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Research Article

RECENT APPLICATIONS AND POTENTIALLY ADMINISTER FUTURE PHARMACO THERAPY OF PULMONARY DRUG DELIVERY SYSTEM

J. Sunil*, G. Venkatesh, B. Brahmaiah and CH. Baburao

Donbosco college of Pharmacy, pulladigunta, 5thmile, Guntur,

Andhra Pradesh, India.

ABSTRACT

Pulmonary route as an noninvasive administration for systemic delivery of therapeutic agents (mainly peptides and proteins) due to the fact that the lungs could provide a large absorptive surface area but extremely thin (0.1 µm – 0.2 µm) absorptive mucosal membrane and good blood supply. However, recent advances show great promise, but pulmonary delivery of peptides and proteins is complicated by the complexity of the anatomic structure of the human respiratory system and the effect of disposition exerted by the respiration process.Pulmonary drug delivery system is a needle free technique.. Now a day'spulmonary drug delivery remains the preferred route for administration of various drugs. It is animportant research area which impacts the treatment of illnesses including asthma, chronic obstructivepulmonary disease and various diseases. Drug is delivered directly to the conducting zone of the lungs.In this article, we summarize recent advances in applications of pulmonary drug delivery system.previously pulmonary drug delivery is used for management of Asthma and COPD only but dueadvancement in application nowadays Pulmonary drug delivery is useful to treat Diabetes, anginapectoris, cancer , bone disorders ,migraine,tuberculosis,acute lung injury and others[1].

Keywords: Administration, Inhalation, Aerosol, Lung, future pharmaco therpy

INTRODUCTION

Pulmonary route have been used to treat various respiratory diseases for centuries. Ancient inhalation therapies included the useof leaves from plants, vapors from aromatic plants, balsams, and myhrr. However, around the turn of the 19th century, with the invention of liquid nebulizers, these early treatments developed into legitimate pharmaceutical therapies. In the 1920 s adrenaline was introduced as a nebulizer solution, in 1925 nebulizer porcine insulin was used in experimental studies in diabetes, and in 1945pulmonary delivery of the recently discovered penicillin was investigated. Steroids had been introduced in the mid 1950s for the treatment of asthma and nebulizers were enjoying widespread use. In 1956 the pressured metered dose inhaler (Pmdi) was introduced, over the past 5 decades, helped by the advances in molecule designand drug discovery the(Pmdi)has risen to become the main stay of asthma treatment .2Over the decade certain drugs have been sold in compositions suitable for forming drug dispersion for pulmonary delivery to treat various conditions in humans. Such pulmonary drug delivery compositions are designed to be delivered by inhalation by the patient of a drug dispersion so that the active drug within the dispersion can reach the lung. It has been found that certain drugs given by pulmonary route are readily absorbed through the alveolar region directly into blood circulation.

Pulmonary route possesses many advantages over other routes of administration for the treatment of specific disease states, particularly lung associated large protein molecules which degrade in the gastrointestinal conditions and are eliminated by the first pass metabolism in the liver can be delivered via the pulmonary route if deposited in the respiratory zone of the lungs. Devices used to deliver drug by pulmonary route area based on one of three platforms pressurized metered dose inhaler, nebulizer and dry powder .In the treatment of disease, aerosol administration represents a valuable means by which a therapeutic agent may bedelivered.[3]

ADVANTAGES OF PULMONARY DRUG DELIVERY

Inhaled drug delivery puts drug where it is needed. It requires low and fraction of oral dose i.e. drug content of one 4 mg tablet of salbutamol equals to 40 doses of meter doses. Pulmonary drug delivery having very negligible side effects sincerest of body is not exposed to drug. Onset of action is very quick with pulmonary drug delivery. Degradation of drug by liver is avoided in pulmonary drug delivery. In asthma and diabetes requires long term treatment if it is given by pulmonary drug delivery safety is maximum because rest of body isnot exposed to drug.[4]

