Drug Delivery Methods, Applications and New A Horizon of Conjugated Drugs

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Abstract

Diseases and drugs are an inevitable part of our lives. People used several techniques to make the drug efficient. Biological molecules are chiral molecules; such as proteins, sugar, fat, hormones etc. Most of the market available drugs are chiral drugs. Nature's molecules are chiral too. It can be isomer or in enantiomeric forms. Pure enantiomers are hard to produce. Mist, skin patch, intravenous techniques are already used. Now molecular techniques are more efficient to deliver drugs in proper places. Every cellular mechanism is energy driven. Phosphorylation helps with energetic reactions. During epigenetic change, methylation and acetylation take place. New Cancer or Alzheimer's drug target this acetylation or methylation sites. Peptides can be attached with drugs for better penetration in cells or for stability. Amino acid Arginine helps with cell penetration. Dendrimers (branched polymer), chitin, dextrose has used for drug delivery purposes. PEGylation helps the drug to roam in the blood for long time. It is biodegradable. siRNA or miRNA is now widely used to silence genes. Hydrophilic double stranded siRNA is negatively charged, and it can be packaged with positively charged nano-particles. Quantum dot technology is used very often in nanotechnology. Now it's application has started for drug delivery purposes. Some plant viruses are ineffective in human and it is a good cargo for drugs. DNA and in situ hybridization is an effective technique for target-specific drugs. Nano particle like gold, mesoporous silica nanoparticles which carry surface positive charge, attaches negatively charged DNA very tightly and helps to deliver deep inside the cell. Novel metals are good molecular cargo. Chitosan is a polycationic polymer and dissolves easily in an acidic environment. It has capability to release drug slowly, and that makes it a good medium for drug delivery by oral pills. miRNA are microRNAs, people have started using those RNAs to silence disease-specific genes. Quantum dots are gaining popularity due to its less toxicity, surfactant-free attachment and target specific delivery. New emerging method started using fullerene (C60). The carbon atoms of fullerene, do not attach with surrounding carbon atoms; these characteristics make it a good vehicle for drugs. Carbon-hydrogen (C-H) bonds breaks down much faster than carbon-carbon (C-C) bonds. This property holds the fullerene structure intact. Cancer, infectious bacteria, and artificial Ebola have tested with fullerenes. Polyethyleneimine can be tagged with nucleic acid or nano particle.

This poster carry an overview of various research projects that was addressed by the researchers.

Introduction

Internalization of drug is a challenge in in-vitro research. A majority of the rare peptides was hydrophobic due to their high percentage of less common hydrophobic amino acids. Arginine tails improve the solubility of these peptide, and increase cell penetration. Peptides can be attached with drugs for better penetration into cells or for stability. Amino acid Arginine helps with cell penetration. Natural compounds give less side effect. Dendrimers (branched polymer), chitin, dextrose has used for drug delivery purposes. PEGylation helps the drug to stay stable in the blood stream for long time; if a small molecule get considered as a drug. A long inert peptide tail or vitamin tail keeps it stable in the blood and helps to find the surface receptor. It is biodegradable. Although net surface charge should be under consideration when a new drug comes in mind.

Methods

- Particle bombardment method was used to deliver drug candidate or a gene.
- Point mutation was used to check the functionality of that gene with positive and negative control.
- Cell Culture took place with nano particles.
- Peptide conjugated drug delivery tested through regular cell culture. Data collected at 24, 48, 36 and 76 hours.
- DNA and nanoparticle conjugated drug delivery in cell was dose dependent. DNA conjugated drug delivery also takes place with heat shock micro- injection.
- Slow drug delivery through Fullerene.
- Glycan or chitosan attached drug delivery through cell culture.
- DNA purification takes place by column chromatography.
- Candidate drug get purified by HPLC, HPLC- Tandem Mass Spectroscopy.

Results:

- Peptide attached drug has good percentage of uptake in the human body.
- Gold nano particles wrapped with DNA or drug is a good delivery system for particle delivery.
- Fluorescent microscopy images shows internalization of drugs.
- Poly Arginine tail helps to attach peptide with cells and helps to internalize drugs.
- Carbohydrate attached drugs get absorbed in the system. Human body absorbs natural molecule fast.
- DNA purification took place by column chromatography.

Carbon nanotube or Fullerenes C60 - C120 for slow steady drug delivery

Figure 1. A carton of drug delivery system

Future Research Approach- Hypothetical Vitamin and Antibody Conjugated Drugs

Figure 3. Hypothetical design of a conjugated drug

Bacteriophage for drug delivery

Figure 2. Drug delivery mechanism

Figure 4. Confocal Microscopy image of MDA-MB-231 cells, orthogonal/three dimensional view of cells. Poly Arginine containing peptide drug attached on cell membrane and inside the cells.

Effect of Nullomer Peptide "9R" on MDA-MB-231 Human Breast Cancer Cell Line 4/26/10

MTT Assay, started with 3000 cells, 48 hours incubation

Figure 5. Dose curve of a candidate peptide drug

The power house of the cell - mitochondria

Figure 6. A important sub-organelle target in the cell to cure various diseases, most of the biosynthetic pathways are energy driven and mitochondria produces ATP molecules.

