THE USE OF NANOTECHNOLOGY IN MEDICINE

Florentina BURLACU[1]

Grațiela Doina GHIOALDĂ LUȚĂ[2]

Abstract

Nanotechnology is a new field of science that produces extremely small structures from organic or inorganic materials. These nanoparticles can be used in many fields: medicine, foods, cosmetics, clothing, constructions, furniture, not only in the making of electronics or in the automotive industry. Because of their special properties nanoparticles, also known as nanomaterials, can revolutionize all fields in which they are used. But the domain in which they can bring the most important benefits for human life is medicine. Nanoparticles can be used in the medicine field in the production of drugs and vaccines, and also in diagnostic and investigative tools, etc. Nanomaterials are used with great success in imaging and in the construction of medical devices. Many European citizens have legitimate concerns about the safe use of nanoparticles in medicines. All these concerns can be put aside only through thoroughly testing all the medicines that contain nanoparticles before they will be put on the market for general use.

Keywords: Nanotechnology, State of the Art, New Technology, Medicine, Health

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1. Introduction

Nanotechnology is not good or bad, it only is. The way it is used for the benefit of humanity or against humanity can determine if this discovery is The Holy Grail or the Nemesis for humankind. Nanotechnology can change the world bringing benefits in many important fields, but in medicine it can do miracles, and it can really make the difference between life and death.

Before we can discuss the use of nanotechnology in the medicine field, we must first define the term of nanotechnology.

[1] PhD candidate at The Bucharest University of Economic Studies, Bucharest, Romania, e-mail address: florentina.burlacu@yahoo.com

[2] PhD candidate at The Bucharest University of Economic Studies, Bucharest, Romania, e-mail address: gratiela101@yahoo.com

Artem Oppermann in his article „What Is Nanotechnology?" explains that nanotechnology is the „field of science and engineering that focuses on the design and manufacture of extremely small devices and structures" [2].

These extremely small devices that are smaller than 100 nanometers (nm) can be used in many fields from electronics to medicine, from energy to textiles, their range of applications is very wide [2].

Oppermann says that „nanotechnology refers to any device or product that is created or modified by manipulating matter at the nanoscale. By controlling atoms and molecules, companies can develop nanomaterials no more than 100 nanometers thick and apply these materials to industries like healthcare, sports and electronics" [2].

Nanotechnology is so important because it can be utilized to create materials and to develop devices and systems that have unique properties and functions. The extremely small size of the materials that are used in nanotechnology allows them to have different physical and chemical proprieties than the same materials have when they are at a larger scale [2].

The author of this article explains that „Due to their small size, nanomaterials have a large surface area-to-volume ratio, which can lead to increased reactivity, strength and conductivity" [2].

Because nanomaterials are exceptionally small in size, they can be incorporated very easy in a vast variety of products and processes such as medical treatments, electronic devices, energy production, environmental remediation, etc. Nanomaterials are used not only for improving the already existing products, but also for creating new ones that have an increased durability [2].

We are using nanotechnology in our daily life and some of us don't even know it. Nanotechnology is used in the making of electronics - smartphones, laptops, televisions, etc., cosmetics - foundations, moisturizers, etc., sporting goods - equipment, etc., clothing - outdoor gear, athletic wear, etc., sunscreen, furniture, adhesives, automotive, etc. [2].

Many are wondering how nanotechnology is made and how exactly nanomaterials are created. Nanomaterials are developed using the following methods:

- *Top-down approaches* – are using procedures like lithography, laser, chemical etching or mechanical milling to carve into a larger piece of material and to reduce it to nanoscale. They are used for making integrated circuits in electronics.
- *Bottom-up approaches* – are utilizing techniques such as chemical synthesis or self-assembly to build up materials from smaller components such as atoms or molecules. This is the way the synthesis of nanoparticles is created.
- *Self-assembly* – uses techniques such as template-assisted self-assembly or directed self-assembly to create materials or structures that are able to organize themselves into the desired nanoscale structure. For example, these techniques are used in the production of block copolymers.

