REVIEW

The state of nanomedicine in Sri Lanka: challenges and opportunities

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Abstract

Nanomedicine is rapidly expanding in the world due to its potential impact in alleviating various critical problems related to health. In this short review, we highlight the developments in nanomedicine in Sri Lanka through the work carried out by various scientists within the country. Potential challenges in the field and obstacles for conversion to clinical products will also be discussed. Even though there are limited contributions in relation to nano-drug carriers, antibacterial agents, and bone prostheses, the research focused on vaccine development, diagnosis, and imaging tools, and high-throughput screening platforms have not been developed. The main emphasis has been on therapeutic applications and anticancer drug delivery. Many hybrid biocompatible materials have been developed for drug delivery applications; however, work has been limited to in vitro studies due to various reasons. These findings can be extended to in vivo studies by strengthening the collaboration between nanotechnologists and health-related scientists, whose contribution at the clinical stages is paramount. Because of the slow pace of infrastructure development and related policies for clinical trials, many discoveries are terminated at the publication stage. Therefore, product development and commercialization are very challenging in the Sri Lankan context. The attraction of venture capitalists, investors, and government commitment represent current challenges for the product development and implementation of nanomedicine applications within the country.

1. Introduction

The design and use of nanomaterials for addressing health issues continue to attract increasing attention. Nanomedicine is one of the major fields in nanotechnology applications and has the potential to address many problems related to health. Research in nanomedicine encompasses many areas, including drug delivery, antibacterials, wearable devices, vaccine development, and implants, employing various hybrid materials. Worldwide, many of these developments are starting to appear in successful clinical trials, and some have even translated into viable clinical products.

The main approaches to research in nanomedicine include the designing, production, delivery, and imaging of drug systems, with high specificity and fewer side effects (Pautler & Brenner, 2010; Boulaiz et al., 2011; Ventola, 2012). The difference between nanomedicine and conventional medicine is that in nanomedicine,
drug and disease site interactions can be manipulated at the molecular levels (Owen et al., 2016). In addition, tools operating at the nanoscale to treat and diagnose diseases can also be categorized under nanomedicine (Pautler & Brenner, 2010; Boulaiz et al., 2011; Ventola, 2012; Donnellan et al., 2017; Riehemann et al., 2009). Unlike conventional therapies such as surgery, radiation, and chemotherapy, nanomedicine allows marked differentiation of diseased cells, to make smart decisions either to kill these cells or to repair them to regain the functionality (Riehemann et al., 2009). Further, the potential of nanomedicine to provide tangible solutions for the deadliest diseases, such as cancer, human immunodeficiency virus, dengue, zika, and SARS, have been identified.

Additionally, another important milestone in nanomedicine is the establishment of point of care diagnostics, which can easily be applied to screen many people for a disease. Surface-modified biochips developed to diagnose cervical cancer are one such example. In population screening of certain diseased conditions like cervical cancer, the modification of the surface of biochips has allowed the quick identification of certain marker proteins secreted by diseased cells (Riehemann et al., 2009). Therefore, nanomedicine would be an ideal, reliable, specific, sensitive, and a sustainable practice for any country to uplift their health standards and quality of life. In developing countries, a large fraction of conventional treatment options, which are non-viable due to high cost and poor efficiency, can be substituted by nanomedicine, provided the cost is low (Pautler & Brenner, 2010; Boulaiz et al., 2011; Ventola, 2012; Riehemann et al., 2009).

2. State of Nanomedicine Research in Sri Lanka

In the Sri Lankan context, nanomedicine is a relatively young field, due to the lack of many qualified and experienced scientists in this area. However, there is a great potential with the limited number of scientists who are actively associated with research in nano-drug carriers, antibacterial agents, and bone prostheses. These include development of bone prostheses (Rajapakse et al., 2016), drug encapsulation, for example, Vitamin C (Samantha Dissanayake et al., 2015), targeted cancer treatment (Katuwavila et al., 2016a; Weerasuriya et al., 2017; Nwokwu et al., 2017; Manatunga et al., 2017; Manatunga et al., 2018a), and developing antimicrobial agents (Peiris et al., 2017; Rathnayake et al., 2018). Rajapakse et al. have actively engaged in nano hydroxyapatite-based biomaterials (Fig. 1) (Rajapakse et al., 2016; Wijesinghe et al., 2017) in artificial prosthesis research, and their contribution has hugely benefited patients who suffered bone injuries. This was initiated and developed during the civil war period in Sri Lanka, when many people suffered from severe injuries.
bone injuries because of explosions. With a strong collaboration between several research groups including scientists, doctors, and engineers, prostheses based on biomaterials and other inorganic materials were manufactured and were successfully transplanted to orthopaedic patients.

