IJCRT.ORG ISSN : 2320-2882

INTERNATIONAL JOURNAL OF CREATIVE RESEARCH THOUGHTS (IJCRT)

An International Open Access, Peer-reviewed, Refereed Journal

A OVERVIEW OF AN DRY POWDER INHALATION DOSAGE FORM

Sanchali Sahadeo Pingale, Mr. Prof. Dr. Pravin Cholke

Nikhil Nityanand Yerkal , Mr. Prof . Mahesh Harale

Author : Sanchali Sahadeo Pingale ,

Nikhil Nityanand Yerkal

Dharmaraj shaikshink pratishathn College Of Pharmacy Walki , Ahmednagar .

ABSTRACT

Dry powder inhalation remedy has been proven to be an powerful technique for treating breathing sicknesses like bronchial allergies, Chronic Obstructive Pulmonary Diseases and Cystic Fibrosis. It has additionally been extensively prevalent and utilized in scientific practice. The contemporary coronavirus (COVID-19) pandemic additionally has improved such hobby and is greater ability programs of dry powder inhalation remedy in vaccines and antivirus drug. Many organizations at the moment are prioritizing the improvement of dry powder inhalers (DPIs) above pressurized . formulations of bronchial allergies drugs. A well-designed DPI and the best powder method can optimize the effectiveness' of inhaled drug remedy. ADPI ought to be capable of supply medicines efficiently for maximum sufferers and an offer a dose that doesn't range with inspiratory float rate.

Keywords

DPIS , PMDIS, Pdds.

1.INTRODUCTION

1.1 Pulmonary drug delivery

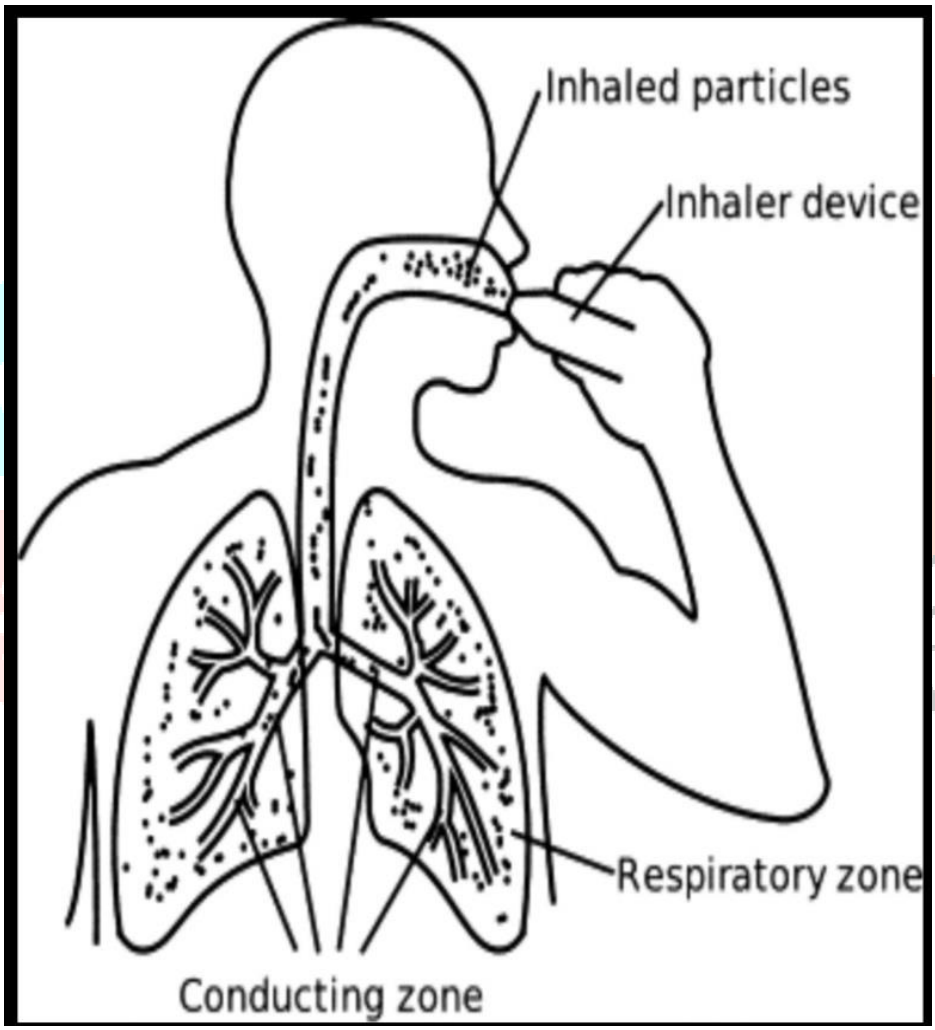
Dry powder inhalation remedy has been proven to be an powerful technique for treating respiration illnesses like asthma, Chronic Obstructive Pulmonary Diseases and Cystic Fibrosis. It has additionally been extensively regularly occurring and utilized in medical practice. The modern coronavirus (COVID-19) (1)

