The Pharma Innovation

ISSN: 2277- 7695
CODEN Code: PIHNBQ
ZDB-Number: 2663038-2
IC Journal No: 7725

Received: 26-05-2013
Accepted: 29-07-2013

Vol. 2 No. 6 2013
Online Available at www.thepharmajournal.com

THE PHARMA INNOVATION - JOURNAL

Application of Nanotechnology and Biocomputation for Treatment of Cancer : A Review

Ashish Shrivastava [1] and H. K. Garg [2*]

1. Department of Biotechnology, C.S.A. Govt. P. G. Nodal College, Sehore - 466001 (India). [Email : akshrivastava333@gmail.com; Tel: 09301667033]
2. Department of Zoology, Sarojini Naidu Govt. Girls Post Graduate (Autonomous) College, Shivaji Nagar, Bhopal - 462016 (India)

Nanotechnology promises to provide quicker, reliable and affordable tools and applications to diagnose and treat an array of diseases to make human lives healthier. In the present review, an effort has been made to study how nanotechnology can help to address them. All at once, the possible role of biocomputation, as a means to specify cancer drug therapy, with an aim to apply the results in clinical settings, especially the modeling of drug delivery via nanoparticles, has also been worked upon. Biocomputation could save lives and enhance the quality of cancer treatment through tailor-made therapy for each individual patient, reducing the time and costs involved. With these ideas in mind, a pilot study was taken to work out system-level biocomputation of tumor growth and cancer therapy. While re-examining the merits of nanotechnology, its application in cancer chemotherapy and its likely challenges in a biological setting, have also been counted.

Keyword: Nanotechnology, Biocomputation, Nanoparticles, Cancer.

1. Introduction

Nanotechnology implies to manipulation, precision-placement, modeling and manufacture of material at the nanometer scale, where one meter is equal to 1 billion nanometers [15]. There are many conservative treatments today that consume a lot of time and are quite expensive. Using nanotechnology, surgical instruments of fine precision and dexterity that can operate on the cells and even molecules - something well beyond today's medical technology, can be developed. Though the clinical arsenal for treatment of cancer has been significantly extended in recent years with the application of new drugs and therapeutic modalities, however, the three basic approaches are still in vogue - surgical resection, radiation and chemotherapy. The latter one is first and foremost directed at metastatic cancer, which often has a poor prognosis. Notwithstanding the fact that significant proportion of research investment is focused on recuperating the efficacy of chemotherapy, which is often considered as the lone hope in treating a cancer patient, the challenges with chemotherapy cannot be over sighted. These include drug resistance by tumor cells, toxic effects on healthy tissue, inadequate targeting and impaired transport to the tumor. To this may be added, scheduling of proper drug dosage and determination of optimal drug concentration. At last, drug release kinetics, at the site of tumour, is another crucial aspect of chemotherapy.

2. Advantages of Nanotechnology

Cancer drug therapy, involving nanotechnology, offers several promising features over conventional drugs. Nano scale devices are two

orders of magnitude smaller than tumour cells, making it possible for them to interact directly with intracellular organelles and proteins. Owing to their molecule-like size, nano scale 'tools' may be capable of early diagnosis of disease using least amount of tissue, even down to a single malignant cell [18]. These tools may not only prevent disease by monitoring genetic damage, but also treat cells *in vivo* while minimizing interference with healthy tissue. By combining different kinds of nano scale tools on a single device, it may be possible to run multiple diagnostic tests simultaneously [19]. In particular, it is hoped that cancer drug therapy involving nanotechnology will be more successful in targeting malignant cells and sparing healthy tissue. In this regard, the role of nano particles, loaded with chemotherapeutic drugs, has been receiving much attention. Research and development in this area are expected to dramatically increase its importance in the days to come.

