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Recent Advanced Approaches in Protein and Peptide Drug Delivery System: A Review

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ABSTRACT: Protein and Peptide drug delivery system are the Novel drug Delivery System. Proteins and peptides are the most abundant components of biological cells. They exist functioning such as enzymes, hormones, structural element and immunoglobulin. The twenty different naturally occurring amino acids join with each other by peptide bonds and build polymers referred to peptides and proteins. Although the distinction between peptides and proteins are peptide contains less than 20 amino acids, having a molecular weight less than 5000, while a protein possesses 50 or more amino acids and its molecular weight lies abovethis value. The most of pharmaceutical proteins and peptides areabsorbed IM, IV and Subcutaneous route of Absorption, but the oralroute is more convenient for absorption ofprotein as compared toother. Various problems associated with administration of protein andpeptide drugs are needed to overcome by different pharmaceutical approaches. Severalapproaches available for maximizing pharmacokinetic and pharmacodynamics properties arechemical modification, formulation vehicles, mucoadhesive polymeric system, use of enzymeinhibitors, absorption enhancers, penetration enhancers etc. The Present Review is describedStructure, classification of Protein, Need, Advantages, Function of protein and peptide drugdelivery system. Route of Absorption, Pharmaceutical approaches, Incorporation of DDS,Stability aspect, Applications, Recent Advances and Marketed formulation of Protein andPeptide drug delivery system.

Keywords: Protein, Peptide, Parenteral, Non-Parenteral, Pharmaceutical approaches,
Novel drug Delivery System, immunoglobulin

I. INTRODUCTION

The Protein and Peptide is a Novel Drug Delivery System and it is a Novel approach of drugdelivery system. Protein and Peptides are the Most Abundant Material of Living system andBiological cell. Its act has Hormones, Enzymes, Structural Elements andImmunoglobulin's.It is also important take part in Several Metabolic Process,Immunogenic Defence as well as its take part in several Biological activities.Proteins arethe one of the most abundant Organic molecule in Biological System, the term Protein firstused has Berzelius. The term Protein is derived from a Greek word Proteios MeansHolding the first Place. Proteins are the high molecular weight mixed polymer of Alphaamino acids joined together the Peptide Linkages. In Protein mainly contain Carbon,Nitrogen, Oxygen and Sulphur Molecule. Protein are the compounds having linear chainamino acids are held Together by the Covenant Linkages is called has Peptide Bonds.Peptides are the Condensation Product of Alpha Amino acids. The alpha amino groupof one molecule of amino acid are condensed alpha carboxyl group of another aminoacids. Protein are occurs in every part of all living cells for giving nutritional activity forproviding a body building ability. It is Important Molecule for the Plant and Animal cells.In Protein is mainly act has Enzyme for catalysis of Biochemical reactions, It is applicable forthe Transportation of Metabolites and Gene. It is applicable for giving a definite shape,strength to the cell and tissues.

It is having a One of the Most Important Applicability to control the Metabolic Pathways, PH, Osmotic Pressure and Temperature.The ProteinInsulin Regulates the Blood sugar level.In case of Peptide the two amino acids are condensed to fromdipeptides, threeforms Tripeptides, Four to from Tetra peptide and Peptide for the 2-20amino acids are Polypeptides. The Polymers of 100 and more than 100 Amino acidcalled has Proteins.The Proteins are classified into two types first is depending on thesolubility of proteins and another is complexity in structure of proteins. In fist case on thebasis of solubility they are classified into two

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types Globular Protein and Fibrous Proteins,The proteins are soluble in water or common salts known has Globular proteins and the theproteins are insoluble in Water and common solvents are called has Fibrous Proteins. Insecond case on the basis complexity Proteins are classified in three types Fist is simpleprotein it can contains only one amino acids, second is conjugated proteins it can containsamino acids and non protein parts, and third Derived Proteins it is hydrolysis product formedby the action of the physiological agents like heat, chemical agent, and enzymatic actions onthe Protein molecules.

