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Review Article

Polyaminoacid: revolutionizing drug delivery through advanced nanocarrier systems

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ABSTRACT

Polyaminoacid are smart nanocarriers and striking aspirant material for drug delivery. Amino-acids can be effortlessly ionized positively or negatively. Commonly used polyaminoacid chains are polylysine, polyarginine, and polyglutamic acid. Polyaminoacid polymers can also be synthesized in the laboratory and are called synthetic polyaminoacid polymers. Polyaminoacid are sensitive to acidic pH and are degraded by acid and enzymes in the lysosome, the amino acids are released and the conjugated drug portion is also released. Block polymers are versatile and multifunctional in drug delivery. PEG-copolymers can be utilized for drug targeting, organ imaging and drug delivery purpose. Only water soluble polyaminoacid can be utilized for drug delivery and other biomedical applications. The advantage of using Polyaminoacid is that they are biocompatible, biodegradable, pH sensitive, provide nutrients to the tissue upon cleavage, are conjugated with drug, proteins, and antibodies, and can be amalgamated with other polymers such as chitosan, nanoparticle synthesis with other composite material is possible. The active drug loading is highly efficient, intracellular drug delivery possible, it can cross many physiological and anatomical barriers such as the blood brain barrier, self – assembled property, delivery of prodrugs etc. Biomedical applications include cancer cell targeting, gene transfer, gene delivery, siRNA transfer, miRNA, gene silencing, intraocular delivery, intracellular delivery, brain delivery, radiological imaging, bone tuberculosis, cosmetic use, colonic drug delivery, delivery of prodrug. Therefore, polyaminoacid are versatile in drug delivery systems.

Keywords: Polyaminoacid, Biomedical application, Nanoparticle, Drug delivery, Polymers

INTRODUCTION

Polyaminoacid are smart nanocarriers and striking aspirant material for drug delivery. Amino acids can be effortlessly ionized positively or negatively.[1,2]

This quality imparts them unique characteristics which makes them suitable for the impetuses sensitive materials.[1,2]

Commonly used polyaminoacid chains are polylysine, polyargnine, polyglutamic acid.[3,4]

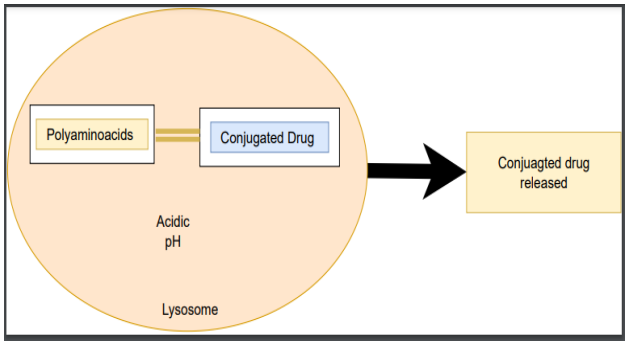

Figure 1: Graphical abstract.

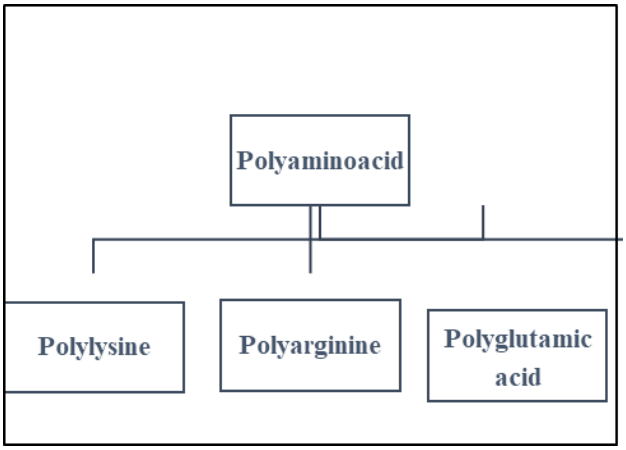

Figure 2: Commonly used polyaminoacid.