In 1925 nebulizer porcine insulin turned into utilized as a component of trial studies in diabetes, and in 1945 pulmonary delivery of the recently discovered penicillin turned into investigated. Steroids had been presented in the mid1950s for the treatment of bronchial allergies and nebulizers have been appreciating a ways attaining use. In 1956 the forced metered dose inhaler (pMDI) turned into

introduced, over the past 5 decades, help t the advances in molecule design and drug discovery the pMDI has land up to grow to be the primary live of a bronchial allergies treatment. (2)

Pulmonary route possesses numerous 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 be delivered. (3).

1.2: Schematic representation of pulmonary drug delivery system [4]



General Requirement of DPIs

DPIs need to meet the subsequent requirements

: a. Particle Size of API Active Compound have to be inhalable. In order to capable of by skip into the lungs, it have to be found in debris of length approximately 1 to ten μm. Such micro high-quality debris may be received through micronization, managed precipitation from appropriate solvent[7).

b. Drug content material uniformity

order to assure that the affected person receives the identical dose each time, it's far essential that every pill or blister in a single-dose gadget include the identical quantity of powder and medicinal drug whilst in a multi-dose gadget; the reservoir have to launch the identical quantity of powder and drug each time .[8]

c. Content uniformity

at extraordinary airflows Drug transport from a DPI relies upon at the affected person's respiratory pattern. This means that the dose must be launched in precisely the identical manner at low respiratory and at a excessive respiratory rate. Content uniformity at extraordinary airflows is consequently extraordinarily essential for a DPI [7]

d.Stability of powder

in opposition to humidity and temperature. Because the particle length distribution of lactose is extraordinarily essential for the motion of a DPI, the lactose have to be covered in opposition to particle length increase. The primary assets liable for particle length increase is an undesired of temperature and relative humidity. Controlling the temperature and relative humidity accom aggregate panied through garage in the best packaging are essential for Stability. [7]

Advantages of pulmonary drug delivery system

1. The massive protein molecules which is probably degrade in gastrointestinal tract and removed through first byskip metabolism are given through pulmonary course which keep away from first byskip metabolism

2. Pulmonary Drug Delivery System has negligible aspect impact because the relaxation of frame isn't always uncovered to drugs given with the aid of using pulmonary path offers brief onset of action .

3. Pulmonary transport additionally gives the ability for higher and possibly greater inexpensive remedy or prophylaxis of breathing and systemic diseases.