- *Physical vapor deposition* – vaporizing a material to form a thin film used in the coating of various objects such as cutting tools.
- *Chemical vapor deposition* – uses a technique that makes a gas to react to a surface in order to create a thin film of the desired material. This procedure is used in the production of thin films for solar cells [2].

There are four main types of nanomaterials that are used in nanotechnology:

1. ***Carbon-based nanomaterials*** – are being made up of carbon nanotubes produced through carbon-based vapor deposition. In order to obtain such materials carbon is heated and added up after a reaction between a surface and a catalyst takes place.
2. ***Metal-based nanomaterials*** – they consist of quantum dots that are created by growing in a solution, under very specific conditions, nanoscale crystals of two different elements.
3. ***Dendrimers*** – are nanoparticles that are composed of a core, inner shell and outer shell. They can be constructed in two ways: starting from the core or starting from the outer shell.
4. ***Nanocomposites*** – are formed of either multiple nanomaterials or a blend of nanomaterials and much larger materials. The result is stronger metals, plastics and other substances [2].

Using nanotechnology brings a lot of benefits: enhanced medical treatments - creating more targeted and effective drugs, diagnostic tools and medical devices, improved materials, increased energy efficiency, improved water filtration and purification, improved food safety and agriculture [2].

But we must never forget the potential risks of nanotechnology: health and environmental risks - we can't predict with accuracy the long-term health effects of exposure to nanomaterials, nanotechnology in food could be harmful for humans and also for the environment, economic risks - nanotechnology can produce economic and financial inequality and job displacement and ethical risks - using nanotechnology as a weapon in the military field or in surveillance [2].

Nanotechnology can change the world as we know it. Because it can be applied in many fields it can really improve the quality of the human life. But in our humble opinion in the medicine field nanotechnology can bring the most important and valuable thing in the world: health, healing and life for all human beings.

2. Problem Statement

In his book „Current Advances in the Medical Application of Nanotechnology" Mark Slevin explains that in the medical field nanotechnology will help implement „new therapies, more rapid and sensitive diagnostic and investigative tools for normal and diseased tissues, and new materials for tissue engineering" [5].

Nanotechnology plays an important role in biomedical research and clinical medicine. Due to their small size nanoparticles can deliver drugs exactly into the targeted diseased cells or into exact locations within the tissue, which increases drug concentrations locally and reduces systemic toxicities. Nanoparticles can also be used in achieving sustained drug release after only one injection. Nanotechnology can help improving medical imaging and diagnosis techniques [5].

Mark Slevin explains that „nanomedicine is the medical use of molecular-sized particles to deliver drugs, heat, light or other substances to specific cells in the human body. Engineering particles to be used in this way allows detection and/or treatment of diseases or injuries within the targeted cells, thereby minimizing the damage to healthy cells in the body." [5].

In order to increase the efficiency and to reduce the side effects it is important to direct the drugs exactly where the disease is localized. This is possible with the help of some nanoparticles that have only 150 nm in diameter, they are made from biodegradable polymer poly (d,1-lactic-co-glycolic acid) and poly (ethylene glycol) and have been developed especially for encapsulating drugs, specific proteins or antibodies which can be attached to artificial RNA strands – aptamers. These nanoparticles are picked up by specific cells in which they dissolve in order to discharge the drug or the protein [5].

Slevin says that the treatment of a disease depends on the identification of a target and the delivery of a therapeutic agent which either causes a function to be restored, switches off inappropriate activity, or destroys the diseased cell in the case of cancer [5].

Nanotechnology is used not only in the production of drugs, but also in the development of vaccines for humans.

In the book „Micro- and Nanotechnology in Vaccine Development" edited by Mariusz Skwarczynski and István Tóth, the authors of chapter 5 Neeland, de Veer and Scheerlinck explain that nanoparticles can function as both a delivery system and an adjuvant to increase immunity [4].

