International Journal of Nanotechnology and Applications
ISSN 0973-631X Volume 11, Number 3 (2017), pp. 277-283

http://www.ripublication.com

Magnetic Nanoparticle / Magnetic Fluid Approach to Control Neuromuscular Degeneration in Friedreich's Ataxia

[1]Swasti Wagh and [2]D.K.Wagh

[1]M.Sc. (Applied Mathematics),
[2]Ph.D. Retired professor.of Mathematics, Shri G.S. Institute of Tech. &SC. Indore, (MP), India,

Abstract-

The paper describes Friedreich's Ataxia (FRDA), a rare genetic disorder which causes imbalance, in-co-ordination of limb movements and neuromuscular degeneration. Then it explains the genetics of FRDA and the cause of degeneration. Understanding of the cause of degeneration leads us to suggest magnetic nanoparticle approach to control degeneration in FRDA.

INTRODUCTION –

Nanotechnology is concerned with creation and utilization of material devices of nano scale. Because the building blocks of living organism- proteins and cell parts are of nano size, this technology finds promising applications in biotechnology and medicine[1]. The nanotechnology has played a vital role in various biomedical applications such as biomarkers, biosensors, molecular imaging, drug and gene delivery, probing DNA structures, targeted drug delivery and cancer treatment. In this paper, we propose a magnetic nanoparticle approach to control degeneration in Friedreich's Ataxia (FRDA) which is a genetic neuro-muscular degenerative condition of progressive nature and is incurable till today.

The sec. 1 deals with Ataxia and its types. In sec 2 we discuss genetics of FRDA. In sec 3 we explain role of frataxin gene .Sec4 is devoted to nano particles, nanotechnology & Sc., magnetic fluids and their application in biotechnology & medicine. In Sec.5 and 6 we explain cause of degeneration in FRDA and magnetic

nanoparticle approach to control degeneration. In the last sec. some concluding remarks are given.

1. ATAXIA AND ITS TYPES-

We begin with what is Ataxia? Ataxia is a neuromuscular degenerative condition of progressive nature .Initial symptoms are imbalance, gait disturbance and in-co-ordination in limb movements. There are two types of Ataxias—(1) Acquired ataxia and (2) Non acquired ataxia or genetic ataxia.

1) Acquired ataxias are non genetic and are caused because of various environmental factors or structural damage to cerebellum and spinal cord.

Many of these ataxias are curable.

2) Non acquired ataxias are genetic and hence are inherited ataxias. No cure is available for these till now. These are further classified as–

i) Dominant ataxia
for e.g. Spinocerebellar Ataxia (SCA), Episodic Ataxia and DRPLA (dentato-rubro-pallido-luysian atrophy) are autosomal dominant ataxia.

ii) Recessive ataxia

For e.g. Friedreich's Ataxia, Ataxia Telegansia.

This paper is on Friedreich's Ataxia which is a recessive genetic ataxia. Friedreich's ataxia (FRDA)[2,3] is a genetic, progressive, neurodegenerative movement disorder, with onset of symptoms at a mean age between 10-15 years.

FRDA is predominantly a neurodegenerative disease. It manifests in initial symptoms of poor coordination, such as gait disturbance, and the patient becomes helpless and totally dependent on others in course of time. It can also lead to scoliosis, heart disease (cardiomyopathy), slurred speech, diabetes etc.Till now there is no cure of FRDA or any treatment which can control degeneration, and the patient has to lead a miserable life.

2. GENETICS OF FRDA –

FRDA is an autosomal recessive inherited[2,3] disease caused by trinucleotide (GAA) expansion of the *FXN* (frataxin) gene. Autosomal recessive means that an individual develops symptoms of FRDA if he has inherited two mutated or abnormal copies of the *FXN* gene. If an individual has one mutated FXN gene (allele) and one normal FXN gene (allele) then the individual does not show symptoms of FRDA, but he is a FRDA carrier .The individual is normal if both-copies of FXN gene are normal.

If we denote the normal FXN gene by 'F' and diseased (non functioning) gene by 'f', then genotype-

1. (f,f) is FRDA patient
2. (f,F) or (F,f) are carriers of FRDA
3. (F,F) is normal

FRDA is the most common of autosomal recessive ataxia.