RECENT ADVANCES IN PULMONARY DRUG DELIVERY INCLUDES

Recent Advances in technology of pulmonary drug delivery

Recent advances in pulmonary drug delivery devices

Recent Advances in formulation of pulmonary drug delivery

Recent Advances in applications of pulmonary drug delivery

RECENT ADVANCES IN PULMONARY DRUG DELIVERY DEVICES

Following types of inhalation devices are present

Inhalation drug delivery system by- metered dose inhalers

Inhalation drug delivery system by —dry powder inhalers

Inhalation drug delivery system by -nebulizer

RECENT ADVANCES IN FORMULATION OF PULMONARY DRUG DELIVERY

Effective inhalable medication are produced by drug formulation. Formulation stability is another challenge in producing pulmonary drug delivery. Formulation is responsible for keeping drug pharmacologically active, it must be efficiently delivered into the lungs, to the appropriate site of action and remains in the lungs until the desired pharmacological effect occurs. Depending upon disease condition effective formulation release drug, such as insulin for diabetes, must be deposited in the lung periphery to ensure maximum systemic bioavailability. . Thus, a formulation that is retained in the lungs for the desired length of time and avoids the clearance mechanisms of the lung may be necessary. Research into dry powder formulations has been an area of growth in recent years and will be the focus of this section. Various techniques are used to made advances in dry powders formulation for inhalation involves either, micronization via jet milling, precipitation, or spray drying using various excipients, such as lipids and polymers, or carrier systems like lactose.

Recent role pulmonary delivery inpatients on ventilators

Aerosols to patients on ventilators have received much accepted by doctors as well as patient in 1990. Some studies of early delivery techniques documented low (2.2%) deposition in the lung with half retained in the nebulize rand considerable inter subject variability. Recently to improve inhalation coordination of patient devices like Baby mask are mostly used. This mask is attached to spacer for small tidal volumes and low inspiratory flow rates infant and young Childers..By using baby mask we can easily give medication to child up to 2years this is recent advancements in applications of pulmonary drug delivery.

Pulmonary delivery in cystic fibrosis

Nowadays cystic fibrosis is very common disease .Pulmonary delivery played an important role in the management of CF for decades. The main aim of aerosol system is to deliver drugs to infants and chidrens. Recently following drugs are given by pulmonary route for cystic fibrosis.

I) **N-Acetylcysteine**

N-acetylcysteine (NAC) is Mucolytic agents have been used by pulmonary route to help in sputum clearance. It will help to liquefy tenacious secretions and make their clearance easier. Recently newer mucolytic agent, nacystelyn, has been developed for delivery viaa dry powder inhaler.

II) **Recombinant human deoxyribonuclease aerosol**

Rerecentaly deoxyribonuclease is given by pulmonary route .Recombinant humandeoxyribonuclease aerosol mainly used toliquefy secretions in CF patient.

III). **Tobramycin-spray dried**.
Tobramycin powders containing Nanoparticles for pulmonary delivery.Tobramycin is widely used to treat patients with CF. Overall, evidence suggests improved lung function and probably
reduced hospitalization when tobramycin is part of maintenance therapy in cf.

New use of pulmonary delivery indiabetes
Diabetes is a syndrome of disordered metabolism and inappropriate hyperglycemia resulting from a deficiency of insulin secretion orresistance. Diabetes can cause a heart attack, stroke, blindness, kidney disease, nerve damage and other serious health problems. Themost common form of this therapy is twice-daily subcutaneous injections of insulin. This type of treatment is painful and as a result encourages noncompliance by up to half of the diabetics. Peptides and/or proteins are becoming more important in medication. When taken orally, peptides and/or proteins are degraded by theproteolytic enzymes in the gastrointestinal tract, and might be impermeable to the intestinal mucosa due to their hydrophilicity and large molecular size. As a result, systemic delivery of these macromolecular drugs and other therapeutic and diagnostic agents has been limited to the parenteral route. Repeated injections are required due to the short half-lives of peptide/protein drugs.14The first attempts atintra pulmonary delivery were made in the 1920s . However, almost 50 years feasibility of arolosied insiulin was demonstrated Initial observations were soon confirmed by others revealing a more rapid absorption and clearance compared to subcutaneous administered insulin. Several companies are working on insulin inhalers than any other insulin delivery option. Insulin inhalers would work much like asthma Inhalers. The products fall into two main groups the dry powder formulations and solution, which are delivered through different patented inhaler systems. E.g. Novel pMDI formulations for pulmonary delivery of proteins.[31,32,33,34,35,36.]