SYNTHESIS OF SYNTHETIC POLYAMINOACID POLYMERS

Polyaminoacid polymers can be also synthesized in laboratory and are called synthetic polyaminoacid polymers.[5]

METHODS OF SYNTHESIS

Polyaminoacid structural chunks are manufactured by careful shielding of proportioned oligoethylenimine ancestors followed by introduction of a carboxylic acid.[6] Also synthesized by thermal polycondensation reaction, and keeping the thermal temperature as low as 100^0 C.[7,8] Polymerization of N-carboxyanyhydrides can be used. For production of polyaminoacid, "chemical interaction of poly-dichlorophosphazene-IV with amino acid esters."[9] Technique of utilizing microwaves for the synthesis of polyamino acids have been demonstrated.[10] Primary or secondary amines are made to react with polysuccinimide can be used for synthesis.[11]

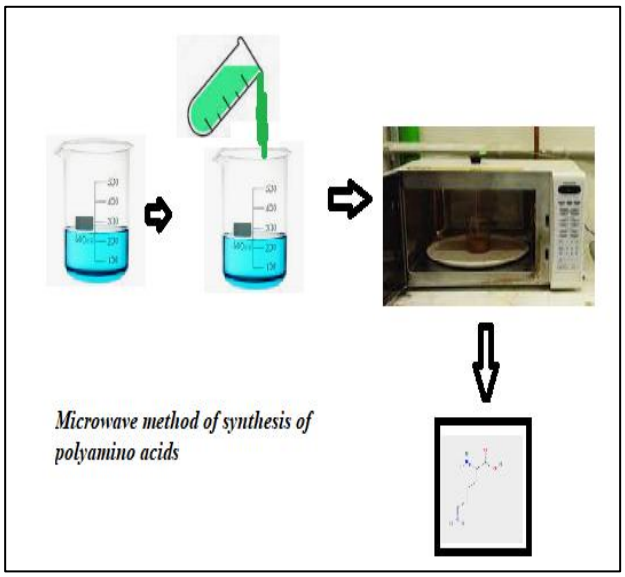

Figure 3: Method of synthesis.

Goal in synthesizing of polyaminoacid-the main goal is to protect the function of amino acids.[12]

Polymeric nanoparticle synthesis done by spray dryin.[13]

MECHANISM OF INTRACELLULAR DELIVERY

Polyaminoacid are sensitive to acidic pH and are degraded by acid and enzymes in the lysosome.[14,15] The amino acids are released and the conjugated drug portion is also released.[14,15] The most important point is that such a conjugated drug with polyaminoacid indwell in mature intracellular lysosomes.[14,15]

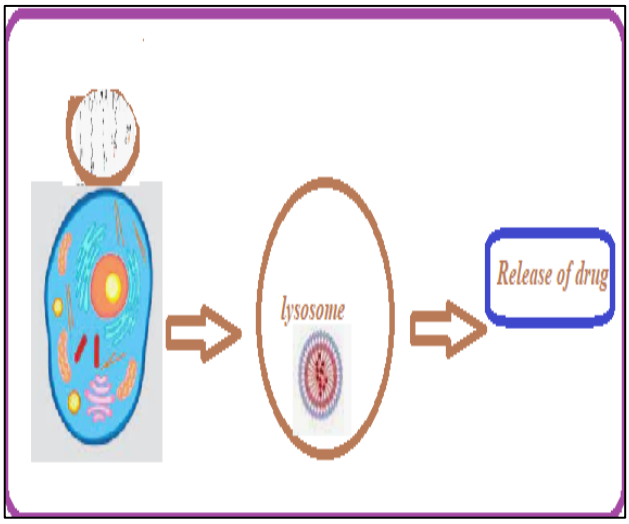

Figure 4: Mechanism of intracellular delivery.

Disintegration of PEG-poyaminoacids

Kumar et al such conjugated PEG-polyaminoacid polymers can be completely disintegrated in reductive environment.[16]

Block co-polymers

PEG-polyaminoacid: block copolymers have been synthesized with the unique function and feature of detaching PEG.[17] Block polymers are versatile and multifunctional in drug delivery.[18] PEG-copolymers can be utilized fordrug targeting, organimaging and drug delivery purpose.[19,20]

Essential criteria for the biomedical application of polyaminoacid: Only water soluble Polyaminoacid can be used for drug delivery and other bio-medical application.[21]

ADVANTAGE

Advantages are are-biocompatible, biodegradable, pH sensitive, provide nutrition to the tissue on cleavage, conjugated with drug, protein, antibody, can be amalgamated with other polymers such as chitosan, nanoparticle synthesis possible with other composite

material possible, drug loading is highly efficient, wide range of biomedical and pharmaceutical application, intracellular drug delivery possible. The charge on biomaterial can be helpful in synthesis, conjugation and drug delivery application. Can cross many physiological and anatomical barrier such as blood brain barrier and p-glycoprotein, self-assembled property, delivery of prodrugs and easy metabolism and easy clearance from body.[1-63]

