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The Recent Advances in the Nanotechnology and Its Applications - A Review

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Abstract: *Nanotechnology is one of the most promising tools for the current revolution in agri-food sector. Nanotechnology approaches provide novel and innovative ways to improve crop yield and to reduce the use of harmful crop protection agents. nanotechnology has great advantages in food sector like detection of pesticides/toxicants in food items, development of food storage and packaging materials, enhancement of shelf life of foods, nanoencapsulation of food nutraceuticals or bioactive molecules, detection of pathogens in food materials, enhancement of food taste, color and odour. This domain includes better understanding of living and thinking systems, revolutionary biotechnology processes, synthesis of new drugs and their targeted delivery, regenerative medicine, neuromorphic engineering, and developing a sustainable environment. Nanobiosystems research is a priority in many countries and its relevance within nanotechnology is expected to increase in the future. The realisation that the nanoscale has certain properties needed to solve important medical challenges and cater to unmet medical needs is driving nanomedical research. In the future, we could imagine a world where medical nanodevices are routinely implanted or even injected into the bloodstream to monitor health and to automatically participate in the repair of systems that deviate from the normal pattern. The continued advancement in the field of biomedical nanotechnology is the establishment and collaboration of research groups in complementary fields.*

Key Word: *Nanotechnology, Nanocapsulation, Nanobiosystems, Drug delivery, Cancer therapy, Nanodevices.*

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I. Introduction

Nanotechnology literally means any technology on a nanoscale that has applications in the real world. Nanotechnology encompasses the production and application of physical, chemical, and biological systems at scales ranging from individual atoms or molecules to submicron dimensions, as well as the integration of the resulting nanostructures into larger systems. Nanotechnology is likely to have a profound impact on our economy and society in the early 21st century, comparable to that of semiconductor technology, information technology, or cellular and molecular biology [1].

Science and technology research in nanotechnology promises breakthroughs in areas such as materials and manufacturing, nanoelectronics, medicine and healthcare, energy, biotechnology, information technology, and national security. It is widely felt that nanotechnology will be the next Industrial Revolution. Nanometer-scale features are mainly built up from their elemental constituents. Examples include chemical synthesis, spontaneous self-assembly of molecular clusters (molecular self-assembly) from simple reagents in solution, biological molecules (e.g., DNA) used as building blocks for production of three-dimensional nanostructures, and quantum dots (nanocrystals) of arbitrary diameter (about 10–105 atoms). The definition of a nanoparticle is an aggregate of atoms bonded together with a radius between 1 and 100 nm. It typically consists of 10–105 atoms [2].

A variety of vacuum deposition and nonequilibrium-plasma chemistry techniques are used to produce layered nanocomposites and nanotubes. Atomically controlled structures are produced using molecular-beam epitaxy and organometallic vapor-phase epitaxy. Micro- and nanosystem components are fabricated using top-down lithographic and nonlithographic fabrication techniques and range in size from micro- to nanometers. Continued improvements in lithography for use in the production of nanocomponents have resulted in line widths as small as 10 nm in experimental prototypes. The nanotechnology field, in addition to the fabrication of nanosystems, provides impetus for the development of experimental and computational tools [3].

The discovery of novel materials, processes, and phenomena at the nanoscale and the development of new experimental and theoretical techniques for research provide fresh opportunities for the development of innovative nanosystems and nanostructured materials. The properties of materials at the nanoscale can be very different from those at a larger scale [4]. When the dimension of a material is reduced from a large size, the properties remain the same at first, then small changes occur, until finally when the size drops below 100 nm, dramatic changes in properties can occur. If only one length of a three-dimensional nanostructure is of nanodimension, the structure is referred to as a quantum well; if two sides are of nanometer length, the structure is referred to as a quantum wire. A quantum dot has all three dimensions in the nano range. The term quantum is associated with these three types of nanostructures because the changes in properties arise from the quantum-mechanical nature of physics in the domain of the ultrasmall.

The potential of nanotechnology have been recognized by many industries, and also commercial products are being manufactured. The main areas of nanotechnology application are in electronics, photonics, pharmaceuticals and cosmetics, food and finishes for surfaces and textiles. Nanoscience is defined as the study of phenomena and the manipulation of materials at the atomic, molecular and macromolecular scales, where the properties differ from those at a larger scale. It is also explained as the control of matter on an atomic and molecular scale with at least one characteristic dimension measured in nanometer. Moreover, it is defined as the design, production and application of structures, devices and systems through control of the size and shape of the material at nanometre scale.