Pulmonary drug delivery will continue to evolve, and respiratory care practitioners are on the forefront to assist and potentially administer future pharmacotherapeutic agents.

Pulmonary drug delivery continues to be an exciting and evolving method for new pharmaceutical agents. Recent data has estimated that the global pulmonary drug delivery technologies market may reach US$37.7 billion by 2015.[1] Aerosol-based formulations offer a number of advantages, including limited systemic side effect profile, alternatives to self-injections, and limited dependence on infusion delivery devices. Based on this need, the pharmaceutical industry is investing major resources in aerosol drug delivery and biotechnology, including research in particle engineering, dry powder formulations, protein and peptide-based therapeutics, dispersion technology, drug delivery methods, and drug delivery device design. This research is leading to a frontier of newer pharmacotherapeutic alternatives to be administered for aerosol delivery. These comprise antibiotics, antidiabetic agents, analgesics, antiemetics, nicotine replacement, hormone therapy, and vaccines. As pharmaceutical technology advances, the future of pulmonary drug delivery via aerosol will continue to represent another alternative delivery method for patients. The potential result of this new technology is improvement in health care-related outcomes, including decreasing disease-related patient morbidity and mortality.

RECENT TREND IN APPLICATIONS OF PULMONARY DRUGDELIVERY
Apart from asthma and COPD recently pulmonary drug delivery isused for following indication

- Insulin by Aerosol
- Treatment of Migraine
- Nicotine Aerosol for Smoking Cessation
- Aerosols for Angina.
- Aerosol Vaccination.
- Alpha 1 Antitrypsin
- Aerosols in Transplantation
- Pulmonary arterial hypertension
- Acute Lung Injury
- Surfactant Aerosol
- Gene Therapy via Aerosol
- In Cancer chemotherapy
- Pentamidine Aerosol
- Amphotericin B
- Gentamycin aerosol
- Ribavirin Aerosol
- Zanimivir R/C with revolizer for swine flue.
- Aerosols used in clinical investigations of disease

- Inhaled Drug Delivery for Tuberculosis Therapy.
- Pulmonary delivery of lower molecular weight Heparin.
- Controlled delivery of drugs to lungs
- Pulmonary delivery of drugs for bone disorders
- Pulmonary delivery of opioids as pain therapeutics.

CONCLUSION

The lung has served as a route of drug administration for thousands of years. Now a day's pulmonary drug delivery remains the preferred route for administration of various drugs. Pulmonary drug delivery is an important research area which impacts the treatment of illnesses including asthma, chronic obstructive pulmonary disease and various diseases. Inhalation gives the most direct access to drug target. In the treatment of obstructive respiratory diseases, pulmonary delivery can minimize systemic side effects, provide rapid response and minimize the required dose since the drug is delivered directly to the conducting zone of the lungs .It is a needle free several techniques have been developed in the recent past, to improve the Quality of pulmonary drug delivery system without affecting their integrity. Because of advancement in applications of pulmonary drug delivery it is useful for multiple diseases. So pulmonary drug delivery is best route of administration as compare to other routes.

