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A Review on Dry powder Inhaler

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Abstract

Abstract: A Dry powder inhaler (DPI) is a device that disperses medication into the lungs. DPIs are frequently used to treat respiratory conditions such as asthma, bronchitis, and COPD. In recent years, interest in Dry powder inhalers as an effective and ecologically responsible means of medication delivery to the lungs has increased. Dry powder inhaler can meet these goals only with an efficient metering system, and a carefully selected device. It is mainly classified into three classes: Nebulizer, pMDI, DPI. DPIs, which administer medication to the lungs in the form of a dry powder, are an alternative to pMDI. To ensure that the patient receive the same dose each time at a varied airflow rate, API particles must be present in the size range of 1 to 10m.DPI are formulated using four types of formulation strategies such as; Drug additive, Drug carrier, Drug free, Drug carrier additive. The "Twin Stage Impingner" completes the investigation of lung deposition. The inward breath device, which is primarily divided based on measurements into single-unit and multi-dosage stores, is crucial to achieving appropriate delivery of breathed in medication to the lung.

Keywords

Dry powder inhaler, Inhalation device, Pulmonary route, Carrier particle, Patient complaints.

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INTRODUCTION

PULMONARY DRUG DELIVERY SYSTEM:

In the current research sector, the pulmonary route of drug delivery is becoming increasingly significant as it allows for pharmaceutical emphasis. Especially transporting to the lung for both localized and systemic therapy. The purpose of the study is to investigate the technical, physiological, and effectiveness aspects of the innovative pulmonary route of drug targeting and various drug delivery systems, including metered dosage inhalers (MDI), dry powder inhalers(DPI),nebulizers, etc [1] Pulmonary Drug Delivery System serves as major route of drug administration for thousands of years .Ancient inhalation therapies include the use of leaves from plants vapors from aromatic plants, balsams, and myrrh. It is mainly used for systematically acting drugs such as peptide and protein, as well as for drugs that are designed to act locally on the lungs themselves for the treatment of asthma, Chronic Obstructive Pulmonary Diseases, (COPD) or Cystic Fibrosis(CF).[2] [3] Diabetes trial investigations began with nebulized porcine insulin in 1925 and in 1945 pulmonary delivery of the recently discovered penicillin was investigated. For the treatment of asthma, steroids had been introduced in the middle of the 1950s and nebulizers were widespread use. The Pressurized metered dosage inhaler was first launched in 1956, and during the last 50 years with the aid of developments in molecular design and drug discovery, it has evolved into the main stay of asthma treatment. Throughout the decade, specific medications have been sold in forms that can be formed into drug dispersion for pulmonary delivery to treat a variety of human illness. Such pulmonary drug delivery compositions are made to be inhaled by the patient, allowing the active medication included in the composition to reach the lung. 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 valuable means by which a therapeutic agent may be delivered [2,3,4]

ADVANTAGES OF PULMONARY DRUG DELIVERY SYSTEM [2,5,6]

1. Drugs given by pulmonary route gives quick onset of action.
2.Pulmonary drug delivery system has negligible side effect as the rest of the body is not exposed to drugs.
3.Pulmonary drug delivery system is needling free technique.
4.Respiratory tract provide a large surface area which is highly permeable for absorption of drug into the blood.
5.It is non-invasive drug delivery system.

Inhaled drug delivery systems can be divided into three principal categories:

*pMDIs
*DPIs
*Nebulizers

NEBULIZERS

In this system, aerosols are generated from solution or suspension of the drug in an appropriate solvent. These are utilized mostly in hospital and ambulatory care settings for delivering doses over multiple breadths, and to infants, elderly and critically ill patients. These formulations may contain preservatives to reduce microbial growth [7,8]
Nebulizers have been used in medicine since the middle of the nineteenth century. In this technique, the medication solution or suspension is suspended in a suitable solvent. While some medications are insoluble or unstable in solution, it is still possible to produce suspensions known as heterogenous systems. In a solution, the active ingredient is dissolved in a solvent to form a homogeneous phase. Nebulizers are incredibly good at producing mists of very small droplets that have good pulmonary deposition. The nebulizer platform uses an air jet or ultrasonic mechanism to atomize an aqueous-based medicinal solution.[1, 9]

ADVANTAGES OF NEBULIZER [10]

1. High doses of medication can be used.
2.Easy formulation handling and requires less coordination of patient.

DISADVANTAGES OF NEBULIZER [11,12]

1.Equipment is expansive which is hard to transport
2.Nebulizers are not typically used for chronic-disease management because they are larger and less convenient, and the aerosol is delivered continuously.