The structure of Protein is mainly classified into four types First is Primary Structure of Protein the Primary structure of protein is referred as the number, natureand sequence of amino acids along with polypeptide chain, In this structure the N terminal ofamino acids always shown in left end of Polypeptide and C terminal of amino acid shown inright side, The best example of Pri. Structure is an Insulin Molecule. The Secondarystructure of protein in which the Long Polypeptide chain are folded or collided in a differentGeometric arrangements. The two types of arrangements of secondary structure of ProteinAlpha helical Structure and Beta Pleated sheet. In tertiary structure of proteins are the threedimensional coiling and folding of the chain, stabilized by the interaction between thesequences of amino acids, this folding results the (R-) group is side chai amino acids, theseinteraction are mainly (H-) bonded Interactions. The final shape of the tertiary structure ofprotein is an elapsed, globe and any other irregular shape. In Quaternary structure of Proteinsare the two or more polypeptide chain hold together by non covalent bond to give thequaternary structure of the proteins, Haemoglobin has Example of Quaternary structure ofProteins. Proteins and Peptide are applicable Endogenous functioning to maintain theBiological Environments. The discovery of Numerous Hormones and Peptides areApplicable for the Pharmaceutical and Biopharmaceuticals, It is applicable inPathophysiology of the Human diseases, The important application in Protein and Peptide inMedical Practices, Drug discovery Processes and Research activities.[11,20]

Need Of Protein And Peptide Drug Delivery System

1) The protein and peptides are very important in biological cells and Organic Molecules.
2) Now a days R-DNA technology and hybridoma techniques also used in protein and peptide based pharmaceuticals.[10]

Structure Of Peptides And Proteins:

A primary structure of amino acids individual arrangement, secondary coiled α-helix and pleated sheets, tertiary three dimensional arrangement and quaternary association of ternary forms.[10]

STABILITY OF PROTEINS:

Proteins are only marginally stable under physiological conditions. Forces such as hydrophobic, electrostatic interactions and hydrogen bonding act more as stabilizing factors. Protein degradation pathways such as chemical, physical and biological as showed in Fig. 1 presents a challenge to formulation scientists, for the development of stable pharmaceutical preparations. The measures to improve chemical and physical stability are summarised in Table

1. Biological stability can be improved by co-administration of enzyme inhibitors or by altering 3D structural orientation.[1,2,3]

Table 1: Stability aspects of proteins and peptides

S. No.	Stability	Problem	Overcome /Prevention
1	**Chemical Instability**		
A	**Deamidation**	Spontaneous degradation and loss of amino acid sequence homogeneity Denaturation, increase the immunogenicity	Buffer composition, lowering of Ph
B	**Oxidation**	Air, residual peroxide content, or intense fluorescent light, may lead to the decomposition of protein and peptide	Lyophilisation, Use of antioxidants, chelating agents, protection from light.
C	**Proteolysis**	Exposure to Harsh conditions	Storing at cold and sterile

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		such as high pH, high temperature or proteolytic enzyme	conditions
D	**Disulfide exchange**	It alters its 3 dimensional structures and results in its biological activity.	By thiol scavengers such as P-mercuribenzoate, N-ehylmaleimide, Copper ions.
D	**Racemisation**	Racemisation may form peptide bonds that are sensitive to proteolytic enzymes.	Addition of thiol scavengers such as P- mercuribenzoate, N-ehylmaleimide, Copper ions, may prevent susceptible sulphur and disulphide.
E	**β-elimination**	β-elimination of cystine residue leads to destruction of disulphide bonds of protein, due to high temperature.	Blocking thiol group
2	**Physical Instability**		
A	**Aggregation and precipitation**	Ionic complexation, salting out, charge neutrality close to the isoelectric pH, and results in limiting solubility of the molecule. Increase in thermal motion of the molecule due to agitation.	Use of nonionic surfactants to prevent aggregation and sugars to stabilise the proteins
B	**Denatured protein**	It may lead to the decrease in solubility, alteration in surface tension, loss of crystallizing ability, changes in constituent group reactivity and molecular profile, vulnerability to enzymatic degradation, loss of antgenicity and loss of specific biological activity.	Maintaining pH, ionic strength and temperature.
C	**Adsorbed protein**	If the peptide and protein drug entities are adsorbed at interface there may reduction in concentration of drug available to show its function	Use of Surfactants, smooth glass walls and reduces in excess agitation.