3. ROLE OF FRATAXIN GENE –

FXN gene encodes frataxin protein[4] which is localized in the mitochondria. The function of frataxin protein is not entirely clear, however, the primary role of frataxin protein is the activation of iron-sulfur (Fe-S) clusters biogenesis in the mitochondria. Frataxin protein works as an iron chaperone, a companion of iron particle. It holds iron and takes it to sulphur to form iron-sulphur cluster. Iron-sulfur clusters are required for mitochondrial electron transport chain to generate energy in the form of adenosine triphosphate (ATP).

4. NANO PARTICLES, NANOTECHNOLOGY AND MAGNETIC FLUID

Nanoparticles are very small particles of size of only about few nano meters , where 1 nano meter = 10^{-9} meter, i.e. one billionth of a meter .The nanoparticles have novel optical, electronic and structural properties that are not available in individual molecules or bulk solid. Nano science and technology is concerned with the study and preparation of nano particles of different materials and their applications in other fields of science such as physics, chemistry, biology, medicines, material engineering etc.

Living organisms are made up of cells and proteins. The cells are typically of about 10 micron size (1 micron = 10^{-6} meters) and their parts are even smaller. Proteins have a size of about 5 nano meter. So the applications of nanotechnology are very promising in biology and medicine[1,5 to 16] .
Some of these applications are

- Drug and gene delivery[5]
- Bio detection of pathogens
- Detection of proteins
- Probing of DNA structures
- Tissue engineering
- Tumor destruction via heating (Hyperthermia)[11]
- Separation and purification of biological molecules and cells

- MRI contrast enhancement
- Phagokinetic studies.

MAGNETIC FLUID –

Magnetic fluid[22] is a suspension of magnetic nanoparticles in a liquid carrier. This fluid can be made to flow by applying magnetic field gradient. It was first synthesized by Rosensweig, a scientist of NASA, in 1965 to tackle the problem of circulating heat and injecting fuel in space ships in gravity free regions. Because of wide applications of magnetic fluid in technology, several methods have been developed to prepare magnetic fluid. For medical applications, body compatible magnetic fluids which can be safely injected in human body are also available. Some biomedical applications of nanoparticles and magnetic fluid are described below[13]:

Nanotechnology has helped to increase the effectiveness of treating cancer in certain situations. Magnetic field hyperthermia can be made more effective by using biocompatible super paramagnetic nanoparticles. These help in heating cancerous tissue by creating oscillations that produce heat from friction. This heat damages the cancer tissue. The gold nanoparticles have a typical property that they can identify cancerous tissue. When the cancer tissue is identified a laser can be used to explode the particles to damage the cancerous tissue. The effectiveness of radiation therapy in cancer treatment can be increased by gold nanoparticles. These are body compatible, radio sensitizer and can increase dose deposit. The increase in dose creates free radicals which damage the cancerous tissue.

Nanoparticles have also been used in orthopedic implants. They increase the biocompatibility of the implants which results in longer life span of the implant.

Nanoparticles are also used for effective drug delivery. It is also possible to prepare nanoparticles which are sensitive to specific PH value. These particles remain in certain conformation protecting the drug till it reaches the target having specific PH value. In response to this specific PH value of the target, nanoparticles change conformation shape and release the drug. With the use of magnetic nanoparticles, it is possible to control the speed of drug delivery at the target and it is also possible to skip the regions quickly where the drug has adverse effects.

5. CAUSE OF FRDA -

In FRDA, because of GAA expansion in FXN gene, production of frataxin protein is reduced. The level of frataxin protein in affected individuals drops to nearly 5% to 30% of that in healthy individuals. Low frataxin protein level leads to insufficient

biosynthesis of Fe-S clusters. This affects the process of energy production in mitochondria and iron metabolism. Thus, there is gradual reduction of ATP energy in mitochondria and besides this increase in iron accumulation on the cell, accelerating the gradual death of the cell. With the lapse of time more and more cells die and neuromuscular degeneration becomes more and more prominent. Ultimately, the FRDA patient becomes totally dependent on others for his day to day activities and also becomes the victim of many other associated problems.