4. Pulmonary Drug Delivery System is needle free technique. [5]

2.DRY POWDER INHALER

A Dry powder inhaler (DPI) is a tool that supplies remedy to the lungs with inside the shape of a dry powder. DPIs are generally used to deal with respiration ailments inclusive of asthma, bronchitis, emphysema and COPD even though DPIs have moreover been applied as part of the remedy of diabetes mellitus. DPI is specially labelled into Active and passive. [6]

The dry powder platform carries devices that generate an aerosol right now from 1 to 5 μm duration drug powder, or mixtures with excipients. Excipients applied in DPI are used as carrier for Active Pharmaceutical Ingredient (API). Most usually used carrier is Lactose Monohydrate. [7]

DPIs are an possibility to the aerosol-based definitely inhalers usually called metered-dose inhaler (MDI)

Advantages of DPIs

1. Require little or no coordination of actuation and inhalation .

2. Formulation Stability

3.propepllent free design

4. Flowability[7]

3. Dry powder inhalation: past

DPIs are already regarded on account that mid-eighteenth century from Vincent Alfred Newton's UK patent 1161 [9] His device, supposed to supply pulverized potassium chloride, turned into in no way synthetic on an commercial scale, however. This, incontrast with the Aerohalor of Abbott, which turned into released almost one hundred years later in 1948 and used for the shipping of penicillin and norethisterone, a bronchodilator[10]

These inhalers contained a lactose primarily based totally drug system in small drugs or 'sifters'. For the improvement of the primary tool advertised on this period, the Fisons Spinhaler® (1967), the excessive dose (20 mg of cromogly cate sodium, that's too excessive for MDIs) turned into the principle driver[10] More than 10 years later and after extensive debate approximately the nomenclature,Staniforth (1987) provided superb arguments to update the name 'ordered' by 'adhesive[11]

Micronized tablets for transport with this reservoir inhaler are converted through spheronization into gentle aggregates (at the beginning with out micronized lactose) to acquire a carrier-loose formulation. Nearly all DPIs evolved earlier than 2010 have been so-known as passive.

4. Dry powder inhalation: present

New inhaler concept developments may easily stretch over periods of 10-15 years. What was started several years ago may not reach the patient in the next half a decade. The patent literature may tell what is going on but cannot reveal which developments will be successful; only few of the patented inventions reach the market. Therefore, the boundary between past and present is blurred, and for the sake of continuity, the period from approximately 1990 onwards will be considered (at least partly) as the present.

five mainstream developments can be distinguished

related primarily to dry powder inhalation:

(1) 'repair actions' for the design weaknesses of the early inhaler concepts

(2) formulation of high-dose drugs ('particle engineering')

(3) development of inhalers and formulations for vaccines and systemically acting drugs

(4) understanding (and controlling) pulmonary drug deposition and distribution from DPIs.

(5) miscellaneous innovative developments. [11]

5 . DRY POWDER INHALATION :FUTURE

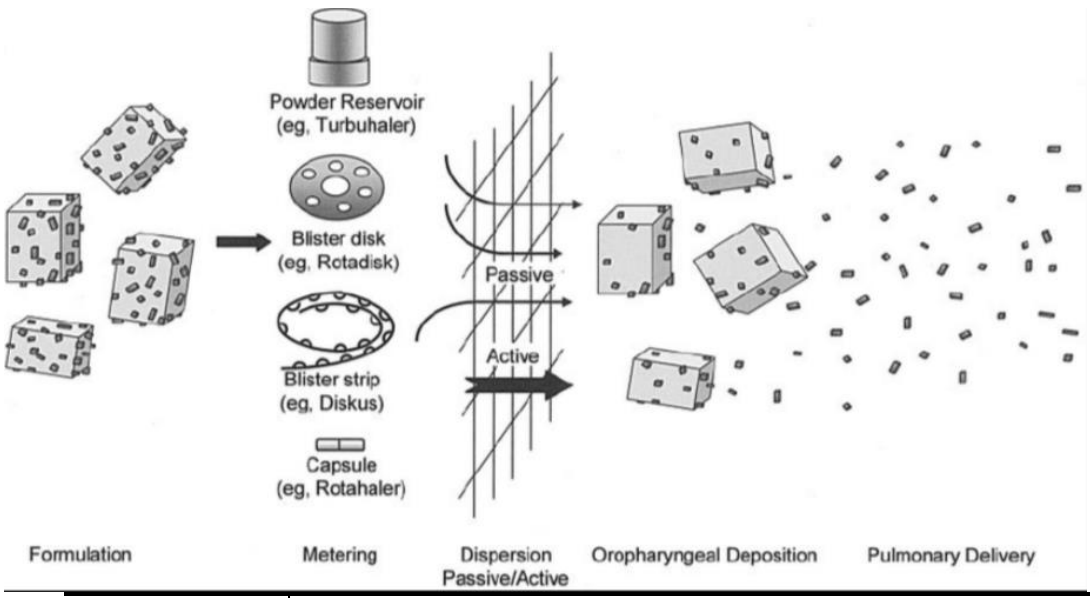
In 1995, it was written: 'it is possibly the "power assisted"multidose dry powder inhalers which represent the real "new wave" of powder aerosol delivery' [12] Today, 20 years later,no active DPI has been successful on the market yet. In the early 1990s, also the first manuscripts about the promising perspectives of aerosolized medication for gene and peptide therapy were published.[13] It was

