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Protein Drug Delivery System

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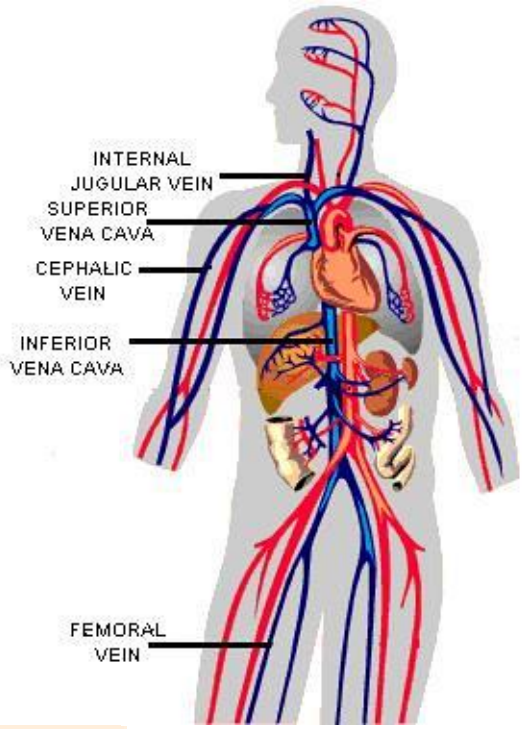
Abstract

Protein and Peptide drug delivery system are the Novel drug Delivery Revised on 22 Feb 2016,System. Proteins and peptides are the most abundant components of Accepted on 13 Mar 2016biological cells. They exist functioning such as enzymes, hormones, DOI: 10.20959/wjpps20164-6425structural element and immunoglobulin. The twenty different naturally occurring amino acids join with each other by peptide bonds and build *Correspondence for polymers referred to peptides and proteins. Although the distinction Authorbetween peptides and proteins are peptide contains less than 20 amino Sagar Kishor SavaleDepartment of acids, having a molecular weight less than 5000, while a protein Pharmaceutics, R. C. Patel possesses 50 or more amino acids and its molecular weight lies above Institute of Pharmaceutical this value. The most of pharmaceutical proteins and peptides are Education and Research, absorbed IM, IV and Subcutaneous route of Absorption, but the oral Shirapur 425405, Dist. Dhule route is more convenient for absorption of protein as compared to Maharashtra

INTRODUCTION

The Protein and Peptide is a Novel Drug Delivery System and it is a Novel approach of drug delivery system.[1] Protein and Peptides are the Most Abundant Material of Living system and Biological cell.[Hormones, Enzymes, Structural Element.[5] It is also important take part in Several Metabolic Process, Immunogenic Defense as well as its take part in several Biological activities.[6] Proteins are the one of the most abundant Organic molecule in Biological System, the term Protein first used has Berzelius.[7,] The term Protein is derived from a Greek word Proteios Means Holding the first Place.Proteins are the high molecular weight mixed of Alp polymer ha amino acids joined together the Peptide Linkages is called has Peptide Bonds.Peptides are the Condensation Product of Alpha Amino acids.



NEED OF PROTEIN AND PEPTIDE DRUG DELIVERY SYSTEM

The protein and peptides are very important in biological cells and Organic Molecules.2. In the Absence of proteins and peptides causes diseases like Diabetes mellitus. (Causeddue to the lack of protein called INSULIN3. Now a days R-DNA technology and hybridoma techniques also used in protein and peptide based pharmaceuticals.

ADVANTAGES OF PROTEIN AND PEPTIDE DRUG DELIVERY SYSTEM1.

Erythropoietin is mainly used for production of RBC.2. The protein Tissue plasminogen activator is used for Heart attack, Stroke.[Oxytocin is used in management of labor pain.4. Bradykinin increases the peripheral circulation.]5. Somatostatin decrease bleeding in gastric ulcer.

FUNCTIONS OF PROTEIN AND PEPTIDE DRUG DELIVERY SYSTEM1.

Transport and storage of small molecules and biological molecules.]2. Coordinated motion via muscle contraction.3. The Mechanical support from fibrous protein.[4. Generation and transmission of nerve impulses.5. Enzymatic catalysis in biochemical reactions.