PROTEIN DELIVERY:

The formulation design and delivery of protein drug delivery involves not only protection of protein/peptide from enzymatic degradation but also aid in enhancing its absorption without altering in biological activity**.** Hence there are several techniques involved for the successful delivery of proteins and peptides for their specific site of action.[7,8]

ADVANTAGES OF PROTEIN AND PEPTIDE DRUG DELIVERY SYSTEM[5,6]

1. Erythropoietin is mainly used for production of RBC.
2. The protein Tissue plasminogen activator is used for Heart attack, Stroke.
3. Oxytocin is used in management of labour pain.
4. Bradykinin increases the peripheral circulation.
5. Somatostatin decrease bleeding in gastric ulcer.
6. Gonadotropin induce ovulation.
7. Insulin maintain blood sugar level.

FUNCTIONS OF PROTEIN AND PEPTIDE DRUG DELIVERY SYSTEM[9,10,11]

1. 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.

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5. Enzymatic catalysis in biochemical reactions.
6. The Immune protection through antibodies.
7. The Control of growth and differentiation via hormones.

CHEMICAL MODIFICATION:

A chemical modification of peptide and protein drugs improves their enzymatic stabilityand/ormembrane penetration of peptides and proteins. It can also be used for minimizing immunogenicity. Protein modification can be done either by direct modification of exposedside-chain amino acid groups of proteins or through the carbohydrate part of glycoproteinsand glycol-enzymes.

Modifications of individual amino acids combined with the substitution of one more L-aminoacid with D-amino acids can significantly alter physiological properties. This wasdemonstrated by vasopressin analogs 1-deamino-8-D-arginine vasopressin (DDAVP) and[Val4, D-Arg8], arginine-vasopressin (dVDAVP), hereafter called desmopressin and deaminovasopressin, respectively. While the former involves deamination of the first amino acidand replacement of the last L-arginine with D-arginine, the latter also has the fourth amino acidchanged to valine. While the natural vasopressin is orally active in the water-loaded rat at largedoses, desmopressin is twice as active at the 75th fraction of the dose, which is attributed toenhanced membrane permeation and enzymatic stability. Desmopressin absorption was shownto be passive and by the paracellular route across the rat jejunum and site dependent in rabbits.Whether the chemical modification alters the transport pathway, however, remains to be unknown.

Increasing the hydrophobicity of a peptide or protein by surface modification using lipophilicmoieties may be of particular benefit to transcellular passive or active absorption by membranepenetration or attachment, respectively; or it may simply aid in the increased stability of theprotein.[13,19,15]

ENZYME INHIBITORS:

The choice of protease inhibitors will depend on the structure of these therapeutic drugs, and the information on the specificity of proteases is essential to guarantee the stability of the drugs in the GI tract20. The quantity of co-administered inhibitor(s) is essential for the intestinal permeability of a peptide or protein drug.

For example, enzyme degradation of insulin is known to be mediated by the serine proteases trypsin, α-chymotrypsin and thiol metalloproteinase insulin degrading enzymes. The stability of insulin has been evaluated in the presence of excipients that inhibit these enzymes. Representative inhibitors of trypsin and α-chymotrypsin include pancreatic inhibitor and soybean trypsin inhibitor, FK-448, Camostat mesylate and aprotinin. Inhibitors of insulin degrading enzymes include 1,10-phenanthroline, p-chloromeribenzoate and bacitracin reported the use of a combination of an enhancer, sodium cholate and a protease inhibitor to achieve a 10% increase in rat intestinal insulin absorption.

Thiomers are promising candidates within as enzyme inhibitors. Hutton et al. first reported the inhibitory properties of poly (acrylates) on intestinal proteases. They found a strong reduction of albumin degradation by a mixture of proteases in the presence of carbopol 934P. A subsequent study by Lueben et al. showed that polycarbophil and carbopol 934P were potent inhibitors of the proteolytic enzymes trypsin, α-chymotrypsin and carboxypeptidase A. As a result of the covalent attachment of cysteine to polycarbophil, the inhibitory effect of the polymer towards carboxypeptidase A, carboxypeptidase B and chymotrypsin could be significantly improved. This polycarbophil-cysteine conjugate also had a significantly greater inhibitory activity than unmodified polycarbophil on the activity of isolated aminopeptidase N and aminopeptidase N present on intact intestinal mucosa.

Another approach to enzyme inhibition is to manipulate the pH to inactivate local digestive enzymes. A sufficient amount of a pH-lowering buffer that lowers local intestinal pH to values below 4.5 can deactivate trypsin, chymotrypsin and elastase.