anticipated that 'in the near future, optimal formulations will be combined with modified aerosol delivery devices to achieve reproducible dosing'.Again 20 years later, it has to be acknowledged that still more efficient aerosol devices are needed, that formulations have to be safer and bioavailability has to be improved. [14]. These examples show how difficult it is to predict the future of DPI therapy. Many large biopharmaceuticals may eventually appear to be unsuitable for inhalation. Smaller molecules, on the other hand, such as levodopa, loxapine, and (locally acting) iloprost or sildenafil (MWs ≪1 kDa) seem to have considerably greater future perspective. Currently, the treatment of infectious lung diseases with inhaled antibiotics is in the spotlight. An advantage is the deposition directly at the site of infection, which makes higher local concentrations, and thus, a more effective therapy possible without increasing the adverse systemic effects. Higher concentrations also could make drug-resistant organisms susceptible to the antibacterial drugs again. Some inhaled dry powder antibiotics are on the market already (e.g. TOBI from Novartis and Colobreathe from Forest Laboratories for CF therapy) or are expected to obtain approval soon (Ciprofloxacin DPI from Bayer HealthCare for bronchiectasis therapy). For all these drugs, classic capsule inhalers are used. Therapy for diseases such as TB is much more challenging because of the higher doses involved. For the future, the success of pulmonary TB treatment may depend on the development of efficient novel high-dose DPIs and synergistic drug combinations to minimize the number of inhalations. Some studies with proven synergistic effect of antibiotic combinations have recently already been reviewed .[15]

6. Principle of dry powder inhaler design

Most DPIs contain micronized drug mixed with larger carrier particles, which prevents aggregation and helps flow property. The dispersion of a dry powder aerosol is directed from a static powder bed. To generate the aerosol, the particles must be moved. Movement can be brought about by several mechanisms viz.; Passive and Active. Passive inhalers employ the patient's inspiratory flow. When the patient activates the DPI and inhales, airflow through the device creates shear and turbulence; air is introduced into the powder bed and the static powder blend is fluidized and enters the patient's airways. 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 Deposition of drug into the lungs is determined by the patient's variable inspiratory airflow. Inadequate drug carrier separation leads to low deposition of drug into the lung which affects the efficiency of DPI. Different dispersion mechanisms have been received for DPIs[16)

6.1 schematic representation of DRY POWDER INHALER DESIGN [16]