6. MAGNETIC NANOPARTICLE/MAGNETIC FLUID APPROACH TO CONTROL DEGENERATION IN FRDA -

Nano technology may solve this problem. In place of frataxin protein, we can introduce magnetic-nano particles in the body to pickup iron particles, and using external magnetic field, we can direct them to sulphur to form iron-sulphur clusters. Thus iron-sulphur clusters can be formed even in the absence of frataxin protein in FRDA patients. When the formation of iron-sulphur clusters will not stop in FRDA patients, the process of respiration in mitochondria will continue to produce energy in the form of ATP. As iron particles are utilized in formation of iron-sulphur clusters, no free iron is left to get deposited on cells and cause their death. Thus both the problems of FRDA, i.e. the loss of ATP energy and cell death due to iron accumulation can be controlled. In the beginning of FRDA, this approach is expected to control degeneration completely. However, in acute cases degeneration may be controlled at least partially.

7. CONCLUDING REMARKS -

Materialization of the approach will require selection of proper body compatible magnetic nano-particles / magnetic fluid, identification of locations where it is to be introduced and external magnetic field to be applied to pickup iron particles and direct them to sulphur. A set of in vitro and in vivo experiments are required to be planed to study iron-sulphur clusterization.The study of possible side effects and their remedy is also essential.

REFERENCES:

[1] Ov salata, Applications of nanoparticles in biology and medicine, Journal Nanotechnology 2004,2:3

[2] Frequently asked questions about ataxia. National Ataxia foundation (NAF) publication 2014.

[3] Friedreich Ataxia Booklet published by Ataxia UK 2015.

[4] Role of frataxin Wikipedia, the free enclopedia, (https://en.wikipedia.org/wiki/frataxin).

[5] Lavan DA-, Meguire R, (2003), small –scale systems for in-vivo drug delivery. Nat. biotechnol-21:-1184-91.-Allen TM, Cullis PR,(2004)Drug delivery systems entering the main stream, Science 303,1818-1822.

[6] Cavalcanti A, Shirinzadeh B, Freitas RA, Hogg T, (2008), Nano robot architecture for medical target identification,Nanotech.19:15.

[7] {2010) Nanotech In targeted cancer therapy, University of Waterloo.

[8] Nie S , Xing Y , Kim GJ , Simons JW ,Nanotech applications in cancer , Annu Rev. Biomed Eng 9,2257-88.

[9] Wong HL, Wu XY , Bendayan R, (2012), Nanotechnological advances for the delivery of C NS therapeutics. Adv .Drug Deliv. Review 64,686-700.

[10] Pankhurst QA. Connolly J, Jones SK, Dobson J, Applications of magnetic nanoparticles in biomedicine. J.Phys D: Appl. Phys. 2003, 36, R167-R181.

[11] Yoshida J,Kobayashi T, Intra cellular hyperthermia for cancer using magnetite cationic limposomes.J. Magn Magn Mater, 1999, 176-184.

[12] Taton TA,nanostructures as tailored biological probs. Trends Biotechnol 2002, 20, 277-279.

[13] Medical applications of nanoparticles.univ. of Michigan(pdf).https://www.uniflint.edu

[14] Whitesides GM, The right size in biotechnology, 2003, 21, 1161-65.

[15] C.N.Ramchand and Saiyed Zainulabedin M, Advancement in the field of medicine and biotechnology.International work shop on recent advances in nanotechnology of magnetic fluids, Jan 22-24, 2003 at NPL New Delhi.

[16] Ivo Safarik and Mirka Safarikova, Magnetic nanoparticles and biosciences. .International work shop on recent advances in nanotechnology of magnetic fluids, Jan 22-24, 2003 at NPL New Delhi.

[17] D.K.wagh, Swasti wagh and Jitendra Binwal, Viscosity of magnetic fluid in terms of size distribution parameters of magnetic particles. .International work shop on recent advances in nanotechnology of magnetic fluids, Jan 22-24, 2003 at NPL New Delhi.

[18] D.K.Wagh and S.D.wagh, Blood flow considered as magnetic fluid flow, in Physiological fluid dynamics III Narosa publishing house 1992, pp.311-315.

[19] D.K.Wagh and Ashima Avashia,Investigation of the effect of magnetic field on

microcirculation using porous flow approach, Advances in physiological fluid dynamics Narosa publishing house 1995,pp.156-158.

[20] D.K.Wa gh and Ashima Avashia, on the viscosity of magnetic fluid, Journal of magnetism and magnetic materials Elsevier, 153, (1996) pp. 359-365.

[21] D.K.Wagh and Ashima Avashia, on the thermal conductivity of magnetic fluid, Japanise journal, Journal of applied physics Vol. 35(1996) pp. 3518-3521.

[22] R.E.Rosensweig, Ferrohydrodynamics, Cambridge University press .1985