THE FUNDAMENTAL OF NOVEL DRUG DELIVERY SYSTEM; METHODOLOGY, ROLE OF NANOTECHNOLOGY; NANOPARTICLES IN PHARMACEUTICAL RESEARCH.

[Kushwah Nilesh] [1], Yezdani Umama, [Mohammad Gayoor khan][1]

[Manish kushwah] [1], Kumar Ayush.

[Department of Pharmacy, Truba Institute of Pharmacy, Bhopal India] [1]

Department of Pharmacy Practice, MRM college of Pharmacy, Hyderabad India.

Department of Pharmacy Practice, (M.M.C.P) M.M.D.U Mullana Ambala Haryana, India.

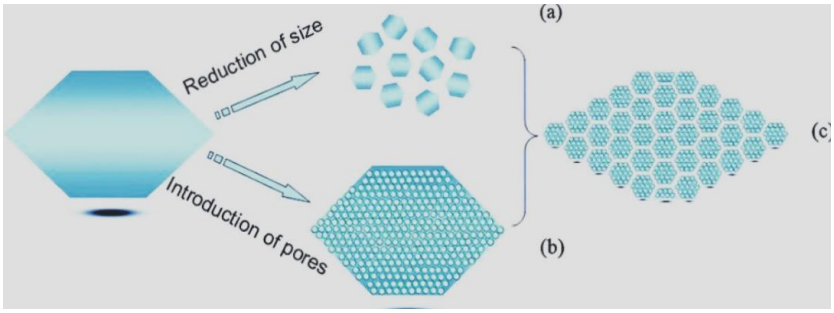
Abstract:

Novel Drug Delivery system is the New and advanced branch of Pharmaceutical branch in this field covered Nano Particles, Nanosomes, etc. This system is advanced & very easy to understand the Pharmacokinetic and Pharmacodynamic behavior of drug since, which approach of the development of optimal drug delivery system. This system cover several discipline includes Silver Nanosomes control phlebovirus using in RT- PCR Detection, targeted Drug delivery system is also part of novel drug delivery, Novel drug delivery system is also applicable for Alzheimer's disease as well. Novel drug delivery system is divided into various disciplines for example – Nanotechnology; Nanotechnology is the study of extremely small structured molecule (size of 0.1 to 100 nm). Nano medicine is a new competitive field of science and technology. Nano medicine ranges from the medical applications of non material's and biological devices to Nano electronic biosensors used in medical field. Nanotechnology, or systems/device manufacture at the molecular level, and it is a multidisciplinary scientific field undergoing explosive development. In future it is widely used in Pharmaceutical and many novel nanoparticles and Nano devices are expected to be used, with an enormous positive impact on human health. In short NDDS maintain the drug concentration in therapeutic range for longer period of time. The future aspects of Novel Drug delivery system are broad; covering all field related to Nano device, Nano Medicine, Nano Particles, Nano somes etc.

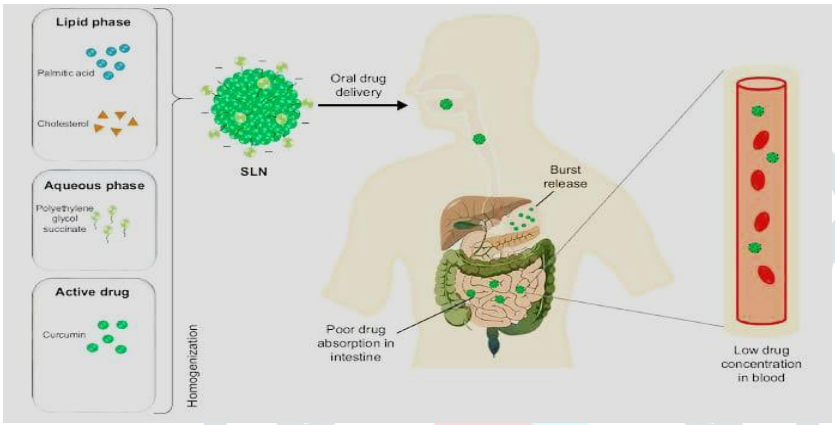
Keywords- *Nano Particles, Alzheimer's Disease, Nanosomes, Nano device, Nanotechnology, carbon Nano- Tubes.*

