

PAST AND PRESENT TRENDS OF DRY POWDER INHALER DEVICES: A REVIEW

*Sharath Chandra Reddy, Kapileshwar Swain, H.G.Shivakumar, VNSK Varma, Mahesh G.

Department of Pharmaceutics, JSS College of Pharmacy, JSS University, S. S. Nagar, Mysore, India-570015

*Corresponding Author's E-mail: sharathreddy341@gmail.com

ABSTRACT:

Administration of dry powder inhalers (DPIs) for the management of respiratory diseases has improved significantly in modern lifetime. Currently there is a vast margin of available DPIs that differ not only in the design-plan, effective operational techniques that are requisite, output features and the delivery of drug across an assortment of inhalation pattern. Diverse patient population possibly make choice of individual types of DPI as it is precisely easier to use when in comparison to the other types and preferring the right DPI which shall fulfil a particular requirement for patient will certainly enhance the patient compliance along with the therapy. For instance some DPIs are found to put forth a greater resistance against inspirational flow rate contrast to others which undoubtedly affects the total emitted dose (TED) and also the fine particle fraction (FPF) of aerosol that has been released. As a consequence an individual patient may receive different doses of drug while inhaling from the different DPIs. For that reason, it is essential that the prescriber should be in complete knowledge of the characteristics of different types of DPI, in order to prescribe the device which is most appropriate to the individual patient's needs. The present study sights the features of currently accessible DPIs, evaluates their effectiveness, usage, patient acceptability, drugs administered by that inhaler. The variation in output characteristics, availability and patient's selection between the available devices has revealed to have an effect on treatment efficacy and patient compliance through therapy. Altering the DPI that has been prescribed to the patient to a cost effective or a generic device may consequently affect disease control and thereby amplify the cost of treatment.

Keywords: Dry powder inhaler; Total emitted dose; DPI design; Resistance; Patient acceptability; Fine particle fraction.

INTRODUCTION:

The key rationale for the introduction of DPIs is the irremediable damage that is caused to the ozone layer by the chlorofluorocarbon propellants (CFC)¹ that are frequently used in pressurised metered dose inhalers (pMDIs) for the well gain the Pharmaceutical industry consequently made a firm decision to the development of nonchlorofluorocarbons (CFC) propellants for use in pMDIs and also DPIs which do not make use of any propellant, though the provoked thought of making the reformulation by the change of propellant that is used in pMDIs that are based on hydrofluoroalkanes replacing CFC there are some problems as it is not so simple to substitute with each other producing a similar properties. The first such DPIs were similar to the SpinhalerTM, for example salbutamol² and beclometasone dipropionate³ delivered via the RotahalerTM (GlaxoSmithKline) and Ipratropium bromide delivered by the AerohalerTM (Boehringer- Ingelheim)⁴. Dose emission from some of these DPIs was less than that from that of pMDI and therefore the recommended doses from the DPIs were double those from a pMDI. Gradually, a next generation of novel DPIs became available with extensively different designs, operating characteristics and improved drug delivery to the lung. Some devices contained a reservoir of drug such as the TurbuhalerTM (Astra Zeneca), ClickhalerTM (Innovata Biomed), and EasyhalerTM (Orion), while other devices had individually sealed unit doses of drug, such as the DiskhalerTM (GlaxoSmithKline) and DiskusTM (GlaxoSmithKline). Some DPIs, such as the ClickhalerTM and EasyhalerTM were designed to resemble pMDIs as

closely as possible while other devices, such as DiskusTM, were designed to facilitate easy use and patient acceptability.

Considerations of an ideal device:

1. A device which is simple to use, carry, contains multiple doses, protects the drug from moisture and has a dose indicator.^{5,6,7,8}
2. Should have accurate and uniform dose delivery over a wide range of inspiratory flowrates.^{9,10}
3. Consistent dose delivery throughout the life of the inhaler and consistency of dose when compared to other similar inhalers.¹¹
4. Optimal particle size of drug for deep lung delivery¹².
5. Suitability for a wide range of drugs and doses.
6. Minimum adhesion between drug formulation and devices.¹³
7. Product stability in the device.
8. cost-effectiveness.¹⁴

First generation DPI devices:

First generation DPI devices are single unit dose devices which are breath activated. The dose delivery is dependent on particle size and deagglomeration of drug - carrier agglomerates or drug carrier mixtures delivered by patient inspiratory flow.

Spinhaler:

Spinhaler is a single dose dry powder inhaler device produced by Aventis. Spinhaler, launched by Fisons in the late 1967.¹⁵ It is similar to that of rotahaler which can allow one capsule at one time. The Spinhaler device has been used regularly each day by many asthmatics without mishap¹⁶. It consists of plastic rotar (propeller), piercing needles, and mouth piece shown in the fig.1¹⁷. The spinhaler should be helded in upright position with the mouth piece pointing downwards, the body should be unscrewed from the mouth piece then the capsule should be placed firmly into the cup of the propeller and fix it back to the mouth piece. The capsule can be pierced by sliding the outer sleeve.

Advantages:

1. Spinhaler is a very safe device
2. The Spinhaler minimised the need for accurate coordination by the patient, while also giving

manufacturers the opportunity to formulate powders, which had important advantages regarding shelf-life stability.

Disadvantages:

1. As it is a single dose device it is loaded each time before use.
2. Spinhaler formulations have difficulty of administration and intolerance of use in some patients.

Drugs administered by using spinhaler :

Salbutamol sulphate, Bactomethasone dipropionate, Salbutamol + Bactomethasone dipropionate are the drug administered through spinhaler.

Studies conducted on spinhaler:

Spinhaler showed lowest fine particle fraction (10%) than diskhaler (23%) and turbuhaler (35-40%) at 50-60 l/min.