Nanotechnology and nano-engineering stand to produce significant scientific and technological advances in diverse fields including medicine and physiology. In a broad sense, they can be defined as the science and engineering involved in the design, synthesis, characterization, and application of materials and devices whose smallest functional organization in at least one dimension is on the nanometer scale, ranging from a few to several hundred nanometers. A nanometer is one billionth of a meter or three orders of magnitude smaller then a micron, roughly the size scale of a molecule itself (e.g., a DNA molecule is about 2.5 nm long while a sodium atom is about 0.2 nm).

Nanotechnology provides innovative means of controlling and structuring food. Recently, nanotechnology has become an active research field in food science, especially related to the development of functional foods with improved functionality and value. Nanostructured colloids (nanocolloids) are nano-sized materials that can be inherently present in food, or they can be formed because of food processing technologies such as milling, homogenization, emulsification, electrospraying, spray-drying, supercritical CO2-based techniques, gelation, foaming, etc.

According to the European Commission, “Nanomaterial” means a natural, incidental or manufactured material containing particles, in an unbound state or as an aggregate or as an agglomerate and where, for 50% or more of the particles in the number size distribution, one or more external dimensions is in the size range of 1–100 nm. In specific cases and where warranted by concerns for the environment, health, safety or competitiveness, the number size distribution threshold of 50% may be replaced by a threshold between 1 and 50% [5].

Nanotechnology, a recently developed field of science which could even fit into a person’s fingernail is mainly an inter-disciplinary branch of physics, chemistry, biology and engineering sciences, rapidly growing to radically transform electronics, automobiles, agriculture, food and various other industrial systems. Nanomaterials/ nanostructures with unique physical, chemical and mechanical properties can be synthesized by applying this attractive technology which may find applications in industrial sectors of global market.

Synthesized nanomaterials are characterized by high end equipments SEM, TEM, AFM, DLS zeta, X-ray diffraction, DSC, TGA, fluorescence, FT-IR and UV-Vis spectroscopy for their morphology and other attributes like size, stability, surface charge, degree of crystallinity, presence of surface functional groups, and thermo sensitivity **[6].**

Classification of Nano Materials

Nano materials can be classified dimension wise into following categories:

Classification Examples

- Nano rods, nano wires have dimension less than 100 nm.
- Tubes, fibers, platelets have dimensions less than 100 nm.
- Particles, quantum dots, hollow spheres have 0 or 3 Dimensions < 100 nm.

On the basis of phase composition, nano materials in different phases can be classified as,

- The nano material is called single phase solids. Crystalline, amorphous particles and layers are included in this class.
- Matrix composites, coated particles are included in multi-phase solids.
- Multi-phase systems of nano material include colloids, aerogels, Ferro fluids, etc.

Effect of nanotechnology in food industries

The applications of nanotechnology have been recognized by many industries. Even though foods are complex biological systems and also undergo a variety of processing. The discoveries made in nanotechnology also give impact to the food industry, due to the effect of biological and biochemical functionality of the system during the processing. Therefore, nanotechnology tries to help this problem to measure, control and manipulate the matter at the nanoscale level to change those properties and functions in a beneficial way. Besides that nanotechnology is also used as a means to understand how physicochemical characteristics of nano-sized substance can change the structure, texture and quality of foodstuffs **[7].**

Many major areas in food production may benefit from nanotechnology which is development of new functional materials, microscale and nanoscale processing, product development and methods, instrumentation design for improved food safety and biosecurity, storage, transportation and traceability. The rapid development in food industries improved tastes, colour, flavour, texture and consistency of foodstuffs, increased absorption and bioavailability of nutrients and health supplements, new food packaging materials with improved mechanical, barrier and antimicrobial properties, nano-sensors for traceability and monitoring the condition of food during transport and storage. The effect of nanotechnology in food industries is illustrated in Figure -1.