Graphical Abstract -

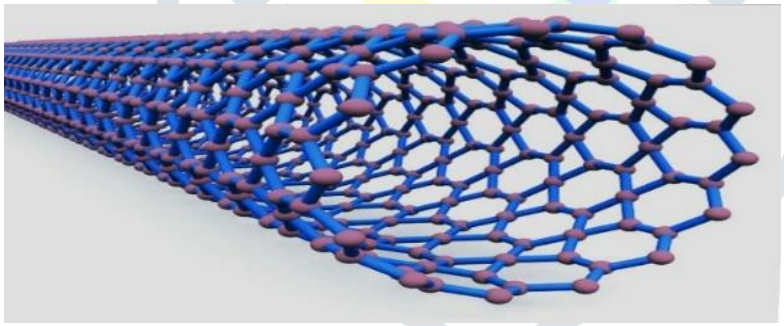
Novel Drug Delivery advanced branch of Pharmaceutical, and in this system the understand of Pharmacodynamic and Pharmacokinetic behaviour we can studied which directly approach to the development of optimal drug delivery system, NDDS maintain the drug concentration in therapeutic range for longer period of time in addition, may deliver the content to the site of action if so desired as per requirements.



(a) NANOSIZED CRYSTAL



(b) SOLID LIQUID NANO PARTICLES



(c) CARBON NANO TUBE

FIGURES: 1.1 (a) Nano sized crystal (b) Solid Liquid Nano Particles (c) Carbon Nano Tube.

I. INTRODUCTION Novel drug delivery systems is the new system Recent advances in the understanding of pharmacokinetic & pharmacodynamic behaviour of drug need optimum approach for Drug Delivery system, drug concentration in therapeutic range for longer period of time There are several advantages of novel drug delivery systems over conventional drug delivery.

1. Better patient compliance may be ensured.

2. Optimum therapeutic- drug concentration in the blood or in tissue may be maintained over a prolonged period of time.

3. Pre- determined release rates of extended period of time may be achieved.

4. Frequent dosing and wastage of the drug may be reduced or excluded.

II. NOVEL DRUG DELIVERY SYSTEM

Various drug delivery systems have been developed and some of them under development with an aim to minimize drug degradation or loss, to prevent harmful side effects and to improve drug bioavailability and also to favour and facilitate the accumulation of the drug in the required bio- zone (site). There are no. Of novel carries which have been established and documented to be useful for controlled and targeted drug delivery. Localized drug delivery devices provide drug action through spatial or temporal control of drug release (usually rate- limiting) in the vicinity of the target. Targeted drug delivery provides drug action by using carries either for passive or active targeting or one base or self programmed approach, usually anchored with suitable sensory devices, which recognize their receptor at the target.

Ocusert

A truly continuous, and controlled- release and zero – order kinetic fashion was achieved using ocusert. First marketed by Alza Corporation, California, the pilocarpine ocusert improved the non compliance problems, low intra -ocular drug bioavailability and potential systemic side effect of pilocarpine.

Reservoir- Type drug delivery system in the reservoir- type drug delivery systems, drug is encapsulated in the drug reservoir compartment whose drug – releasing surface is covered by a rate- controlling an embryonic polymer membrane. The drug in the reservoir compartments can be drug in liquid – or solid type dispersion of drug in a liquid or solid type dispersion medium.

The drug in the reservoir compartments can be drug in liquid – or solid type dispersion of drug in a liquid or solid type dispersion medium.

III. TARGETED DRUG DELIVERY

The targeted drug delivery system if appropriately engineered can be provided the desired therapeutic response without or with side effects associated with conventional drug dosage form. In 1902, Paul Ehrlich proposed the concept of magic bullet. He postulated that therapeutic molecules like drugs; vaccines or macromolecules such as DNA, etc could be successfully delivered to desired therapeutic site in the optimal quantity.

