Research article Available online www.ijsrr.org ISSN: 2279–0543

International Journal of Scientific Research and Reviews

# Analysing Nanotechnology in the Paediatrics Medicinal science with reference to the Central Nervous System

**BasakSayan***

Department of Polymer Science and Technology,University of Calcutta
92. A.P.C Road, Kolkata-700009, India
Email- sayancu15@gmail.com

## ABSTRACT

Nanotechnologyhas been an impeccable scientific tool to address and overcome pharmaceutical a biological drawbacks such as poor aqueous solubility, low physicochemical stability and insufficient bioavailability. Because conventionally the development of paediatric treatments usually relied on the previous experience in adults and the clinical testing being carried out in anaged environment, there do not exists approved paediatricnanomedicines yet. While various chemotherapeutic agents can be utilized to improve the survival rate of patients with ovarian cancer, their distribution throughout the entire body results in high normal organ toxicity.Further, all the existenttreatments for paediatric science pertaining to the Central nervous system are either of less efficiency or comprise of higher level of cellular Cytotoxicity. This short review deals with the two common tumours of the central nervous system occurring in children and the currentscientific advances applied on it with respect to nanotechnology. In addition, we have discussed on the benefits of using nanotechnology to address the complications in the central nervous systembecause of its small size (10-100 nm) of particles which improves circulation and enables superior accumulation of the therapeutic drugs at the tumour sites, especially in infants.

**KEYWORDS-** Nanotechnology, Paediatrics, Medulloblastoma, Astrocytoma

***Corresponding author**

**SayanBasak***

Department of Polymer Science and Technology,

University of Calcutta

92. A.P.C Road, Kolkata-700009, India

Email- sayancu15@gmail.com

## 1. INTRODUCTION

There exist several researches which demonstrated that children have a very different capacity and a pathway for drug absorption. Several theories claim perhaps it is because of their bio distribution, metabolism and excretion with respect to adults[1]. Furthermore, several pharmacokinetic studies have showed that the dynamics and the environment in which a drug acts on a child's body is completely different from that of an adult due to the direct adjustment of the dose to the body weight/surface ratio. If the paediatric population is divviedinto five groups namely newborn infants (0–27 days), infants and toddlers (28 days-23 months), preschool children (2–5 years), school children (6–11 years) and adolescents (12–16/18 years), we will see that each group exhibits differentlevel of intestinal mobility, drug conjugation and delivery system along with pH transition. Incas of inhalatory products, the cognitive development can also effect the drug formulation and the possible clinical trials[2-5]. The toxicology aspect with respect to thenanoparticle used in the drugshould be thoroughly tested because children show a higherresponse to the particle deposition. A very famous citing example is that several nano DDS comprising of the biocompatibility liposomes have reached clinical phase in case of adults but it is still restricted to trials in children. This short review is aimed to focus on the tumours of the central nervous system using nanoscience as a solution, keeping paediatric science on the backdrop.

## 2. ANALYSING THE TUMOURS OF THE CENTRAL NERVOUS SYSTEM

### 2.1*MEDDULOBLASTOMA*

As far as the Central nervous System is concerned, Medulloblastoma is one of the major malignant paediatric neoplasms. It is a very aggressive and invasive primary brain tumour localized in the cerebellum and the posterior fossa with a high tendency to metastasize[6]. Lu et al had carried out a survey which resulted that the incidence of this particular disease is approximately 9.6 cases per million children and the current survival rate is 65%. Although the figures have improved from a drastic 30% to 65% in 2015, the science is still striving more every day to improve the survival rate. It is worth noting that Medulloblastoma in children and adults are genetically and histologically different and they have been recently classified into four well defined molecular groups. The challenge lies in the fact of identifying the correct phasic disease and proposing the proper therapy for the same, which implies to the importance of the paediatric clinical trials[7]. The cellular and molecular mechanisms that genesised, maintain and overlapsthe progression of Medulloblastoma remain constant though the Hedgehog signalling pathway has been related to the development of one type of the disease.

Drugs such as vismodegib had been proposed by various scientistswhich is currently under clinical trialsin adults and this could eventually expand the therapeutic drug design in children. Other cellular targeted drugs based on microRNA have been a prime focus for the scientists because of its high repository effect. These short non-coding RNA sequences (22 nucleotides) regulate transcriptional and post-transcriptional stages of gene expressions[8-9].

Keeping these of the pharmacokinetic potential of thesemolecular targets, the first investigations at the overlaying areas of Medulloblastoma and nanotechnology employed commercially available liposomal formulations approved for the treatment of adult tumours. A major reason for the above assertion was that since patients, especially adults enter into several sub classes of Medulloblastoma was found to be the best suitedfor clinical trials from both a regulatory and an ethical perspective.Boiardi et al. studied the safety and functionalization of daunorubicin-loaded liposomes in adult patients with advanced recurrent gliomas and Medulloblastoma. The results pertaining to Medulloblastoma turned out werepositive[10]. Piccaluga in the early 2000 synthesised a drug framed on the similar composition with added agents (DuanoXome®) for the clinical evaluation in relapsedmeningeal acute myeloidleukaemia. The reports suggested that since liposomes over mines the blood brain barrier system; they can be a potent treatment agent for the tumours of the Central Nervous System. Since then, only countable preliminary studies explored nanotechnology platforms to improve the therapy of Medulloblastoma[11-15].