3. Challenges of Nanotechnology

There are limitless challenges in the handling nanotechnology for clinical treatment of cancer. First, there are basic physical issues with matter at such a small scale. Since matter behaves differently at the nano scale than it does at micro and macro levels, most of the science at the nano scale has been dedicated to basic research to understand how matter behaves on this scale [19]? Since nano materials have large surface areas relative to their volumes, phenomena such as friction are more critical than they are in larger systems. The small size of nano particles may result in significant delay or quickening in their intended actions. They may gather at unintended sites in the body or provoke unexpected immune system reactions. Cells may even adapt to the nano particles, modifying the body's behavior in unforeseen ways [19]. The efficacy of nano particles may be adversely affected by their interaction with the cellular environment. For instance, the reticulo-endothelial system (RES) may clear nano scale devices, even 'stealth' versions, too rapidly for them to be effective because of the tendency of RES to phagocytose nano particles. Nano particles can be taken up by dendritic cells [16] and by macrophages [14]. RES accumulation of nanoparticles could potentially lead to a compromise of the immune system. On the other hand, larger nanoparticles may accumulate in larger organs, leading to toxicity [19]. Perhaps the biggest issue of all is that the physically compromised tumour vasculature may prevent most of the nano devices from reaching the target cells by vascular transport or diffusion. Alterations in the tumor vasculature may adversely affect the convection of the nano devices in the blood stream. Local cell density and other stromal features may hamper drug or nano device diffusion through tumour tissue.

4. Chemotherapy *via* Nano particles

Chemotherapy using nano particles has been studied in clinical trials for several years and numerous studies have been published in this regard. Two liposomally delivered drugs are currently on the market: daunorubicin and doxorubicin. These encapsulated drugs can be formulated to maximize their half-life in the circulation.

Nano scale drug delivery systems for chemotherapy can be either polymer based or lipid based. Polymers, which are usually larger than lipid molecules, form a solid phase, such as polymeric nano particles, films and pellets, while lipids form a liquid (or liquid crystalline phase), such as liposomes, cubersomes, micelles and other emulsions [17]. While polymer based systems are considered biologically more stable than lipid based systems, the latter are generally more biocompatible. Polymer based systems might possess good drug targeting ability because their uptake may be different for cells in different tissues. In fact, Feng & Chien (2003) have suggested that a combination of polymer and lipid based systems could combine their benefits and shun their respective drawbacks. An example of such a nano particle would be a liposomes-in-microspheres (LIM) system, where drugs are first loaded into liposomes and then encapsulated into polymeric microspheres. This way both hydrophobic and hydrophilic drugs can be

delivered in one nano particle. The bioactivity of peptides and proteins would be preserved in the liposomes, whose stability is protected by the polymeric matrix.

5. Biocomputation

Biocomputation serves as a mathematical tool to examine the fundamental physical principles that affect delivery and degradation of nano particles in cancer treatment. It provides a better understanding of the interaction between nanotechnology and living tissue thereby saves time and resources by providing a coherent framework to predict experimental outcomes. The major challenge of biocomputation is to fit in these physical principles into a biologically relevant model for tangible bio-numerical product. It is difficult to prepare a model from nano particle (10−9 m) to tumor (10−3 m) scale, not only for the reason that matter behaves very differently in each, rather because simulation may require integration of multiple hierarchies of models, each differing in several orders of magnitude in terms of scale and qualitative properties.

Modeling of drug delivery encompasses the formulation of quantitative descriptions for drug transport in biological systems to : i)evaluate feasibility of new drug delivery methods; ii) to estimate dose response and toxicity; and iii) to speed up experimental and clinical evaluation. Modeling principles apply to both procedures and technologies. In the treatment of cancer, it is hoped that biocomputation will ease formulation of optimal treatment models that would allow administration strategies for chemotherapy to get the most out of benefit while down-sizing the side effects [17].

Biocomputation based theoretical results could potentially be validated by correlation of numerical predictions with *in vitro* and *in vivo* data of a particular patient's cancer response to chemotherapy. In turn, these experimentally and clinically validated biocomputation results may be employed to design tailored therapy *in silico* using computer simulations. Biocomputation of targeted and controlled drug delivery *via* nano particles is not only expected to offer novel insight into *in vivo* drug delivery, but also simulate the therapeutic effects of the delivery device. Since there are no encompassing mathematical models that can apply to all conceivable physical and chemical processes in product development, it is important to develop an adequate theory in view of drug delivery & diffusion, polymer swelling & degradation, osmotic, steric, magnetic, and charge effects [17].

6. Discussion

Studies embarked in the past few years acclaim nanotechnology to be a highly effective method of cancer treatment or diagnosis. However, speculations are going on to verify the prospects of nanotechnology in sure cure for cancer and replacing the traditional treatments such as chemotherapy and radiotherapy. The incredibly fast rate at which nanotechnology has been developing indicates that this speculation could become reality quite soon. On 3rd March 2009, the Journal of Cancer Research published the findings of an investigation on *'Cancer-Specific Transgene Expression Mediated by Systemic Injection of Nano particles'* [4]. Though this study had been carried out on mice, yet the efforts are on to extend these trials on human beings to make a sure cure for metastatic tumours.