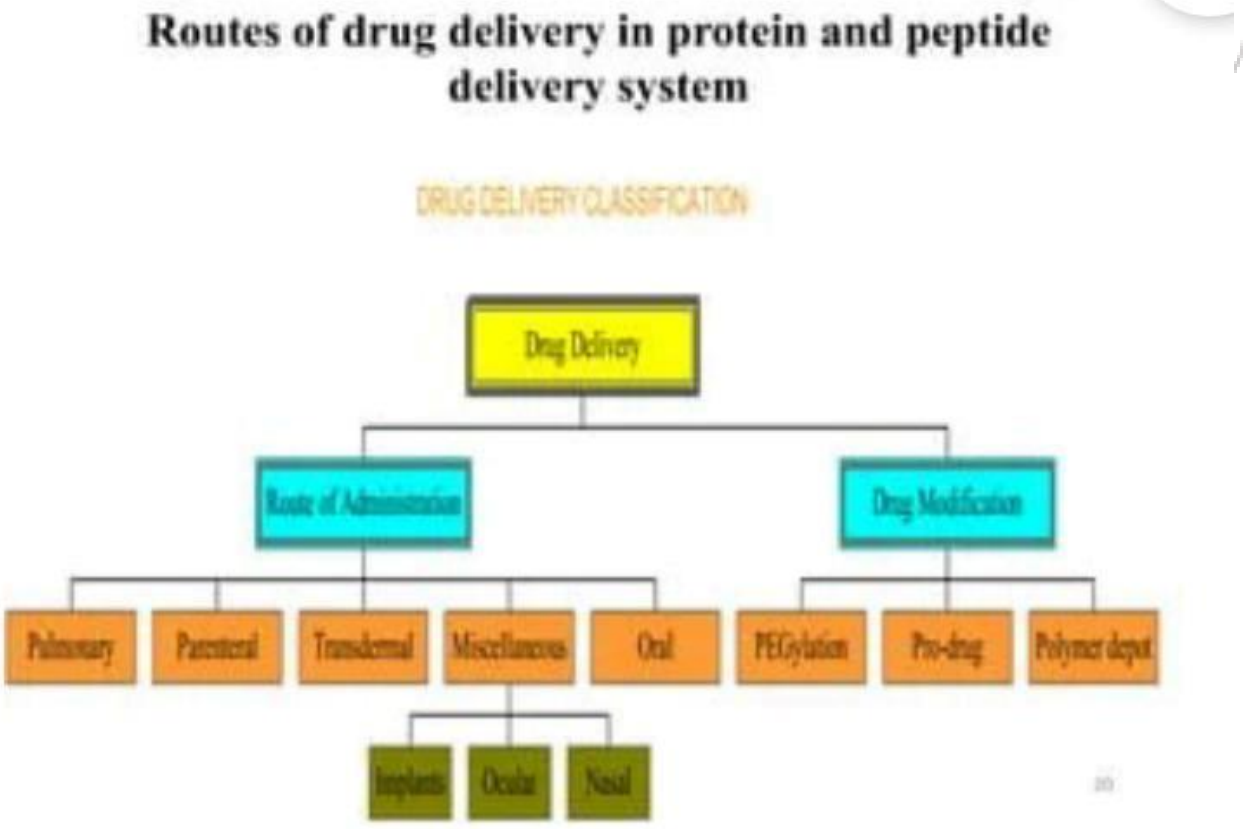
ROUTES OF ABSORPTION

The Proteins and Peptide drug delivery system in which Most of the Pharmaceutical Proteins and Peptides Formulations are the Formulated as a Solution, suspension, Emulsions and they are delivered in Invasive or Parenteral Route such as Intra muscular route (IM), Intravenous route (IV) and Subcutaneous route (SC) Injections. But, These all routes are arises its own Difficulties such as, Poor Patient Compliance, The pain and discomfort associated in this route (to inject injection in same site again and again it can arises Pain) and it is a Inconvenience to treat the Paediatric Patients. The oral route of administration in protein and peptide is suitable as compared to parenteral route, The Oral route having a One of the most convenient route of drug administration, in this type of route no pain and discomfort was arises and Maintained the Higher Patient Compliances or Acceptance. But, The Development oral Protein and Peptide Drug delivery arises several

Problems for their Oral Administration of Drugs. This Problem is arises There Unfavourable and Undesirable Physicochemical Properties are such as The Large molecular size of the drug molecules, drug undergoes susceptibility to Biological and Enzymatic degradations, The oral drug having a short Plasma Half Life as compared to other drugs, it can having high Immunogenicity, The tendency of Protein undergoes Aggregations, Adsorption and it can undergoes Denaturation's, The Major Problem Orally Administered Proteins and Peptides are having a Lesser Bioavailability or Less Bioavailability is having a less than 1%. The other route f administration of protein and peptide is arises success for the administration of Proteins and Peptide drugs, the routes are Oral, Buccal administration, Intranasal administration, Pulmonary administrations, Transdermal, Rectal and Ocular administration