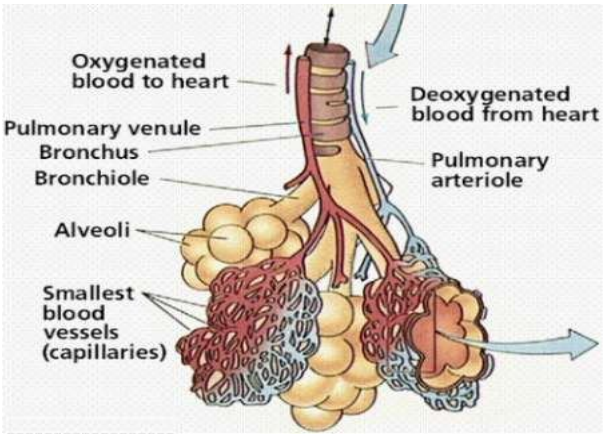

Fig. 2: Blood flow on lungus and structure of alveoils

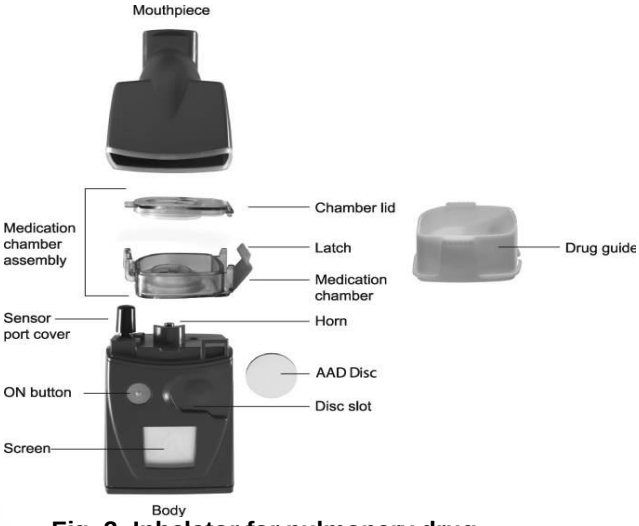

Fig. 3: Inhalator for pulmonary drug delivery

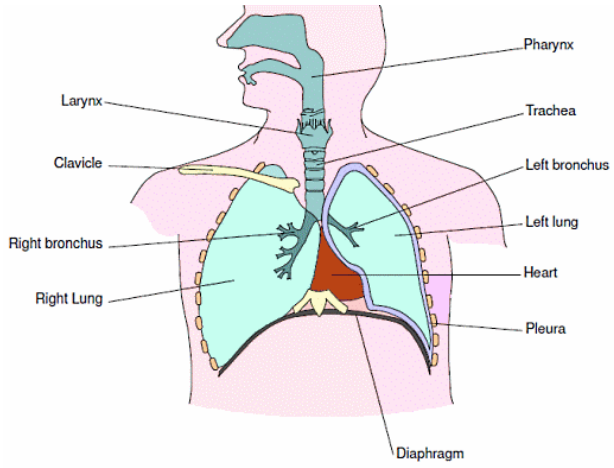

Fig. 1: Lungs view

Fig: 4: Pulmonary drug delivery via aerosol

Abbreviations

1. NAC- N-acetylcysteine
2. CF - cystic fibrosis
3. IDDS - Inhalation drug delivery system
4. COPD - chronic obstructivepulmonary disease.

