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Providing nano packaging standards for pharmaceutical products in accordance with international laws

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ABSTRACT
Today, nanotechnology is known as one of the newest methods in improving the quality, health and packaging of referee materials. Polymer nanocapsules have a special ability to store and release the carrier substance. Packaging is one of the important issues in the field of storage of medicinal materials, and the use of nanoscience can improve the quality and efficiency of packaging materials. Many of the materials that are currently used for packaging pharmaceuticals are non-degradable, which increase environmental pollution. Recently, polymer nanocomposites have been considered for the packaging of pharmaceuticals, which protect the products from physical damage and pollution. Also, smart packaging systems are made with the help of nano-sensors that are sensitive to the release of chemicals caused by the spoilage of medicines and by changing the color, it warns of the spoilage of the medicinal substance. In this article, different types of nanoparticles along with their different applications, the use of nanocomposites, nanosensors and are investigated. Also, in recent years, the rapid growth of nanotechnology has raised challenges in the field of health and safety of nanomaterials. Standardization is one of the first steps to assess and control risks resulting from nanotechnology. This study was conducted with the aim of reviewing the national standards of Iran in relation to the safety, health and environmental aspects of nanotechnology

Keywords: Nanotechnology, Nanoparticles, Nanomedicine, Packaging, Antimicrobial, Medicine, Standard, Environment

1. INTRODUCTION

Packaging of pharmaceuticals is one of the mainlevels in the production of pharmaceuticals, the importance of which is not hidden from anyone in the durability and useful life of pharmaceuticals. Whilst, the use of nanotechnology in the packaging of pharmaceuticals is an essential part and its importance is increasing every day [1-5]. The main part of employing this approach is to maintain the safety of medicinal materials, somainconsiderationslike the packaging type and the amount of its antimicrobial properties (determining the type of nanoparticles suitable for obtaining to the desired antimicrobial property) should be considered. Advancement in smart packaging to increase the useful life of pharmaceuticals is the purpose for Pharma Company. These packaging systems can repair tears and small holes based on environmental conditions (such as changes in temperature and humidity) and inform the consumer about the corruption of the medicinal substance.

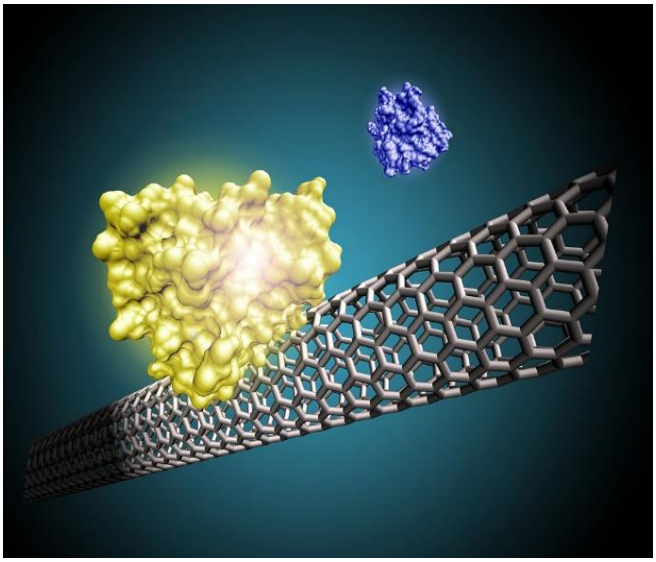

Figure 1: Application of nano in packaging technology with carbon nanotubes to prevent contamination

Nanotechnology is the application of scientific knowledge to manufacture, manipulate and control nanoscale materials [6]. In a general comparison with micromaterials, nanomaterials have more specific surface area and special physical, chemical, electrical, magnetic, mechanical, thermal, and optical characteristics that distinguish them from other materials. It differentiates in larger sizes [7]. The advances of recent decades in the field of nanotechnology promise the production of new nanomaterials with special physical and chemical properties. These advances have made it possible to use nanomaterials in all fields, as well as in medicine pharmaceutical production and packaging purposes [8] with the emergence of nanotechnology. Nanomaterials that are produced or consumed in industries or laboratories have exposed employees, consumers and the environment to a new generation of airborne hazards [9]. Concerns about nanomaterials increased when in vitro and in vitro studies in vivo confirmed their biological and toxic effects for living organisms [10] studies by one of the researchers in the In-vitro environment show that nanomaterials such as carbon-based nanomaterials may lead to cell death of human lung epithelial cells [8,11] Epidemiological studies confirm Major occupational exposures to nanomaterials occur due to their accumulation in the air and their inhalation. In this regard, the recent studies of the researchers of the same study confirm the presence of reactive oxygen species as a biomarker of oxidative damage in the air samples of workers exposed to nanomaterials [12].