PROPERTIES OF PROTEINS AND PEPTIDES

he Protein are the most abundant biological and organic molecule they are soluble in water and it can formed a Colloidal solution with water. Protein and Peptides are physicochemical and Metabolically Stable System. In case oral administration of Protein and Peptide Drug delivery system Several Properties can affect the rate of absorption of Protein and Peptide in oral drug delivery system, the properties are such as, Absorption Properties, In case of Absorption Properties Molecular weight and size of the particle, Conformational studies and Steriospecification of Three Dimensional Arrangements in Space, Immunogenicity of drug molecules. Are affected the rate of Absorption of Protein and Peptide in Oral drug delivery systems. Another one is Physicochemical Properties such as, solubility and Lipophilicity of drug is major Criteria of absorption of drug, The aggregations and Hydrogen bonding of drug in oral administrations, The Physicochemical Properties are



the major Criteria for the drug absorption in oral drug delivery systems, The drug absorption oral drug delivery system it an mainly arises two main Problems are the Metabolic degradation of Various forms of Protein and Peptides by interaction with the various Proteolytic Enzymes, and it is having Less Membrane Penetration Abilities. This all Criteriaassociated in Properties of Protein and Peptide drug delivery system is Applicable for determination of various Problem associated in oral drug delivery system and it is important to give idea on the

basis Properties to prevent the problems in drug administration in oral Protein and Peptide in Oral drug delivery Systems.

PHARMACEUTICAL APPROACHES

The Chemical Modification of Protein and Peptide Drug Delivery System of Drugs is Important to Improve the Enzymatic Stability as well as Membrane Permeations. It is Applicable for the reducing the Immunogenici

The Chemical Modification is Includes in Two Types of Modifications as Follows:

Amino acid Modification

Hydrophobization

1.Amino acid Modifications

2.Modification of amino acid is one of the important approach in which the Substitution of the D- amino acid and L- amino acid is important to alter the Physiological Properties of Protein and Peptide Drug Delivery System

Example: Desmopressin and Deaminovasopressin are the two important analogs of vasopressin, former involves deamination of first amino acid and replacement of last Larginine D-arginine to give Deaminovasopre

3.Hydrophobization:It is having an important approach for the Lipophilic Moieties.

Example:

NOBEX INSULIN by the Palmitoylatios.

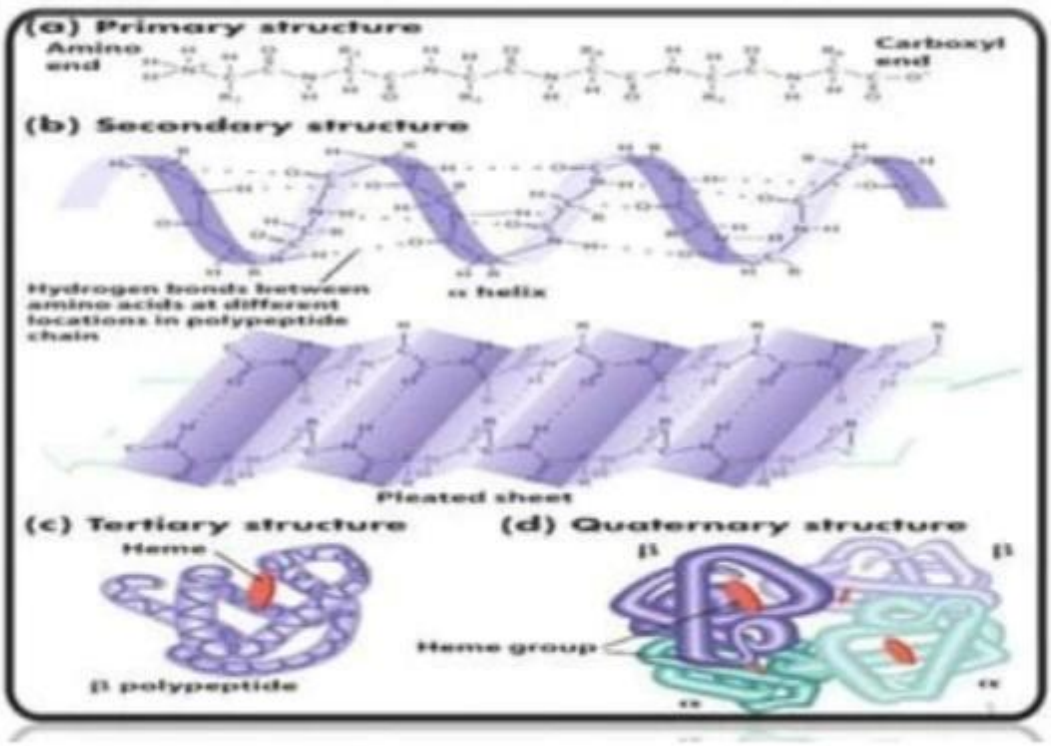
Description of Example:Conjugation of the Insulin Molecule to the 1, 3-dipalmitoylglycerol containing a free amino acid groups of glycine, Phenylalanine and Lysine molecule to from mono and insulin is important to facillated the transfer the insulin across the mucosal membrane of the large intestines. It is important to improve the Stability against the enzymatic degradations.