PMDIs

A PMDI is a device that releases medication into the air in precisely regulated doses after mixing it with a propellant and filling a canister with it. The container, metering valve, and actuator are the three main parts of a standard are the three main parts of a standard metered dose inhaler [MDI].

ADVANTAGES OF PMDIs [7,8]

1.Simple to use
2.Convenient and small
3.Low cost
4.Accurate metering performance.

DISADVANTAGES OF PMDIs [2,5,6]

1.Limited to the treatment of upper airway conditions because of it emits the dose at high velocity, which makes premature deposition in the oropharynx.
2.Contains propellant such as Chlorofluorocarbon (CFC) which depletes the ozone layer.
3.pMDI is limited to certain drugs that are stable in a propellant.

DRY POWDER INHALERS:

A DPI is a device that delivers medication to the lungs in the form of dry powder. [7,8]A dry powder formulation of an active drug is given for local and systemic action via the pulmonary route using DPIs. Dry powder Inhaler (DPI), where the medication particles (5m) are blended with an appropriate large carrier (such as lactose) to optimize the flow characteristics and dose uniformity. Patients must use their own energy to deagglomerate and aeroionize the formulation powder. To do this, a significant degree of turbulence is required to break up the big agglomerates into smaller, fine, and inhalable particles.[13]

Types of DPIs	Pressure drops across the device	Required inspiratory flow(L/min)	Example
Low resistance DPIs	< 5Mbar 1/2 L/min^{-1}	>90	Aerolizer, Breezhaler
Medium resistance DPIs	5-10Mbar 1/2 L/min^{-1}	50-60	Turbohaler, Accuhaler / Diskus, Novolizer, Ellipta
High resistance DPIS	>10 Mbar 1/2 L/min^{-1}	<50	Easyhaler, Twisthaler

GENERAL REQUIREMENTS OF DPI:

DPIs must meet the following requirements.

a. Drug content uniformity

In order to guarantee that the patient gets the same dose every time, it is important that each capsule or blister in a single-dose system contain the same amount of powder and medication while in a multi-dose system; the reservoir must release the same amount of powder and drug every time. [12,14,15]

b.Flowability

For the right amount of powder to produce a DPI, this attribute must be sufficient. Since practically all active substances have poor flowability, the carrier must provide the good flow.[7,8]

c. Particle Size of API

Active compound must be inhalable. To able to pass into the lungs, it must be present in particles of size about 1-5micro meters. Such microfine particles can be obtained by micronization, controlled precipitation from suitable solvent, or by spray drying if the procedure conditions are suitable.[7,8]

d. Content uniformity at different airflows

The patients breathing pattern affects how much medication is delivered through a DPI. This implies that the dose has to be released in exactly the same way at low breathing and a high breathing rate. Content uniformity at different airflows is, therefore, extremely important for a DPI.

e. Stability of powder against humidity and temperature

The protection of lactose against particle size expansion is necessary since lactose particle size distribution is crucial to the action of a DPI. The key factor causing particle size expansion is an unfavourable mixture of temperature and relative humidity. For stability, its crucial to regulate to regulate the temperature an relative humidity, then store items in the right packaging. [12,14]

ADVANTAGES OF DPI [16,17,18,19]

1.Formulation stability:

DPIs are preferred as stable formulations since they are often made as one- phase, solid particle blends. Due to their lower energy state and lower rate of chemical deterioration, dry particles are less likely to react with contact surfaces.

2.Propellant-free design:

pMDI contains propellants such as CFCs and hydrofluoroalkanes which are ozone-depleting and greenhouse gases. Production of CFC propellants was banned from january1,1996, to stop the depletion of ozone layer. Hence, pMDI was replaced by DPI which does not contain propellant. Hence, DPIs are environmental friendly formulation.