Contact with nanomaterials in the work environment may be caused by the release of nanomaterials from powders, liquids or a solid matrix that occurs during their production, consumption or recycling [13] Working with dry powders has the greatest risk of release and contact as a result [14]. Predictions indicate that by 2030, seven million workers around the world will be in contact with nanomaterials [15] The development of standards is considered as a fundamental step in the assessment and control of the risks of nanotechnology [13] Simultaneously with the emergence and very rapid progress Nanotechnology, various organizations around the world have tried to compile and publish standards, guidelines, frameworks, methods, and new approaches for working with nanomaterials [16-19]. One of the most important organizations active in this field is the International Standard Organization (ISO). In this organization, a technical committee named "Technical Committee for Nanotechnologies" (ISO/TC 229: Nanotechnologies) develops and publishes standards related to working with nanomaterials [11]. One of the active working groups in this committee is the "Healthy, Safety and Health, Safety and Environmental ("Nano Technologies") is Aspects of Nanotechnologies (ISO/TC 229/WG 3) [17]. According to what was said, the importance of standards in evaluating and controlling the risks of nanomaterials is clearly defined. Therefore, the main goal of this study is to analyze the content and review the national standards compiled in the field of nanotechnology in relation to the aspects of safety, health and environment in the pharmaceutical field.

2. METHOD

In recent years, nanoparticles have played an important role in medical science and have many applications, including contrast agent in imaging and drug delivery to tumors. The picture below is a general diagram of the types of nanoparticles and their main applications in biomedicine.

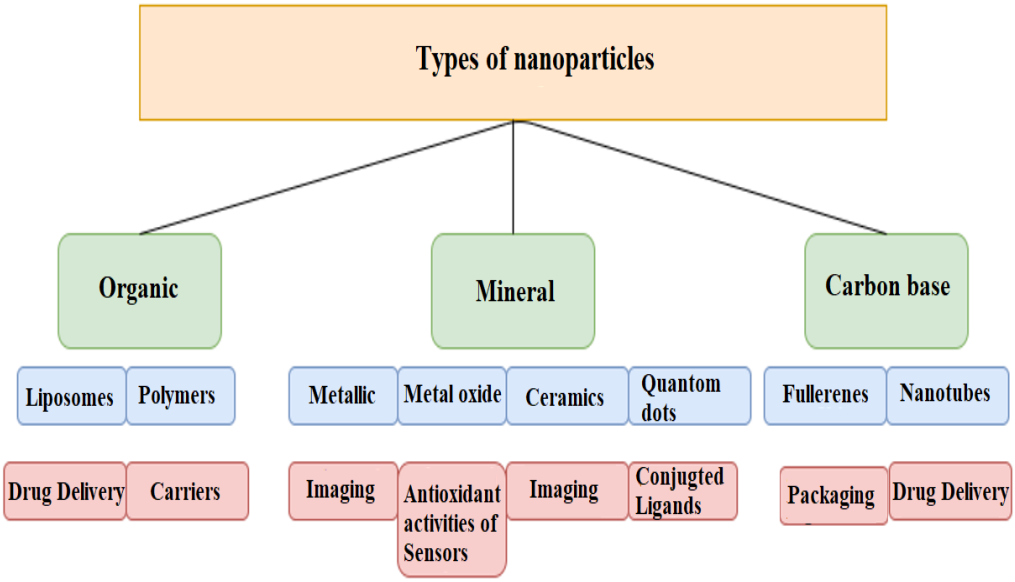

Figure 2. Nanoparticles used in medicine

2.1 Types of nanoparticles

1- Nano clay

Clay nanoparticles are one of the most studied nanoparticles.The reason for this attention is their cheapness, easy access and good performance.Clay can be used as a nano layer and with a thickness on the nano scale.Its minerals are mostly montmorillonite (bentonite) and it is often considered a commercial nano material.Clay nanoparticles are usually considered as two-dimensional plates with a very small thickness (about nanometers).Two special features of nanoclay that play an important role in the production of nanocomposites are: 1. The layers are opened from each other and dispersed in the polymer matrix. 2. Their surface modification for better interaction between the polymer matrix and nanoparticles [2, 20].