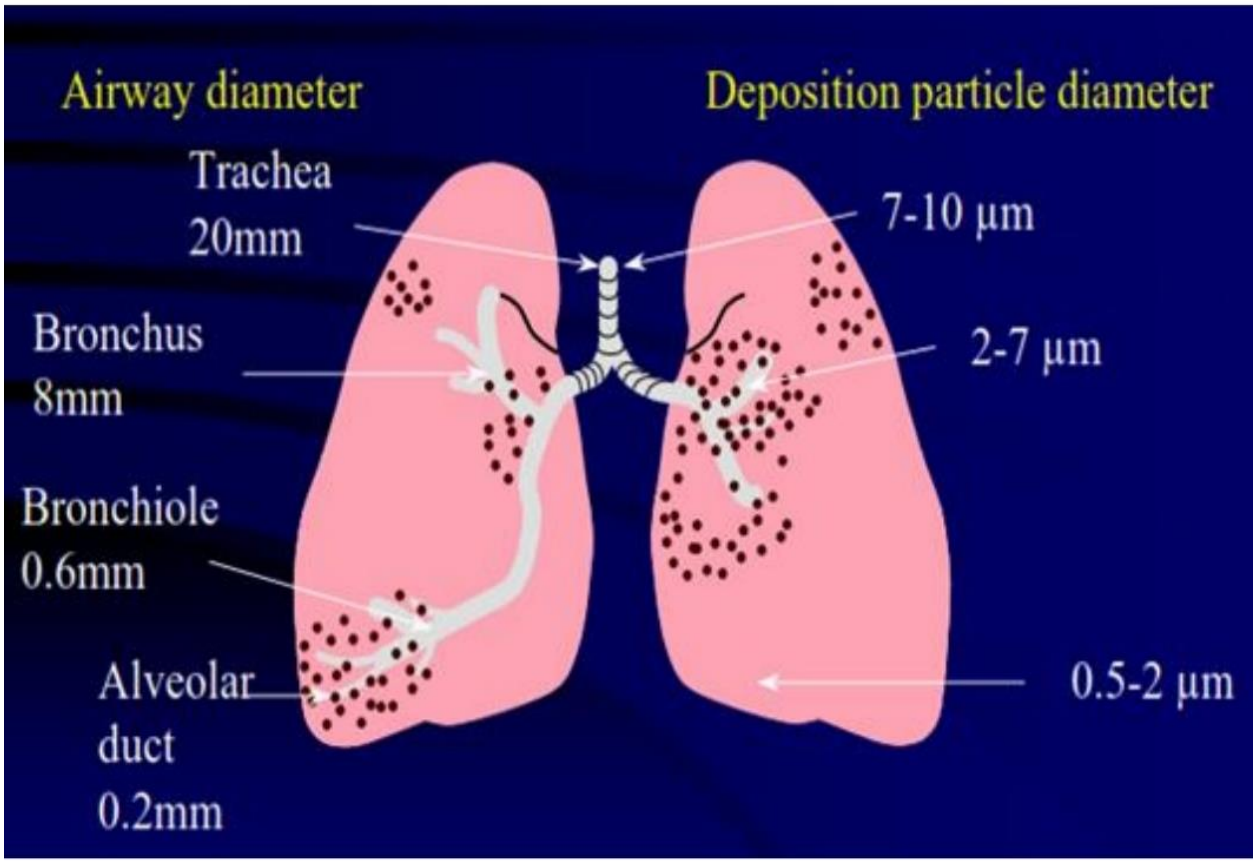
6.2 DPI design issues

The design of a DPI must be coordinated with the formulation of the drug.Inhaler design, particularly the geometry of the mouthpiece, is critical for patients to produce an airflow succulent to lift the drug from the dose chamber or capsule, break up the agglomerates in a turbulent airstream, and deliver a dose to the lungs as therapeutically elective ¢ne particles. [18] The air£ow generated by inhalation directly determines particle velocity and hence the ease with which particles are DE agglomerated. The materials used in the construction of DPIs and characteristics of the formulation (26 ^28) eject electrostatic charge accumulation. Some formulations,as well as inhaler materials, accumulate and retain electrostatic charge more strongly than others, and this will eject both drug retention within these inhalers as well as delivered aerosol behaviour.[19]