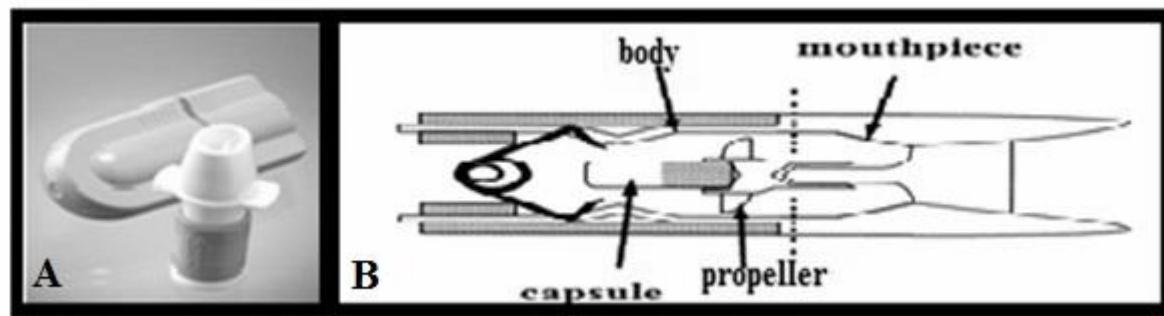


Figure 1: The spinhaler. A) Pictorial Representation B) Schematic Diagram

Rotahaler:

Rotahaler is a single dose dry powder inhaler device produced by GlaxoSmithKline. The capsule filled with inhalation must be placed or pushed into the square hole until the level of the capsule matches to that of the top of the square hole by holding the rotahaler vertically. Now the rotahaler is helded vertically and the barrel must be twisted sharply backward and forward which makes the capsule to separate into two parts (cap and body) and inhaled through the mouth piece adapter¹⁸.

Advantages:

1. It has small convenient size and can be used by most of the patients.
2. No need of breath coordination

Disadvantages:

1. Every time each dose must be loaded
2. Difficult for those with restricted finger or hand movement to load the rotahaler.
3. Not suitable for all ages because of its high inspiratory flow rates requirement.
4. Capsules may sometime affected by humidity.

Drugs Administered By Using Rotahaler:

Table 1: DPI administered through rotahaer

Drug	Strength	Brand
Baclomethasone dipropionate	200mcg, 400 mcg	Becotide rotahaler
Salbutamol	200 mcg	Ventolin rotahaler

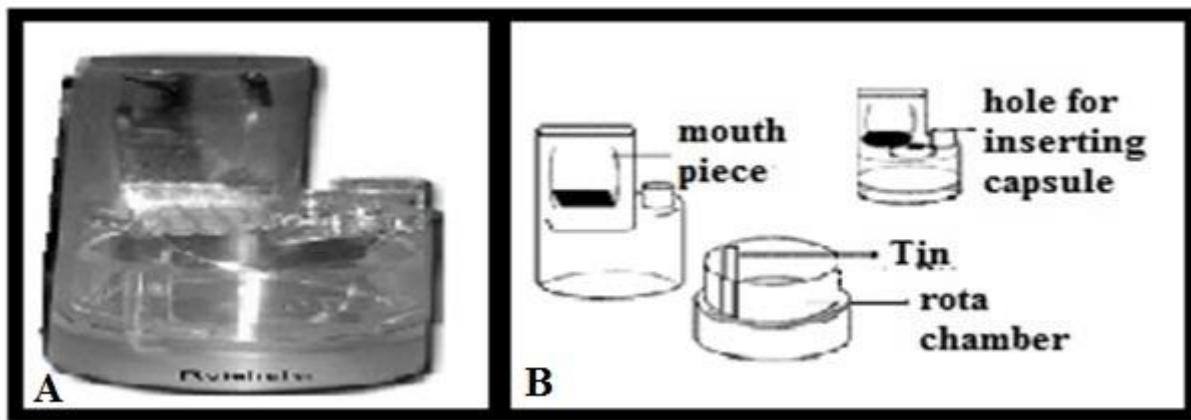


Figure 2: The Rotahaler A) Pictorial Representation B) Schematic Diagram

Cyclohaler:

cyclohaler is a single dose dpi device produced by Pharmachemie. The caps of the cyclohaler was separated and turn the mouth piece adapter by holding the device at the base and the capsule is placed in the compartment of the inhaler and the mouth piece was brought back to the closed position. The capsule was pierced by squeezing the two blue buttons inward on the base of the inhaler and the inhalation was inhaled through the mouth piece¹⁹.

Advantages:

With low intrinsic resistance it releases 70 % of the metered dose at an inspiratory flow of 28 l/min.

Drugs administered by using cyclohaler:

Table 2 indicates the formulation which are administered through cyclohaler

Table 2: DPI administered through cyclohaler

Drug	Strength	Brand
Budesonide	200,400 mcg	Mifloneide®
Formoterol	12 mcg	Foradil®
Beclomethasone	50,100,250 mcg/100,200,400mcg	Becotide®, Miflasone®
Salbutamol	-----	Sultanol®

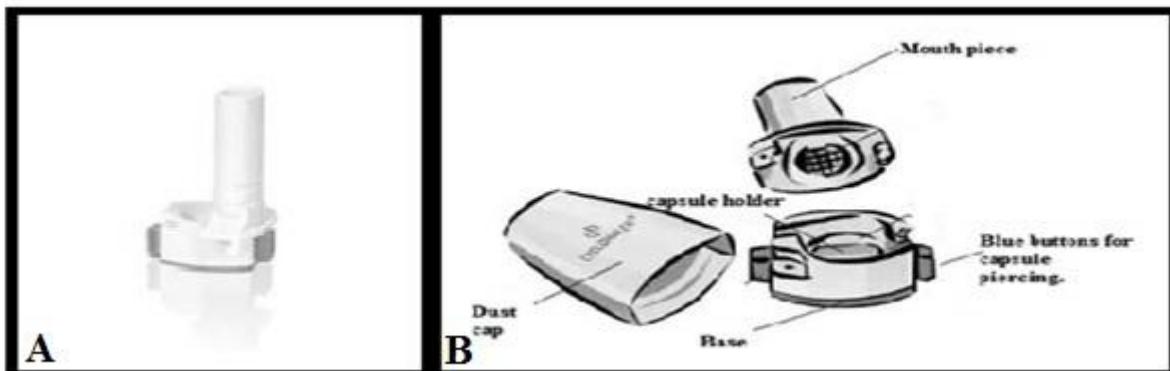


Figure 3: The cyclohaler A) Pictorial Representation B) Schematic Diagram

Twin Caps²⁰

It is a Single dose dpi device produced by Hovione. TwinCaps®, a two-component inhaler with a single step to inhalation, approved in October 2010 for marketing in Japan with Daiichi Sankyo's Inavir® influenza anti-viral product. Two dose compartments are filled directly with drug powder and immediately closed by inserting them

into the inhaler body. In use, the patient pushes the dose compartment sideways and aligns the first dose compartment with the mouthpiece. With the inhaler ready for use, inhalation can take place. For the second dose, the patient pushes the dose compartment in the other direction and inhales again.