Many Sri Lankan scientists have reported a sizable amount of work related to anticancer drug delivery systems. Most of these drug delivery systems are based on chitosan alginate nanoparticles (Katuwavila et al., 2016a; Katuwavila et al., 2016b) or liposomes (Samantha Dissanayake et al., 2015; Pamunuwa et al., 2016; Pamunuwa et al., 2015; Menikarachchi et al., 2016; Nwokwu et al., 2017). They have been tested on various cancer cell lines such as breast (Katuwavila et al., 2016a) and lung (Nwokwu et al., 2017) cancer. Even though there is a good potential of these drugs to act against cancer cells, none has reached the clinical stage. In addition, in vitro studies on successful biocompatible nanocarriers with magnetic targeting properties (Fig. 2) have been well explored for many naturally available anticancer agents (Manatunga et al., 2017; Manatunga et al., 2018a) towards breast and liver cancer cells.

It has also been recognized that there has been a marked increase of kidney diseases among the rural population in Sri Lanka mainly due to the accumulation of chronic biological and chemical toxins in drinking water. Because of this requirement of the country, many research groups have focused on developing materials to remove biological toxins, heavy metals, and other dye contaminants in drinking water using biocompatible nanocomposites (Udayakantha et al., 2015; Jayaweera et al., 2018; Manatunga et al., 2016; Manatunga et al., 2018b; Fernando et al., 2015), and one such approach is depicted in Figure 3. Application of some of these materials in water purification systems is already established (Wasana et al., 2016).1

3. Barriers on Development or Implementation of Nanomedicine in Sri Lanka

Most of the nanomedicine research in Sri Lanka involves simple techniques due to high cost for advanced methodologies, and therefore, advanced techniques such as lithography are not yet entertained. This is mainly due to the lack of investment towards the challenging nanomedicine research, which requires

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1CERTKiD - Centre for Education, Research and Training on Kidney Diseases - https://www.pressreader.com/sri-lanka/sunday-times-sri-lanka/20170312/283940292478123 (Accessed on 07/03/2018).
state-of-the-art facilities. It is evident that most of the anticancer drug delivery approaches terminate at the in vitro studies without reaching the in vivo level due to lack of facilities in maintaining animal models for the purpose of conducting preclinical trials. Maintaining nurseries, labour, and artificial induction of certain diseases in these models have been a significant additional cost. In addition, administrative burdens, ethical clearance, and the unwillingness of patients to undergo human clinical trials (Ventola, 2012) have further restricted the expansion of nanomedicine in a country like Sri Lanka.

On the other hand, there are other important issues related to public health, such as public sanitation and infectious diseases. Therefore, it is vital to search for potential nanomedicines, not only for cancer but also for other prevailing health conditions, such as dengue, human rabies, leptospirosis, viral hepatitis, tuberculosis, and diabetes. More importantly, these diseases need active contributions from nanomedicine not only for the treatment but also for the prevention.

Lack of funding for the potential projects could be considered as a major reason for the discontinuity of research after publications. In this context, specific procedures for government funding are a timely requirement, and therefore, launching the Nanotechnology Initiative in Sri Lanka in order to strengthen capacity and sustain economic growth is an important milestone. However, the cooperative participation of regulatory agencies, concerned public groups, healthcare professionals, and academia in this field is still scarce. Out of these, professionals in the medical field play a major role by researching the effectiveness of new products, thereby encouraging the funding agencies to support the research (Pautler & Brenner, 2010).

The Sri Lanka Institute of Nanotechnology is a research institute that acts as the national body, which is primarily engaged with nanotechnology-based research and development in Sri Lanka. Sri Lanka Institute of Nanotechnology was established as a public-private partnership between the government of Sri Lanka and a few private companies. The National Research Council of Sri Lanka is also actively engaged in building up private public partnerships to gather the potential research and development activities and the interested industries to contribute towards the economic development of the country. At the same time, thinking beyond the publication level is important to strengthen product-oriented research, where much concern should be given to intellectual property and patenting (Konig et al., 2015), which may build up a strong platform to attract interested commercial parties. It is believed that both intellectual property and commercial parties should interconnect as research and development continues (Reynolds et al., 2018).