3.Require little or no coordination of actuation and inhalation:

Incorrect use of pMDIs found that poor coordination of actuation and inhalation caused decreased asthma control in a substantial proportion of patients treated with corticosteroids pMDIs. Whereas DPIs are activated by the patients inspiratory airflow, they require little or no coordination of actuation and inhalation.

4.Other advantages of DPI:

- Less potential for extractable from device components.
- High drug dose carrying capacities.DPIs can deliver a range of doses from<10mg to more than 20mg through one short inhalation.

DISADVANTAGES OF DPI:[16,17,20]

1.More expensive than pMDIs

2.Potential for dose uniformity problems

3.Development and manufacture more complex and expensive

4.Dependency on patients inspiratory flow rate and profile.

FIG: SINGLE –DOSE DPIs AND MULTI-DOSE DPIs

Formulation strategies for Dry Powder Inhaler [2]

Efficacy of DPI is mainly depending on flow property of powder which is mainly affected by strong interparticle forces which make the cohesive bulk powder agglomerate. The vander waals force, electrostatic force and capillary force are the three different interparticle forces. When the particles are sufficiently close to one another (0.2-1.0 nm) and tiny(20m or less), the vander waals force is detectable. The vander waals force can be dramatically altered by surface roughness, geometrical structure, and particle deformation. When particles with different work functions are brought into contact, electrostatic force can result from the potential difference. The powder becomes sticky as a result of the coulomb attraction. In order to construct liquid bridges between the particles in close contact, fluid condenses in the spaces between them, creating capillary force.

To overcome these difficulties different types of formulation strategies for DPI(Fig) are used as follows.

a. Carrier Free

The active therapeutic element in the carrier-free technique can be a single chemical, a composite made up of multiple compounds, or it can be contained within small particles. From crystallization and milling to spray drying and supercritical fluid, there are many different production methods. Because they cannot generate the best particle shape, narrow particle size distribution, low surface energy, or avoid amorphous material, crystallization and milling were determined to be inadequate for preparing pulmonary medicines. The medication particle intended for inhalation needs to be less than 5 micrometers in size [1,12]

b.Drug Carrier

It is difficult to administer 1g or 1mg of pharmacological doses into the tiny blisters for dry powder inhalers. The fact that the ideal particles are between 1 to 5m makes it difficult to entrain powder by inhalation as well. To improve their flow and to boost the volume of each dose, the drug molecules are therefore combined with bigger particles. These carrier particles can have geometric sizes between 50 and 100m. If properly prepared, coarse particles in the fine particle bed can act as an additional agitator or turbulence promotor to aid in the fluidization of the fine particles.[1] Disadvantage of this strategy include carriers generally deposit in the mouth along with many drug particles adhered to them which leads to less drug reaching the lungs.

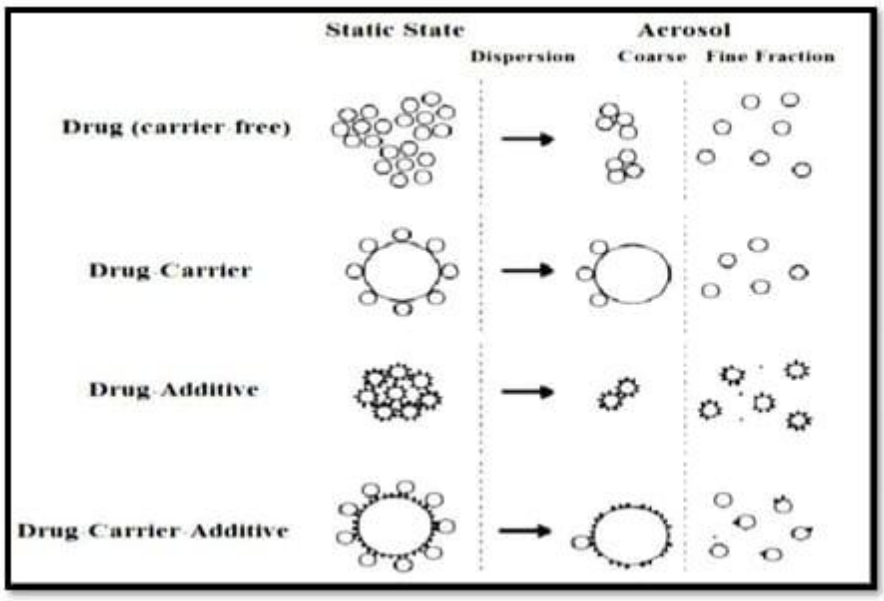
c.Drug Additive

The addition of finer particles can also improve the fluidization quality of drug fine powders. Additives such as submicron silica (0.5-3wt %), alumina(29nm), aerosol 200 (12nm) were used.