The more frequently used nanoparticles in the development of vaccines are the following:

- *Virus-like particles (VLPs)* – 20-800 nm – are self-assembling nanoparticles that morphologically resemble infectious virions but lack infectious viral nucleic acid.
- *Aluminum salts and related inorganic particles (eg. $CaPO_4$, silicates, or gold)* – 25-1000 nm – many conventional vaccines use as adjuvant aluminum salts because they bind antigens through charge and hydrostatic interactions in order to enhance absorption by dendritic cells.
- *Immune stimulating complexes (ISCOMs)* – 40 nm – are nanoparticles that resemble with a cage. They are made up of Quil A (saponin adjuvant), cholesterol and phospholipids.

- *Viral sized inert polystyrene rigid nanoparticles* – 40-50 nm – they enhance the absorption by the dendritic cells at 40-50 nm viral-like size and can conjugate antigen.
- *Micelles* – 40-200 nm – the hydrophobic core is able to hold hydrophobic antigens or peptides coupled to the outer soluble layer.
- *Emulsions* – 50-600 nm – are oil-in-water formulas that transport antigens inside their core.
- *Liposomes* – 100-400 nm – are phospholipid bilayer vesicles with a water core in which the antigen is encapsulated.
- *Polymer nanoparticles [chitosan, poly (lactic-co-glycolic acid) - (PLGA), polyglycolic acid (PGA)]* – 40 nm-large gels – are being evaluated for development, they form gels and stable spheres to absorb or conjugate [4].

The authors of this study are convinced that the manipulation of the innate response through nanoparticles has a deep and important effect on the induced adaptive immune reaction. The addition of pathogen-associated molecular patterns (PAMPs) as adjuvants frequently results in serious inflammation at the injection site and the local lymph node [4].

It was discovered that associating these pathogen-associated molecular patterns to nanoparticles can result in a lower reactogenicity and at the same time maintaining or enhancing immunogenicity. Consequently, nanoparticles could really improve the clinical result of the next generation of effective adjuvants [4].

The researchers give a fair warning that if the pharmaceutical companies want to use these new technologies in the development of commercial products, they all need to improve their understanding of these new adjuvants. And the most important thing is that they have to address issues relating to safety including biodistribution and degradation of the nanoadjuvants [4].

In the last 4 years nanotechnology was used on a large scale in the development of vaccines. Nanoparticles were used in both anti-Covid-19 vaccines developed by Pfizer-BioNTech and Moderna [1].

The goal of the powerful pharmaceutical companies is to develop a multivalent vaccine for all the 20 known influenza A and B virus sub-types. This new generation of influenza vaccine is developed with the help of modified messenger RNA (mRNA) and lipid nanoparticles [3].

But the vaccine industry is not the only one that utilizes with great success nanotechnology. Another medical field in which nanoparticles can bring great change and start a revolution is imaging, diagnostics and medical devices.

The use of nanotechnology in medicine led to advances in early detection, imaging, and treatment of disease. The possibility to utilize nanoparticles in order to diagnose, treat and monitor disease progression without surgery, biopsy, or other invasive methodologies may increase the rate of survival, improve the quality of life and also reduce the costs [6].

The advances in bioconjugation and self-assembly made possible the development of „smart" targeted nanoparticles, which combine targeting molecules with therapeutic and/or imaging agents all in one extremely small particle. These nanoparticles make possible the delivery of imaging agents and drugs to the disease sites, resulting in the production of high contrast images with low levels of noise and also in an increased efficiency of the therapy with reduced adverse side effects [6].

Some nanoparticles have been developed from various naturally occurring organic building blocks such as: lipids, proteins, polymers. And others were produced from inorganic materials: gold, silica, iron [6].

More than 25 nanoparticles or platforms how they are also referred as in this study have been approved for clinical use. We mention here only one of them that has been used for imaging: the superparamagnetic iron oxide nanoparticles that were developed as contrast agents for magnetic resonance imaging (MRI) [6].

Although inorganic nanoparticles have some advantages like wide availability, controlled shape and size, and easy surface manipulation, but at the same time they have poor stability under aqueous conditions and low cellular transfer efficiency. Instead, lipid-based nanoparticles like liposomes and micelles can carry significant payloads of drugs, but they experience poor stability in vivo [6].

