now fluorescence is the technique that it has advantage of less time, acts particularly on targeted sites, high accuracy and with ionising radiation risk. The tumour identification is the major challenge for x-rays, DRC and ECG. Fundamental change in surgery will be a benefit to surgeons to do surgery faster. The development in bioimaging that is analysis of real time body process is the technique used for reducing of tumours by nanoprobes by analyzing the body parts. The NIR-2 fluorescence technique is also used for efficient and quick surgery<sup>27</sup>.

### Recent Applications of Nanoparticles

The nanotechnology was recently highly developed in medical science and nanoparticles, nanomaterials

are obtained recently from the bulk materials like gold, silver and silica which are produced physically or biochemically<sup>28</sup>. The main reason of change in nanoparticle is due to their physical, chemical and biological properties. There are many reasons to increase in nanoparticle use in drug delivery system as image distribution agents for medical purpose. Now a days the cancer treatment is based on chemical therapeutic drugs mainly involved in chemotherapy or radiotherapy to destroy cancer cells. This treatment causes health issues and side effects to the patient. Gold particles due to their unique size and shape are produced by UV rays, IR radiation, chemical and biological ways. The gold nanoparticles have advantage of compatible with body, cytotoxic properties of nanoparticles, that is less base on surface area, size and shape based on this the nanoparticles are evaluated.

Gall bladder cancer is the most common biliary tract disease it has characteristics of increase in growth and high damage to patients. Some of cytotoxic agents which are used in advanced biliary tract disease causes reduce in death rate and infections<sup>29</sup>.



**Fig2:** Applications of Nanotechnology are Scaffolds, Drug delivery systems, Vascular grafts, Skin tissue repair and Medical implants.

The route of administration of drug for eye is ophthalmic application but it doesn't enter into eye by crossing of barrier only few amount is entering into the eye<sup>30</sup>. Even though the eye is protected by barriers the eye is still effected by the tissue damage leads to immediate surgery. The tissue damage of eye lens is the major cause for 50% of blindness in world. The main cause of tissue damage is growing old is generally associated with external factors like u v rays and external injury causing accident and genetics. The nanoparticles have capacity to enter into the transparent layer of eye. The nanoparticles have a major advantage is that is it has reduced size and easily enter into blood circulation. The SLN-NAC major function is taking of nanoparticles by eye tissue, attachment to layer of eye cells process of clearing from eye tissue region. The nanoparticles has size ranging from 10\_400 nm will enter into deeper layer of inner layer of tissue for not arising of damage of eye lens tissue. The SLN-NAC technique is used for preventing tissue of lens by reducing the dosage by injecting through injection. The SLN\_NAC technique prevent the damage of inner layer of eye.<sup>30</sup>

Lung diseases are day by day increasing in the population it causing financial and physical burden on the patients.<sup>31</sup> The two types of lung cancer are small cell lung cancer (SCLC) and non-small cell lung cancer (NCLCs). The elastic matrix major cause for extending and recoil of lung tissue.<sup>31</sup>

Nanotechnology is the latest technique used for the treatment of diseases.<sup>32</sup> Exosomes have an evident to have high drug delivery to produce desired result as compared to polymers. Lack of confirm to stand and purification is major aim to for starting of

exosomes technique into the clinical study. The researchers in the recent two decades identified the exosomes the basic advantage of short time, high specificity, low toxicity and high efficacy.<sup>32</sup>

The increase people suffered with neurological disorders, functional loss of neuron, which is a major cause in the society.<sup>33</sup> The pollution of air is the one of main cause of increase in health problems. The people dying due to air pollution is high. The particulate matter in size is 2.5  $\mu\text{m}$  (PM2.5) the increase in people exposed above this is increased by 20% from 3.2 to 4.5millions according to survey in 2015. The dangerous consequences occur in brain if CNS more exposed to particulate matter, heavy metals and toxic materials. The safety of nanoparticles is based on their size, shape and surface area.<sup>33</sup>

