INTERACTION BETWEEN GROUP OF VITAMINS AND NANO DRUGS TO BRAINSTEM GLIOMA PROTEIN AND REDESIGNING THE CHEMICAL STRUCTURE

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ABSTRACT

Brainstem Gliomas are amongst the most subtle and deadliest disease in the field of cancer. It provides treatments include surgery, clinical approach, radiotherapy, and chemotherapy. Blood Brain Barrier (BBB) is very important part allows to circulate blood from brain to body parts. Provides difficulty in delivering nano-molecules efficiently into the brain and offers the medical side effects depends upon characteristics of drugs even that can be used to indicate the effectiveness of drugs in similar tumors. This challenge is to identify how efficiently applied drugs works in central nervous system. Bioinformatics approach in nanomedicine helps to find out the presence of drug molecules present in the body, where they are needed and where they will do the best. I.e. The delivery of drug in BBB focuses on increasing the bioavailability and curate cancer with updated redesigned Drug and protein interaction. So, it is all about to make efficient redesigned drug and view it in 3D. Our novel approach focuses on redesign and apply efficient ligand through BBB to the Mutated Brainstem Glioma sequence using CADD tools, comparing the efficiency with existing drugs and view it in systematic proposed 3D visualization tool.

Index Terms: Brainstem glioma; Blood-brain barrier (BBB); Nano drug; Central nervous system; CADD; 3D visualization tool

I. INTRODUCTION

The drug is one of the most prominently used organic small molecule that starts the function of a biological molecule such as proteins, carbohydrates etc, which results in a therapeutic benefit to the patients. The delivery of drug in brain cancer focuses on increase in bioavailability. So it is all about targeting the molecules and delivering drugs incorrect accuracy. Analyzing the cost among different nanomedicine applied on gene sequence in the human body and noted it, showing variation of protein cells with the use of best nanomedicine. The first phase is find the most efficient nanodrugs for brainstem glioma and redesigning its chemical structure. So, we can reduce the side effects of nanodrugs by combining the structure of suitable vitamins. It will make our project in a much more efficient manner in the nanomedicine field.

Bioinformatics has opened an application field Computer Aided Drug Design (CADD) for increasing need for new drugs. CADD is efficient of growing the amount of novel drug compounds in body. This application can provide much more advanced and healthy medical drugs and it increases the computing ability to find drug and advance process. CADD provides chemical and biological information about ligands and targets to identify and optimize new drugs. To using this CADD we can store, manage and analyze quickly increasing resources has given rise to the field. The CADD application can be of two categories such as structural based and ligand based. CADD depends on the capabilities such as to determine, to study and analyze the 3D structures of biological molecules. The ligand based CADD approach involves the analysis of ligands to interact with a target of interest to analyze their chemical structures.

Brainstem Gliomas are one of the most damaging kinds of brain cancer and are related with a poor diagnosis and incurable child cancers. Brain stem gliomas starts in the brain or spinal cord tissue and are usually spread through the nervous system. Blood Brain Barrier (BBB) controls the delivery of therapeutic molecules into the brain and need to check different pharmaceuticals in each stage that have been applicable for the glioma tumors. The Nanomedicine field provides design, efficient drug with least side effects. Nanodrug redesigning for brainstem glioma by reducing the side effects of already existing nanodrugs. It will make our project in a much more efficient manner in the nanomedicine field. I.e. it will be lead to identifying the most efficient nanodrug for brainstem glioma. The project is to develop a computational tool for predicting the structure of biomedical with Nanodrug interaction on brain stem glioma disease sequence with respect to central nervous system and comparing the results, calculate efficiency.

II. REVIEW OF LITERATURE

Prashanth and Wilson [1]] proposed that Molecular Dynamics of Water-Mediated Interactions of a Linear Benzimidazole-Biphenyl Diamidine with the DNA Minor Groove, which provides a linear conformation with a radius curvature and which does not equivalent to the DNA minimal groove shape. It also provides a better understanding of how water couples the linear database and compounds to the minor groove for tight binding without a large contribution to the entropy of binding. Krishnan Namboori et al., [2] proposed that The ApoE gene of Alzheimer's disease (AD): Functional, Integrative Genomics and the ApoE gene is responsible for the Alzheimer's disease, which has been examined to find functional values of Single-Nucleotide Polymorphisms (SNPs) in body. Both natural and mutant protein structures were analyzed along with the stabilization residues to determine all SNPs of ApoE. The mutation in R132S has analyzed as the most significant effect on functional variation. Bipin Nair et al., [3] proposed that an approach for identifying the presence of factor IX gene in DNA sequences using position vector ANN. The predicts the presence of genes in the DNA sequence. This paper proposes an approach for training the system to identify a specific gene by providing relevant protein sequences and identifying exact