Apparently, the solution for all these limitations are the nanomaterials that are made up of plant viruses. Viral nanoparticles (VNPs) have many qualities and come in many shapes and sizes. In nature the viral capsid has as a main function the protection of its genome under various environmental conditions, therefore the VNPs are naturally stable and monodisperse. The viral nanoparticles are able to combine the strengths of inorganic and lipid-based materials [6].

The viral nanoparticles are derived from plants or bacteria and are able to deliver an ideal basis for the development of targeted imaging agents and „drug delivery vehicles". Virus-like particles (VLPs) are a subset of viral nanoparticles (VNPs) that can be produced at a large scale. VLPs lack any genomic replicative information and because of that they are safe, being non-infectious and non-hazardous for humans and animals [6].

The authors of this study explain that „VNPs and VLPs are self-assembling systems that are highly symmetrical, dynamic, polyvalent, and monodisperse, rendering them one of the most advanced nanomaterials produced in nature. They offer the advantages of biocompatibility and biodegradability over synthetic inorganic nanoparticles. In addition, they are extremely robust and well characterized and can be produced in large quantities within a short period of time." [6].

The structure of the viral nanoparticles makes it possible for them to be modified in several ways in order to allow the loading of drugs, imaging agents and other nanoparticles in their internal cavity, as well as chemical conjugation of targeting ligands on the external surface for the delivery in a specific tissue [6].

The application of nanotechnology in medicine has the potential to bring health and to cure all the incurable diseases. Also, this new technology can increase the life expectancy of all people on the planet.

But for this massive and revolutionary change in medicine to happen it is necessary for two things:

1. to test the long-term effects that nanoparticles have on human health and if they can be utilized without generating serious side effects and health problems,
2. the small group of rich people that have the patent for nanotechnology to wish to use the nanoparticles for the right causes and in the benefit of all humans.

We continue this article with the research questions that this paper is trying to answer.

3. Research Questions/Aims of the research

The questions we would like to find answers for are the following:

Have Europeans heard about nanomaterials?

Do Europeans have concerns about the negative impact of nanomaterials?

Do Europeans want to be informed about the products that contain nanomaterials especially the medicines?

We believe the answer to all the above questions is affirmative.

The objective of this article is to demonstrate that the citizens from the member states of the European Union are aware of the existence of nanotechnology and nanomaterials (nanoparticles). Europeans are to some extent informed about this subject and have legitimate concerns and questions when it comes to the use of nanoparticles especially in food, medicines and cosmetics.

4. Research Methods

We used in this article mainly the qualitative method in order to obtain the extensive data about the use of nanotechnology in the medicine field. Quantitative analysis is also used, especially when we present and interpret the statistical data. The following techniques are used in this paper: a case study on the use of nanoparticles in medicine, and the analysis of the theoretical works in the nanotechnology field.