7. Lung Deposition Study

The deposition of inhaled particles in the human respiratory tract depends fundamentally on the particle properties and the way the patients breathe at the time of delivery. The vital size characteristic for deposition is called aerodynamic diameter: it is determined by the
actual size of the particle, its shape, and its density. A small amount of particles in the aerodynamic size range of approximately 3.5–6 μm can penetrate to some extent at moderate inspiratory flow rates beyond the central airways into the peripheral region of the lung, while particles less than 3.5 μm and greater than approximately 0.5 μm will largely bypass the bronchial airways during inhalation and penetrate almost entirely
to the deep lung Larger particles are ruled by their inertial mass and will affect in upper airways due to their inertia. This impaction is exacerbated by higher inhalation flow rates, and even at controlled inhalation flow, oropharyngeal deposition indicates very high levels of inter- and intra subject variability Larger particles are ruled by their inertial mass and will affect in upper airways due to their inertia. This impaction is exacerbated by higher inhalation flow rates, and even at controlled inhalation flow, oropharyngeal deposition indicates very high levels of inter- and intra subject variability. [17]

7.1 Diagrammatic representation of lung deposition study [17)



8. Classification of DPI Device[20)

Dry powder inhaler devices are mainly classified by two type

1.single unit dose

2. Multi unit dose

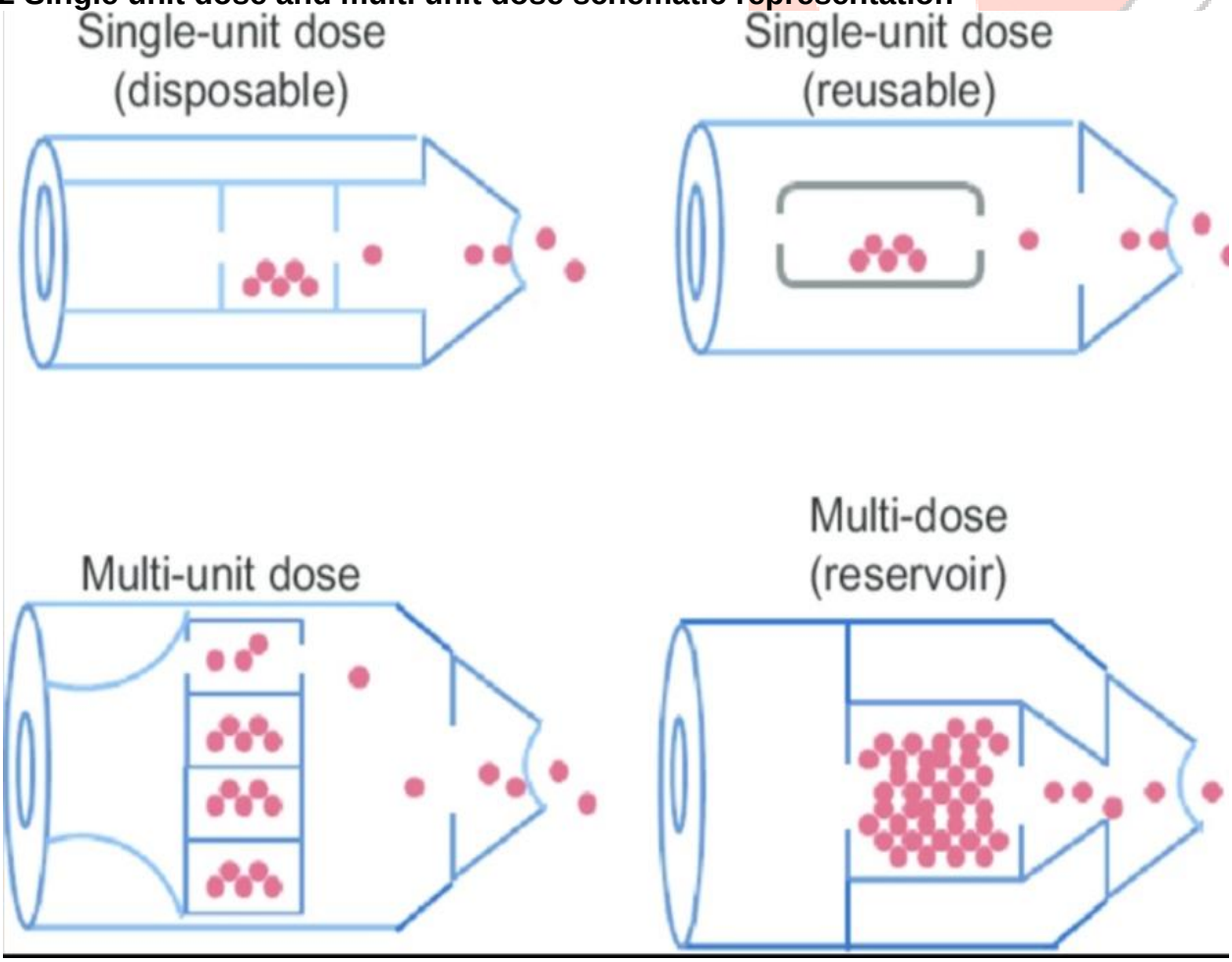
A. Single-unit dose ….