ENZYME INHIBITORS

The enzyme (protease) inhibitors are the enzymatic approach of the Protein and Peptide drug delivery systems. GIT and Liver is play important role in Metabolizing of the Protein and Peptides into smaller fragments of the two to ten amino acids with the help of the variety of Proteolytic Enzymes. This Protease inhibitors are CO-administered with Protein and Peptide to alter the Environment for the Enzyme stability to supress the Proteolytic activity. The enzyme proteases inhibiters are divided into four types they are Aspartic Proteases (Pepsin, Rennin), Cystinyl Proteases (Papain, Endopeptidase), Sternly Proteases (Thrombin, Trypsin), and Metallo Proteases (Carboxypeptidase).

PENETRATION ENHANCERS

Penetration enhancers are the one of the most important Component of Protein and Peptides formulation is responsible for the Disruption of the Mucosal Barriers and applicable to improve the Membrane Permeations of Large Macromolecular substances lie Proteins and Peptides. The Several classes of compounds are mainly



used has a permeation enhancers a

such as Surfactant (Polysorbate, SLS, Pluronic F-68), Chelating agent (EDTA), Fatty acids (Sodium Carprate), Mucoadhesive Polymeric systems (Thiomers, Cellulose derivatives), Phospholipids (PC). The basic Mechanism of Penetration enhancers are the, detergent and surfactant molecules are the increases the transcellular transport of the drug material is responsible to disrupting the structure of the lipid bilayer of lipid membrane are having more permeability. Another mechanism is the calcium chelates are the responsible for the Exert the action of complex formation of the calcium ions and they are passing through the tightjunctions and they are facillated the Paracellular transport of the hydrophilic drugs materials. Fatty acids are the important for the improving the paracellular absorption by phospholipasesC activations and upregulation of intracellular Calcium ions, is leading to the contraction of actine myosin filaments.

FORMULATION VEHICLES

The Protein and Peptide Drug Delivery system is important for the Oral Delivery of Protein and Peptides can be successfully achieved by using various carrier systems are like

1. Dry Emulsion
2. Microspheres
3. Liposomes
4. Nanoparticles

1.Dry Emulsion:

•It is important application in drug delivery system s to prevent the instabilities of the long term storage of multiple emulsions. The novel approach at which multiple emulsion is replaced by dry emulsions. Dry Emulsion is prepared by the Spray drying, Lyophollization and evaporation Techniques. In dry emulsion preparation application of the PH responsive polymers like HPMCP, is important for the emulsions are the enteric coated and site specific achieved.

2. Microspheres: The uniform distribution of drug in oral drug delivery in Protein peptides drug are known as Microspheres. The PH responsive microspheres are the mainly used in oral delivery for the protection of the stomach from proteolytic degradations and Protection upper portion of small intestine from proteolytic degradations.

3. Liposomes: LiposomesNanoparticles are the small microscopic vesicles in which aqueous volume is entirely enclosed by the membrane composed lipid molecules. Liposomes in drug delivery system, the encapsulation of the insulin with sugar chain portion of mucin and PEG

•completely suppressed the degradation of the insulin molecules in intestinal fluid. The uncoated from of liposomes are suppressed it on partially surface coating of the liposomes molecules in PEG or mucin gained resistances against dagestion by salts and increased the stability of GI tract.