locations of splice junctions in DNA sequences. Pranita et al., [4] proposed that Computer-aided drug design: an innovative tool for modeling the strategies for CADD is extent the structural and other information existing about the target and the ligands. The CADD drug discovery in recent years have demonstrated the potential rate of CADD in drug development. The drug design using CADD application provide design of drug with least side effects and high potency. The journal of pharmaceutics and drug delivery research [5] proposed makes a contribution in advancing knowledge for drug delivery research [5]. Molecular modeling allows to use computers to envision the molecules means demonstrative molecular structures. Zaixing Yang et al., [6] had proposed Nanoparticles with their large special structure amenability and excellent mechanical and electrical properties that becomes a best candidate for high efficiency nanomedicines in both diagnostics and therapeutics. Drug development and Research had proposed cancer science and therapy nanomedicine is the use of nanoparticles in medical practice for improving imaging, drug delivery and therapy [7]. Nanophoto-thermolysis and nanophotohyper-thermia are two new techniques which exploits strong light absorption properties of nanoparticles to generate heat in the body. Hadar Zaman [8] had proposed an approach for Addressing Solubility through Nano Based Drug Delivery Systems for developing new methods to overcome poor solubility in drug development residues a challenge for the pharmaceutical production. It is estimated recently discovered chemical entities are insoluble. So, it provides less efficiency in interaction of drugs and sequences. Wim et al., [9] had proposed an approach for Drug delivery and nanoparticles: Applications and hazards. The use of nanotechnology in treatment are more specifically drug delivery is set to spread rapidly. Now many elements are under analysis for drug delivery and more precisely for cancer therapy. Anwunobi et al., [10] proposed an Recent Applications of Natural Polymers in Nanodrug Delivery. Natural polymers can't enjoy the healthiness of easy flexibility to design as compared to synthetic polymers, but their excellent biocompatibility and protection makes them very important in the research of various drug delivery systems. But not mentioned the drug and protein interaction. Ariel Gilert and Marcelle Machluf [11] proposed an approach for Nano to micro delivery systems: targeting angiogenesis in brain tumors. There is an urgent need to develop delivery platforms, which will avoid such hurdles and qualify the distribution of antigenic drugs into the tumor bed. Dimendra et al., [12] proposed that treatment of cancer by using nanoparticles as a Drug Delivery for understanding of the differences between cancer cell and its normal counterpart. If we do not understand cancer, we cannot control and eliminate it. Singh et al., [13] based on research conducted, human brain tumors are focused on the molecular and cellular study of the tumor mass. It focuses on how it will take lot of steps to recognize the stem cells in brain. Janet et al., [14] discuss the major forms of resistance and new possibilities in nanomedicine to overcome side effects of brain tumor. It mainly focusses on advanced nanomedicine benefits in cancer therapy and efficiency of several methods in medical field. Groot et al., [15] describing epidermal growth factor receptor (EGPR) may be one of the effective application in working with glioma patients. So, In this approach they are taking different clinical activities and evaluate the changes in the EGPR. It also evaluating the changes curation of cancer in glioma patients.

III. Problem Formulation

The existing method brainstem gliomas are not nearly as common in adults as they are common in children also. They can be difficult to diagnose and are challenging to treat. Clinical studies of this diagnosis are few and generally small. Because of these factors, the understanding of the biology of adult brainstem glioma is incomplete. The childhood brainstem gliomas may show some sign or symptoms initial stage of the cancer is analyzed and keep remaining for a few months or years. Some cancer treatments may cause side effects after the treatment also. The side effects like physical problems, changes in mood, feelings, thinking, learning or even memory. The clinical trials are the best treatments. These clinical trials are the part of the cancer research process, which helps to find out the new tumor treatments that are safe and effective or better than the standard treatment, which finds the most efficient nanodrug for brainstem glioma. Indeed, not a single complete approach is powerful enough to offer a sustainable break through glioma treatment. So, the future application is a combined effort of making the approach in much more efficient manner.

IV. Problem Definition

In our proposed methodology used for nanodrug redesign for brainstem glioma. Brainstem gliomas are one of the most complicated and high-risk brain tumor that are associated with a poor diagnosis and incurable child tumors. Brainstem gliomas starts in brain or spinal cord tissue and that spread throughout the nervous system. Nanodrug for brainstem gliomas by reducing the drawback of already existing methodologies. The project is to develop a computational tool for predicting the structure of biomedical with nanodrug interaction on brain stem glioma disease sequence with respect to central nervous system and comparing the results, calculate efficiency. We were reduce the drawbacks by redesign the efficient nanodrug with least side effects.