2- silver nanoparticles as antimicrobial materials in food packaging

The use of silver nanoparticles in single-layer packaging containers as additives, due to being impervious to oxygen and moisture, can prevent the growth of bacteria and molds in the packaging and, as a result, increase the shelf life of the productand not changing its appearance and physical characteristics.The size of silver particles is uniform (65-65 nanometers and on average 25 nanometers).These particles have high purity, good dispersion, and a quasi-spherical shape.In the ionic state, its antimicrobial effect is greater, but it is toxic.Because its nanoparticles have more surface area than larger particles, it is chemically more active than large silver particles.Nano compounds used in packaging sometimes have antimicrobial properties, and as a result, the packaging itself plays a role as an antimicrobial agent.Among the most widely used nano compounds used in these packages, we can mention silver nano particles, although nano oxide and chlorine nano oxide can also be used.But so far, it has been proven that silver nanoparticles are the most effective antimicrobial against bacteria, viruses and other eukaryotic microorganisms.The physical characteristics of nanomaterials, such as size and shape, surface characteristics, and their chemical composition can cause toxic effects.For example, silver nanoparticles produce reactive oxygen species that increase the reaction of molecules and create free radicals, and ultimately cause swelling and damage to proteins and membranes.The high antibacterial effect of nanosilver may cause the destruction of beneficial bacteria in the body and around us [3].

3-Titanium dioxide nanoparticles

Titanium dioxide nanoparticles are one of the most widely used semi-conducting nanoparticles with special hydrophilic and photocatalytic properties, absorb ultraviolet light and are antibacterial, and are effective against pathogens transmitted through food, including Salmonella, Vibrio parahemolyticus, and Listeria monocytogenes under UV light. [4]They are widely used in making polymer nanocomposites for the purpose of food packaging.These nanoparticles are very efficient in absorbing short-wavelength light, and this approach is used for UV protection in sunscreens and textiles [6].

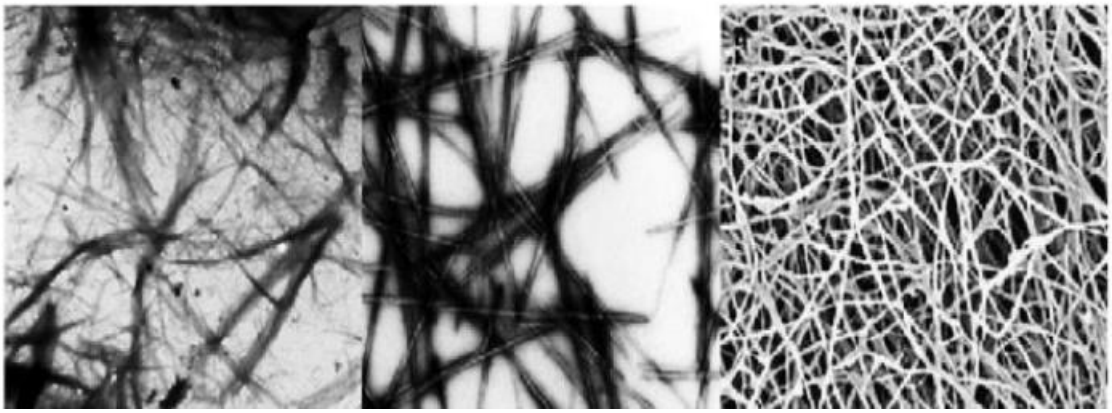

Figure 3. Electron microscope images of bacterial nanocellulose-cellulose nanocrystals-cellulose nanofibers

4- Zinc oxide nanoparticle

Zinc oxide nanoparticles belong to the wurtzite family and have properties such as semi-conductivity, piezoelectricity and pyroelectricity.These unique properties make zinc oxide particles the richest nanostructured materials.Also, these particles are safe and can be used in medical applications easily and uncoated, and are widely used in cosmetics and health industries.These special properties of zinc oxide can create various research fields in the future[5].