IV. THE GENERAL CONCEPT OF TARGETED DRUG DELIVERY SYSTEM

Minor Access- Drug carrier-circulation – it is divided into 2 parts 1.target tissue 2. Non-

Targeting Tissue – Major Pathway Major Access – target drug/carrier- circulation it is divided into 2 parts

1. Target tissue

2. Non-Target Tissue- Minor Pathway.

V. CLASSIFICATION OF VARIOUS TYPE OF TARGETING STRATEGIES

DRUG TARGETING- is basically divided into 2 parts Passive & active

1) Passive- •EPR effect •localized delivery
2) Active- • Ligand receptors • Antigen- anybody • Aptamer

VI. DRUG TARGETING ALZHEIMER'S

Alzheimer's disease accounts for sixty to eighty % of dementia cases. Alzheimer's is the commonest type of dementia, a general term for amnesia and other intellectual abilities serious enough to interfere with everyday life.

Stages of Alzheimer's disease

Alzheimer's has no current cure, however, treatments for symptoms are available and research continues. Although current Alzheimer's disease treatments cannot stop Alzheimer's from progressing, they can temporarily slow the worsening of dementia symptoms and improve quality of life for those with Alzheimer's disease and their caregivers.

Factors

Alzheimer's disease (AD) is a progressive neurodegenerative disease for which no cure exists. There is a considerable need for new therapies that provide improved symptomatic benefit and disease-slowing capabilities. In recent decades there has been substantial progress in understanding the molecular and cellular changes associated with AD pathology.

Over the last thirty years, researchers have made remarkable progress in understanding healthy brain function and what goes wrong in Alzheimer's disease. The following are examples of promising targets for next-generation drug therapies are:

1. Inflammation, 2. Tau-protein, 3. Beta-amyloid

1) Inflammation

Inflammation is the key to Alzheimer's brain abnormality. Scientists have learned a good deal concerning molecules involved within the body's overall inflammatory response and are working to higher understand specific aspects of inflammation most active in the brain. These insights could purpose to novel anti-inflammatory drug treatments for Alzheimer's disease.

2) Tau-protein

Tau protein is the chief element of tangles, the other hallmark brain abnormality. Researchers are investigation methods to stay tau molecules from collapsing and twisting into tangles, a process that destroys a vital cell transport system.

3) Beta- Amyloid

Beta-Amyloid is the chief element of plaques, one hallmark Alzheimer's disease brain abnormality. Scientists now have an understanding of how this protein fragment is clipped from its parent compound amyloid precursor protein.

VII. NANOTECHNOLOGY RELATION

Nanotechnology is the study of extremely small structures as it deals with materials in the size of 0.1 to 100 nm. Hence, in Greek "nano" means "dwarf". The application of nanotechnology in medicines and pharmaceuticals and its advancement in it has revolutionized the twentieth century Nanomedicine will result in products that are better, faster and also cheaper. Nanotechnology involves work by reducing the size of large structures to smallest structure (i.e. from top down), e.g. photonics applications in Nano electronics and Nano engineering, top-down or to the bottom up, which involves changing individual atoms and molecules into nanostructures and more closely resembles chemistry biology.
Nanotechnology works on the matter at dimensions in the nanometer scale length (1-100 nm) by a special scale that is being designed to calculate the activity of the nanoparticles (nanoscale) and hence can be used broadly in various fields.

Applications of Nanotechnology:

- Space exploration.
- Energy and Environment
- Health and Medicine
- Early diagnosis and screening

Uses:

1. Nanoparticles may also be used for the simultaneous tagging of multiple biomolecules, both inside as well as outside the cells to monitor disease progression.