Advantages:

Pre-Filled, disposable, low-cost device is needed, with extreme ease of use²¹.

Studies conducted on twin caps:

1. In in-vitro tests, the minimum flow rate at which TwinCaps® has been shown to deliver 95% of the nominal dose is 20 litres per minute
2. TwinCaps® uses a patented dispersion mechanism in which the dose compartment becomes a highly turbulent chamber, maximizing fine particle fractions. FPFs ranging from 25% to 70% have been

obtained, at flow rates of 35 litres per minute (pressure drop 4kpa).

Applications:

TwinCaps has been approved in Japan for the delivery of a long-acting neuraminidase inhibitor for the cure and prevention of influenza.

Drugs Administered By Using Twin Caps:

Anti-virals and antibiotics for lung infection, Oncological drugs, pulmonary hypertension drugs are administered through twin caps.

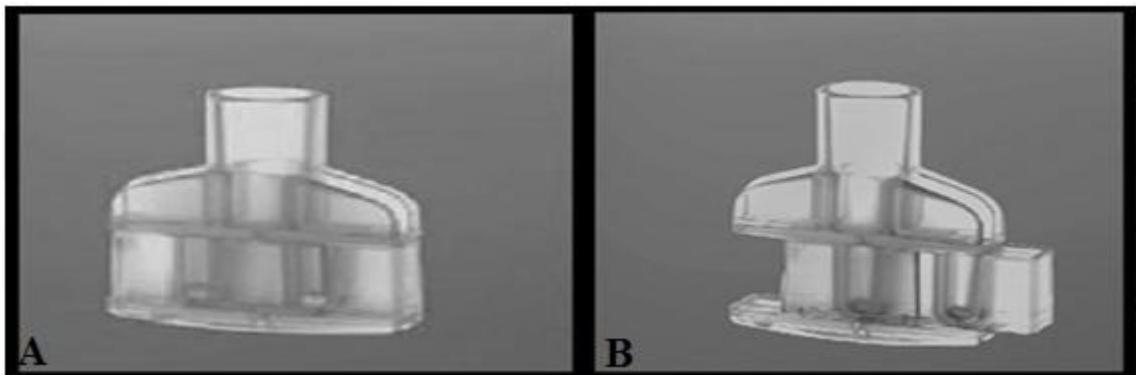


Figure 4: Twin caps A) closed position B) open position

Flow Caps:²²

Flow caps, a single unit dose DPI device produces by havione. FlowCaps® is a capsule-based, re-fillable, passive dry-powder inhaler, holding up to 14 capsules. It is pen-shaped. It is a simple dry powder inhaler that delivers the powder contained in a capsule. The device, trademarked FlowCaps® is a manual device without any kind of motor or active assistance, thus inhalation occurs under the patient's energy.

Advantages:

1. FlowCaps® is one of the most versatile inhalers, able to deliver doses in the low-microgram range, to multi-milligram (depending on API properties, up to 10 mg has been successfully delivered).

2. Emitted dose was found to be 80% and fine particle fraction was to be found in the range of 30-70% of emitted dose.
3. Usable at low airflow rates, from as low as 20 litres per minute and nominal rate 35 litres per minute.
4. Inexpensive due to simple, durable construction.
5. Delivers with high efficiency and low inspiratory effort.

Drugs Administered By Using flow Caps:

Table 3 indicates the formulation which are administered through flowcaps

Table 3: DPI administered through flowcaps

Drug	Strength	Brand
Salbutamol sulphate	200 mcg	Flowcaps

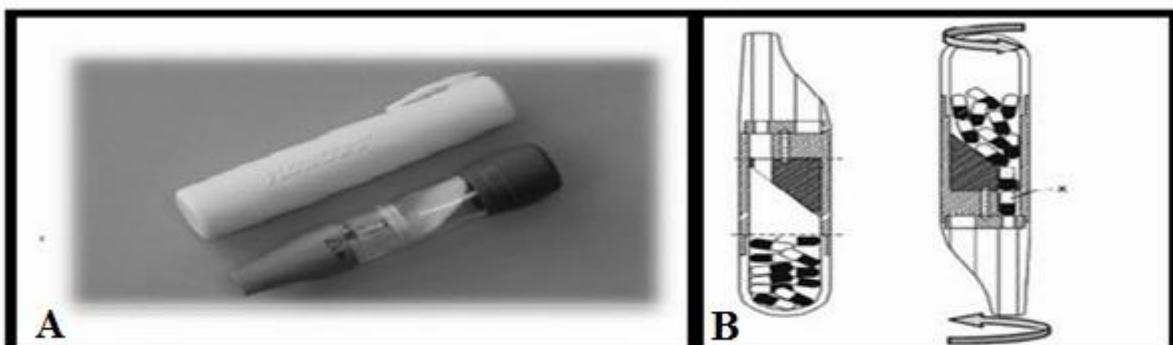


Figure 5: Flowcaps A) Pictorial Representation B) Schematic Diagram

Aerohaler:

Aerohaler is a multi-unit dose dpi device produced by boehringer-ingheim.it consists of mouth piece , magazine. for operation , the mouthpiece was opened, the magazine was slightly turned in clockwise direction until the mark is pointing a particular number , to load six capsules , the mark should point number six and then the magazine was pushed back downwards. the capsules are placed into the holes of the magazine and the inhaler was closed until the click sound was heared. nad the inhalation was inhaled through the mouth piece.

