Nanotechnology based drug delivery systems

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Introduction

In the past century, nanotechnology has been a prominent theme for many science fiction writers. However, thanks to recent developments in chemistry and manufacturing, we are now able to bring things that were once unimaginable into fruition. The field of nanotechnology refers to the research, development and the production of materials under the size of 100 nanometers (nm). Over the past decade, the scientific community has experienced a boom in the research and development of nanotechnology. New technologies are being released with thousands of dollars of funding behind them. In this paper, the benefits, disadvantages, applications, governmental policies and recommendations of nanotech based drug delivery will be discussed.

Overview

At the forefront of the nanotechnology revolution lies in the field of nanomedical drug delivery. Nanomedical drug delivery is the concept of using minute nanomaterials (NM) to act as carrier substances for drugs. These nanocarriers will then be injected into the bloodstream and deposit drugs at specific cells. Compared to conventional drugs which target on a macro scale, nanocarriers are able to target on the micro scale, leaving neighbouring healthy cells unharmed. This precision will ultimately lead to benefits such as reduced drug dosages and reduced side effects. When tested in the lab, these particles have shown a high degree of success within lab animals. Currently, several forms of suitable nanocarriers exist. The most prevalent ones include nanocrystals, various forms of organic nanoplatforms

(such as liposomes) and inorganic platforms, such as gold nanoparticles. Next, the benefits of nanotechnology will be discussed.

Benefits

Nanotechnology based drug delivery systems are able to deliver a wide range of benefits to the human body, increase the effectiveness of conventional drugs and eliminate the short falls of conventional methods. As mentioned before, nanocarriers are able to target specific cancerous cells while leaving healthy cells alone. The cause of this phenomenon is attributed to the enhanced Permeability and retention effect (EPR). (Bamrungsap, et al, 2012) Molecules who possess the EPR property have a tendency to accumulate at specific cancerous cells, leaving normal healthy cells largely alone. Indirectly, EPR can be attributed to a reduction in drug dosage, reduced side effect intensity, enhanced efficacy and reduced toxicity. (Bamrungsap et al, 2012) Another benefit of nanocarriers compared to conventional drugs is that their physical properties such as size, surface area, and functionality can be easily modifiable. This is seen nanocarriers based on liposomes. In addition to being easily modifiable, liposomes are known for their ability to reduce side effects, toxicity and reducing drug clearance. (Bamrungsap et al, 2012) Nanocarriers are also able to be adapted to release drugs depending on environmental triggers. These environmental triggers can vary from physical (temperature), chemical or biological signals. Commonly seen in polymeric nanoparticles, this property allows drugs to remain inert unless they are activated by an environmental trigger. Hence, they only activate when they are required. (Bamrungsap et al, 2012) Nanoparticles such as gold nanocarriers are able to act as drug “

reservoir” (Bamrungsap et al, 2012). This allows drugs to have a slow release into the targeted area. Finally, nanocarriers such as liposomes have the ability to isolate drugs away from the environment. This allows for more efficient drug delivery as the drug will not be carried away by other bodily fluids. (Bamrungsap et al, 2012) Through the application of nanotechnological drug delivery, we can expect to see difficult to treat diseases such as cancer to be significantly less invasive, more tolerable, and more treatable to the patient. In turn, with better survival prospects for the world’s number 4 most deadly disease, (WHO, 2014) we could expect to see a sizable increase in the average human lifespan. In the next session, the risks and disadvantages of nanotechnology will be discussed.

Risks/Disadvantages

Despite nanotechnology being vastly beneficial to the individual and society, there are extreme risks involved with every new technology. Nanotechnological based drug carriers are no exception. In recent years, with the rapid development of nanotechnology, the field of nanotoxicology has also developed in order to study the toxicity of nanoparticles toward organisms. (Bamrungsap et al, 2012) Nanoparticles differ greatly from the largely harmless micron sized particles. Nanoparticles have been linked to changed body distributions and triggering of blood clots. In addition, nanoparticles have been linked to more traditional particle related illnesses such as inflammation and lung cancer. However, nanoparticles are significantly more difficult to remove from the body and can also cause mitochondrial damage, platelet aggression, and cardiovascular diseases.