In a single-unit dose device, the drug is formulated as a micronized drug powder and carrier system and supplied in individual gelatine capsules, which are then embedded into the device for a single dose and expelled and discarded after Single unit dose device is further classified into Single unit dose, Single use disposable. In single unit dose; capsule containing dry powder for inhalation are used. These capsules are replaced after used. In case of single use disposable device; powder for inhalation is filled in dose cavity.[fig 1.1]

B. Multi dose reservoir.

Multi dose reservoir is further classified as; multi unit dose, multi dose reservoir. The multi-unit dose device utilizes factory metered and sealed doses packaged in a way that the device can hold multiple doses without having to reload. commonly , the packaging comprises of replaceable disks or cartridges, or strips of foil polymer blister packaging that may or may not be reloadable. This pre-packaged does have the upside of being protected from the environment until use, and ensuring sufficient control of dose uniformity. In case of multi dose reservoir type; device stores the formulation in bulk, and has a built in mechanism to meter individual doses from the bulk upon actuation. One of the main disadvantages of these devices is moisture ingress into the reservoir from patient exhalation or environmental humidity during the life of the product which leads to decrease in flow rate of powder for inhalation. Fig (2.2)

8.2 Single unit dose and multi unit dose schematic representation



9.DRY POWDER INHALER INCLUDES..