d.Drug Carrier Additive:

An additional particle type may be added to the formulation to improve may be a fine particle such as fine particle of the same composition as the carrier, which could function as a physical spacer, or possibly by occupying high-energy sites such as clefts in the carrier surface.

DIFFERENT TYPES OF FORMULATION



FORMULATION OF DPI

Formulation of DPI Mainly includes three steps:

1.API Production

2.Formulation of API with or without carriers

3.Integration of the formulation into the device.

API PRODUCTION:

Drug particles should be no larger than 5 m. It should fall between 2 and 5 m. Typically, throughout the bulk drug production process, the drug particle size is not adequately controlled. In a separate unit operation, the size of the drug particle must be decreased. There are many methods for reducing the size of materials, including grinding, spray drying, and superficial fluid extraction. There are many different kinds of mills used to reduce the size of pharmaceuticals, but only a few of them are suited for DPI to do so. The ball mill, high peripheral speed mills like jet mill, and mills with a range of 2 to 5m. High-velocity particle-particle collisions in the jet mill reduce particle size. The milling chamber filled with raw materials. The nozzles feed high-pressure nitrogen, which accelerates the solid particles to sonic speeds. When the particles collide, they break. Larger particles are subjected to greater centrifugal forces as they fly around the mill and are pushed to the outer edge of the chamber. The mill Center discharge stream is where small particles leave the machine.

A pin mill uses mechanical impact to grind material, both by particle-particle and particle-solid collisions which can produce 1micrometer particles. It is equipped with a series of concentrically mounted pins located on a spinning rotor and stationary stator plate. Powder is fed to the milling chamber and transported through the milling chamber by centrifugal force. The finished milled product is gathered at the bottom. The ball mill is a cylindrical device that rotates while being filled with balls and a substance to be grind into powder. The medication is dissolved in water or a solvent and sprayed into a heated expansion chamber as a fine mist during spray-drying. Small amounts of medication are left behind when the droplets dry, and these particles gather near the chamber base.[21,22,23]

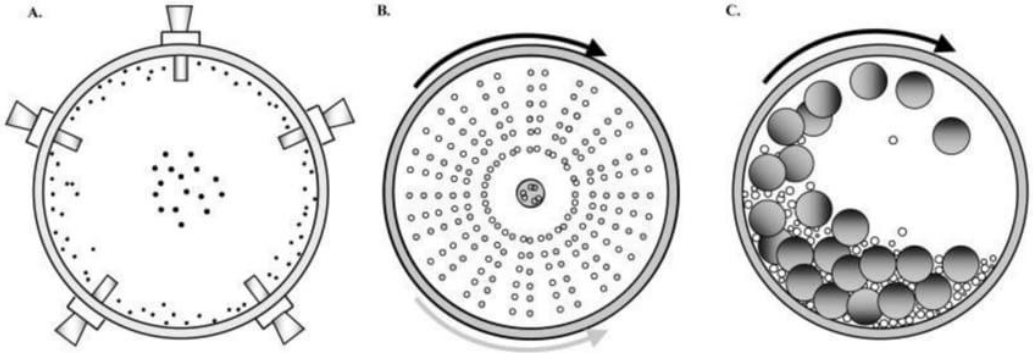


FIG: Cross- sections of 3 mills commonly used to create micron-size particles A: Jet mill B:Pinmill C: Ball mill.