DISADVANTAGE

Since this type of polymers, block polymers can cross protective barriers and bypass P-gp, their limitation and challenge is that the use of such polymer-based delivery during gestation may lead to toxicity and foetal damage.[1-63] Since the polymer can cross the placental barrier, further studies are desirable to overcome thislimitation.[1-63]

BIOMEDICAL AND PHARMACEUTICAL APPLICATIONS

Polyaminoacid polymers are promoted as tool for drug delivery.[22]

Oncology applications

Polyamino acids are comprehensively studied for drug delivery of anti-cancer drugs.[23] Kuang et al for-cancer treatment polyaminoacid composite ZnO and mesoporous silica nanoparticle with the charge-reversal propertie scan be exploited for cancer therapy. Nano particles of Polyaminoacid are having potential in cancer treatment.[24] Superparamagnetic iron nanoparticles i.e. SPION surrounded by polyaminoacid nanogels can be used for treatment of nano-particles.[25] PEGlyated-polylysine co-polymer has excellent features for drug delivery especially for anti-cancer drugs.[26] Poly (ethylene glycol)-poly (lysine) block copolymer-ubenimex conjugate targets amino peptidase and exerts an antitumor effect in hepatocellular carcinoma stem cells.[27] Polylysine dendrigraft loaded with doxorubicin can be used for excellent delivery in human being.[28]

Magnetic coated non-vector with polyarginine can be utilized for siRNA especially in cancer cell lines.[29] Polyamino acid based nanocarriers are responsive to reactive oxygen species and can be utilized to target cancer.[30] Poly-L-glutamic acid can be used for cancer therapy.[31] Various cancer of the lung, colon, uterus, ovaries, testis ,stomach can be treated with polyaminoacid polymers.[32] Polyaminoacid and chitosan with interferon gamma are used for targeting colorectal cancer.[33]

Drug loading

PEG-polyaminoacid: block copolymers have been amalgamated with unique function and feature of detaching PEG.[34]

Bone tuberculosis: Anti-tuberculosis medications can be amalgamated in calcium sulphate and polyaminoacid composite constituents in bone tuberculosis lesion demonstrated constant upshot of all three drugs in combination.[35]

Gastrointestinal drug delivery

Polyaminoacid polymers can be effectively used for drug delivery in ulcerative colitis, inflammatory disease of colon since they have affinity for mucus membrane and display bio-adhesive properties.[36]

Micro rocket to carry drug can be made with Polyaminoacid to deliver drug to the stomach.[37] Poly-amino acid complexed with dextran can be used for colon delivery useful for the colonic disorders.[38]

Intracellular drug delivery

Nanoparticles with poly-γ-glutamic acid for enhanced intracellular medication.[39] Such type of approach can be used for the delivery of genes, siRNA, silencing gene and delivery drugs to the nucleus.[39,40] Polyarginine also improves intracellular drug delivery.[41,42]

Intraocular and retinal drug delivery

Synthetic polymers and polyaminoacid polymers can be used for retinal drug delivery.[43]

Cosmetic use

Asan anti-wrinkle and anti-aging agent using polyaspartic acid polymer.[44]

Increase bioavailability of drugs

ε-poly-L-lysine and β-cyclodextrin sulphate are useful in loading proteins, and peptides and can be protected from breakdown in stomach and increase absorption from the intestine thus increasing bioavailability.[45]

Gene transfer

Polylysine has great potential as a non-vector for gene transfer and gene delivery.[46-48]

miRNAs delivery

Polyaminoacid can be applied for therapeutic delivery of miRNAs.[49]

Radiological application

Polylysine can be used for imaging and tumour targeting.[50] Polyarginine can cross the blood brain barrier and is utilized for brain imaging application.[51,52]

Endocrine and metabolic disorder

Diabetes mellitus: Polyaminoacid complexed with chitosan. Such fabricated nanoparticles can be exploited for the delivery of insulin. Fabrication of chitosan with poly-g-glutamic amino acid polymer assembled nanoparticles can be for oral insulin delivery.[53,54]

Controlled release

Polyamino acid polymers can be used for controlled drug release technology.[55]

Food industry

Polyamino acids are used as antimicrobial additive in the food industry.[56]

Antimicrobial effect

PEG-Polyamino acids have an antimicrobialeffects.[57] Polyaminoacid and zinc oxide nanoparticle have an antibacterial effect.[58]