Zucker and Barenholzrecently fabricated a matrixed liposomal combination of vincristine and topotecan co-encapsulated in the same nanocarriers to simultaneously deliver themto human Medulloblastoma cell line with positive results. Although thestudies of the same in invivo model are pending, scientists are striving hard to develop an alternative drug delivering strategyhighlighting paediatrics. Lim and co-workers developed curcumin-loaded nanoparticlemade of N-isopropylacrylamide, vinylpyrrolidone and acrylic acid(NanoCurc®) and demonstrated a dose-dependent decrease in the growth ofDaoy and D283Med cell lines in vitro especially when subjected to an infant's body. The most interesting contribution of this project was that the changes in the CD-133 characterised stem like spherical projections were turned out to be synchronouswith the clinical trials of children[16]. Moreover, the gene regulated expression of IGF-1, STAT3 and GIL1 which are majorly responsiblefor the growth of Medulloblastoma showed depreciation when subjected to the nano curcumin.

The relevance of in vitro assays shouldnot be overestimated, especially because this type of cancer is characterized by the fast dissemination and the invasiveness of its cells in differentareas of the CNS and the conservation of an intact blood–brain barrier.

It is generally difficult to create the analogous human environmentespecially in intermitted stages on infancyto measure the exact efficacy of the system[17]. Meng et al had developed the in vitro model of the brain tumour in these exact environments. The next challenge, after this would be the development of an appropriate xenograft model to study the pharmacokinetics within a children system response.

The last semi decade had seen the emergent of theranostics which is a blend of therapeutics and diagnostics as a new concept to address the problem of this disease treatment. Sun et al. used super paramagnetic nanoparticles comprising of $Fe_2O_3$ surface-modified with PEG and chlorotoxin, a peptide isolated from scorpion venom that shows great affinity for neuroectodermic cells, to deliver an antitumoral drug (methotrexate) and an MRI agent to Medulloblastoma (D283) and glioma (9L/lacZ) cell lines and toamurinexenograftgliomasmodel simultaneously. The same ligand was used to target a nano-vector/DNA complex to Daoy cells[18-19].

## *2.2. ASTROCYTOMA*

Astrocytoma is another class of intracranial brain tumoursimilar to that of Medulloblastoma originated in gliomal cells called astrocytes. It can develop in any zone of the brain andalso in the spine spacing the risk for the disease to spread throughout the entire Central nervous system very quickly[20]. Based on the recognition of anaplasia (nuclear atypia,cell pleomorphism, mitotic activity, endothelial hyperplasia and necrosis) and histological analysis, theWHO classifies astrocytomas accordingto growing malignancy into grades I (polycystic and subependymal giantcell astrocytomas), II (pylomyxoid, peomorphicxanthoastrocytomas andDiffuseastrocytomas), III (anaplastic astrocytoma) and IV (glioblastomamultiform).

Lower grades of astrocytomas are considered to be the benign tumours having the highest occurrence rate amongst the infants. The present prognosis is good, though it depends on the brain mass lost after surgical resection. Since, these tumours are quite heterogeneous in nature;the improvement pathway is quite complicated as they could be effective in one type and ineffective in the other[20].

This also challenges the conduction of clinical trials which might have an impeccable role in the paediatricscience. Only a few preliminary studies addressed the use of nanotechnology to treat this type of cancer, most of them focusing on high grade astrocytomas that are more characteristic of the adult population. Themost common nanocarriers was PEGylated and ligand-conjugated liposomes, most often loadedwith campthotecin,limestoneor doxorubicin[21-22].

## 3. CONCLUSIONS

The nanoscience has taken aprospective route to address the Tumours of the central nervous system from the past decade. The Australian Centre for Nan medicine at the University of New South Wales (Sydney, Australia) had carried out a research which showed that the fate of pediatricnanomedicine seems to be intimately linked to the progresses made in the implementation of these innovative therapies in adults, which is further constrained by the absence of a rigid framework of regulation. In other words, fromanethical perspective, the support of the implementation of the "Precautionaryprinciple" what would make the implementation of nanotechnology inchildren a possibility only in the long-term range and after very extensive andmeticulous research. In the same way, diseases which have a less survival factor in case of children should receive a specialattention to assure better medical treatment[23]. The most effective and the primary responses should be to be the foundation of research clusters in academia and industry that address, in a focused and multidisciplinary way, the treatmentof each single disease at the paediatric level. Otherwise, the current adult–child gap is expected to undergo a further deepening and the paediatric patients left onemore time behind.