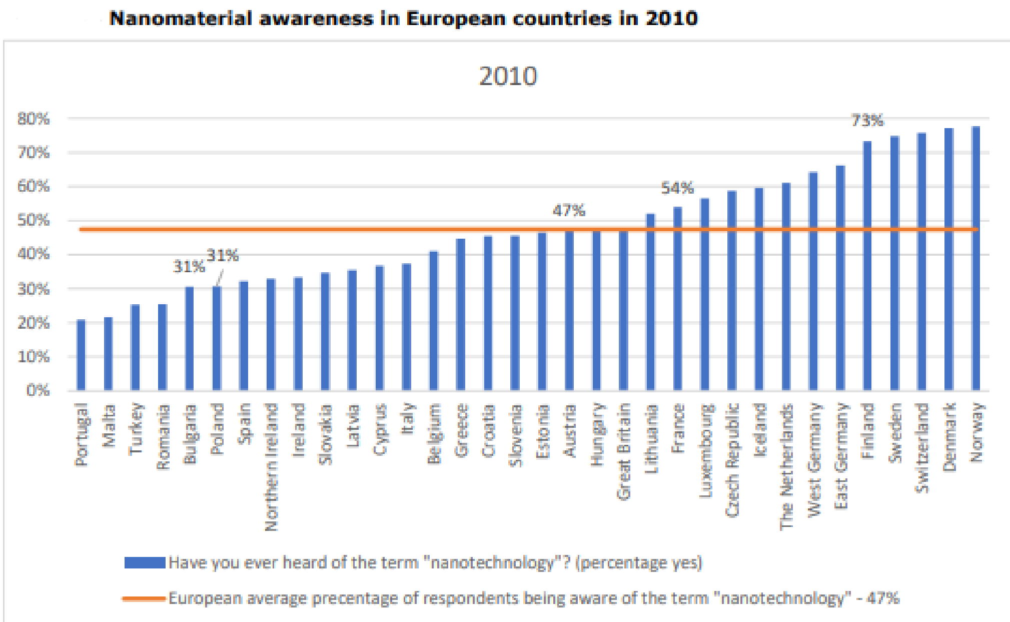
5. Findings

When it comes to nanotechnology statistical data is a little hard to find especially on open access journals. We don't understand why but ordinary people are also reserved in answering some questions about this subject.

The statistical data we are using come from a study that was commissioned by the European Chemicals Agency (ECHA) and was published in November 2020. The previous mentioned study „Understanding Public Perception Of Nanomaterials And Their Safety In The EU. Final report" is published on The European Union Observatory for Nanomaterials (EUON).

EUON is an entity funded by the European Commission and is being hosted and kept in existence by the European Chemicals Agency (ECHA). The European Union Observatory for Nanomaterials provides information about the existing nanomaterials on the EU market [7].

In the study „Understanding Public Perception Of Nanomaterials And Their Safety In The EU. Final report" it is presented a graphic that shows the European citizens awareness regarding the nanomaterials in the year 2010.



Graphic 1. Nanomaterial awareness in European countries in 2010[3]

[3] Source: *Understanding Public Perception Of Nanomaterials And Their Safety In The EU Final report,* November 2020, p. 42.

At the question „Have you ever heard of the term „nanotechnology"?" we can see illustrated with the blue columns the percentages of the „yes" answers in every European state. The red horizontal line fixed at 47% shows the average percentage of the European respondents that are aware of the term „nanotechnology".

From Graphic 1 we can easily see that the five countries that have the highest percent of knowledge about nanotechnology (over 70%) are with only one exception from the Northern Europe (Norway, Denmark, Switzerland, Sweden, Finland).

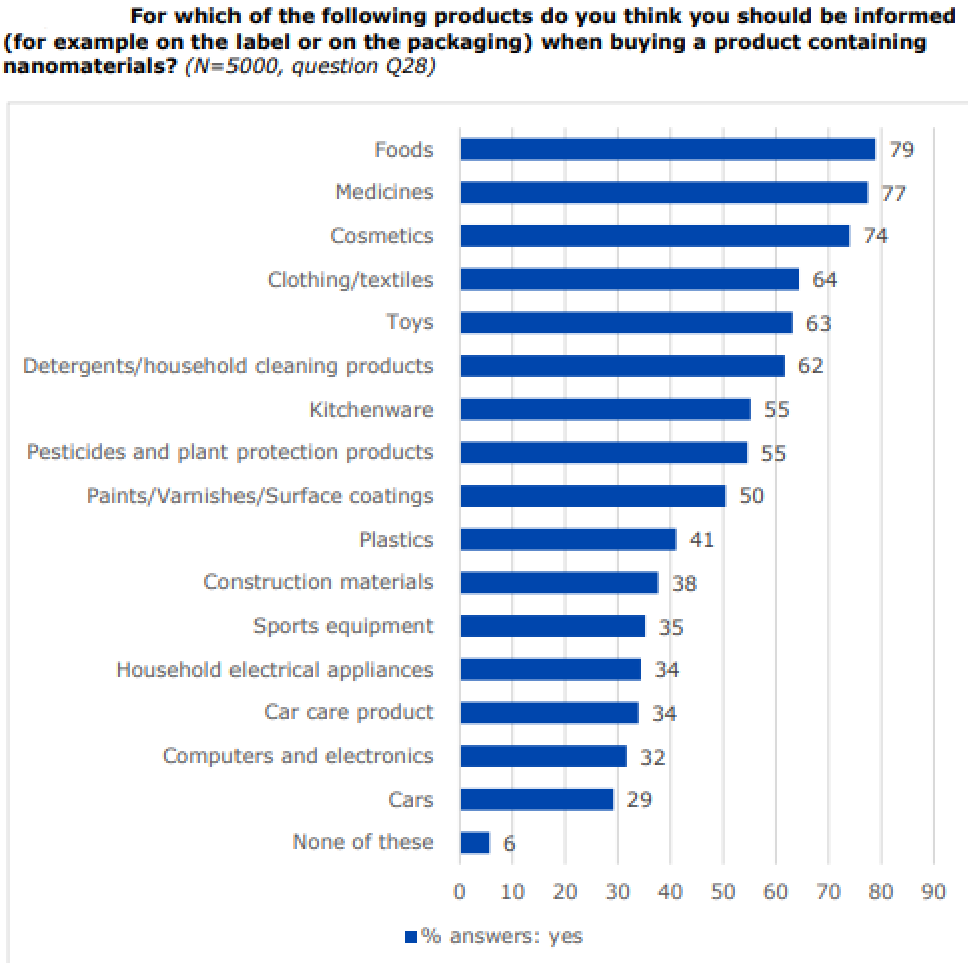
On the other hand, the European states that have the lowest level of awareness when it comes to nanotechnology (under 30%) are Portugal, Malta, Turkey and our country Romania.