Sustained release device

Polymers are utilized for sustained release manoeuvre.[59]

Nanoparticle synthesis

Polyaminoacid can be used for the nanoparticle synthesis.[60]

Tissue engineering

Poly-l-lysine and PEG biomaterial are used for tissue engineering.[61]

Protein delivery

Protein can be delivered to specific cells, dendritic cells using polyaminoacid nanoparticle.[62]

Theranostic agents

Polyaminoacid polymers are used as the theranosticagents.[63]

Target specific delivery

Target specific delivery is possible with Polyaminoacid that will deliver intracellular drug. Such approach can be useful in the treatment of diabetic nephropathy and various molecular target such as NADPH Oxidase, TGF –beta, HDAC enzymes etc can be easily targeted.[50-63]

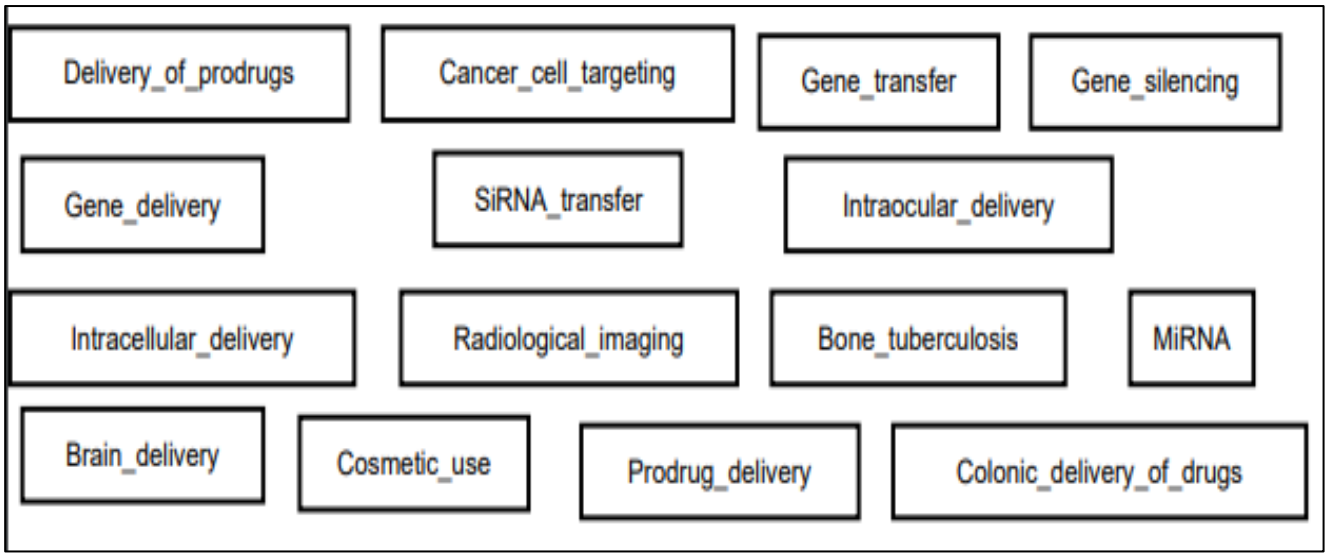

Figure 5: Overview of biomedical application.

CONCLUSION

Polyaminoacid are biocompatible, biodegradable, pH sensitive, provide nutrients to the tissue upon cleavage, are conjugated with drugs, proteins and antibodies, can be amalgamated with other polymers such as chitosan, nanoparticle synthesis with other composite materials is possible, the drug loading is highly efficient, wide range of biomedical and pharmaceutical applications, intracellular drug delivery is possible, charge on biomaterial can be helpful in synthesis, conjugation and drug delivery application. Can cross many physiological and anatomical barrier such as blood brain barrier, self-assembled property, delivery of prodrugs etc. Biomedical applications include cancer cell targeting, gene transfer, gene delivery, siRNA transfer, miRNA, gene silencing, intraocular delivery, intracellular delivery, brain delivery, radiological imaging, bone tuberculosis, cosmetic use, colonic drug delivery, delivery of prodrug. Thus, polyaminoacid find versatile applications in the drug delivery system. Since such type of polymers, block

polymers can cross protective barriers and bypass P-gp. The limitation and challenge is that the use of such polymer-based drug delivery during gestation may lead to toxicity and foetal damage as the polymer can cross the placental barrier. Further studies are desirable to overcome this limitation.

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