Formulation of API with or without carriers:

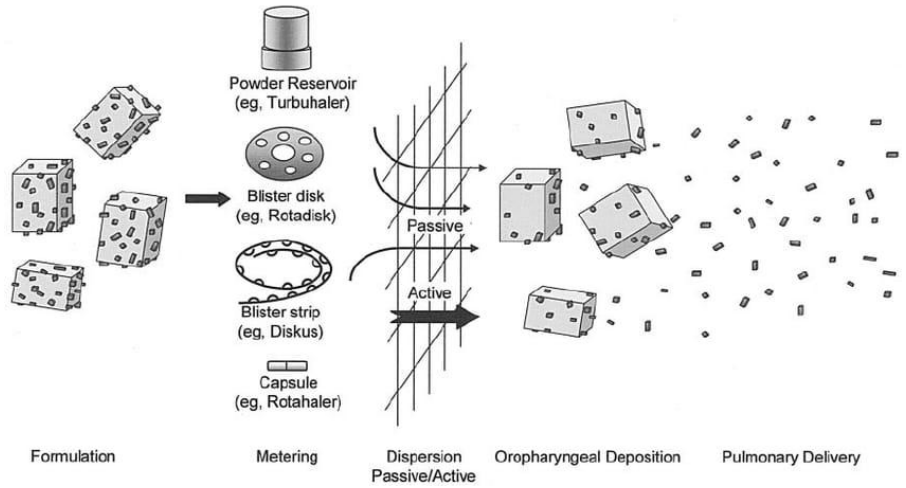
Drugs and carriers are combined in the blending process. Inadequate mixing can bring about poor dose uniformity. In many cases inadequate mixing cannot be overcome just by expanding the blending time. Blender choice, rotation speed, capacity, and fill level are all parameters for optimization which affects the blend homogeneity [24].There are high energy active sites on the surface of the coarse carrier particles thereby prompting to a strong adherence of the drug particles to the coarse particles(Particle size >20micrometers).Expansion of fine carrier particles(Fines <10micrometers) saturates the active sites of coarse carrier particles mostly, to which, then, micronized drug is attached. Hence, drug adheres to passive sites, i.e., less energy sites and facilities the disaggregation of the micronized drug during inhalation.

Integration of the formulation into device:

The combined mixture is then put into reservoirs, blisters containing multiple doses, or capsules for use with an inhaler. The automatic filling procedure is dependent on the metering systems design.

Principle of dry powder inhaler design:

A static powder bed is used to conduct the dispersion of a dry powder aerosol. The particles need to be transported in order to produce the aerosol. Several mechanisms, including passive and active ones, can cause movement. Inhalers that are passive use the patients inspiratory flow. The static particle blend is fluidized and injected into the patient airways when the patient activates the DPI and inhales, causing airflow through the DPI and inhales, causing airflow through the device to induce shear and turbulence. There, the drug particles separate from the carrier particles and are carried deep into the lungs, while the larger carrier particles impact in the oropharynx and are cleared. Several power- assisted devices (pneumatic, impact force, and vibratory) have been created or are actively being developed for aerosol formation. In these DPIs known as active –dispersion DPIs are not offered commerically.[21,22]



PRINCIPLE OF DRY POWDER INHALER DESIGN

DPI DEVICE:

The primary inhaler parts are same for all type of devices on the market and many in development. Dry powder inhaler device consists of powder formulation, dose measuring system ,powder deagglomeration principle and mouthpiece.[25,26]

Ideal Characteristics for DPI Device:

1.Device should be easy to use and convenient to carry.
2.Contain multiple doses
3.Protect the drug from moisture.
4.Minimum adhesion between drug formulation and devices
5.Accurate and uniform delivery of doses over wide range of inspiratory flow rate.

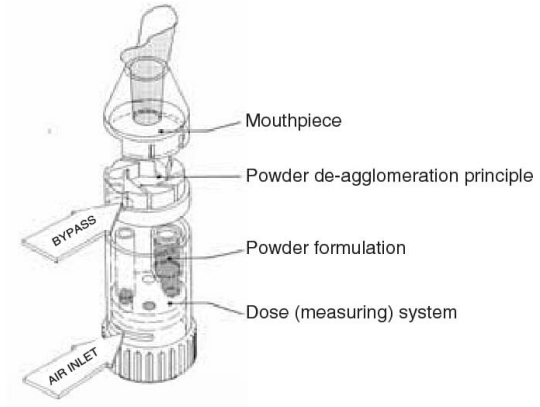


FIG: Primary functional design elements of dry powder inhaler

THE MAIN CLASSES OF DPIS, BASED ON THEIR INTRINSIC RESISTANCE, AND PRESSURE DROP ACROSS THE DEVICE

Capsule-based device:

These DPI Devices often have a chamber in which a capsule is inserted. When the patient presses the button, pins or twists inserted in the capsule cause it to break with external force. The patient breathes in the powder once it has been discharged. [24,27]

Capsule-based devices listed below.