The environmental changes and climatic change, increased in population and growth of infected individuals the occurrence superficial mycosis is increased and leads to death in recent years.<sup>34</sup> The dermatomycosis causes itching, patches on toes, skin rashes on thighs. It slowly spread to hair or nails causes loss of hair and deformation of nails. There are many therapeutic methods used to treat the mycosis. The basis requirement and its fulfilment have been satisfied by using of nanoparticles due to their ease of applications and their size, shape. The mostly used nanoparticles are silver nanoparticles and gold nanoparticle. The problems are arising due to the use of microbial resistant agent this causes the choosing of antimicrobial agents. Due their broad spectrum silver particles are used for antibiotics, Gold particle are used as surgical treatment purpose.<sup>34</sup>

Nanoparticles are materials which are 0.1million times smaller than the hair.<sup>35</sup> These are widely used for the medical purpose due to their size and bioavailability. These are very smaller in size that can be seen under microscope. They are classified as organic and inorganic nanoparticles. There are many advantages of nanoparticles in biotechnology are, ease of separation, catalytic reactions, storage of energy and biological fluids. Nanoparticles also have some disadvantages toxicity issue and radiation problems. To avoid radiation safety measures should be followed. These act on the surface of the particles that causes the cancer, mutation problems. The nanoparticles are used individually or in conjugation with other molecules for good response on neuron cells. Nanoparticles have capability of promoting and acting on the neuronal cells in internal and external conditions.<sup>35</sup>

Acquired immune deficiency syndrome (AIDS) was first identified in 1981 .The people suffering with HIV are 20 million in that 10 million people are dying due to this disease.<sup>36</sup> Every year 1.5million people are newly effected with HIV. The HIV mainly effect on CD41 T lymphocytes, this causes damage to the immune function which is known as AIDS. While CART evidenced to force viral load in patients. The delay in development and reduce in viral transmission. CART is unable prevent the HIV in infected individuals. The iron nanoparticle plays an important role in imaging and distribution in the body of plants or animal body due to their magnetic resonance. Nanoparticle system is measured based on the nanoscale systems .The carbon nanotubes are latest nanoparticles used in the treatment of HIV due to their chemical and physical properties.<sup>36</sup>

Nanotechnology has been highly developed in past 10 years.<sup>37</sup> Nanotechnology mimics the function in one dimension. The nanoparticles which have least size will have physicochemical properties which is distinguished from other macro or micro molecules. When nanoparticles with small size come in contact with body of plant or animal body, in human the interactions are mainly influenced by physicochemical properties. Many interactions in the body, immunological response and crossing across barriers based on particle size considerations. Based on the biochemical properties and particle size it is used in treatment of HIV and AIDS. The Nano carriers are size about 10nm and 100nm is used as therapeutic agent is combination on their surface which cause the increase in dissolution, bioavailability and solubility but their own activity get not effected.<sup>37</sup>

The nanotechnology is the latest technique used to treat diseases. Nanomaterials usage was highly increased. Carbon tubes are one of nanomaterial which was introduced in 1991. It is used because of it has properties of individual electrical, mechanical and structural properties. Due to this advantage which is used in small scale biological, electrical and mechanical advantages. The mice has to be injected with NP, MWCNTs, and MWCNTs+NP to identify the toxicity. Antioxidant against protecting parameters was measured to toxicity in gene but no toxicity was observed when administered at 5 mg/kg was administered .If dose of oxidative is not occurred, this causes toxicity in liver and DNA damage and reduce in sperm count.<sup>37</sup>

Nanoparticles of 100nm in size are generally used as vehicles in drug delivery systems such as biodegradable materials like polymers.<sup>38</sup> These are taken more by body cells rather than macromolecules for effective transfer of materials and drug delivery systems for medicative advantage the drug get attached to the surface of the particle. The targeted drug delivery system can control the drug that entering into the body of plants or bacteria. Nanoparticles are generally used for the drug delivery systems on target on organs with high stability, effectiveness, easily enter into blood circulation. Cancer is the one of the most dangerous disease in world to identify and treat the disease due to their imaging and therapeutic agents in blood brain barrier system, from the recent studies found that the nanoparticles are used in treatment of cancer .The nanoparticle Apolipoprotein E drug is used to inject it into blood brain barrier system.<sup>38</sup>

Coronary artery disease is the main reason for death of 4 million people in the European countries. The development of pharmaceuticals and medical treatment was improved but it is not controlling the reducing myocardial function and heart cell loss. PU and PU-LN1 were injected into the mice through skin for systemic determination of their Biocompatibility and tissue response. Scaffolds is the main reason of changing of composition of heart ECM that is improved with reason of positively effect of CPC in case of dividing, rejoining, time, specificity distinguished towards smooth muscle and cardiac muscle.<sup>39</sup>