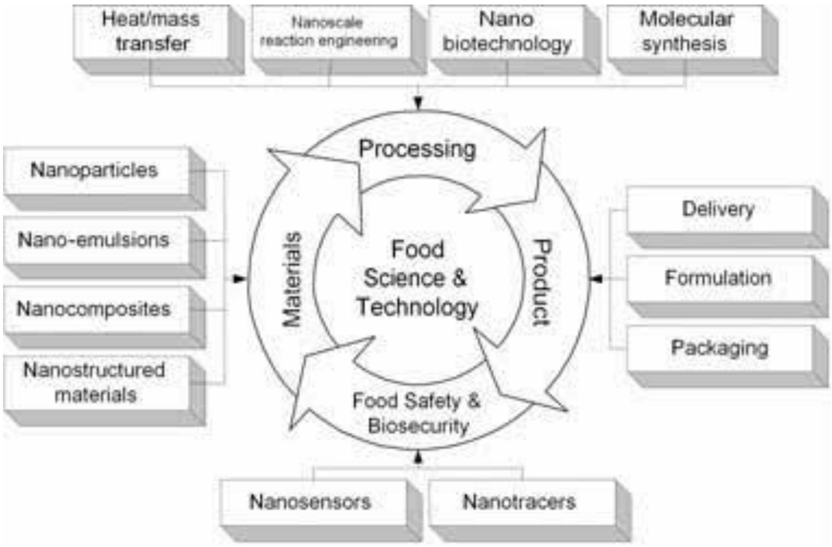

FIGURE -1: EFFECT OF NANOTECHNOLOGY IN FOOD INDUSTRIES

The term ‘nanofood’ basically deals with the food that has been cultivated, produced, processed and then packed using various nanotechnological aspects or the food in which synthesized nanomaterials have been added. The nanoformulation of the dietary supplements, functional foods, bioactive molecules, and herbal products having medical value is known as nano-nutraceuticals, a term combining nutrition with pharmaceuticals. Food items undergo a variety of modifications at the stage of post-harvesting and processing that bring a change in the biological and biochemical makeup of food. Hence, the nanotechnological advancements in the fields of biology and biochemistry could influence the food industry **[8].**

It has been a challenge and overwhelming task for the scientists engaged with nanotechnology to overcome these limitations. Companies are now developing novel functional foods with improved taste and health benefits. Hence, nanotechnology can be a promising technology to resolve the issues related to food security, shelf life, disease treatment, delivery methods, detection of food contaminants and pathogen, food packaging and protection of the environmental contamination.

Nanotechnology in Medicine

The use of nanotechnology in medicine offers some exciting possibilities. Some techniques are only imagined, while others are at various stages of testing, or actually being used today. Nanotechnology in medicine involves applications of nanoparticles currently under development, as well as longer ranges research that involves the use of manufactured nano-robots to make repairs at the cellular level.

Advancement in the field of nanotechnology and its applications to the field of medicines and pharmaceuticals has revolutionized the twentieth century. Nanotechnology is the study of extremely small structures. The prefix “nano” is a Greek word which means “dwarf”. The word “nano” means very small or miniature size. Nanotechnology is the treatment of individual atoms, molecules, or compounds into structures to produce materials and devices with special properties. Nanotechnology involve work from top down i.e. reducing the size of large structures to smallest structure e.g. photonics applications in nano electronics and nano engineering, top-down or the bottom up, which involves changing individual atoms and molecules into nanostructures and more closely resembles chemistry biology **[9].**

Nanotechnology deals with materials in the size of 0.1 to 100 nm; however it is also inherent that these materials should display different properties such as electrical conductance chemical reactivity, magnetism, optical effects and physical strength, from bulk materials as a result of their small size.

Nanotechnology in Medicine Applications

One application of nanotechnology in medicine currently being developed involves employing nanoparticles to deliver drugs, heat, light or other substances to specific types of cells (such as cancer cells). Particles are engineered so that they are attracted to diseased cells, which allow direct treatment of those cells. This technique reduces damage to healthy cells in the body and allows for earlier detection of disease **[10].**

Nanotechnology in medicine involves applications of nanoparticles currently under development, as well as longer ranges research that involves the use of manufactured nano-robots to make repairs at the cellular level (sometimes referred to as *nanomedicine*). Whatever you call it, the use of nanotechnology in the field of medicine could revolutionize the way we detect and treat damage to the human body and disease in the future, and many techniques only imagined a few years ago are making remarkable progress towards becoming realities.