Discussion

Neutral drug delivery vehicles are the good sources for future study. 9 carbon carbohydrates attach easily with cell membranes. Arginine and other amino acid helps to penetrate cells when they are attached with drugs. Phenol containing natural compounds showed anti microbial and antitumor activity.

Conjugated drugs are in fore front now. Researchers are using various approach to deliver drugs effectively. Such as- Quantum dot conjugated magnetic nano particle, carbohydrate conjugated nano particle. Redox activated metal based prodrugs (Fe, Co, Cu) has future to treat Alzheimer's disease. It can be two step dose dependent method to control the redox level in the cells. Vitamin E conjugated cancer drug can treat and nourish the body at the same time. Although bigger molecules some times unstable in the blood. Micro emulsion can be used as a drug delivery techniques for GI track. Glycan and lipid conjugated drugs helps to attach with bacteria and viruses where cell membrane or cell coat protein is hard cleave. Bioactive glasses are also under consideration to use as a drug delivery method. A piece of DNA or gene gets easily conjugated with tungsten or gold nano particle to make hybrid plants, animals or to create new drugs. The drug delivery process takes place in sterile vacuum chamber, and it is sub-organelle specific. Glucose thread/natural polymer is under consideration to use for surgical procedures. Flavonoids and Shikimic acid pathway products are also a good source of natural medicine, which already got explored a lot, and gives some fundamental thoughts to create something new that will be biocompatible.

Hypothetical long hydro-carbon chain attached with gold nanoparticles that can be conjugated with drugs for in –vitro study.

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9. Zhang Y, Walker J B, Minic Z, Liu F, Goshgarian H, Mao G, Transporter protein and drug conjugated gold nano particles capable of bypassing blood br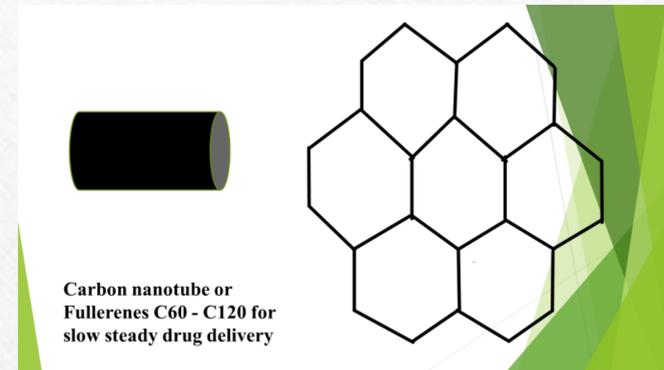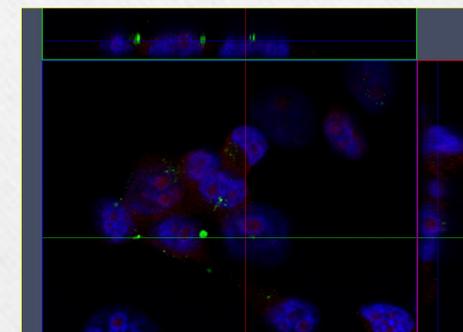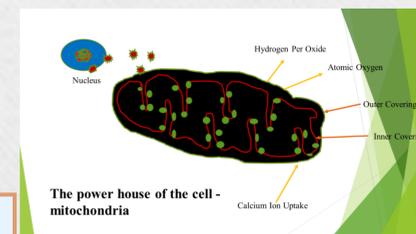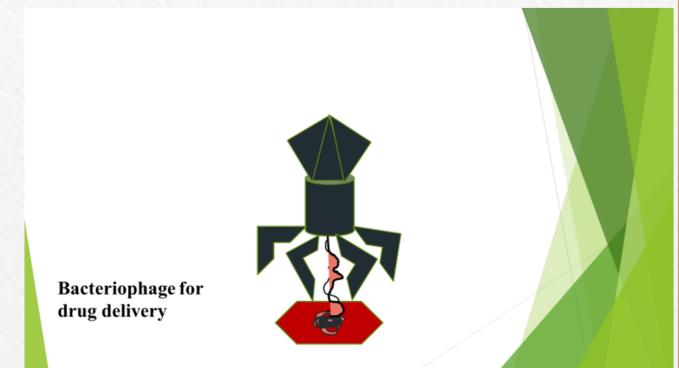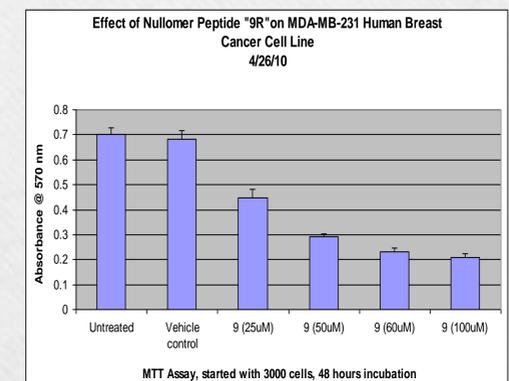ain barrier, Scientific Reports, 2016; 6: 25794.