5-Nanoparticles of silicon dioxide

Silicon dioxide or silica is the most abundant component of the earth's crust.This compound with the chemical formula sio2 has a diamond-like structure and is a white crystalline substance.Its melting and boiling temperature is relatively high and it is found in nature in two crystalline and amorphous forms.

6-Nanoparticles of silicon oxide and silver oxide

They improve the barrier properties against oxygen and carbon dioxide and improve the mechanical properties of packaging.They also have antimicrobial, antifungal and antibiotic properties.

7- Nanocapsules

In recent years, one of the most common fields of application of nanoparticles in the food and pharmaceutical industries has been their use as carriers for food-drugs and bioactive substances.In the case of nutritional supplements, nanotechnology has been used to reduce the particle size of various compounds in order to absorb them.Among several effective methods in the production of nanoparticles, the encapsulation method seems to be the most appropriate method.In this method, the molecules are separated and coated inside the active compound.Therefore, such compounds are immediately and effectively absorbed inside the body

8- Nano sensors

Smart packaging systems are made with the help of nanosensors that are sensitive to the release of chemicals caused by food spoilage and by changing color, it warns of food spoilage.One of the very useful applications of nanosensors is their use in food safety and quality control, which can detect chemical and biological contaminants in very small amounts.Pests, antibiotics and different genes in agricultural products can be detected and analyzed by nano sensors.To ensure food safety, portable nanosensors can be used to detect harmful chemicals, pathogens, and toxins in food [7].

9- Nanocomposites

A composite is a bulky object or a mass that generally includes at least two separate materials with a complementary structure.The smaller the size of the nanoparticles, the more problem it is to distribute them in the polymer matrix.Since nanoparticles are so unstable and tend to aggregate or clump together, and the clumping of nanoparticles is considered a weak point for the polymer matrix.Inorganic nanoparticles with very small particle size make small changes in the nature of polymer materials and if they are designed and formulated correctly, they can enhance the thermal, mechanical, barrier and fireability properties of the polymer.

3. RESULTS

The importance of packaging and storage of medicines is very high. Advanced packaging based on nanotechnology has made it possible to transport materials safely without destroying the taste, structure and quality. In addition, it prevents pollution and maintains mechanical, physiological, physical and chemical properties. According to the studies conducted, the trend of using nano technology in the production, packaging and transfer of medicine is expanding (Figure 1). Nanoparticles used in pharmaceutical packaging can increase drug stability, lightness, heat resistance, and make them stronger in terms of mechanical and thermal performance, as well as less permeability to gases. Also, nanosensors enable detection of microorganisms,

pathogens, simple organic molecules and air/gas in medicines. Nanomaterials and nanotechnologies are still growing as these materials continue to be modified according to their applications and cost-effectiveness.