*Aerolizer
*Rotahaler
*ARCUS
*FlowCaps
*DOTT DPI
*Breeze haler
*Aerohaler,and
*Podhaler Redihaler.

Cartridge-based device

To keep medication powder, these devices have a chamber. The apparatus has a unique mechanism for releasing medications upon inhalation.

Xectovair, Ultrahaler, Spiromax, Swinghaler, PADD, Jethaler, VIP inhaler, and NEXT haler are a few examples of cartridge-based medical equipment. It contains a button that is coupled to a push lever that is tied to a bar that is connected to the powder chamber. It can be applied numerous times.[24,27]

Blister based device:

Blister based devices normally have a ring of aluminum blisters inside the device. One prefilled medication dose is contained in each blister. A Dose counter serves as another dosing indicator on the device. To release the drug powder for inhalation, puncture the blister. As the patient breathes in, a stream of air is produced, which carries the medication powder away. Acubreathe, Acubreathe single dosage, Prohaler, Puffhaler, Multihaler, Gyrohaler, Forspiro, Elpenhaler and Diskhaler as examples.[28,29]

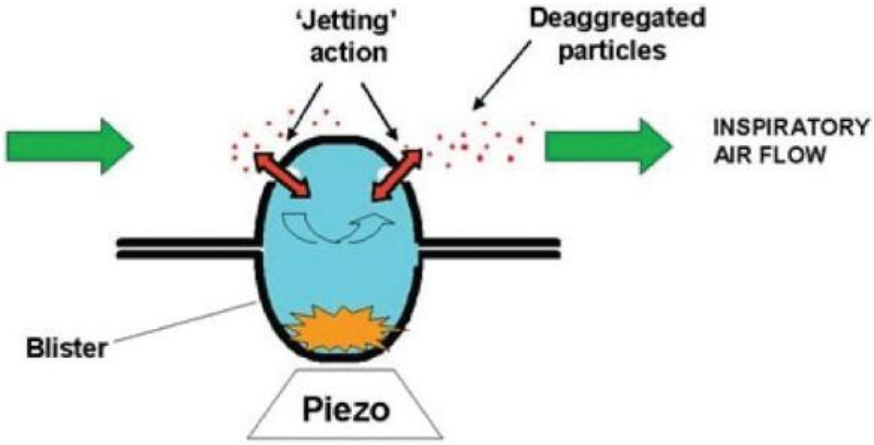


FIG: ILLUSTRATION OF MICRODOSE

CONCLUSION:

The number of diseases that are being considered candidates for the aerosol therapy has increased substantially. Until recently, asthma was only the clear example of a disease that could be treated via aerosol delivery to lungs. We now consider it possible to treat not only asthma and chronic obstructive pulmonary diseases but also systemic disorders such as diabetes, cancer, neurobiological disorders and other pulmonary diseases such as cystic fibrosis and pulmonary infectious diseases.

REFERENCES:

1. Daniher D. I, Zhu J. Review Dry Powder Platform for pulmonary drug delivery. Particuology., 2008, 6: 225-238
2. Derek Ivan Daniher, Jesse Zhu; Review Dry powder platform for pulmonary drug delivery; Particuology. 2008; 6:225–238
3. Siraj Shaikh, Sayyed Nazim, Tarique Khan, Afsar Shaikh, Mohammad Zameeruddin and Aamer Quazi. Recent Advances In Pulmonary Drug Delivery System: A Review. International Journal of Applied Pharmaceutics.
4. http://www.kem.edu/dept/clinical_pharmacology/ACCP_Day1/Session%202/Dr%20Misra%20-%20RECENT%20ADVACNCES%20IN%20LIPOSOMAL%20DPI%20FOR%20PULMONARY%20D.pdf
5. Richard J. Malcolmson and Jonathan K. Embleton. Dry powder formulations for pulmonary delivery. Reviews research focus, PSTT. 1998;1(9):394-398.
6. http://nanoparticles.org/pdf/Gardne r.pdf, David L. Gardner; Factors to Consider in Developing a Dry Powder Inhaler.
7. Kadu P, Kendre P, Gursal K. Dry powder inhaler: A review. J Adv Drug Deliv 2016; 3:42-52.
8. Sahane SP, Bhaskaran S, Nikhar AK, Mundhada DR. Dry Powder inhaler: An advanced technique for pulmonary drug delivery system. Int J Pharm Chem Sci 2012; 1:1027-34.
9. Prime D, Atkins P. J, Slater A, Sun by B. Review of Dry Powder inhalers; Advance Drug Delivery Reviews., 1997, 26: 51-58.
10. . http://nanoparticles.org/pdf/Gardne r.pdf, David L. Gardner; Factors to Consider in Developing a Dry Powder Inhaler
11. Telko M. J, Embleton J. K. Dry Powdr Inhaler Formulation; Respiratory Care.,2005, 50(9):1209-1227.
12. SP. Sahane, AK. Nikhar, S. Bhaskarana, DR.
13. Islam N and Gladki E. Dry Powder Inhalers (DPIs): A review of device reliability and innovation. Int. J. Pharm. 2008; 360:1-11.
14. 13. Dry powder inhalers. [www.lactose.com]
15. Keller M, Walz R. M. Dry Powder for Inhalation, United State Patent Application Publication, Publication No.- US2011/0114092 A1, Publication Date- May 19, 2011.
16. Yadhav N, Lohani A. Dry powder inhalers: A review. Indo Global J Pharm Sci 2013; 3:142-55.
17. Telko MJ, Hickey AJ. Dry powder inhaler formulation. Respir Care 2005; 50:1209-27.
18. Chauhan PS, Popli H. Evaluation study of dry powder inhalers: A concise, systemic review. Int J Curr Adv Res2018; 7:13686-91.
19. Shah ND, Shah VV, Waghamare J. Dry powder for inhalation. Int J Res Rev Pharm Appl Sci 2012; 2:458-72.
20. Ashurst I I, Malton A, Prime D, Sum by B. Latest advances in the development of dry powder inhalers. Pharm Sci Technolo Today 2000; 3:246-56.
21. Martin J Telko and Anthony J Hickey; Dry Powder Inhaler Formulation. Respiratory Care. 2005;50(9):1209-1227.
22. Alagusundaram M, Deepthi N, Ramkanth S, Angalaparameswari S, Mohamed Saleem TS, Gnanaprakash K, Thiruvengadarajan VS and Madhusudhana Chetty C. Dry Powder Inhalers - An Overview. International Journal Research Pharmaceutical Science. 2010;1(1):34-42.
23. Mahavir B. Chougule, Bijay K. Padhi, Kaustubh A. Jinturkar and Ambikanandan Misra. Development of Dry Powder Inhalers; Recent Patents on Drug Delivery & Formulation. 2007;1(1):11-21.

24. Dadarwal D. Dry powder inhaler; special emphasis to formulation, devices, characterization, and process validation protocol: A review. J Drug Deliv Ther 2017; 7:50-4
25. Newman SP and Busse WW. Review Evolution of dry powder inhaler design, formulation, and performance. Respiratory Medicine. 2002; 96:293-304
26. Nazrul Islam and Ellen Gldaki. Mini Review Dry Powder Inhalers (DPIs)- A review of device reliability and innovation. International Journal of Pharmaceutics. 2008; 360:1-11.
27. Asif DF, Munir H, Ghafoor S, Abrar M, Nawaz MN, Ahsan A. Dry powder inhaler devices. J Cell Sci Ther 2017; 8:14.
28. Oyarzun Ampeuri FA, Brea J, Loza MI, Torres D, Alonso MJ. Chitosan hyaluronic acid nanoparticles loaded with heparin for the treatment of asthma. Int. J. Pharm. 2009; 381(2):122-129
29. Frijlink HW, de Boer AH. Trends in the technology-driven development of new inhalation devices. Drug Discovery Today: Technologies 2005; 2(1):47-57.