The improvement of identification and treating of neoplasms and the abnormal growth of brain tumours still leads to death of patients. Magnetic resonance imaging (MRI) is powerful method for preoperative activity of brain imaging identification and restricting of tumour to particular place. The carbonized polymer dots (CPD) present mainly in



internal lysozyme structure. CPD are normally distributed in normal place of tumour effecting glial cells of brain evidence the stage of convenience restricting of tumour to particular organ before the surgery.<sup>39</sup>

#### Personalized anticancer immunotherapy

Cancer neoantigens obtained from somatic mutations happened randomly in tumor tissue represent a different type of targets for immunotherapies including cancer vaccine<sup>40</sup>. This tumor specific neoantigens vaccination reduces the potential induction of central and peripheral suffering as well as the risk of autoimmunity. This vaccines marked therapeutic potential in both preclinical and early phase clinical studies. Nonetheless, remarkable challenges remain in the effective and faithful recognition of immunogenic neoepitopes and the more efficient, safe delivery of the subunit vaccine components for electing potent and robust anticancer T cell responses.

The first step in developing such personalized vaccines is to identification of patient specific immunogenic neoantigen with recent advanced in genomes sequencing technology as well as the MHC epitope database and predictive algorithms, is now becomes possible to identify and screen cancer neoantigens for individual patient. Point mutation and insertion deletion<sup>40</sup>, could be identified by comparing the sequences of tumor and matched healthy tissue. Other methods are also exploited currently to identify the cancer neoantigens besides sequencing of tumor samples.

A large number of methods have been introduced for preparation, formulation and delivery of different cancer vaccines, whole tumor cell lysate nucleotide, protein or peptide-based vaccines dendritic based vaccines viral vectors, biomaterial assisted vaccines and so on. In vitro transcribed mRNA has undergone many preclinical and clinical investigations for therapeutic cancer vaccination with advanced of self-adjuvating activity<sup>40</sup>. Unformulated mRNA could be spontaneously taken up by many kinds of cells through scavenger receptor mediated endocytosis. As a result, only a small part of administered mRNA could be captured by APCs and reach cytoplasm for subsequent translation and antigen presentation.

Antigenic peptide has been extensively exploited for cancer vaccines as it presents several advantages including direct function as pivotal T cell epitope, low toxicity, low cost and ease of synthesis. In pioneered phase 1 clinical study evaluating SLPs based neoantigen cancer vaccine vaccines, a selective pool of twenty SLPs together with adjuvant cutaneous melanoma. During the treatment, seven vaccines

doses were administrated through subcutaneous injection in 20 weeks. Neoantiges could also be delivered by DCs, which plays a key role in antigen presentation in the immune system. Similarly sipuleucel T, DC vaccines targeting nepantigens have been developed and evaluated in a small scale clinical trial. It was found that this vaccine increased the preexisting neoantigen specific TCR repertoire against previously HLA class 1 restricted neoantigens. Biomaterials have been largely investigated for vaccine delivery as they could protect antigen and adjuvant molecules from degradation, enhance lymphoid organs targeting and modulate APCs potential in both preclinical and clinical development. This method is method have been employed to improve the efficacy of peptide or mRNA based neoantigen vaccines.<sup>40</sup>

#### CONCLUSION

Nanotechnology is considered to be a rapid growing science and loads of new applications are being found out on this every year. Nanoparticles have played major role in finding out a source of treating threatening disorders like Cancer, HIV etc. Metallic NPs like Gold nanoparticles have been extensively exploited in treatments of various disorders. Scaffolds have helped in treatment of cardiovascular disorders like coronary artery disease. Several recent studies have concluded that cancer neoantigens obtained from somatic mutations happened randomly in tumor tissue represent an different type of targets for immunotherapies including cancer vaccine and now Biomaterials are being largely investigated for vaccine delivery as they could protect antigen and adjuvant molecules from degradation, enhance lymphoid organs targeting and modulate APCs potential in both preclinical and clinical development. Studies on Carbonized Polymer dots have resulted in finding a solution for decimation of brain tumors.

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#### CONFLICTS OF INTEREST

The authors have declared that there are no Conflicts of interest.

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