V. Existing Methodology

Brainstem gliomas is a challenging disease in medical history with challenging way of treatment options. It includes radiotherapy, chemotherapy and clinical studies of diagnosis are very few and less efficient. Where radiotherapy won't cure the cancer but it used to reduce growth of the cancer, and it lead to control the pain of patients. But it highly causes side effects to nearby tissues of human body. In most of the times it reduces the growth of near tissues and lead to complicated body problems. Even in the case of chemotherapy may experience a variety of side effects such as vomiting, loss of appetite, a major side effects associated with chemo is hair falls out. Medical care of brain cancer is mainly focus on the patients health with less side effects, so it

mainly uses nanodrugs such as Tarceva and Gefitinb. Where tarceva is a nano medicine that interact with tissues and reduce the growth of cancer cells. It mainly gives to ones after the patient is tried with other cancer medicines. But, if you are using tarceva mainly have drawback such as kidney or liver disease, even it can cause skin rash, dryness or other irritation such a back-bone pain etc. so most of glioma patients are using vitamin d. Where vitamin d makes body stronger. Gefitinb nanodrug also has the same side effects. It leads patients to take vitamin d separately. So, using our approach we are making both vitamin D and nanomedicine into a single drug. It will reduce side effects and make more powerful and efficient nanodrug for brain cancer.

VI. Proposed Methodology

A. flow chart

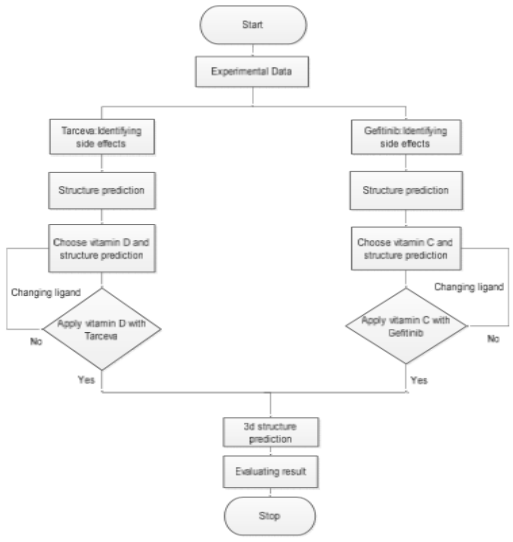

Figure 1: Architecture Diagram of Proposed System

Step 1: Choose the existing drug for the brainstem glioma patients and study about the operations on the data. Take it as the experimental data. Ie, nanodrugs (Tarceva, Gefitinib).

Step 2: Study the processing of nanodrug with protein sequence and identifying side effects of nanodrug.

Step 3: Collecting the historical patient details from hospital and creating report on side effects of drugs in glioma patients.

Step 4: Structural prediction of nanodrug.

Step 5: Study the different vitamins and ligand for reduce side effects of nanodrug.

Step 6: Choose the appropriate vitamin for the nanodrug which leads to reduce the side effects and check the process among them.

Step 7: If vitamin (ligand) produce an efficient medicine with existing nanodrug, with avoiding the side effects. Then lead to process further steps.

Step 8: If the ligand (vitamin) is not processing with existing drug then choose different vitamin and identifying result, with reducing side effects.

Step 9: View the resulted drug in 3D structure and identifying modified codon structure and evaluating result.

Step 10: Evaluating redesigned drug with existing drug and describing efficiency of resultant data.

VII. Experimental Results

The main intention of our project is to try to maximize avoiding other treatments such as radio-therapy, chemotherapy, etc. and making efficient use of redesigning nanodrugs for glioma patients. Using nano-particles over other methods provides killing only tumor cells than killing healthy cells, efficient nano caries in drug delivery provides better control and distribution of molecules into specified tissue. Even redesigning drugs will lead to make more systematic product in the medical field. Because of the side effects of drugs tarceva and gefitinib structure, we are redesigning structure by combining with respect to vitamin D and vitamin C and changing the ligand. So, we are improving the efficiency combines with these vitamins and redesigning the structure of nanomedicine.