Figure 3. In the work carried out by Udayakantha et al. (2015), HAp-curcumin bi-coated granular activated carbon (HAP/C/GAC) and HAp/GAC have been used to remove *Escherichia coli* and *Staphylococcus aureus* bacteria in water (reprinted from K. S. M. Udayakantha, R. M. de Silva, K. M. N. de Silva, and C. Hettiarachchi, *RSC Adv.*, 2015, 5, 64696, DOI: 10.1039/C5RA11518C).

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2,List of Notifiable Diseases in Sri Lanka - http://www.epid.gov.lk/web/index.php?option=com_content&view=article&id=145&Itemid=446&lang=en (Accessed on 13/02/2018).
3,Sri Lanka Institute of Nanotechnology - http://slintec.lk/ (Accessed on 14/02/2018).
4,Private Public Partnership Programs arranged by National Research Council - http://www.nrc.gov.lk/index.php/programs-in-operation/private-public-partnership-programe.html (Accessed on 14/02/2018).
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Lack of a strong industry base and a proper investing body or a venture capitalist has been a major challenge in translation of research up to the product development stage. Investors always expect to have extraordinary performance from these new technologies that can compete with the already available products in the market. Sometimes, the cost also becomes a limiting factor here as they always prefer the new product to be low cost (Pautler & Brenner, 2010). In such cases, attracting the public and the industry by demonstrating long-term health benefits with respect to price will certainly increase the likelihood of these products being purchased.

Establishing a functional platform for nanomedicine is extremely challenging, as there are misconceptions among the public with the word “nano.” It was shown that even the professionals and undergraduates in the medical field have an average knowledge of the therapeutic applications related to nanomedicine (Jaliya et al., 2014). The main reason for such inability is that nanotechnology and nanomedicine are taught at different levels, which are not actually interconnected, creating an obstacle to building up a connection between nanotechnology and nanomedicine. Additionally, allocating funds by the responsible bodies for such purposes and initiating interdisciplinary international collaborative research in nanomedicine will be a good investment for the country.

Finally, the lack of proper standardized protocols regarding safety and potential health risks arising from exposure to nanomaterials is another area that should be properly addressed (Pautler & Brenner, 2010). Therefore, convincing communities to have confidence in the efficacy and safety of nanotechnology-based products may be required. Hence, establishing a procedure for the registration of the local nanomaterials and nanoproducts and setting proper guidelines (i.e., a local agency like the FDA in the USA, which set rules and regulations) to evaluate the life cycle, biocompatibility, and safety of these products in a timely manner, with respect to their exposure to the environment, will eliminate fear and increase customer/patient preference. This is again another type of major hurdle, which has lessened the interest of certain pharmaceutical companies to proceed with product development (Pautler & Brenner, 2010).

4. Conclusions

From the aforementioned broad analysis, which was focused on many subareas of nanomedicine, it is clear that although there is lot of excitement related to nanomedicine, there are many barriers that have impeded the transformation of lab trials into a clinical product. Hence, a dynamic, productive, and socially responsible research platform should be immediately established, to eliminate the barriers that has prevented the development or implementation of nanomedicine in Sri Lanka.

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Conflict of Interest

None declared.

REFERENCES

Boulaiz, H., Alvarez, P. J., Ramirez, A., Marchal, J. A., Prados, J., Rodriguez-Serrano, F., Perán, M., Melguizo, C., and Aranega, A. 2011. Nanomedicine: applications, areas and development prospects. Int J Mol Sci 12:3303-3321. https://doi.org/10.3390/ijms12053303.

Donnellan, S., Stone, V., Johnston, H., Giardiello, M., Owen, A., Rannard, S., Aljayyousi, G., Swift, B., Tran, L., Watkins, C., and Stevenson, K. 2017. Intracellular delivery of nano-formulated antituberculosis drugs enhances bactericidal activity. J Interdiscip Nanomedicine 2:146-156. https://doi.org/10.1002/jin2.27.

Fernando, M. S., De Silva, R. M., and De Silva, K. M. N. 2015. Synthesis, characterization, and application of nano hydroxyapatite and nanocomposite of hydroxyapatite with granular activated carbon for the removal of Pb2+ from aqueous solutions. Appl Surf Sci 351:95-103. https://doi.org/10.1016/j.apsusc.2015.05.092.

Jaliya, S. H. K. M. N., Jayasena, L. D., Kalavitiogoda, S. K. B., Koralagedara, K. I. S., and Kulathunga, P. S. P. N. 2014. Sri Lankan medical undergraduates awareness of nanotechnology and its risks. Educ Res Int 2014:1-11. https://doi.org/10.1155/2014/584352.