2. Nanoparticles can be inserted into living cells as magnetic resonance contrast agents.

Use of Nano Scale and Nanostructures in Diagnosis and Screening

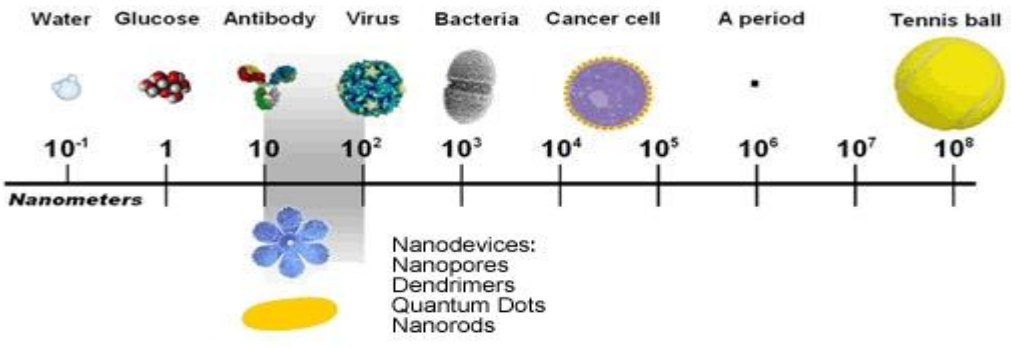


Figure 2: Nano scale and Nanostructure.

The nano scale is the place where the properties of most common things are determined just above the scale of an atom. Nano scale objects have at least one dimension (height, length, depth) that measures between 1 and 999 nanometers (1-999 nm).

VIII. ULTRA FAST DNA SEQUENCING USING NANOPORES

1. The flow of DNA through Nanopores can be used to discriminate low copy numbers of DNA, permitting very rapid genome sequencing.

2. This technology has been even used in electric fields to push RNA and DNA polymers through the central nanopore of a α-hemolysin protein channel mounted in a lipid bilayer.
3. Finally, this technique was also used to sequence a complete codon in an individual DNA strand tethered to a nanopore.
In principle, nanopore detection and characterization of single molecules represent a new methodology for directly reading data encoded in linear polymers.
With single-nucleotide resolution,

Advantages:

1. Low-cost

2. Easy and accurate detection and

3. Future Nano devices may even combine voltage gating with pore size, shape and charge constraints to achieve precise control of ion transport with significant molecular specificity.

Use of Nanotechnology in Health and Medicine

Even today various disease like diabetes, cancer, Parkinson's disease, Alzheimer's disease, cardiovascular diseases, and multiple sclerosis as well as different kinds of serious inflammatory or infectious diseases (e.g. HIV) represent a high variety of serious and complicated diseases that are posing a serious drawback for the mankind. Nano-medicine is an application of nanotechnology that works in the field of health and medication. Nano-medicine makes use of nanomaterials and Nano electronic biosensors. In the future, nanomedicine will benefit molecular nanotechnology. The medical area of nanoscience application has several projected advantages and is potentially valuable for all human races.

IX. DETECTION OF PHLEBOVIRUS BY USING QUALITATIVE REAL TIME (RT) - PCR AND APPLICATION OF SILVER NANOPARTICLES TO CONTROL IT.

The phlebovirus (family- Bunyaviridae) is an enveloped negative-strand RNA virus with a tripartite genome. A method quantifying the small RNA segment by real-time detection reverse transcriptase (RT-PCR) using TaqMan technology and targeting the nonstructural protein coding region was developed and used successfully in-vitro from plasmid sample consisting of RVFV infected Vero cell.

RT-PCR TEST

As this was initially evaluated in animals and then in human samples

The potential antiviral activity of silver nanoparticles formulated as17 Argovit against RVFV was tested on Vero cell culture and type I IF (interferon) receptor-deficient mice by 2 methods was carried out

1. In–vitro: different dilutions of Argovit were administered to an animal infected with a lethal dose of virus or to previously infected cells.