Presystemic metabolism of proteins and peptide drugs can be reduced by co-administration of enzyme inhibitors. Use of proteases and peptidases inhibitors such as soybean trypsin inhibitor, FT-448, Bestatine, Comostate amylase, Leupeptine, Aprotinin. Furthermore, Bacitracin, Amastatin, Boroleucin and Puromycin have been used to avoid enzymatic degradation of drugs such as Leucine enkephalin and human growth hormone[(Table5)[13,14)]

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Table 5: Protein and peptide delivery through co-administration of Enzyme inhibitors.

Enzyme inhibitor	Molecules inhibited	Effect on peptide drugs
Soybean trypsin inhibitor, FK-448	Chymotrypsin	Enhanced intestinal absorption of insulin in rats and dogs. Suppressed digestion of insulin by pancreatic enzymes
Aprotinin	Serine proteases, specifically trypsin, Chymotrypsin, and plasmin	Intraileally administered insulin with aprotinin led to decrease in blood glucose of 30% compared with controls
Puromycin	Serine and metallopeptidases	Improved stability of Leucine enkephalin, and stability and permeability of d-Ala2, d-Leu5 enkephalin (DADLE)
N-acetylcysteine	Inhibits amino peptidase N and has mucolytic properties	--
Bacitracin	Trypsin and Pepsin, amino peptidase N	Used to increase delivery of Insulin, Met-kephamid and Buserelin

ROUTES OF ABSORPTION

The Proteins and Peptide drug delivery system in which Most of the Pharmaceutical Proteinsand Peptides Formulations are the Formulated as a Solution, suspension, Emulsions and theyare delivered in Invasive or Parenteral Route such as Intra muscular route (IM), Intravenousroute (IV) and Subcutaneous route (SC) Injections. But, These all routes are arises its ownDifficulties such as, Poor Patient Compliance, The pain and discomfort associated in thisroute (to inject injection in same site again and again it can arises Pain) and it is aInconvenience to treat the Paediatric Patients. The oral route of administration in protein andpeptide is suitable as compared to parenteral route, The Oral route having a One of the mostconvenient route of drug administration, in this type of route no pain and discomfort wasarises and Maintained the Higher Patient Compliances or Acceptance. But, The Developmentoral Protein and Peptide Drug delivery arises several Problems for their Oral Administrationof Drugs. This Problem is arises There Unfavourable and Undesirable PhysicochemicalProperties are such as The Large molecular size of the drug molecules, drug undergoessusceptibility to Biological and Enzymatic degradations, The oral drug having a short PlasmaHalf Life as compared to other drugs, it can having high Immunogenicity, The tendency ofProtein undergoes Aggregations, Adsorption and it can undergoes Denaturation's, The MajorProblem Orally Administered Proteins and Peptides are having a Lesser Bioavailability orLess Bioavailability is having a less than 1%. The other route of administration of protein andpeptide is arises success for the administration of Proteins and Peptide drugs, the routes areOral, Buccal administration, Intranasal administration, Pulmonary administrations,Transdermal, Rectal and Ocular administrations of Proteins and Peptide.[17]

Properties Of Proteins And Peptides

The Protein are the most abundant biological and organic molecule they are soluble in waterand it can formed a Colloidal solution with water. Protein and Peptides are the 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 Stereospecificity 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 Criteria associated in Properties

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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.[18]

PHARMACEUTICAL APPROACHES

Various pharmaceutical approaches and their outcomes

Approaches	Outcomes
Chemical modification	
a) Amino acid modification	Improves enzymatic stability.
b) Hydrophobization	Improve membrane penetration
Use of enzyme inhibitors	Resist degradation by enzymes present in stomach and intestine
Use of absorption enhancers	Increases membrane permeability
Formulation vehicles	
a) Emulsions	Protects drug from acid and luminal proteases in the GIT. Enhance permeation through intestinal mucosa
b) Microspheres	Prevents proteolytic degradation in stomach and upper portion of small intestine. Restricts release of drug to favorable area of GIT
c) Nanoparticles	Prevent enzymatic degradation. Increases intestinal epithelial absorption
d) Liposomes	Improves physical stability. Increases membrane permeability.
Mucoadhesive polymeric system	Achieve site-specific drug delivery. Improves membrane permeation.