Drug Delivery

In nanotechnology nano particles are used for site specific drug delivery. In this technique the required drug dose is used and side-effects are lowered significantly as the active agent is deposited in the morbid region only. This highly selective approach can reduce costs and pain to the patients. Thus variety of nano particles such as dendrimers, and nano porous materials find application. Micelles obtained from block co-polymers, are used for drug encapsulation. They transport small drug molecules to the desired location. Similarly, nano electromechanical systems are utilized for the active release of drugs. Iron nano particles or gold shells are finding important application in the cancer treatment. A targeted medicine reduces the drug consumption and treatment expenses, making the treatment of patients cost effective. Nano medicines used for drug delivery, are made up of nano scale particles or molecules which can improve drug bioavailability. For maximizing bioavailability both at specific places in the body and over a period of time, molecular targeting is done by nano engineered devices such as nano robots **[11].** The molecules are targeted and delivering of drugs is done with cell precision. In vivo imaging is another area where Nano tools and devises are being developed for in vivo imaging. Using nano particle images such as in ultrasound and MRI, nano particles are used as contrast. The nano engineered materials are being developed for effectively treating illnesses and diseases such as cancer. With the advancement of nanotechnology, self-assembled biocompatible nano devices can be created which will detect the cancerous cells and automatically evaluate the disease, will cure and prepare reports. The pharmacological and therapeutic properties of drugs can be improved by proper designing of drug delivery systems, by use of lipid and polymer based nano particles [12]. The strength of drug delivery systems is their ability to alter the pharmacokinetics and biodistribution of the drug. Nano particles are designed to avoid the body's defense mechanisms **[13],** can be used to improve drug delivery. New, complex drug delivery mechanisms are being developed, which can get drugs through cell membranes and into cell cytoplasm, thereby increasing efficiency. Triggered response is one way for drug molecules to be used more efficiently. Drugs that are placed in the body can activate only on receiving a particular signal. A drug with poor solubility will be replaced by a drug delivery system, having improved solubility due to presence of both hydrophilic and hydrophobic environments [14]. Tissue damage by drug can be prevented with drug delivery, by regulated drug release. With drug delivery systems larger clearance of drug from body can be reduced by altering the pharmacokinetics of the drug. Potential nano drugs will work by very specific and well understood mechanisms; one of the major impacts of nanotechnology and nanoscience will be in leading development of completely new drugs with more useful behaviour and less side effects.

The applications of nano particles in drug delivery Abraxane, is albumin bound paclitaxel, a nano particle used for treatment of breast cancer and non-small- cell lung cancer (NSCLC). Nano particles are used to deliver the drug with enhanced effectiveness for treatment for head and neck cancer, in mice model study ,which was carried out at from Rice University and University of Texas MD Anderson Cancer Center. The reported treatment uses Cremophor EL which allows the hydrophobic paclitaxel to be delivered intravenously. When the toxic Cremophor is replaced with carbon nano particles its side effects diminished and drug targeting was much improved and needs a lower dose of the toxic paclitaxel [15]. Nano particle chain was used to deliver the drug doxorubicin to breast cancer cells in a mice study at Case Western Reserve University. The scientists prepared a 100 nm long nano particle chain by chemically linking three magnetic, iron-oxide nano spheres, to one doxorubicinloaded liposome. After penetration of the nano chains inside the tumor magnetic nanoparticles were made to vibrate by generating, radiofrequency field which resulted in the rupture of the liposome, thereby dispersing the drug in its free form throughout the tumor. Tumor growth was halted more effectively by nanotechnology than the standard treatment with doxorubicin and is less harmful to healthy cells as very less doses of doxorubicin were used [16, 17]. Polyethylene glycol (PEG) nano particles carrying payload of antibiotics at its core were used to target bacterial infection more precisely inside the body, as reported by scientists of MIT. The nano delivery of particles, containing a sub-layer of pH sensitive chains of the amino acid histidine, is used to destroy bacteria that have developed resistance to antibiotics because of the targeted high dose and prolonged release of the drug. Nanotechnology can be efficiently used to treat various infectious diseases [18, 19].

'Minicell' nano particle are used in early phase clinical trial for drug delivery for treatment of patients with advanced and untreatable cancer. The minicells are built from the membranes of mutant bacteria and were loaded with paclitaxel and coated with cetuximab, antibodies and used for treatment of a variety of cancers. The tumor cells engulf the minicells. Once inside the tumor, the anti-cancer drug destroys the tumor cells. The larger size of minicells plays a better profile in sideeffects. The minicell drug delivery system uses lower dose of drug and has less side-effects can be used to treat a number of different cancers with different anti-cancer drugs [20]. **(Peiris et al. 2012).**

Many substances that could, in theory, be used as medicines have the disadvantage that they are hardly, if at all, able to reach the diseased organs or tissues in the body. There are various possible reasons for this:

(1) the substance is hardly, if at all, soluble in water;

(2) the substance is broken down in the body or inactivated before it reaches its target;

(3) the substance is hardly, if at all, capable of passing certain biological barriers (cell membranes, placenta, blood- brain barrier);

(4) the substance distributes nonspecifically to all kinds of tissues and organs.