## 4. REFERENCES

1. S.S. Feng, Nanoparticles of biodegradable polymers for new concept chemotherapy, Expert Rev. Med. Dev. 2004; 1: 115–125.
2. Vila, A. Sanchez, M. Tobio, P. Calvo, M.J. Alonso, Design of biodegradable particles for protein delivery, J. Control. Release, 2002; 78: 15–24.
3. A. Nori, J. Kopecek, Intracellular targeting of polymer-bound drugs for cancer chemotherapy, Adv. Drug Deliv. Rev. 2005; 57: 609–636.
4. Y. Bae, N. Nishiyama, S. Fukushima, H. Koyama, M. Yasuhiro, K. Kataoka, Preparation and biological characterization of polymeric micelle drug carriers with intracellular pH-triggered drug release property: tumor permeability, controlled subcellular drug distribution, and enhanced in vivo antitumor efficacy, Bioconjug. Chem. 2005; 16: 122–130.
5. E.R. Gillies, A.P. Goodwin, J.M.J. Frechet, Acetals as pH-sensitive linkages for drug delivery, Bioconjug. Chem. 2004; 15: 1254–1263.
6. E.R. Gillies, J.M.J. Frechet, pH-responsive copolymer assemblies for controlled release of doxorubicin, Bioconjug. Chem. 2005; 16: 361–368.
7. R.I. Pakunlu, Y. Wang, M. Saad, J.J. Khandare, V. Starovoytov, T. Minko, In vitro and in vivo intracellular liposomal delivery of antisense oligonucleotides and anticancer drug, J. Control. Release, 2006; 114: 153–162.

8. G. Sharma, S. Anabousi, C. Ehrhardt, M.N.V.R. Kumar, Liposome's as targeted drug delivery systems in the treatment of breast cancer, J. Drug Target. 2006; 14: 301–310.
9. S. Bontha, A.V. Kabanov, T.K. Bronich, Polymer micelles with cross-linked ionic cores for delivery of anticancer drugs, J. Control. Release,2006; 114: 163–174.
10. T.Y. Jiang, Z.Y. Wang, C. Chen, F.k. Mo, Y.l. Xu, L.x. Tang, J.j. Liang, Poly(aspartic-acid) derivatives as polymeric micelle drug delivery systems, J. Appl. Polym. Sci. 2006; 101: 2871–2878.
11. J.Z. Du, D.P. Chen, Y.C. Wang, C.S. Xiao, Y.J. Lu, J. Wang, G.Z. Zhang, Synthesis and micellization of amphiphilic brush-coil block copolymer based on poly(e-caprolactone) and PEGylatedpolyphosphoester, Biomacromolecules, 2006; 7: 1898–1903.
12. K.S. Rathore, R. Lowalekar, R.K. Nema, C.P. Jain, Quantum dots: a future drug delivery system, Pharmacol. Rev. 2006; 4: 30–32.
13. Z. Zhelev, H. Ohba, R. Bakalova, Single quantum dot-micelles coated with silica shell as potentially non-cytotoxic fluorescent cell tracers, J. Am. Chem. Soc. 128 (2006) 6324–6325.
14. J. Weng, J. Ren, Luminescent quantum dots: a very attractive and promising tool in biomedicine, Curr. Med. Chem. 2006; 13: 897– 909.
15. Y. Dong, S.S. Feng, Nan particles of poly(D,L-lactide)/methoxypoly(ethylene glycol)–poly(D,L-lactide) blends for controlled release of paclitaxel, J. Biomed. Mater. Res. 2006; 78A: 12–19.
16. H. Zhang, W. Cui, J. Bei, S. Wang, Preparation of poly(lactide-coglycolide-co-caprolactone) nanoparticles and their degradation behaviour in aqueous solution, Polym. Degrad. Stab. 2006; 91: 1929–1936.
17. S. Sajeesh, C.P. Sharma, Novel pH responsive polymethacrylicacidchitosan-polyethylene glycol nanoparticles for oral peptide delivery, J. Biomed. Mater. Res. 2006; 76B: 298–305.
18. J.M. Bergen, H.A. von Recum, T.T. Goodman, A.P. Massey, S.H. Pun, Gold nanoparticles as a versatile platform for optimizing physicochemical parameters for targeted drug delivery, Macromol.Biosci. 2006; 6 : 506–516.
19. V. Dixit, J. VandenBossche, D.M. Sherman, D.H. Thompson, R.P. Andres, Synthesis and grafting of theistic acid-PEG-foliate conjugates onto Au nanoparticles for selective targeting of folatereceptor positivetumor cells, Bioconjug. Chem. 2006; 17: 603–609.
20. J.L. Arias, V. Gallardo, F. Linares-Molinero, A.V. Delgado, Preparation and characterization of carbonyl iron/poly(butylcyanoacrylate) core/shell nanoparticles, J. Colloid Interface Sci. 2006; 299: 599–607.
21. J. Dobson, Magnetic nanoparticles for drug delivery, Drug Dev. Res. 2006; 67: 55–60.

22. J. Yang, H. Lee, W. Hyung, S.B. Park, S. Haam, Magnetic PECA nanoparticles as drug carriers for targeted delivery: synthesis and release characteristics, J. Microencapsul. 2006; 23: 203–212.
23. H. Maeda, J. Wu, T. Sawa, Y. Matsumura, K. Hori, Tumor vascular permeability and the EPR effect in macromolecular therapeutics: a review, J. Control. Release, 2000; 65: 271–284.