Advantages:

A specially designed magazine which tells the number of capsules left in the aerohaler.

Drugs Administered By Using Aerohaler:

Table 4: DPI administered through aerohaler

Drug	Strength	Brand
Ipratropium bromide	40 mcg	Atrovent aerohaler

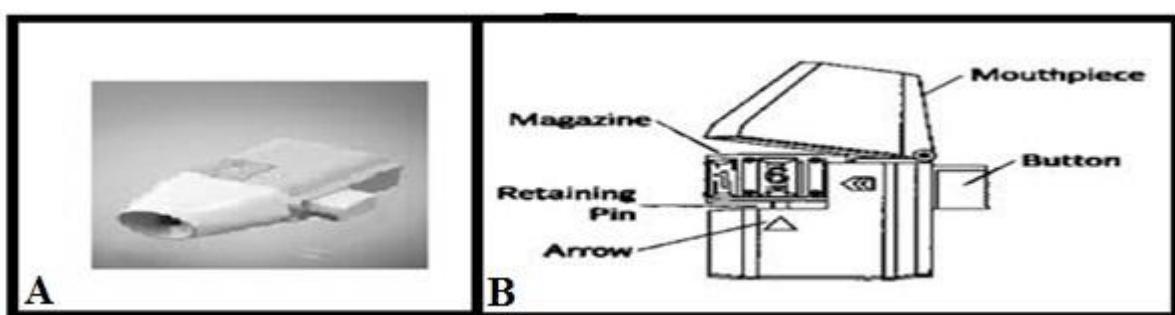


Figure 6: Aerohaler A) Pictorial Representation B) Schematic Diagram

Novalizer:

Novalizer is a multiple dose dpi device produced by ASTA. Pressing down the red dosage button moves the dosing channel backwards releasing powder into the dosing chamber. Simultaneously the tapper knocks against the cartridge – indicated by a noisy double click, so that the powder sinks together and air escapes from the dosing chamber avoiding imprecise dosing. At the same time the colour in the signal window changes from red to green indicating that the inhaler is now ready for inhalation.

Drugs Administered By Using Novalizer:

Table 5 indicates the formulation which are administer through novalizer

Table 5: DPI administered through novalizer

Drug	Strength	Brand
Budesonide	200 mcg	Budelin Novalizer
Budesonide	200,400 mcg	Bijsluiter Novalizer

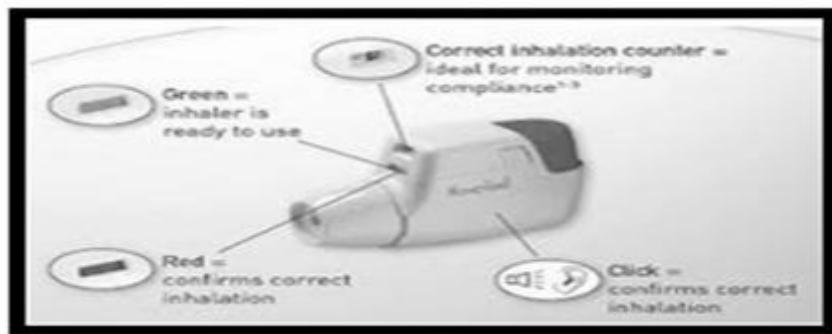


Figure7: Novalizer

Turbuhaler:

Turbuhaler is multidose Dpi device produced by Astrazeneca. Turbuhaler accurately delivers the drug in predetermined doses and it is not possible to exceed the predetermined dose in any case. The dose indicator gives indication to the patient when there are 20 or fewer doses remaining indicated by red mark at the bottom of Turbuhaler. The drug located within this inhaler is formulated as a pellet of a soft aggregate of micronised

drug which may be formulated with or without any additional lactose excipient. The loading of the Turbuhaler must be in upright position and later the usage can be in any position. The Turbuhaler consists of mouthpiece with spiral shaped channels, rotating disk, drug reservoir, turning grip, protective cover with desiccant. when the grip at the base is fully twisted and backed again a single dose is loaded, and the drug get filled into holes of the rotating dosing disc, the size and number of holes can be changed according to the dose .

Under inhalation powder from the holes in dosing disc is lifted into inhalation channel into the deaggregation zone consists of two spiral channels where the powder get deagglomerated under turbulent flow.

Advantages:

1. Do not require any shaking before use unlike pMDI's.
2. All the powder will leave the device with first 200 ml of air inhaled.
3. Easy to use, convenient size and follow the instructions by the patient.
4. No need of breath coordination.
5. Multidose capacity
6. Whistle adapter to asses adequate inspiratory flow available
7. Grip attachment for arthritic or restricted finger movement to load dose.

Disadvantages:

1. No definite guide as to when inhaler is completely empty.
2. Not suitable for all ages.
3. Unless held upright when the loading the turbohaler, the correct dose may not be delivered.

Patient instructions:

1. The patient is advised to inhale forcefully and deeply
2. Keep the device upright until loaded
3. Rinse mouth after use and spit.

Research activities:

15-30% of the dose reach the lungs at 60 l/min and reduces with decrease in flow rate.

