Annals of Translational Medicine & Epidemiology

Open Access

Austin Publishing Group

Editorial

Recent Updates in Peptide Drugs Delivery

Okorochenkov SA*
Department of Organic Chemistry, Palacký University, Czech Republic

***Corresponding author:** Okorochenkov SA, Department of Organic Chemistry, Palacký University, Czech Republic

Received: May 12, 2016; **Accepted:** May 16, 2016; **Published:** May 17, 2016

Keywords

Peptide drugs; Delivery systems

Editorial

During several past decades peptides discovered to be very promising candidates as new therapeutics [1]. Peptides have almost no side effects, show perfect selectivity and do not accumulate in liver. Unfortunately, peptides still did not become mainstream drugs due to the number of limitations. Peptides, with very rare exceptions could not be administrated orally because of fast proteolysis in stomach; they are generally not stable in aqueous solution; finally, peptides are mostly not stable under ambient temperature [2].

Antimicrobial Peptides (AMPs) are a good example which reflects problems of peptide application in medical practice. AMPs were firstly discovered as a key component of insect's innate immunity and later they were found in other species. AMPs demonstrate high activity against wide range of pathogens including Gram-positive and Gram-negative bacteria, yeasts, fungi and viruses. In most cases pathogens show no resistant development towards AMPs [3]. Together with absence of toxic side effects inherent to "traditional" antibiotics it made AMPs one of the most promising classes of future therapeutics on 1990s- early 2000s. Nevertheless there are just few examples of AMPs approved by regulatory authorities for application in clinical practice. Problems with administration by oral and injection way limited their application for treatment of generalized infections. AMPs approved or being on late stage of clinical trials are mostly used for treatment of superficial infections like acne, oral candidiasis or eyes infections [4]. Thus, AMPs felt short of expectations as novel antibiotics.

The number of peptide or protein-based drugs approved by regulatory authorities is slowly increasing year to year but their part in pharmaceutical market still does not exceed 10% [5]. Fortunately, researches both in industry and in academy are gradually leading to overcome challenges of peptide usage in clinical practice.

The driving force for optimization of peptide delivery systems is presence on the market of some irreplaceable peptides and proteins such as insulin and human growth hormone. The successful approaches (optimized in comparison with simple syringe injection) could be roughly divided into three groups: "physical" approaches, "Advanced Delivery Systems" (ADS) and chemical modifications.

"Physical" approaches include advanced methods of injection with reduced pain and traumatic effects. Good examples are devices making micropores in skin of patient facilitating thereby diffusion of therapeutic throw the skin to blood or pump implants which are widely used for the control of insulin level [6]. The non-invasive physical methods for drug delivery employ weak electrical field like iontophoresis techniques for transdermal transport of therapeutic proteins [7]. Another non-invasive solution is laser-assistant techniques for skin penetration, as P.L.E.A.S.E. technology for triptorelin and follicle stimulating hormone delivery [6]. All of these methods display high performance and in some cases could be recognized as an optimal solution. However, fundamental disadvantage of these techniques is necessity to use complex and expensive devices requiring technical support, which results in the limited applicability of "physical" approaches.

The main advantage of ADSs is possible oral administration. Basically, this technique includes incorporation or adsorption of peptide drug on appropriate carrier which serves for controlled release and intracellular delivery of drug and prevents its premature biodegradation. First proposed protein carriers were liposomal systems. "Simple" liposomes composed from lipids and peptide/protein drug usually do not provide significant improvement of bioavailability if administrated orally due to the fast biodegradation of lipids. However, more complex ADSs are much more efficient. Thus, polymerized liposomesOrasome™, where lipids from inner and outer leaflet are covalently bound to each other provides acceptable bioavailability of carried proteins and could be used even for oral vaccination [8]. Other approaches for improvement of liposomes efficiency include addition of auxiliary compounds (positively charged peptides, sugars, immunoglobulins, etc.) and chemical modification of liposomes with peptides, Polyethylene Glycol (PEG) and targeting molecules. Disadvantages of liposomes are their moderate stability, leakage and fusion of encapsulated drug/molecules and relative high cost [8].