1. CHEMICAL MODIFICATION (PRODRUG APPROACH) [21,16,19]

The Chemical Modification of Protein and Peptide Drug Delivery System of Drugs isImportantto Improve the Enzymatic Stability as well as Membrane Permeations. It isApplicable for the reducing the Immunogenicity.

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

1. Amino acid Modification
2. Hydrophobization

1. Amino acid Modifications:

The Modification of amino acid is one of the importantapproach in which the Substitution of the D- amino acid and L- amino acid is important toalter the Physiological Properties of Protein and Peptide Drug Delivery Systems.

Example: Desmopressin and De-aminovasopressin are the two important analogs ofvasopressin, former involves deamination of first amino acid and replacement of last Larginine
D-arginine to give De-aminovasopressin.

Application: The Amino acid modification is important to enhance the MembranePermeability and Maintain the Enzymatic Stability.

2. 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 Lysinemolecule to from mono and insulin is important to facillated the transfer the insulin across themucosal membrane of the large intestines. It is important to improve the Stability against theenzymatic degradations.

ENZYME INHIBITORS (PROTEASE)

The enzyme (protease) inhibitors are the enzymatic approach of the Protein and Peptide drugdelivery systems. GIT and Liver is play important role in Metabolization of the Protein andPeptides into smaller fragments of the two to ten amino acids with the help of the variety ofProteolytic Enzymes. This Protease inhibitors are CO- administered with Protein and Peptideto alter

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the Environment for the Enzyme stability to supress the Proteolytic activity. Theenzyme proteases inhibiters are divided into four types they are Aspartic Proteases (Pepsin,Rennin), Cystinyl Proteases (Papain, Endopeptidase), Serinyl Proteases (Thrombin, Trypsin),and Metallo Proteases (Carboxypeptidase).

PENETRATION ENHANCERS

Penetration enhancers are the one of the most important Component of Protein and Peptidesformulation is responsible for the Disruption of the Mucosal Barriers and applicable toimprove the Membrane Permeations of Large Macromolecular substances lie Proteins andPeptides. The Several classes of compounds are mainly used has a permeation enhancers aresuch 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 tight junctions and they are facillated the Paracellular transport of the hydrophilic drugs materials. Fatty acids are the important for the improving the paracellular absorption by phospholipases C activations and upregulation of intracellular Calcium ions, is leading to the contraction of actine myosin filaments.

FORMULATION VEHICLES[21,22,23,24]

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: Liposomes 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.

4. Nanoparticles: Nanoparticles are Nano sized colloidal structure having size is 10-1000nm. The particles in nanometric 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.

MUCOADHESIVE POLYMERIC SYSTEMS

The mucoadhesive polymeric system is important to prevent the problem associated in Presystemic Metabolism or first pass metabolism and maintain its therapeutic efficacy. The residence time of this drug delivery systems at the site of action and the increasing or decreasing the drug clearance rate.

Examples: Thiomers, polyacrylic acid derivatives and cellulose derivatives. The stronger mucoadhesive properties of thiomers are believed to be based on covalent bonds between thiol groups of the thiomer and cystein- rich domains of mucus glycoproteins. (Higher amount of thiol groups is responsible for the stronger mucoadhesive properties).

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APPLICATION ([20,12,18,15])

1.CVS acing drugs Protein and Peptides (Angiotensin 2 antagonist, Bradykinin, Captopril) is important for the Lowering blood pressure and improving peripheral circulation for Heart failure management.

2.CNS active Protein and Peptides (Cholecystokinin, B-endorphin) is important for the Suppressing appetite and Relieving pain.

3.GI-active Protein and Peptides (Gastrin antagonist, pancreatic enzymes) is important for the Reducing secretion of gastric acid and it is important for Digestive supplement.

4. Immunomodulation of the Protein and Peptides (Bursin, Cyclosporin, and Interferon) is important for Selective B-cell differentiatingharmone Inhibits functions of T-lymphocyte Enhancing activity of killer cells.

5.Metabolism modulating Protein and Peptides (Insulin, Vasopressin) is important for treating diabetes mellitus and treating diabetes insipidus.

CONCLUSION:

Therapeutic proteins and peptides are gaining importance in healthcare system. In recent years,numerous therapeutically potent protein and peptide drugs have been developed. Althoughhighly potent, one of the major challenges to the successful clinical use of this therapeutics islack of an effective delivery method. Parenteral delivery remains still upfront even thoughabundant efforts have been put toward delivering protein and peptide via noninvasive routes.Hence, there is large scope to develop viable delivery systems for the efficient use of these complex therapeutic agents in biologically active form.