Drugs Administered By Using Turbuhaler:

Table 6 indicates the formulation which are administer through turbohaler

Table 6: DPI administered through turbohaler

Drug	Strength	Brand Name
Budesonide	100,200,400 mcg	Pulmicort
Terbutaline sulphate	500 mcg	Bricanyl
Eformoterol fumarate	6,12 mcg	Oxis
Salbutabmol sulphate	50,100 mcg	--

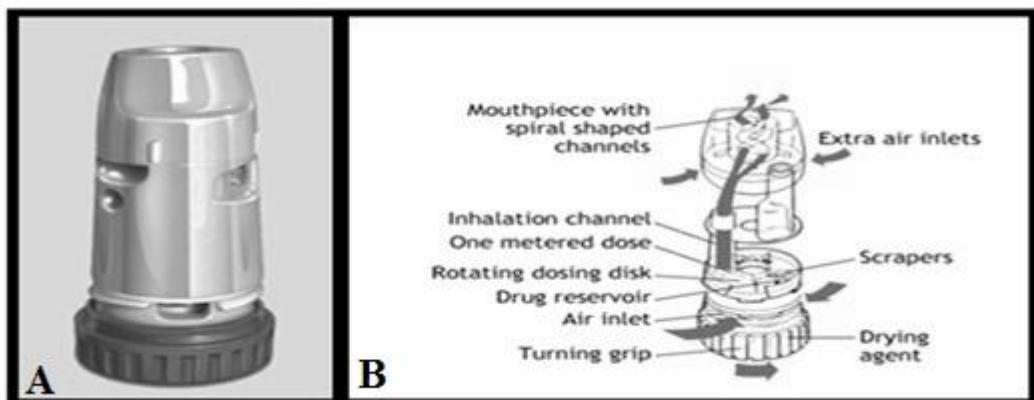


Figure 8: Turbuhaler. A) Pictorial Representation B) Schematic Diagram

Diskhaler:

Diskhaler is a multiunit dose dpi device produced by glaxosmithkline which was alternative to rotahaler²⁴. It consists of medication disk, hinged lid, a piercing needle, and dose indicator. The disk is loaded onto a cartridge unit and slided into the outer body and the piercing needle, punctures the blister so that the medication is inhaled through the mouth piece. The coarse mesh to produce turbulence in the stream of air, leading to deaggregation.

Advantages:

1. Easier to use compared with pMDI's²⁵.
2. Convenient size and design and easy to use.

3. No need of breath coordination.

Disadvantages:

1. limited doses per disk
2. May require more than one inspiration per dose.
3. Not suitable for all ages and require forceful inspiration.

Patient Instructions:²⁶

For loading dose inert disk, slide tray, pierce disk and the inhalation should be quickly and deeply

Drugs Administered By Using Diskhaler:

Table 7 indicates the formulation which are administer through diskhaler

Table 7: DPI administered through diskhaler

Drug	Strength	Brand
Salbutamol	200, 400 mcg	Ventodisks
Baclomethsone Dipropionate	100,200,400 mcg	Becodisks
Salmeterol xinafoate	50 mcg	Servent
Fluticasone propionate	50,100,250 mcg	Flixotide.

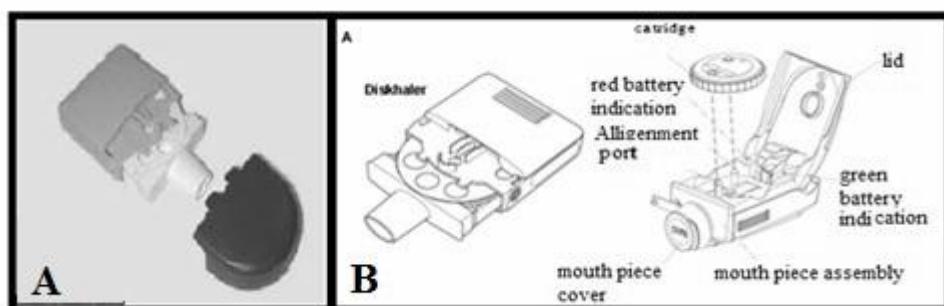


Figure 9: Diskhaler. A) Pictorial Representation B) Schematic Diagram

Diskus (Accuhaler)

Diskus is a multi-unit dose dpi device produced by glaxosmithkline. It is a plastic device, mainly consists of mouthpiece, dose release lever, thumb grip, dose counter, the dosage pack is sealed during the manufacture²⁷. The external lever helps to load new doses. The ratchet-driven index wheel guides the foil strip and aligns each newly - opened blister with air passageways which runs through the top of the body into manifold. This enables the inhaled air to be drawn through the opened blister, aerosolising the contents and delivering the dose through the mouthpiece. As each blister is moved into place, the lid-foil is peeled away from the base-foil by a contracting wheel which collapses progressively as foil collects, thus maintaining alignment of the foils within the device. The spent base-foil is wound into a separate storage chamber designed to retain any residual powder resulting from incomplete inhalation. At each completed movement of the lever the ratchet can be heard and felt to click into place, and an indicator wheel moves on to show the number of doses remaining via a small window in the body. The disc-shaped device should be used in the horizontal plane. The integral outer cover, slid open and closed with the help of a thumbgrip, protects the mouthpiece and the lever. Once opened, the Diskus is primed by sliding the lever back as far as it will go, until a click is heard, followed by inhaling quickly and deeply through the mouthpiece. Closing the outer case automatically resets the lever.

Advantages:

1. Can hold additional doses and easy to use
2. Two hole mouth piece increase turbulence leading to higher deagglomeration .
3. Dose counter indicating how many doses are left.

Disadvantages:

1. Mouthpiece is too shallow.
2. Dose indicator can be reset which may mislead the patient in using the empty inhaler.

Patient instructions:

Open, slide and inhalation should be sucked in quickly and deeply.

Studies conducted:

1. Salbutamol Diskus Showed Low Fine Particle Fraction That Is 28,26,19% At Air Flow Rate 90,60 And 30 Min⁻¹ When Compared With Disk Haler Which Showed 47,40 And 25% Of Fine Particle Fraction At 90,60and 30 Min⁻¹.²⁸
2. Diskus showed 93% accuracy and 93% consistency which compared to diskhaler which showed 56% accuracy and 67% consistency an turbuhaler showed 32% accuracy and 61% consistency²⁹.