In Table 1 we can see illustrated in percentages the concerns about the potential negative impact of nanomaterials on respondents' lives. These numbers must be interpreted having in mind the fact that this view is influenced by the level of people's knowledge about nanomaterials.

VIEW BY LEVEL OF WHAT PEOPLE HEARD ABOUT NANOMATERIALS				
		What people heard about nanomaterials		
Concern level related to nanomaterials	Total	Nothing at all	A little	A lot
Number of respondents	5000	1752	2703	545
I am concerned about possible negative impacts on my life	25%	21%	27%	30%
I am not worried about possible negative impact on my life	38%	23%	45%	57%
I do not know + I do not care	37%	57%	28%	14%

Table 1. Concerns about the potential negative impact of nanomaterials on respondents´ lives[4]

We can see from Table 1 that people with a higher knowledge about nanomaterials have a lower percentage of concern about the negative impact of nanotechnology in their life and at the same time they have a higher degree of acceptance of the new technology. The response „ I don't know" or "I don't care" is used primarily by the people that have no awareness concerning nanomaterials [8].



[4] Source: *Understanding Public Perception Of Nanomaterials And Their Safety In The EU Final report,* November 2020, p. 64.

Graphic 2. For which of the following products do you think you should be informed (for example on the label or on the packaging) when buying a product containing nanomaterials?[5]

In Graphic 2 is shown the list of products or category of products that European citizens want to know if they contain nanomaterials. We can observe that medicines are on the second place with 77% right after foods that are on the first place with 79%. On the third place are situated with 74% cosmetics. On the last two positions in this graphic, we can find computers and electronics with only 32% and cars with 29%.

From Graphic 2 we can deduce the importance that is given by Europeans to the use of nanoparticles in medicines and in the medicine field in general. We are convinced that the majority of the Europeans have heard by now of nanotechnology and nanoparticles and are open to the advances of the medical science. Their only request is to be informed when medicines contain nanoparticles and of course we can presume that they want for this new technology to be thoroughly tested before its usage on a mass scale in medicines and in other consumption products.

6. Conclusion

Nanotechnology is a new field of science that can bring many benefits in the life of humans. Nanoparticles can be used in many domains with stupendous results, but their usage in the medical field has the potential to make miracles happen and to bring health, healing and longevity to all the human beings on this planet. But for this to happen it is very important to be meticulously tested before it can be used on humans.

In our opinion nanotechnology has the power to change the world. The only question is if this change will be in good or in bad. That depends on the small group of people that have the power and control over nanotechnology and the research in this field. Their way of thinking and their interests will shape our future.

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[5] Source: *Understanding Public Perception Of Nanomaterials And Their Safety In The EU Final report,* November 2020, p. 118.

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