Another class of ADSs is Nanoparticles. These carriers could be administrated by different ways including both invasive and non-invasive. Nanoparticles are absorbed by M-cells on Payer's patches in the gut. These ADS can be composed from biodegradable polymers such as chitosan, vitamin B12 - dextran copolymer, poly (lactic-co-glycolic acid) with addition of polyvinyl alcohol, etc [9]. Chitosan nanoparticles attract special interest because they highly improve bioavailability of peptides and proteins during oral and nasal administration. Another interesting sort of nano-sized drug carrier is solid lipid nanoparticles. Their main advantages compared to other carriers are improved stability, enhanced drug content and lower cost [9].

Chemical modification is employed for improving peptides and proteins pharmacological properties. For example, conjugation with fatty acids increases proteins penetration trough the cell membrane by passive diffusion. Another method for protein intracellular

Citation: Okorochenkov SA. Recent Updates in Peptide Drugs Delivery. Ann Transl Med Epidemiol. 2016; 3(1): 1008.

delivery is attachment of targeting molecules which provide protein transport through the membrane into the cell. Moreover, conjugation with cell-penetrating peptides such as oligoarginines also improves proteins delivery [10].

As far as some recombinant protein drugs are exogenous for human organism, they can cause non-desirable immune reaction. An important tool to overcome this limitation is conjugation of protein with PEG. PEGylation makes proteins "invisible" for immune system and if PEGylation extent is chosen correctly, biologic properties of protein remain unchanged [10].

Hence, great number and wide diversity of peptides administration approaches shows itself how complex the task is. Nowadays none of these conceptions could be considered as optimal and universal one. However, in last two decades a great break through has been done in administration of insulin and hormones. These achievements allow to estimate further fast growth of approved protein- and peptide based drugs number.

References

1. Craik DJ, Fairlie DP, Liras S, Price D. The future of peptide-based drugs. Chem Biol Drug Des. 2013; 81: 136-147.
2. Lax R, Meenan K. Challenges for Therapeutic Peptides Part 1: On the Inside, Looking Out. Innovations in Pharm Tech. 2012; 42: 54-56.
3. Wang G, Mishra B, Lau K, Lushnikova T, Golla R, Wang X. Antimicrobial peptides in 2014. Pharmaceuticals (Basel). 2015; 8: 123-150.
4. Okorochenkov SA, Zheltukhina GA, Nebol'sin VE.Antimicrobial Peptides: the Mode of Action and Perspectives of Practical Application. Biochem (Mosc) Suppl Ser B Biomed Chem. 2011; 5: 95-102.
5. Mitragotri S, Burke PA, Langer R. Overcoming the challenges in administering biopharmaceuticals: formulation and delivery strategies. Nat Rev Drug Discov. 2014; 13: 655-672.
6. Lax R, Meenan K. Challenges for Therapeutic Peptides Part 2: Delivery Systems. Innovations in Pharm Tech. 2012; 43: 42-46.
7. Kalluri H, Banga AK. Transdermal delivery of proteins. AAPS PharmSciTech. 2011; 12: 430-441.
8. Akbarzadeh A, Rezaei-Sadabady R, Davaran S, Joo SW, Zarghami N, Hanifehpour Y, et al.Liposome: classification, preparation, and applications. Nanoscale Res Lett. 2013; 8: 102.
9. Ashish JA, Aviral JA, Arvind GA, Satish SS, Pooja HP, jain SK. Peptide and Protein Delivery Using New Drug Delivery Systems. Crit Rev Ther Drug Carrier Syst. 2013; 30: 293-329.
10. Mukherjee S, Ray S, Thakur RS. Solid lipid nanoparticles: a modern formulation approach in drug delivery system. Indian J Pharm Sci. 2009; 71: 349-358.

Ann Transl Med Epidemiol - Volume 3 Issue 1 - 2016
ISSN: 2472-3649 | www.austinpublishinggroup.com

Citation: Okorochenkov SA. Recent Updates in Peptide Drugs Delivery. Ann Transl Med Epidemiol. 2016; 3(1): 1008.