Drugs Administered By Using Diskus:

Table 8 indicates the formulation which are administered through diskus

Table 8: DPI administered through diskus

Drug	Strength	Brand
Salbutamol	200 mcg	Ventolin
Salmeterol	50 mcg	Servent
Fluticasone propionate	100,250,500 mcg	Flixotide
Salmeterol + fluticasone propionate	50+100,250,500 mcg	Seretide

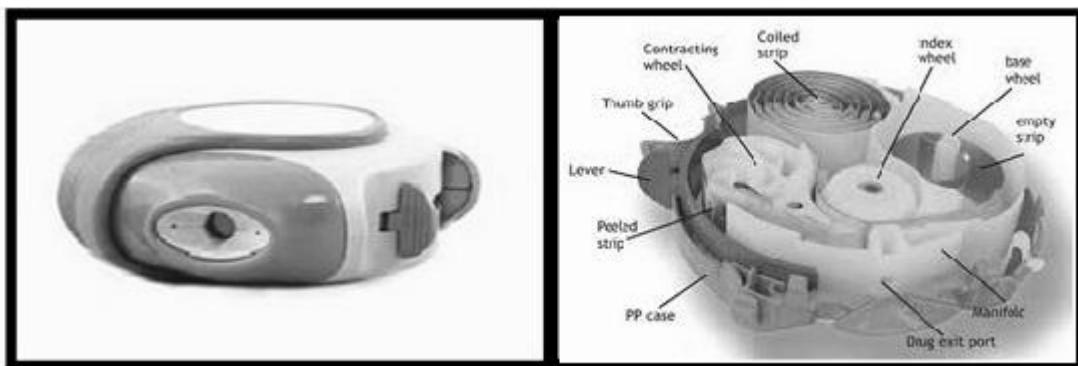


Figure 10: Diskus

Clickhaler:

Clickhaler is a multi-dose dpi device produced by Innovata biomed, click haler consists of 14 plastic components and to two compression springs helps to hold cone tightly and seals the base of the reservoir made of steel, dosing metering elements which consists of metering cone, bulk drug reservoir and compression spring. Due to the gravity the metering cup in the cone are filled as it rotates, carrying the dose of inhalation into the passage, where it aerolises aiding the deaggregation. The dose indicator indicates at last ten doses with red warning.

Advantages:

1. One metered dose delivered at once, reoperation of device automatically removes an unused dose into a waste reservoir.
2. The children Of 6 years of age can achieve active inspiratory flow rates of sufficient drug delivery to lungs^{30,31,32,33,34}.

Disadvantages:

Need a rapid and deep inhalation for optimal dose delivery.

Patient Instructions:

The inhaler should be in upright position, shake and press during priming and inhalation should be steady and deeply.

Research Activities:

A higher proportion of the inhaled dose is delivered into the lungs by clikhaler than baclomethasone pMDI and budesonide turbuhaler^{35,36}.

Drugs administered by using clickhaler:

Table 9 indicates the formulation which are administer through clickhaler

Table 9: DPI administered through clickhaler

Drug	Strength	Brand
Salbutamol	-----	Asmasal
Baclomethasone dipropionate	50,100,250 mcg	Asmabec

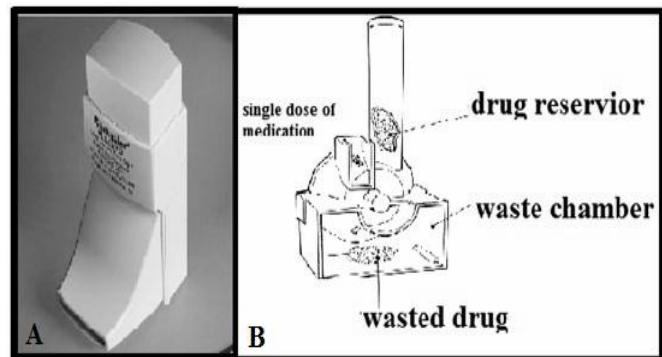


Figure 11: Clickhaler A) Pictorial Representation B) Schematic Diagram

Pulvinal:

Pulvinal is a multiple dose dpi device produced by chiesi farmaceutici. Pulvinal is very similar to that of Turbuhaler by having a mouth piece and basal turning grip and a protective cap which can be unscrewed before use. The priming is done by holding the inhaler in upright position and tapping on the surface to level the powder in metering chamber, then the button on the side of the mouth piece was pressed with one hand while twisting the body a half turn anticlock wise and back again.

Advantages:

Indicates the correct dosing positng by click sound and a red marker when body was twisted and another click sound and the green marker will be indicated when the body is twisted back into the correct position³⁷.

Disadvantages:

It has high resistance to air flow, which made the healthy volunteer unable to reach the flow rate more than 50 lit/min when study conducted on 10 healthy volunteers, during a gamma scintigraphic drug deposition studies

Drugs Administered By Using pulvinal:

Table 10 indicates the formulation which are administer through pulvinal

Table 10: DPI administered through pulvinal

Drug	Strength	Brand
Salbutamol	200 mcg	Pulvinal salbutamol
Baclofemethasone dipropionate	100,200 and 400 mcg	Pulvinal Baclofemethasone dipropionate



Figure 12: Pulvinal

Easyhaler:

Easyhaler is a multiple dose reservoir Dpi device produced by Orion Parma. The sequence of operation and shape is almost similar to that of pMDI.

It consists of seven plastic components and one metering spring. The metering cylinder inside the housing just below the reservoir, which contains sufficient powder for a minimum of 200 doses. the chamber cover is covered by a spring and the overcap, from which two prongs engage directly with ratcheted edges of the metering cylinder. This enables each drug dose to be delivered by pushing down once on the overcap to rotate the metering cylinder. The next dose cavity, filled under gravity with powder from the reservoir, is thus positioned into the mouth piece, through which the drug is inhaled.

Advantages:

1. There is no waste of drug, in case of the double activation the unused dose is returned back to the reservoir.
2. The dose indicator indicated at the last 20 doses with red marker which is connected to ratcheted measuring cylinder.

3. High shielded protective cover is included to reduce moisture penetration into inhaler³⁸.

Disadvantages:

This device have high resistance so require high inspiratory flow rate³⁹.