(Jong & Borm, 2008) In addition to broad nanoparticle risks, various other nanoparticles also have concerns regarding their safety.

One such concern is the potential for cadmium containing quantum dots to release free Cd^{2+} ions. (Jong & Borm, 2008)These ions have been linked to large amounts of cell death when in vitro studies. Another concern is the possibility for Cationic nanoparticles (gold and polystyrene) to cause hemolysis, blood clotting and colon carcinoma in lab rats. Anionic nanoparticles, in contrast, are not known to be toxic. When in high doses, both Anionic and Cationic nanoparticles are both poisonous to the blood brain barrier (BBB). (Jong & Borm, 2008) Similar to cationic and anionic particles, some forms of silica would result in a reduction of cell viability while other forms of silica are rendered to be non-toxic. (Jong & Borm, 2008) Other potentially poisonous nanoparticles include carbon nanotubes, fullerenes, and Dendrimers. (Jong & Borm, 2008) It is clear that no two nanoparticles have the same properties. Hence, it is key for researchers to analyze each nanoparticle on a case-by-case basis.

The final concern is the ability for nanoparticles to contaminate the environment. Owing to their small size, nanoparticles are exceedingly difficult to remove. When nanoparticles are introduced into the water supply, their behavior is relatively unknown. (Wrigth, n. d.). However, nanoparticles do have the tendency to bond with water molecules and porus media. They resist removal when industrial purification is used and whey deposited in soil, they tend to attract other nanoparticles towards them. This is likely to cause marine die offs due to them ingesting toxic nanoparticles. In addition, some studies have shown that the at certain pH levels, there is increased

nanoparticle deposition levels. When nanoparticles enter the air, they behave similar to gasses. They rapidly disperse causing a wide area of contamination. When inhaled in, these particles behave very similarly to how asbestos behaves in the lungs. (Wrigth, n. d.) Hence, before nanotechnology can be widely introduced, extensive testing should be conducted to mitigate any potential risks involved.

Current and Future Applications

Currently, nanocarriers are still considered to be in their infancy. They are too unstable for use and their behavior in humans is also completely unknown. Despite that, in the near future, nanocarriers will be capable of treating a great deal of human ailments with minimal invasiveness. For example, nanocarriers that are coated with the membrane of a red blood cell will be able to circulate around the body for a longer time. (2 days) (Boysen, n. d.) This longer time will provide the nanoparticle more time to attach to cancerous cells. Another application of nanocarriers is to use nano-sized silicon wafers and allowing the wafer to lodge inside the tumor. UV light is then focused upon the tumor, activating the silicon wafers, effectively killing tumor cells. (Roberts, n. d.) Another application for nanoparticles is for treating heart disease. Nanocarriers are able to attach to damaged arteries and apply drugs specifically to that area. Finally, nanotechnology is able to treat for diabetes by releasing insulin depending on environmental triggers. (Boysen, n. d.) Perhaps what could be considered to be the holy grail of nanocarriers is the passage through the BBB. Passage through this barrier means access to the brain. With this passage, treatment for brain tumors

can be less invasive and neurodegenerative diseases such as dementia and ALS could potentially have a cure in sight. (Jong & Borm, 2008)

Governmental Regulation

Currently, in Canada, the development of nanotechnology falls under the regulation of 6 legislations. These regulations are:

- Canadian Environmental Protection Act
- Food and Drugs Act
- Food additive Regulations
- Medical devices Regulations
- Natural Health products Regulations
- Cosmetic Regulations (Government of Canada, 2014)