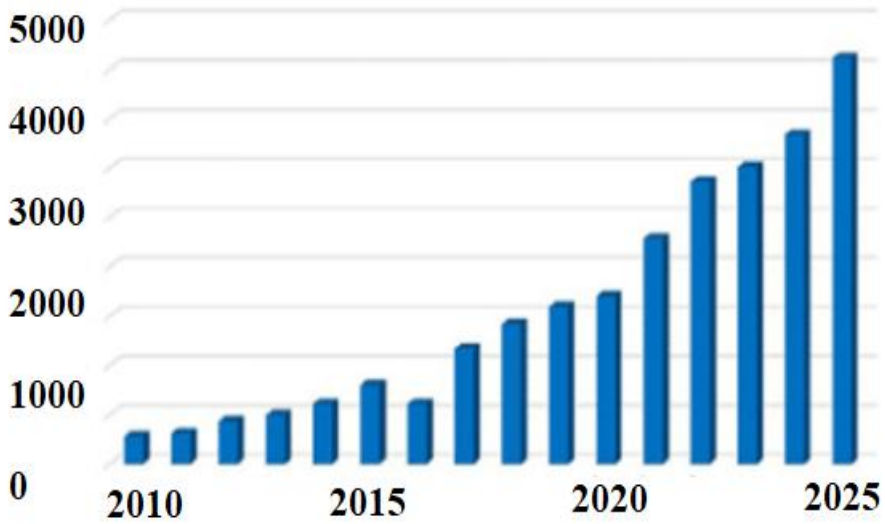

Figure 3. Trends of nanotechnology application in drug delivery

3.1 Medical nanotechnology

Medical nanotechnology in the field of pharmaceuticals has very basic applications, and the strategic goal in this field is to design patient-centered and disease-centered smart and targeted drugs.These drugs have specific action power and carry with them the ability to sense the damaged environment in the tissue and decide how to transfer it and the required amount (Dose) and avoid side effects and sensitizing. The design of materials used inDrug packaging (drug capsule material) is also one of the most important research topics in pharmaceutical nanomedicine.Some of the useful drugs are very toxic and if the capsule is opened before reaching the specific goal, they can cause side effects or reduce their effectiveness. Current researches in this field show that if the substances used inDrug capsule containing nanoparticles (in the size of 1).100 nanometers, compared to the materials that contain larger particles (microns), it has a larger surface-to-volume ratio, the size of the holes in the capsule wall is smaller, and the capsule will have better solubility. In such conditions, the structural propertiessuch capsules are completely different.These advantages increase the penetration and distribution of the drug by the capsule.

3.2 The use of edible films in packaging of pharmaceuticals

Today, the pollution caused by biopolymers has turned everyone's attention to the use of biodegradable materials, and during the last two decades, the study of biodegradable materials derived from proteins and carbohydrates has expanded widely, which can replace It is a suitable choice for synthetic polymers obtained from petroleum derivatives. Biodegradable packages that are edible and can be used together with pharmaceuticals are divided into edible films and coatings. Edible films are produced as a thin layer before being used in the packaging of pharmaceuticals, and then they are used for packaging like synthetic polymers. Unlike films, edible coatings are formed on the medicinal substance. Edible films and coatings have unique advantages compared to synthetic polymers. Biodegradability, very good prevention of the exchange of respiratory gases and as a result controlling the breathing of drugs, prevention of the transfer and exchange of aromatic and flavor compounds, as well as product protection against mechanical damage are among the most important advantages of edible films and coatings [8].

3.3 Laws of nanomedicines (packaging and consumption)

In this section, the rules and regulations governing the packaging and consumption of carrier materials in the field of pharmaceutical packaging have been evaluated using the Pharmacopoeias model in pharmaceutical and global health organizations.The advantages of packaging with nano materials in the field of pharmaceuticals can be mentioned as follows: improvement of barrier properties against liquid, gas and vapor (clay polymer nanocomposites).Creating more stability.Lighter weight.Greater resistance and protection against light, heat and moisture.Protection against pathogens and spoilage agents.Diagnosis of pollution.The checklist provided based on the World Health Organization and the American Health Organization is presented as follows:

Table 1: Criteria for the use of nanotechnology in the field of medicine

performance	physicochemical characteristics	Application type
microbial test results	the size of the nano material used and the morphology	Manufacturing or importing
heavy metal test results	nano-material concentration	Countries consuming
information related to the safety aspects of nano materials	type of coating	Product formulation with the name and effective amounts and additives
the approval of nano materials from health authorities	the concentration of polymorphic compounds	The effective ingredients of the nano product
approved by EPA	nano solvent residue	Manufacturing method
Studies related to Toxicology	Decomposition material	The advantage of using nanoparticles used
Material sensitivity	Microscopic images and particle size distribution	

4. CONCLUSION

Nano knowledge as a new technology has provided potential possibilities for improving the quality and safety of the pharmaceutical industry. The most application of nano technology is in the field of packaging and detection of pharmaceutical pathogens. This knowledge has caused a huge transformation in the packaging industry due to the modification of the structure of materials at the molecular level, and now the possibility of their industrial production is available. For the widespread use of nanotechnology in the packaging of pharmaceuticals, important issues must be considered. The most important of them is the issue of safety, because nanoparticles may enter the drug from the packaging containers of pharmaceuticals. However, more comprehensive research is needed in order to investigate the impact of the contact of different nanoparticles with food on human health in the long term due to their ability to pass through the cell membrane. Many concerns for the optimal selection of nanomaterials and operating conditions that affect human and animal health and well-being can be solved with the cooperation of experts and researchers to develop innovative materials and products to improve health care and thus balance the life cycle system. We will fix it. The widespread use of complex multi-layer films for packaging products leads to problems in recycling due to the complex structure, which leads to an increase in waste and thus affects the ecosystem all over the world. Therefore, it is recommended to select biopolymer materials for specific applications such as pharmaceutical packaging that can be recycled or dissolved.

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