Jayaweera, H. D. A. C., Siriwardane, I., De Silva, K. M. N., and De Silva, R. M. 2018. Synthesis of multifunctional activated carbon nanocomposite comprising biocompatible flake nano hydroxyapatite and natural turmeric extract for the removal of bacteria and lead ions from aqueous solution. Chem Cent J:1-14. https://doi.org/10.1186/s13065-018-0384-7.

Katuwavila, N. P., Perera, A. D. L. C., Dahanyake, D., Karunaratne, V., Amaratunga, G. A. J., and Karunaratne, D. N. 2016b. Alginate nanoparticles protect ferrous from oxidation: potential iron delivery system. Int J Pharm 513:404-409. https://doi.org/10.1016/j.ijpharm.2016.09.053.

Katuwavila, N. P., Perera, A. D. L. C., Samarakoona, S. R., Soysa, P., Karunaratne, V., Amaratunga, G. A. J., and Karunaratne, D. N. 2016a. Chitosan-alginate nanoparticle system efficiently delivers doxorubicin to MCF-7 cells. J Nanomater 2016:1-12. https://doi.org/10.1155/2016/3178904.

Konig, H., Dorado-Morales, P., and Porcar, M. 2015. Responsibility and intellectual property in synthetic...
biology: a proposal for using Responsible Research and Innovation as a basic framework for intellectual property decisions in synthetic biology. EMBO Rep 16:1055-1059. https://doi.org/10.15252/embr.201541048.

Manatunga, D. C., De Silva, R. M., De Silva, K. M. N., De Silva, N., and Premalal, E. V. A. 2018b. Metal and polymer-mediated synthesis of porous crystalline hydroxyapatite nanocomposites for environmental remediation. R Soc Open Sci 5:1-15. https://doi.org/10.1098/rsos.171957.

Manatunga, D. C., de Silva, R. M., de Silva, K. M. N., de Silva, N., Bhandari, S., Yap, Y. K., and Costha, N. P. 2017. pH-responsive controlled release of anti-cancer hydrophobic drugs from sodium alginato and hydroxyapatite bi-coated iron oxide nanoparticles. Eur J Pharm Biopharm 117:29-38. https://doi.org/10.1016/j.ejpb.2017.03.014.

Manatunga, D. C., de Silva, R. M., de Silva, K. M. N., and Ratnaweera, R. 2016. Natural polysaccharides leading to super absorbent hydroxyapatite nanoparticles for the removal of heavy metals and dyes from aqueous solutions. RSC Adv 6:105618-105630. https://doi.org/10.1039/C6RA22662K.

Manatunga, D. C., de Silva, R. M., Nalin de Silva, K. M., Neelika Malavige, G., Wijeratne, D. T., Williams, G. R., Jayasinghe, C. D., and Udagama, P. V. 2018a. Effective delivery of hydrophobic drugs to breast (MCF-7) and liver (HePG2) cancer cells: a detailed investigation using Cytotoxicity assays, fluorescence imaging and flow cytometry. Eur J Pharm Biopharm. https://doi.org/10.1016/j.ejpb.2018.04.001.

Menikarachchi, M. A. S. K., Katuvawila, K. A. N. P., Ekanayake, E. W. M. A., Thevanesam, V., Karunaratne, D. N., and Karunaratne, D. N. 2016. Release behaviour of amoxicillin from chitosan-coated liposomes derived from eggs. J Natl Sci Found Sri Lanka 44:167-173. https://doi.org/10.4038/jnfsr.v44i2.7997.

Nwokwu, C. U. D., Samarakoone, S. R., Karunaratne, D. N., Katuvavila, N. P., Pamunuwa, G. K., Ediriweera, M. K., and Tennikeon, K. H. 2017. Induction of apoptosis in response to improved gedunin by liposomal nano-encapsulation in human non-small-cell lung cancer (NCI-H292) cell line. Trop J Pharm Res 16:2079-2087. https://doi.org/10.4314/tjpr.v16i9.6.

Owen, A., Ramnard, S., Bawar, R., and Feng, S.-S. 2016. Interdisciplinary nanomedicine publications through interdisciplinary peer-review. J Interdiscip Nanomedicine 1:4-8. https://doi.org/10.1002/jin2.1.

Pamunuwa, G., Karunaratne, V., and Karunaratne, D. N. 2016. Effect of lipid composition on in vitro release and skin deposition of curcumin encapsulated liposomes. J Nanomater 2016:1-19. https://doi.org/10.1155/2016/4535790.