The supervision of the use and production of nanoparticles falls under the responsibility of Health Canada and Environment Canada. The role of Environment Canada is to evaluate the ecological impact a nanoparticle will have while Health Canada is responsible for evaluating the risks a particle has on human health. (Government of Canada, 2014) A regulatory framework for Nanoparticles does not exist as of right now. However, a 2-phase plan is currently being discussed. The first phase of the plan involves the continued partnership with various international organizations such as ISO and OECD to create a standardization. This phase also involves the notification of the public and various industries. Simultaneously, Voluntary information and mandatory information submission will occur. The purpose of this is to build a strong framework on the development of nanotechnology. During voluntary information submission, information is remains confidential

under section 313 of the CEPA. If mandatory information submission were to occur, they would fall under the jurisdiction of sections 46 and 71. These require the company to not only submit the required documents but also to answer potential questions to the best of their ability. Finally, legislative amendments will be made the CEPA in order to suit nanotechnology better (Environment Canada, Health Canada, 2007). In phase 2, the adoption international standardizations will occur. ISO/TC 229 will be applied into law. In addition, monitoring for Significant New activities will occur. (sNAC) a sNAC is defined as “ a significantly greater quantity or concentration of the substance in the environment” or a significantly different manner or circumstances of exposure to the substance” (Environment Canada, Health Canada, 2007). If any substance meets this criteria, they would be deemed as toxic under CEPA 1999. The current regulations in place are evidently not enough for the rapidly developing nature of nanotechnology. However, if the framework is implemented, (in addition to the recommendations of ISOTC 229) it should be meet all the demands of nanotechnology satisfactorily.

On the international level, there are several organizations in charge of overseeing the development of nanotechnology. One such group is the OECN working party on nanotechnology. This group is in charge of addressing the political, scientific, technological, and innovation related aspects of nanotechnology. (Government of Canada, 2014) Another group is the OECD working party Manufactured Nanomaterials. This group is responsible for addressing issues of health and environmental impact caused by the manufacture of nanomaterials. (Government of Canada, 2014) Finally, the International organization for standards Technical Commission (ISO/TC) is

responsible for developing a set of nomenclature specific to nanomaterials. This is done under the bill ISOTC 229. Addressing the problem of nomenclature will identify gaps in knowledge and identify the need to invest more in nanotechnology. In addition, ISOTC 229 will make it easier to facilitate the exchange of legal documents regarding nanomaterials. (ISO/TC, 2011)

Public Perception

Public perception is currently a key factor in the acceptance of nanotechnology in society. Currently, it is assumed that the average civilian has low knowledge of nanotechnology. In surveys conducted by the Woodrow Wilson in 2006, 42% respondents said that they did not know anything about nanotechnology. When the same study was conducted again in 2009, 37% of respondents indicated no knowledge of nanotechnology. In contrast, 24-31% of respondents indicated a high degree of knowledge in nanotechnology. (Besley, 2010) In another study, the majority of respondents chose “[nanotechnological] benefits outweigh the risks” between 3 choices. The other two choices were “ benefits will equal the risks” and “ risks outweigh the benefits”. (Besley, 2010)

Contrary to many new technologies, nanotechnology has been reported in a positive light in the press. Studies done in 2004 have shown that the technological benefits of nanotechnology have been more frequently reported. The risks and disadvantages have been shown to be rarely reported. (Besley, 2010)

Cost

As with any new technology, the initial costs are expected to be high. However, as mass production occurs and inefficiencies in the production like are smoothened out, it can be assumed that the price of nanocarriers will drop drastically. According to the United States National Nanological Initiative, the impact of nanotechnologies is expected to reach a $2. 4 billion by 2015. (National Nanotechnological Initiative, n. d.)

Conclusion

As evidenced from this paper, the benefits of nanotechnological are substantial. In the near future, they can developed to treat cancer and can potentially treat incurable diseases such as dementia with direct cell targeting. However, the risks of such new technologies cannot be ignored. As stated before, nanocarriers have been directly related to be toxic towards biological organisms. In addition to several risks, a lack of legislation and international standardization causes the development of nanoparticles to be unregulated. However, this is no reason to stop the development of nanotechnology. In contrast, this is a reason to invest even more into the field of nanotechnological based drug delivery to see what the future unlocks. Although there currently are several side effects associated with then, it is important to keep in mind that this field is in its infancy. With correct government legislation and support, drug delivery based nanotechnology can yield great benefits, ultimately extending the human lifespan and raising the human standard of living.

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