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

REFERENCE

[1]. Banga A.K. and Chein Y.W, Systemic delivery of therapeutic peptides and proteins, Int. J. Pharmaceutics, 1988; 48: 15-50

[2]. Banerjee P. S. and Ritschel W. A., Int. J. Pharm. 1989; 49: 189-197.

[3]. Chein Y. W., Lelawongs P., Siddiqui O., Sun. Y. and W. M. Shi. W. M; Faciliated trandermal delivery of therapeutic peptides/proteins by iontophoretic delivery devices. J. Control. Rel., 1990; 13: 263-278.

[4]. Siddiqui O., Sun Y., Liu J. C. and Chein Y. W., Faciliated transdermal transport of insulin. J. Pharm. Sci., 1987; 76: 341- 345.

[5]. Sibalis D., Transdermal drug applicator. U. S. Patent, 1987; 4: 708-716.

[6]. Meyer B. R., Electro-osmotic transdermal drug delivery, in: 1987 Conference Proceedings on the Latest Developments in Drug Delivery Systems, Aster Publishing, Eugene, Oregon, (1987), 40.

[7]. Meyer et al. Transdermal delivery of human insulin to albino rabbits using electrical current. Am. J. Med. Sci., 1989; 297: 321-325.

[8]. Okabe K., Yamaguchi H. and Kawai Y., New iontophoretic transdermal administration of the beta blocker metaprolol. J. Control. Rel., 1986; 4: 79-85.

[9]. Chein Y. W., Siddiqui O. and Liu J. C., Transdermal iontophoretic delivery of therapeutic peptides/proteins. I. Insulin. Ann. N. Y. Acad. Sci., 1988; 507: 32-51.

[10]. Tahami. Alkhaled and Singh J., Recent patent on drug delivery and formulation, 2007; 1:65-71.

[11]. Vyas S.P. and Khar K.R., Targeted and controlled drug delivery, Novel carrier system, CBS publishers and distributors, New Delhi.561.

[12]. Chein Y.W., Novel drug delivery systems, volume 50, second edition, 715.

[13]. Pekar A. H. and Frank B. H., Conformation of proinsulin. A comparison of insulin andproinsulin self-association at neutral pH. Biochemistry, 1972; 11: 4013-4016.

[14]. Banga AK etal; Hydrogel-based iontotherapeutic delivery devices for transdermaldelivery of peptides-protein drugs. Pharm Res 1993; 10: 697-702.

[15]. Lee Ycetal;. Effect of formulation on the systemic absorption of Insulin from enhancerfree ocular devices. Int J Pharm 1999; 185: 199-204.

[16]. Burgess DJ etal; editors. Biotechnology and Pharmacy. New York: Chapman and Hall;1993; 116-51.
[17]. Aurora Jetal; delivery of protein and peptide –challenges and opportunities. Business Briefing: Future dry discovery, 2006; 38-40.
[18]. John M.etal; Shanafelt.Enhancing exposure of protein therapeutics. Drug Discoverytoday: Technologies 2006; 3: 87-94.
[19]. Yanagi H et al. Effect of inclusion complexation of decanoic acidwith _-cyclodextrin onrectal absorption of cefmetazole sodium suppository in rabbits. Yakugaku Zasshi. 1991;111: 65-69.
[20]. Lin SY and Yang JC, Effect of _-cyclodextrin on the in vitro permeation rate an d in vivo rectal absorption of acetaminophen hydrogel preparations. Pharm. Acta Helv., 1990; 65: \ 262-268.
[21]. Arima H et al. Use of water soluble _-cyclodextrin derivatives as carriers of anti inflammatory drug bi phenylyl acetic acid in rectal delivery. Yakugaku Zasshi. 1992; 112: 65-72.
[22]. Brouard A et al. Rectal administration of carbamazepine gel. Clin. Pharm. 1990; 9: 13–14.
[23]. Levy R et al. Metabolism of Antiepileptic Drugs. Raven Press, New York. 1984; 61–71. 24. Graves NM et al. Relative bioavailability of rectally administered carbamazepine suspension in humans. Epilepsia., 1985; 26: 429–433.