REFERENCES

1. Siraj Shaikh, Syed Nazim, Afsar Shaikh, Tarique Khan, Zameeruddin Md, Quazi Majaz and Shailesh Chalikwar. Ali-Allana College of pharmacy Akkalkuwa Dist, Nandurbar, Maharashtra, India. 2R.C.Patel college of pharmacy,Shirpur Dist Dhule, Maharashtra, India.
2. Michael T. Newhouse, Encyclopedia of Pharmaceutical Technology, second edition, Dekker, New York Informa Healthcare USA. 2000;19:1279-1285.
3. Derek Ivan Daniher and Jesse Zhu. Review on dry powder platform for pulmonary drug delivery, www.sciencedirect.com, Particuology 2008;225–238.
4. Henderik W Frijlink and Anne H de Boer. Trends in the technology-driven development of new inhalation devices, drug discovery today. Technology. 2005; 2(1).
5. Albert HL Chow, Henry HY and Tong, Pratibhash Chattopadhyay and Boris Y Shekunov. Particle Engineering for Pulmonary Drug Delivery," Pharmaceutical Research. 2007; 24(3):411-433.
6. David A Edwards, Abdelaziz Ben-Jebria and Robert Lange.Recent advances in pulmonary drug delivery using large, porous inhaled particles. J Appl Physiology. 1998;85(2):379-385.
7. Rohan Bhavane, Efstathios Karathanasis and Ananth V Annapragada. Agglomerated vesicle technology. a new class of particles for controlled and modulated pulmonary drug delivery, Journal of Controlled Release. 2003;15-28.
8. Paul J Atkins, Timothy M Crowder. The Design and Development of Inhalation Drug Delivery Systems. modern pharmaceutics by Marcel Dekker,1-31.
9. Manfred Keller. Innovations and perspectives of metered dose inhalers in pulmonary drug delivery. International journal of pharmaceutics. 1999;186:81-90.
10. Costas Kaparissides, Sofia Alexandridou, Katerina Kotti and Sotira Chaitidou. Recent advances in novel drug delivery systems. Azojono. 2006.
11. Henrik Luessen Tytonis BV. Pulmonary drug delivery new perspectives on inhalers and inhalables. ON drug Delivery Lt. 2007.
12. Callion ONM. Jet nebulizer for pulmonary drug delivery. International journal of pharmaceutics. 1996;1-11.
13. Le Brun PPH, de Boer AH, Heinemann HGM and Frijlink HW. A review of the technical aspects of drug nebulisation.
14. Labiris NR and Dolovich MB. Pulmonary drug delivery. "Part II: The role of inhalant delivery devices and drug formulations in therapeutic effectiveness of aerosolized medications", Br J Clin Pharmacol. 2003;56(6):600–612.
15. Anthony Moran astec project ltd. Next generation of automated pulmonary drug delivery system", OndrugDelivery Lt. 2007 .
16. Hao-Ying Li and Peter C Seville. Novel PMDI formulations for pulmonary delivery of proteins, International Journal of Pharmaceutics. 2009;1-6.
17. Kathryn Senior. New technology for pulmonary drug delivery. PSTT. 2000;3(8).
18. Charles Hiller F. Therapeutic Aerosols An Overview froma Clinical Perspective", modern pharmaceutics marcel Dekker.
19. Clark AR. Medical aerosol inhalers. Past, present and future. Aerosol Sci Technol. 1995;22:374–391.
20. Grossman J. The evolution of inhaler technology. J Asthma.1994;31:55–6
21. Newman SP and Clarke SW. Inhalation devices and techniques. In: Clark TJH, Godfrey S, Lee TH, editors. Asthma. 3. London: Chapman & Hall; 1992;469–505.
22. Pedersen S. Inhalers and nebulizers: which To choose and why. Rasp Med. 1996;90:69–77.
23. Ganderton D. Targeted delivery of inhaled drugs: current challenges and future goals. J Aerosol Med. 1999;12(1):s3–s8.
24. Dolovich M. New propellant-free technologies under investigation. J Aerosol Med.1999;12(1):s9–s17.

25. Michael T. Newhouse, “Encyclopedia of Pharmaceutical Technology”, Informa Healthcare USA, Page no.1279-1285.
26. Publication Ref No.: IJPRD/2011/PUB/ARTI/VOV-2/ISSUE-12/FEB/018 ISSN 0974 – 9446.
27. International Journal of Pharma Research and Development – Online
28. www.ijprd.com
29. Derek Ivan Daniher and Jesse Zhu. Review on Dry powder platform for pulmonary drug.
30. Delivery,www.sciencedirect.com, Particuology (2008)225– Henderik W. Frijlink, Anne H. de
31. Boer, Trends in the technologydrivenDevelopment of new inhalation devices,
32. Drug discovery Today.technology,Elesevier 2005;1(2).
33. David A Edwards, Abdelaziz Ben Jebria and Robert Lange.Recent advances in pulmonary drug delivery using large, porous inhaled. Particles. J Appl Physiology 1998;85:379-385,
34. www.cipladoc.com
35. David A. Edwards, Andre´ X. Valente, Jonathan Man and Nicolas Tsapis Harvard University, Cambridge, Massachusetts, U.S., “Recent Advances Related to the Systemic Delivery of Therapeutic Molecules by Inhalation”, modern pharmaceutics marcel Dekker. 2004;1-10
36. David R Owens, Geremia B Bolli and Bernard Zinman. Future options for insulin therapy, current science. 2002;83(12):1548-1554.
37. Gowthamarajan K and Giriraj T Kulkarni. Oral Insulin – Fact or Fiction? Resonece. 2003;38-40.
38. Al Tabakha MM and Al Arida. challenges in insulin drug delivery system. Indian journal of pharmaceutical science. 2008;278-284.
39. Naryani R. oral delivery of insulin making needless”, trends biometer.artifs.organ. 2001;159(10):12-16.
40. Jaleh Varshosaz. Insulin Delivery Systems for Controlling Diabetes. Recent Patents on Endocrine, Metabolic & Immune Drug Discovery. 2007;1:25-40.