1.Aerolizer

2.diskus

3.Ellipta

4.Flexhaler

5.Handhelar

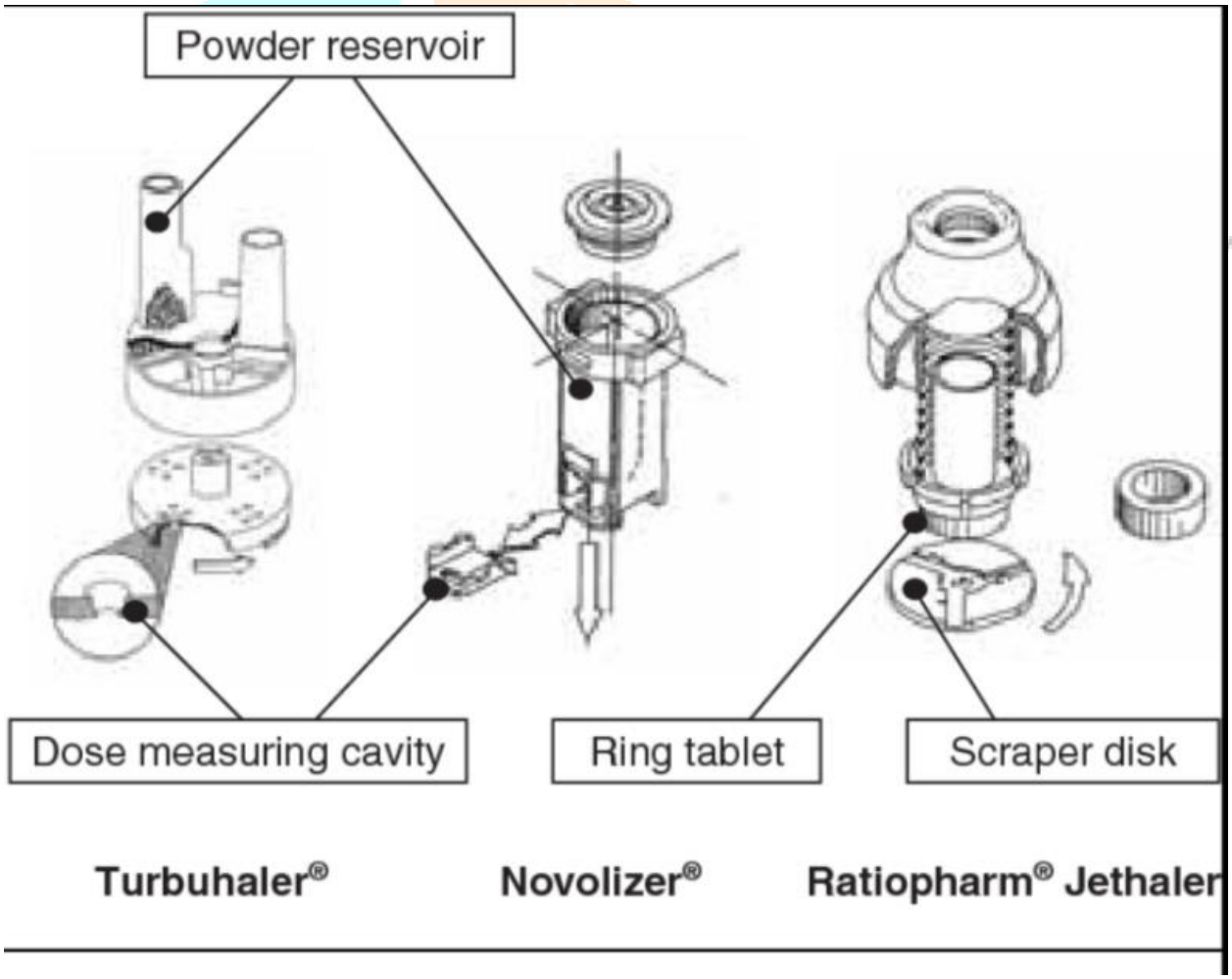
6.Neohaler

7.Pressair

8.Rotahaler

9. Turbuhaler

10. Accuhaler



10.Propellant

In the DPIs there is no use of any propellants.

11.Expert opinion

Many reviews on dry powder inhalation have been published since 1985, but clear visions or strategies for improved DPI design and future DPI development were scarcely presented. Most reviews are confined to a state-of-the-art description with in vitro and in vivo performance data Also, new tools and techniques for DPI device and formulation design have been reviewed and a few have provided characteristics of an ideal DPI without presenting a strategy for achieving these characteristics. Many reviews do have the same key design factors in common, however, such as simplicity, cost-effectiveness, safety, and flow rate-independent lung deposition. Also, the needs for reduction of patient errors and device-formulation integrated development are frequently mentioned. How different is daily practice. The many generic devices on the market increase the number of different inhalers used by the same patient, and it is known that this contributes to the number of patient errors Future improvement of the inhalation therapy is, therefore, primarily served by reducing the number of different inhalers used by the same patient for the same therapy. However, in practice, several plastic manufacturers and consultant agencies continue to develop new DPIS

14. Conclusion

There is now clear evidence that many major players in inhaled drug delivery are prioritizing development of DPI products However, companies developing DPIs face many challenges, and must often make compromises. For instance, seeking solutions to technical problems associated with optimizing pharmaceutical performance may introduce incompatibilities with patient compliance issues. Multidose (reservoir) devices tend to target drug to the lungs more anciently than multiple unit dose devices but tend to have poorer dose uniformity. While it is unlikely that an ideal DPI will ever appear, it is at least possible to list some of the characteristics of an ideal DPI.

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