1. Redesign of the Drugs for Brainstem glioma
   - Redesigning of Erlotinib (Tarceva)

A) Erlotinib (Tarceva)

Tarceva is a one of the most usable cancer medicine interact with nano-cells in patients and reduce growth of cells. The mutation happens in the Epidermal Growth Factor Receptor (EGFR) gene represent abnormalities in Glioblastoma. Active ingredient Erlotinib medicine in Tarceva (called as tyrosine kinase inhibitor) interacts with the tyrosine enzyme generated by EGF and cancer receptor. In mammalian melanin synthesis, tyrosine enzyme is one of the key enzyme. Two different cell types can be produced by pigments are pigmented epithelial cell of the retina and the melanocyte, a cell of neural-crest origin.

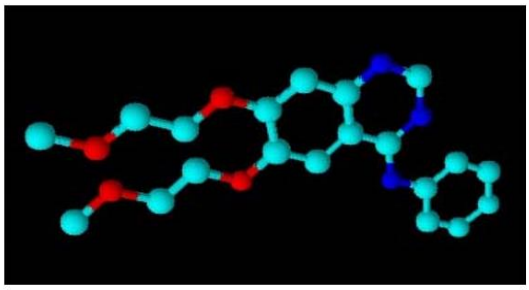

Figure 2: 3D molecular structure of tarceva.

B) Vitamin D

Drug interactions are reported among the people who take vitamin D and Tarceva together. This will analyze the effectiveness and drug interactions between vitamin D and Tarceva. Vitamin D is one of many nutrients of our bodies to stay healthy. Some of the functions of the vitamin D helps brain development and anti-cancer effects. Vitamin D is naturally occurring substance that causes very few side effects, even when administered at high doses and it kills brain stem glioma cells.

Figure 3: Moliocular structure of vitamin D

C) Redesigning of Tarceva and Vitamin D

Tarceva has side effects of such as body pain, stabbing chest pain tightness in the chest difficult or labored breathing, etc. So, we are adding vitamin D structure with tarceva structure and redesigning into a new one. So, it will reduce side effects of tarceva and lead to make body of patients stronger and also the structure display using our 3d structure tool.

2. Redesigning of Iressa (Gefitinib)

A) Iressa (Gefitinib)

It is a drug used to control growth of cancer stem cells in the human body, where in which it act as the EGFR inhibitor and control signaling and growth of cells. Using the epidermal growth factor receptor target cells in body. It is also used in clinical trials for other types of cancer.

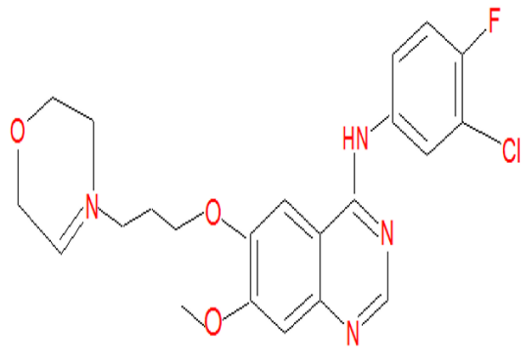

Figure 4: structure of Gefitinib.

B) Vitamin C

Vitamin C is a dietary supplement, which is used to prevent scurvy and used as a essential nutrient involved in the repair of tissues. Vitamin C can reduce tumor death in brain cancer patients which also produce an aggressive free radical in the tumor environment but not in the environment of healthy cells. Vitamin C with radiation, affects the survival of cancer cells isolated from glioblastoma brain tumors compared to survival of normal cells.

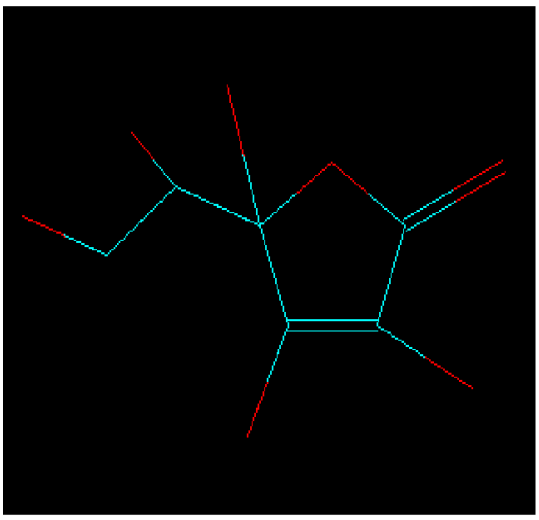

Figure 5: 2d structure of Vitamin C

C) Redesigning of Gefitinib and Vitamin C

The common side effects of iressa include skin reactions, nail disorders, eye pain or irritation, etc. The alergetic reaction including difficulty breathing, closing of the throat are also the weakness of gefitinib. So we are adding vitamin C structure with gefitinib structure and redesigning into a new one.so it will reduce side effects of gefitinib and lead to make body of patients stronger and also the structure display using our 3d structure tool.