Substances of this kind are, therefore, ineffective or lead to undesirable adverse side effects. As long as a hundred years ago, German microbiologist Paul Ehrlich conceived of the idea of using "magic bullets" to direct medicines at their target more effectively [21]. This idea was taken up again at the end of the 1960s and researchers have since been developing such drug delivery systems [22].

Application of Nanoparticles in Cancer

Due to the small size of nano particles can be of great use in oncology, particularly in imaging. Nano particles, such as quantum dots, with quantum confinement properties, such as size-tunable light emission, can be used in conjunction with magnetic resonance imaging, to produce exceptional images of tumor sites. As compared to organic dyes, nano particles are much brighter and need one light source for excitation. Thus the use of fluorescent quantum dots could produce a higher contrast image and at a lower cost than organic dyes used as contrast media. But quantum dots are usually made of quite toxic elements.

Nano wires are used to prepare sensor test chips, which can detect proteins and other biomarkers left behind by cancer cells, and detect and make diagnosis of cancer possible in the early stages from a single drops of a patient's blood [23].

Nano technology based drug delivery is based upon three facts:

i) efficient encapsulation of the drugs,
ii) successful delivery of said drugs to the targeted region of the body, and
iii) Successful release of that drug there. Nano shells of 120nm diameter, coated with gold were used to kill cancer tumors in mice by Prof. Jennifer at Rice University. These nano shells are targeted to bond to cancerous cells by conjugating antibodies or peptides to the nano shell surface. Area of the tumor is irradiated with an infrared laser, which heats the gold sufficiently and kills the cancer cells [24, 25].

Cadmium selenide nano particles in the form of quantum dots are used in detection of cancer tumours because when exposed to ultraviolet light, they glow. The surgeon injects these quantum dots into cancer tumours and can see the glowing tumour, thus the tumour can easily be removed. Nano particles are used in cancer photodynamic therapy, wherein the particle is inserted within the tumour in the body and is illuminated with photo light from the outside. The particle absorbs light and if it is of metal, it will get heated due to energy from the light. High energy oxygen molecules are produced due to light which chemically react with and destroy tumours cell, without reacting with other body cells. Photodynamic therapy has gained importance as a noninvasive technique for dealing with tumours [26].

The applications of various nano systems in cancer therapy are summarized as [27].

• **Carbon nano tubes:** 0.5–3 nm in diameter and 20–1000 nm length, are used for detection of DNA mutation and for detection of disease protein biomarker.

• **Dendrimers:** less than 10 nm in size are useful for controlled release drug delivery, and as image contrast agents.

• **Nano crystals:** of 2-9.5 nm size cause improved formulation for poorly-soluble drugs, labeling of breast cancer marker HeR2surface of cancer cells.

• **Nano particles** are of 10-1000 nm size and are used in MRI and ultrasound image contrast agents and for targeted drug delivery, as permeation enhancers and as reporters of apoptosis, angiogenesis.
• **Nano shells** find application in tumor-specific imaging, deep tissue thermal ablation.
• **Nano wires** are useful for disease protein biomarker detection, DNA mutation detection and for gene expression detection.
• **Quantum dots,** 2-9.5 nm in size, can help in optical detection of genes and proteins in animal models and cell assays, tumor and lymph node visualization.

The Application of Nanotechnology

Nanotechnology has the potential to have a revolutionary importance on medical diagnosis and therapy. This technology become an indicator of solution especially in early detection of cancer cells before anatomical and physiological chance occur in infected cells. A major challenge in cancer diagnosis in the 21st century is to be able to determine the exact relationship between cancer biomarkers and the cancer and to be able to noninvasively detect tumors at an early stage for maximum therapeutic benefit. Significance of nanotechnology in cancer cell is diagnosis of tumor cell at starting of proliferation. The current technique of detection of cancers cells in mammography needs the tumor cells/proliferated cells reach in cell mass a minimum of 1 million cells whereas Nanotechnology detection of cancer cells specially breast cancer with cells mass 100- 1000 cells proliferated beyond the normal phase [28-30]. Nanotechnologies enable diagnosis at the single-cell and molecule levels and some can be incorporated in current molecular diagnostic methods, such as biochips. [31-35]

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