2. In-vivo: Viruses were pre-incubated with Argovit in different dilutions before inoculated in cell/mice.

MATERIAL AND METHODOLOGY

Cell, virus and mouse sera

In vero cells

Cells were grown in 5% co2 at 37o in 199 culture medium (M199) which was supplemented with 10% inactivated fetal calf serum. RVFV strains like MP12, ZH548, ZH501, 74HB59, clone 13 and also the closely related various other phleboviruses like Toscana, Icoaraci, and Belterra were grown in vero culture.

In vivo culture

Mice were inoculated intraperitoneally with 104PFU of RVFV strain ZH548 and blood was collected at different times post inoculation by veinal puncture at the retro-orbital sinus.

Real-time PCR

The amplified reaction mixture contained 2 µl of cDNA in a final volume of 20 µl, and the reaction was carried out with the Light Cycler fast-start DNA Master hybridization probes kit (Roche Diagnostics, Meylan, France),[12] MgCl2 at a 3.5 mM final

concentration, the primers NS3m and S432 at 0.5 μM final concentrations, and the fluorogenic probe CRSSAr at a 0.5 μM final concentration.18 PCR was carried out in the, Light Cycler (Roche) for 45 cycles at 95°C for 15 s and 60°C for 1 min.

X. ASSAY OF ANTIVIRAL ACTIVITIES

Glycyrrhizin, ribavirin, and 6-azauridine were purchased from Sigma-Aldrich (St. Quentin-Alpha 2b interferon

Treated cells

Confluent layers of Vero cells in 24-well tissue culture plates were infected with 0.1 ml of diluted viral suspension (0.01 TCID50 per cell), and 2 ml of maintenance medium containing the test compound at an appropriate concentration was added (4 wells per concentration).

Diagnosis

RT-PCR is the fastest and the easiest method of detecting RVFV in both animals and human but other methods that can even be employed for this are: Differential diagnoses includes brucellosis, Bluetongue, Wesselsbron disease, enterotoxaemia, Bovine ephemeral fever, vibriosis, trichomonosis, Nairobi sheep disease, heart water, ovine enzootic abortion, toxic plant ingestion, etc.

Use of Silver Nanoparticles for the Control of Rvfv

Silver has been known from a very long for its potent anti microbial activity and also various different formulations of silver nanoparticles the use of silver nano particles for the treatment is the most appropriate one as it contains many advantages like Non emergence of resistance variance, contains anti-inflammatory effect, antimodulatory effect, Safer use, Low price. Argovit is a formulation of silver nanoparticles that is being used commercially which has shown broad spectrum of antimicrobial activity.

Methods

1. Silver nanoparticle preparation.
2. Virus cells and normal cell preparation.
3. Cell visibility.
4. In-vitro infection experiment.
5. RVFV infection of mice.
6. Treating some mices with argovit.
7. Testing the treated and untreated cells.

XI. RESULT

The assay sensitivity range was 75 -100% and specificity was 90-100% depending on the comparison. It had overall sensitivity of 96%, positive prediction value 98.5% and specificity upto 96%. It reveals the useful application of silver nanoparticle in the control of important zoonotic pathogen.

XII. CONCLUSION

The Nanotechnology which is Advanced and Scientific Branch for Pharmaceutical research the future of this discipline is very well in terms of research, productivity, etc. The Nanoparticles also play great role in treatment of phlebovirus, Alzheimer' etc. Novel Drug delivery & drug targeting is new techniques which is used in pharmaceutical science. Like targeting drug delivery, vaccine delivery, Gene therapy, commercial development of novel carries (liposome's) Novel Drug Delivery System are: Optimum dose at the right time and right location, Efficient use of expensive drugs, their excipients and by reduction in the production cost, Beneficial to patients, better therapy, improved comfort and standard of living.

XIII. REFERENCES

1. Umama Yezdani., Nilesh Kushwah , Arvind Verma, Fazal Khan , Mohd. Gayoor Khan et al. Application of Nanotechnology in Diagnosis and treatment of various disease and its future advance in medicine. World journal of Pharmacy and Pharmaceutical science., 2018;Vol.7 Issue (11) : 1611-1633. DOI: 10.20959/wjpps201818-12703

2. Nilesh Kushwaha, Fazal Khan, Vipul Patel, Mohd. Gayoor Khan et al. Microencapsulation. International Journal of research methodology Ijrm.Human., 2017 Vol. 1 (2): 35-42.