Pamunuwa, K. M. G. K., Bandara, C. J., Karunaratne, V., and Karunaratne, D. N. 2015. Optimization of a liposomal delivery system for the highly antioxidant methanol extract of stem-bark of Schumacheria castaneifolia Vahl. J Chem Pharm Res 7:1236-1245.

Pautier, M., and Brenner, S. 2010. Nanomedicine: promises and challenges for the future of public health. Int J Nanomedicine 5:803-809. https://doi.org/10.2147/IJNN.513816.

Peiris, M. K., Gunasekara, C. P., Jayaweera, P. M., Arachchi, N. D. H., and Fernando, N. 2017. Biosynthesized silver nanoparticles: are they effective antimicrobials? Mem Inst Oswaldo Cruz 112:537-543. https://doi.org/10.1590/0074-02760170023.

Rajapakse, R. M. G., Wijesinghe, W. P. S. L., Mantilaka, M. M. M. G. P., Chathuranga Senaratna, K. G., Herath, H. M. T. U., Premachandra, T. N., Ranasinghe, C. S. K., Rajapakse, R. P. V. J., Edirisinhe, M., Mahalingam, S., Bandara, I. M. C. C. D., and Singh, S. 2016. Preparation of bone-implants by coating hydroxyapatite nanoparticles on self-formed titanium dioxide thin-layers on titanium metal surfaces. Mater Sci Eng C 63:172-184. https://doi.org/10.1016/j.msec.2016.02.053.

Rathnayake, R. M. N. M., Jayasekara, S. K., Huang, H. H., Yoshimura, M., Wijayasinge, H. W. M. A. C., Ratnayake, R. R., and Pitawala, H. M. T. G. A. 2018. Convenient process to synthesize reduced needle platy graphite silver nanocomposite: a prospective antibiotic against common pathogenic microorganisms in the environment. Mater Res Exp 5:1-12. https://doi.org/10.1088/2053-1591/aaa613.

Reynolds, L. J., Contreras, J. L., and Saranoff, J. D. 2018. Intellectual property policies for solar geoengineering. Wiley Interdiscip Rev Clim Change 9:1-12. https://doi.org/10.1002/wcc.512.

Riehemann, K., Schneider, S. W., Lugner, T. A., Godin, B., Ferrari, M., and Fuchs, H. 2009. Nanomedicine - challenges and perspectives. Angew Chem Int Ed Engl 48:872-897. https://doi.org/10.1002/anie.200802585.

Samantha Dissanayake, D. M. D. S., Karunaratne, D. N., and Chandani Perera, A. D. L. 2015. Enhanced liposomal encapsulation of ascorbic acid by the liquid crystal β6-isosteryl-β-d-glucopyranoside. Mol Cryst Liq Cryst 613:94-102. https://doi.org/10.1080/10704246.2015.1047297.

Udayakantha, K. S. M., de Silva, R. M., de Silva, K. M. N., and Hettiarachchi, C. 2015. Biocompatible nano hydroxyapatite-curcumin bi-coated antibacterial activated carbon for water purification. RSC Adv 5:64696-64703. https://doi.org/10.1039/C5RA11518C.

Ventola, C. L. 2012. The nanomedicine revolution; part 2: current and future clinical applications. P T 37:582-591 http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=3474440&tool=pmcentrez&rendertype=abstract.

Wasana, H. M. S., Aluthpatabendi, D., Kularatne, W. M. T. D., Wijekoon, P., Weerasooriya, R., and Bandara, J. 2016. Drinking water quality and chronic kidney disease of unknown etiology (CKDu): synergic effects of fluoride, cadmium and hardness of water. Environ Geochem Health 38:157-168. https://doi.org/10.1007/s10653-015-9699-7.

Weerasooriya, D. R. K., Wijesinghe, W. P. S. L., and Rajapakse, R. M. G. 2017. Encapsulation of anticancer drug copper bis(8-hydroxyquinoline) in hydroxyapatite for pH-sensitive targeted delivery and slow release. Mater Sci Eng C 71:206-213. https://doi.org/10.1016/j.msec.2016.10.010.

Wijesinghe, W. P. S. L., Mantilaka, M. M. M. G. P., Rajapakse, R. M. G., Pitawala, H. M. T. G. A., Premachandra, T. N., Herath, H. M. T. U., Rajapakse, R. P. V. J., and Wijayantha, K. G. U. 2017. Urea-assisted synthesis of hydroxyapatite nanorods from naturally occurring impureapatite rocks for biomedical applications. RSC Adv 7:24806-24812. https://doi.org/10.1039/C7RA02166F.