VIII. Conclusion

Nanomedicine provides more efficient new tools and treatments comparing to earlier diagnostics like chemotherapy, radiotherapy etc. Cancer Commonly, tumor cells speeding can be detected by cancer biomarkers. Drug delivery in brain cancer mainly focuses on increasing the bioavailability over a period of time. There are many types of treatment in brain cancer. Such as radiation therapy, chemotherapy, targeted therapy, alternative electric field therapy. Existing systems explains these different types of treatments with large side effects and vary from person to person. So, it is all about targeting the molecules and delivering drugs in correct accuracy. We are improving the efficiency by combining nanodrugs with vitamins and redesign the structure and visualizing the protein structure in in 3d model.

References

[1] Prashanth and W. Wilson, D., Molecular Dynamics of WaterMediated Interactions of a Linear Benzimidazole-Biphenyl Diamidine with the DNA Minor Groove. Journal of American Chemical Society 131: 76 (2009).

[2] Krishnan Namboori, P.K., Vineeth, K., V.B. Rohith, Hassan, I.A., Sekhar, L.A., Sekhar, A.A. and Nidheesh, M.A., The ApoE gene of Alzheimer's disease (AD). Functional and Integrative Genomics 11:519-522 (2011)

[3] Bipin Nair B.J., K. Syed Khamarudheen, Ranjitha H.S., Department of Computer Science, Amrita School of Arts and Sciences, Mysuru Campus, Amrita Vishwa Vidyapeetham, Amrita University, India. An approach for identifying the presence of factor IX gene in dna sequences using position vector ANN

[4] Pranita P.K., Cynthia Hawkins Matthieu F., Dumont Kawasaki, E.S., Player, A., Nanotechnology, nanomedicine, and the development of new, effective therapies for cancer.Nanomedicine: Nanotechnology. Biology and Medicine 1(2): 101-109 (2005).

[5] The journal of pharmaceutics and drug delivery research, Fred Laningham Sarah S., Donaldson, Fred Laningham, Paul Graham Fisher, Journal of clinical oncology, Advances Toward an Understanding of Brainstem Gliomas, From the Department of Radiation Oncology; Department of Pediatrics, Neurology, and Neurosurgery.

[6] Zaixing Yang, Marcos Dellaretti, M.D., German Reyes Botero, Karima Mokhtari, Nadine Martin-Duverneuil, Jean-Yves Delattre, Florence Laigle-Donadey Integr Biol (Camb) Nanoparticles with their large space of structural amenability and excellent mechanical and electrical properties. PMC (2014)

[7] De Jong, W.H., Borm, P.J., Drug delivery and nanoparticles: applications and hazards. International Journal of Nanomedicine 3(2): 33 (2008)

[8] Hadar Zaman H., Addressing Solubility through Nano Based Drug Delivery Systems West Yorkshire, Bradford, BD7 1DP, UK

[9] Wim H De Jong, Paul J.A., Borm, Drug delivery and nanoparticles: Applications and hazards, Int. J. Nanomedicie 3(2): 133–149 (2008)

[10] Anwunobi, A.P. and M. O. Emeje, Recent Applications of Natural Polymers in Nanodrug Delivery, Nanoscience Group, National Chemical Laboratory, Pune, India

[11] Ariel Gilert, Marcelle Machluf, Nano to micro delivery systems: targeting angiogenesis in brain tumors, Journal of Angiogenesis Research (2010).

[12] Dimendra J. Patel, Pratik A. Mistri, Jatin J. Prajapati, Department of pharmaceutics, Baroda College of Pharmacy, Limda, Vadodara – 391760, Treatment of cancer by using Nanoparticles as a Drug Delivery.

[13] Singh S.K., Ian D. Clarke, Mizuhiko Terasaki, Victoria E. Bonn, Cynthia Hawkins, Jeremy Squire, Peter B., Dirks, Identification of a Cancer Stem Cell in Human Brain Tumours.

[14] Markman, J.L. et al., Nanomedicine therapeutic approaches to overcome cancer drug resistance. Advanced drug Delivery Reviews 65(13): 1866-1879 (2013).

[15] De Groot, J.F., et al., Phase II study of carboplatin and erlotinib (Tarceva, OSI-774) in patients with recurrent glioblastoma. Journal of Neuro-oncology 90(1): 89-97 (2008).