7. Conclusion

Nanotechnology, thus, undeniably has a potential to be the most effective and optimum form of future treatment and diagnosis of cancer. Not only have nanowires and cantilevers been proven for their capability to provide an efficient method of recognizing cancer biomarkers in the blood for different cancers, nano particle composites have also been developed with opposing properties allowing for more accurate diagnosis and location of cancer. Furthermore, nano shells have an extraordinary potential to treat malignant brain tumours, due to their efficacy in delivering drugs across the blood-brain-barrier. This was, until that time, one of the most challenging aspects of cancer treatment.

Although, some rationally viable methods, such as radiotherapy and chemotherapy, are available for treatment of cancer, these techniques have their own risks. For radiotherapy, the proper dosage needed to cure all malignant brain tumours is approximately 12,000 Rads, but such a high dosage may be extremely neurotoxic and fatal. Similarly, chemotherapy has an imposing risks from alopecia to severe fatigue to ototoxicity to neutropenia and then to thrombocytopenia.

8. References

1. Alberts. Molecular Biology of the Cell. Taylor & Francis Group 2002.
2. Araujo RP, McElwain DLS. A history of the study of solid tumour growth : the contribution of mathematical modeling. Bull Math Biol J 2004.
3. Barbolosi D, Iliadis A. Optimizing drug regimens in cancer chemotherapy : a simulation study using a PK-PD model. Comp Biol Med 2001; 31:157–172.
4. Bauer LA. Applied Clinical Pharmacokinetics. Mc-Graw Hill 2001; 26-45.
5. Baxter LT, Jain RK. Pharmacokinetic analysis of the microscopic distribution of enzyme-conjugated antibodies and pro-drugs: Comparison with experimental data. Brit J Canc 1996; 73(4):447–456.
6. Black KL, Ningaraj NS. Modulation of brain tumor capillaries for enhanced drug delivery selectively to brain tumor. Cancer Control 2004; 11(3):165–173.
7. Bonadonna G, Zambetti M, Valagussa P. Sequential or alternating doxorubicin and CMF regimens in breast cancer with more than three positive nodes : ten year results. J Am Med Assoc 1995; 273:542–547.
8. Brigger I, Dubernet C, Couvreur P. Nanoparticles in cancer therapy and diagnosis. Adv Drug Del Reviews 2002; 54(5):631–651.
9. CCO Formulary, Liposomal Doxorubicin, October 2003.
10. Chaplain M, Anderson A. Mathematical modelling of tumour-induced angiogenesis: network growth and structure. Cancer Treat Res 2004; 117:51–75.
11. Costa P, Lobo JMS. Modeling and comparison of dissolution profiles. Eur J Pharm Sci 2001; 13:123–133.
12. Cristini V, Lowengrub J, Nie Q. Non-linear simulation of tumor growth. J Math Biol 2003; 46:191–224.
13. Cristini V, Frieboes HB, Getemby R, Corenta S, Ferrari M, Sinek S. Morphological instability and cancer inussion. Clin Cancer Res 2005.
14. Cui Z, Hsu CH, Mumper RJ. Physical characterization and macrophage cell uptake of mannan-coated nanoparticles. Drug Dev Ind Pharm 2003; 29(6):689–700.
15. Dordal MS, Ho AC, Jackson-Stone M, Fu YF, Goolsby CL, Winter JN. Flow cytometric assessment of the cellular pharmacokinetics of fluorescent drugs. Cytometry 1995; 20:307–314.
16. Elamanchili P, Diwan M, Cao M, Samuel J. Characterization of poly (D,L-lactic-co-glycolic acid) based nano particulate system for enhanced delivery of antigens to dendritic cells. Vaccine 2004; 22(19):2406–2412.
17. Feng SS, Chien S. Chemotherapeutic engineering : application and further development of chemical engineering principles for chemotherapy of cancer and other diseases. Chem Eng Sci 2003; 58:4087-4114.
18. NIH Publication No 04-5489 by National Cancer Institute. Cancer Nanotechnology - Going Small for Big Advances. Jan, 2004.
19. National Cancer Institute (NCI) website at http://press2.nci.nih.gov/sciencebehind /nanotech.