3. DR. H. S CHANDEL., SHARAD P. PANDAY, ARVIND DANGI, ASISH CHAURASIA. MOHD. GAYOOR KHAN et al. Development of Targeted Drug delivery. International Journal of research methodology Ijrm.Human., 2017 Vol. 1 (2): 30-34.

4. Mohammad Gayoor khan et al. The Novel drug delivery system. World Journal of Pharmacy and Pharmaceutical sciences, ISSN 2278 – 4357, 2017 Vol. 6 Issue (7): 477- 487.

5. Unama Yezdani., Mohd.Gayoor et al. THE DRUG TARGETING IN ALZHEIMER'S OR APPLICATIONS & ITS HAZARDS. World Journal of Pharmacy and Pharmaceutical Sciences, ISSN 2278 – 4357, 2018 Vol. 7, Issue (11): 1532-1549.

6. Umama Yezdani,Rohit Verma, Raqshan Jabeen and Pradeep Sintha, Gayoor Khan Khan et al. DETECTION OF PHLEBOVIRUS BY USING QUALITATIVE REAL TIME (RT) - PCR AND APPLICATION OF SILVER NANOPARTICLES TO CONTROL IT. World journal of Pharmacy and Pharmaceutical science., Vol. 7, Issue 10, 2018: 936-952.

7. Zhang W, Wang Y, Lee BT, Liu C, Wei G, A novel nanoscale-dispersed eye ointment for the treatment of dry eye disease. Nanotechnology, 2014; 25: 125101.

8. Nanotechnology and its Applications in Medicine Anna Pratima Nikalje. Department of Pharmaceutical chemistry, Y.B. Chavan College of Pharmacy, Dr. Rafiq Zakaria Campus, Rauza Bagh, Aurangabad- 431001, Maharashtra, India.

9. Nanotechnology in Medicine: The Medicine of Tomorrow and Nanomedicine Logothetidis S Aristotle University of Thessaloniki, Physics Department Lab for Thin Films - Nanosystems & Nanometrology, GR-54124 Thessaloniki, Greece.

10.Gobin AM, O'Neal DP, Watkins DM, Halas NJ, Drezek RA, near infrared laser-tissue welding using Nano shells as an exogenous absorber. Lasers Surg Med, 2005; 37: 123-129.

11. Zhang W, Wang Y, Lee BT, Liu C, Wei G. A novel nanoscale-dispersed eye ointment for the treatment of dry eye disease. Nanotechnology, 2014; 25: 125101.

12. Nishizawa M, Menon VP, MARTIN CR: Metal Nano tubule membranes with electrochemically switchable ion-transport selectivity. Science, 1995; 268: 700-702

13. Drug delivery systems Third edition Vasant V. Ranade, John B. Cannon, Pg no. 56-63.

14. Chemistry & Molecular Aspects of Drug Design & Action E.A Rekko, P.N Kouroankis; Page no. 110-114.

15. The Theory and Practice of Industrial Pharmacy Lachman /Lieberman's (CBS distributors); Page no. 430-437.

16. Targeted delivery of small & macromolecular drugs. Editor- Ajit S. Narang; Page no. 78-83.

17.Fourth Edition Editors Roop k that SP Vyas Farhan J Ahmed Gaurav K Jain ; Page no. 43-51.

18. Munyua P, Murithi RM, Wainwright S, Githinji J, Hightower A, Mutonga D, Macharia J, Ithondeka PM, Musaa J, Breiman RF, Bloland P, Njenga MK. Rift Valley fever outbreak in livestock in Kenya, 2006-2007. Am J Trop Med Hyg, 2010; 83(Suppl 2): 58–64. 28 ref. [PMC free article] [PubMed]