5. Nanoparticles: Nanoparticles are Nano sized colloidal structure having size is 10-1000nm. The particles in manometric sized range of the particles are absorbed intact by the intestinal epithelium and they are the less prone towards the enzymatic degradations. The particle size surface charges are the influencing the uptake of nanoparticle system in GI tract

INCORPORATION INTO DRUG DELIVERY MATRIX

1.EMULSIFICATION

2. EXTRUSION AND SPRAY DRYING3. POLYMERIZATION

1. EMULSIFICATION

In this Process water soluble drugs is first dissolved in the aqueous (water solution) and it is soluble in Organic solvent. The two solutions are mixed with the appropriate Proportion to produce w/o emulsion. This prepared Primary emulsion is emulsified into aqueous solution containing emulsifier to produced w/o/w emulsion. Finally the organic solvent is mainly removed from emulsion by evaporation of solvent under reduced pressure by the filtration and increasing the Temperature.

2. EXTRUSION

The extrusion and Spraying is employed to from microspheres and the core material or matrix containing drug, incorporated as Solution and the Particulate is mainly ejected from the orifice of fine tubes, syringe or nozzles to from micro droplets. The size of droplet is mainly depends upon the Properties of Liquid (melt, solution and suspension) and Orifice diameter to jet velocity.

3. POLYMERIZATION

Polymeriasation in hydrogels having a polymeric drug delivery system preparation by the mixing of monomer with the drug an initiator and a cross linking agents. The Intravascular delivery of the protein via hydro system that is photo polymerized in situ on the inner surface of blood vessel. The □-radiation are producing deleterious effect on integrity of protein molecules one of the drawback of Protein and Peptide drug delivery systems.

•RECENT ADVANCES

PEGylation

PEGylation is a Recent Advancement of Protein and Peptide Drug Delivery systems, PEGylation is a process of attaching the strands of the polymer PEG to most typical peptides fragments that can help to meet the protein and challenges of improving the safety and efficiency of many therapeutic macromolecules such as Protein and Peptides. It is widely used for the modification of proteins and peptides, antibody fragments and oligonucleotides.PEG are the Non-toxic. And non –immunogenic, it is having a specified Hydrophilicity and it is having high Flexibility. PEGylation is important to increases the Bioavailability, it is applicable for the optimized Pharmacokinetics, it is important for Decreasing Immunogenicity, It is important to Decreases the Frequency of administration. The PEGylation is important Mechanism for increasing the molecular weight of the molecules, it can increases the drug solubility and it is applicable for the protection against Proteolytic degradations, it is having an important mechanism to reducing the dosing frequency andmaintain therapeutic activity.

•MATKETED PREPARATIONS AND APPLICATIONS OF PEGylationPEGylated interferon alpha -2a: In Hepatitis B Treatment.PEGylated interferon alpha-2b: In Hepatitis C Treatment.PEGylated liposome containing doxorubicin: In Cancer Treat

TECHNOLOGY

Therapeutic Proteins and Peptides are administered in IV or SC are often too rapid fro of the Circulation and it is need to inject to the frequent order of administration for maintaining their therapeutic level of the blood. Various types of liposomal formulations have been utilized as drug delivery vehicles for sustained release of proteins and peptides like unilamellar or Multilamellar vesicle systems but few deals with the mulltivesicular liposomes are called as ―DepoFoam particles.‖ The DepoFoam technology is capable of accommodating high drug loading and high recovery of drug material, it is having a high Encapsulation efficiency, it is important type of technique is applicable for the sustained delivery of macromolecular drugs. A unique feature of DepoFoam system is that inside each DepoFoam particle, discontinuous internal aqueous chambers ,bounded by a continuous network of lipid membranes render a higher aqueous volume to lipid ratio and much larger particle diameter as compared to SUV's or MLV's. MARKETED FORMULATIONS ,]Product Formulation Route IndicationMetrodin FSH 75 IU i.m. Induction of ovulationPergonal FSH and LH i.m. infertilityProfasi HCG i.m. InfertilityElspar Asparginase i.m. i.v. LeukemiaGlucagon Glucagon i.m. i.v. s.c. HypoglycemiaActhar Corticotropin i.m. i.v. s.c. Hormone Deficiency

Conclusion

Protein and peptide based pharmaceuticals are rapidly becoming a very important class of therapeutic agents and are likely to replace many existing organic based pharmaceuticals in the very near future. Peptide and protein drugs will be produced on a large scale by biotechnology processes and will become commercially available for therapeutic use. This poses an urgent challenge to the pharmaceutical industry to develop viable delivery systems for the efficient delivery of these complex therapeutic in biologically active form. Their need in the clinical & therapeutic regions has intensified the investigation for their convenient & effective delivery through noninvasive system.

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