Studies Conducted:

salbutamol easyhaler showed good correlation with that of ventolin pMDI⁴⁰ and deliver dose and respirable fraction was found to be relatively unaffected after stability studies⁴¹.

Drugs Administered By Using Easyhaler:

Table 11: indicates the formulation which are administer through easyhaler

Table 11: DPI administered through easyhaler

Drug	Strength	Brand
Salbutamol	100,200 mcg	Buventol, Buventol forte.
Baclofemethasone dipropionate	200, 400 mcg	Beclomet Easyhaler.



Figure 15: Easyhaler

Third Generation DPI devices:

These are active devices employs compressed gas or mortar driven impellers or use of electronic vibration^{42,43,44}.

Exubera:

Exubera being an inhalation powder has a white to off-white coloured powder in a unit dosed blister. Each unit dose blister of exubera consists of 1 mg or 3 mg dose of insulin in a homogeneous powder that contains sodium citrate dihydrate, glycine, mannitol and sodium hydroxide. The exubera blister is usually inserted into the inhaler where the patient pumps the handle of the inhaler by pressing a button that causes the blister to get pierced. The insulin inhalation powder is thus distributed into the chamber, letting the patient to breathe in the released aerosolized powder. In standardized *in vitro* test conditions, EXUBERA being a metered dose device delivers a specific amount of insulin dose from the mouthpiece. A small part of the total particle mass as fine particles that are capable of reaching the deep lung is emitted. There can be a retention upto 45% in the 1 mg blister contents, and up to 25% in the 3 mg blister contents in the blister.

Advantages:

Cost effective when compared to that of insulin injection.

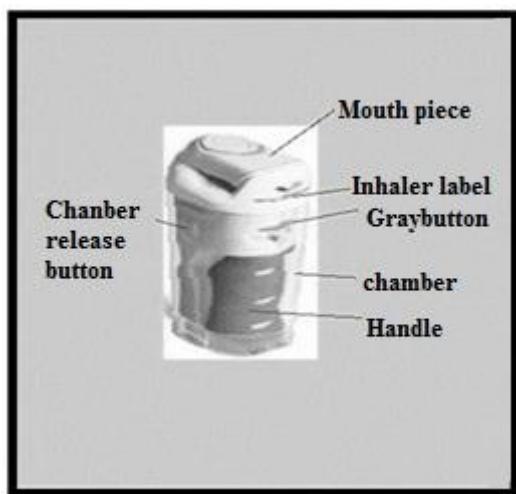


Figure 14: Exubera

CONCLUSION:

The main aim of the article is to emphasize on different DPI devices available dry powder inhalation delivery.

Pulmonary drug delivery is a promising route of administration, being non-invasive and ensuring patient compliance. Till date the production of Inhaler economically with the promising performance is yet to be accomplished. The applications of DPI provide an opportunity to augment the efficiency for aged patients. According to the food and drug administration (FDA) it is recommended to add a necessary part like an integral dose counter as an active part of DPI device. With the advancing technology, the future DPI devices may add other features like dose reminder, audiovisual signals of dose delivery, measurement of flow rates during inhalation. In addition to device design great concern is between interaction between the formulation device, the factors which needs to be given due importance before designing a new device. The consequence of DPI formulation (type of lactose and physicochemical properties of drug), capsule material and inhalers on the charge and polarity of DPI aerosols are dependent on the type of inhaler, carrier size, and capsule size that are considered and used in the experimentation process. Before formulating the factors which influence the formulations must be considered for an ideal inhaler which would result in the product which tend them to be reliable, efficient, user and eco-friendly, and cost effective. Drug delivery mechanism is essential to rationalise design of Devices with promising performance. In days to come the drugs synthesized biotechnologically require the aid of devices which can deliver the drug efficiently targeting the lower airway of lungs. There is a great demand for the innovative DPI's for the treatment of the conditions of like diabetes, cancer, CNS disorders and cystic fibrosis. The recent focus of regulatory requirements mandates that there should be a minimum dependence on the inspiration flow rates of an individual as well as reproducible aerosol performance to attain optimum compliance and activity. The farther development of DPI Products should focus on both inhaler device powder formulation for desired therapeutic benefits over risks. This may also lead to development of a device which is disposable in nature the emancipates the regular cleaning of device time to time, eliminating the concerns for the stability thereby rendering it less expensive and higher patient compliance and safety. Therefore to explore the full potential of DPI's which are of less expenditure and budget to Pharmaceutical Giants and patients innovation of a Novel device with augmented lung targeting, disposition and reliability on device would form a key area in days to come and explore.

REFERENCES:

1. Noakes TJ, CFCs, their replacements and the ozone layer, *Journal of Aerosol Medicine*, 1995, 8, S3-7.
2. Hetzel M, Clark T, Comparison of salbutamol Rotahaler with conventional pressurized aerosol, *Clin Allergy*, 1977, 7, 563-568.
3. Edmunds AT, McKenzie S, Tooley M, Godfrey S, A clinical comparison of beclomethasone dipropionate delivered by pressurized aerosol and as a powder from a Rotahaler, *Arch Dis Child*, 1979, 54, 233-235.
4. Pakes GE, Brogden RN, Heel RC, Speight TM, Avery GS, Ipratropium bromide: a review of its pharmacological properties and therapeutic efficacy in asthma and chronic bronchitis, *Drugs* 20, 1980, 20, 237-266.
5. Ashurst I, Malton A, Prime D, Sumby B, Latest advances in the development of dry powder inhalers, *Pharm Sci Technol Today*, 2000, 3, 246-256.
6. Sheth KK, Innovations in Dry Powder Delivery, in Dry Powder Inhalers in the Treatment of Asthma: A continuing education monograph for physicians,nurses, pharmacists, physician assistants and respiratory therapists, Meniscus, USA, 2002, 3-9.
7. Helen B, Development of inhaler technology, *Med Dev Technol*, 2001, 12, 24-26.
8. Newman SP, Dry powder inhalers for optimal drug delivery, *Expert Opin. Biol. Ther.*, 4, 23-33.
9. Ashurst I, Malton A, Prime D, Sumby B, Latest advances in the development of dry powder inhalers. *Pharma Sci Technol Today*, 2000, 3, 246-256.
10. Chrystyn H, Closer to an 'Ideal Inhaler' with the Easyhaler: an innovative dry powder inhaler, *Clin. Drug Invest*, 2006, 26, 175-183.
11. Newman SP, Busse WW, Evolution of dry powder inhaler design, formulation and performance, *Respir Med*, 2002, 96, 293-304.
12. Clark AR, Medical aerosol inhalers: past, present and future, *Aerosol Sci Technol*, 1995, 22, 374-391.
13. Byron, Peter R, Drug delivery devices: issues in drug development, *Proc Am Thoracic Soc*, 2004, 1, 321-328.
14. Bisgaard H, Automatic actuation of a dry powder inhaler into a nonelectrostatic spacer, *Am J Respir Crit Care Med*, 1998, 157, 518-521.
15. Innovations in Pharmaceutical Technology By Rob Clayborough and Iain Simpson at Sagentia ;74
16. D C QUANTOCK DC: Director of Medical Affairs, Fisons Ltd Pharmaceutical Division, British Medical Journal, Loughborough 1977.
17. Aerosol research [[http://www.aerosols.wustl.edu/ education/Healthaerosol/section04-1b.html](http://www.aerosols.wustl.edu/education/Healthaerosol/section04-1b.html)]
18. National Jewish Health [<http://www.nationaljewish.org/healthinfo/medications/lung-diseases/devices/dry-powder/rotahaler>]
19. Characteristics of the aerolizer/ cyclocaps dry powder inhaler [<http://www.admit-online.info/index.php?id=130&L=0>]
20. Hovione twin caps [<http://www.hovione.com/Twincaps/Twincaps.asp>]
21. Hovione twin caps [http://www.hovione.com/h_press/press-rel/pro_twin_caps]
22. Hovione flow caps [<http://www.hovione.com/Flowcaps/Flowcaps.asp>]
23. Wetterlin K, Turbuhaler: a new powder inhaler for administration of drugs to the airways. *Pharm Res*, 1988, 5, 506-508.
24. Ganderton D, Kassem NM, Dry powder inhalers:Advances in Pharmaceutical Sciences. Ganderton D :London: Academic Press; 1992. P.165-191.
25. Drepaul BA, Payler DK, Qualtrough JE, Beclotide or Becodisks - A controlled study in general practice. *Clin Trials J*, 1989, 26, 335-344.
26. Gustafsson P, Taylor A, Zanen P, Chrystyn H, Can patients use all dry powder inhalers equally well, *Int J Clin Pract*, 2005, 59,149: 13-18.
27. Brindley A, Sumby BS, Smith IJ, Prime D, Haywood PA, Grant AC, Design, manufacture and dose consistency of the Serevent Diskus inhaler, *Pharm Technol Eur*, 1995, 7(1),14-22.
28. Srichana T, Martin GP, Marriott C, Dry powder inhalers: the influence of device resistance and powder formulation on drug and lactose deposition in vitro, *Eur J Pharm Sci*, 1998, 7, 73-80.
29. prime D, Grant A, slater A, woodhouse R, A critical comparison of the dose delivery characteristics of four alternative inhalation devices delivering salbutamol: pressurized metered dose inhaler, Diskus inhaler and Diskus. *Respir med*, 1999, 12, 75-84.
30. Callaghan C, Everard ML, Bush A, Hiller EJ, Ross-Russell R, Keefe P, Weller P, Salbutamol dry powder inhaler: efficacy, tolerability and acceptability study, *Pediatr Pulmonol*, 2002, 33, 189-193.
31. Adler LM, Anand C, Wright FG, Barrett CF, McKeith D, Clarke WIC, Maksimczyk P, Martin GDR, McKinnon C, Raffles AKM, Buck H, Efficacy and tolerability of beclomethasone dipropionate delivered by a novel multidose dry powder inhaler (Clickhalerw) versus a metered dose inhaler in children with asthma, *Curr Ther Res Clin Exp*, 2001, 62, 758-769.
32. Nantel NP, Newhouse MT, Inspiratory flow rates through a novel dry powder inhaler (Clickhaler) in pediatric patients with asthma, *J Aerosol Med*, 1999, 12, 55-58.
33. Parry-Billings M, Birrell C, Oldham L, Callaghan C, Inspiratory flow rate through a dry powder inhaler (Clickhaler) in children with asthma, *Pediatr Pulmonol*, 2003, 35, 220-226.
34. Jones RD, Morice AH, Inspiratory flow rates through a novel dry powder inhaler (Clickhaler) in pediatric asthma patients. *Am J Respir Crit Care Med*, 1998, 157, A124.
35. Warren SJ, Rowe AM, Taylor G, Efficient lung deposition of beclomethasone dipropionate (BDP) via a novel multidose dry powder inhaler compared to a conventional pressurised metered dose inhaler, *Pharm Res*, 1997, 14(11), S131.
36. Warren S, Taylor G, Smith J, Buck H, Parry-Billings M, Gama scintigraphievaluation of a novel budesonide dry powder inhaler using a validated radiolabeling technique, *J Aerosol Med*, 2002, 15, 15-25.
37. Pitcairn G, Lunguetti G, Ventura P, Newman S, A comparison of salbutamol inhaled from a new dry powder inhaler, at two inhaled flow rates. *Int J Pharm*, 1994, 102, 11-18.
38. Malinen A, Laurikainen K, Silvasti M, Toivanen P, Nieminen NM, New model of Easyhaler is clinically equally effective as compared with the former model. *Eur Respir J*, 1997, 10 (25), S127.
39. Steckel H, Muller BW, In vitro evaluation of dry powder inhalers: drug deposition of commonly used devices, *Int J Pharmaceutics*, 1997, 154, 19-29.
40. Vidgren M, Silvasti M, Vidgren P, Easyhaler multiple dose powder inhaler—practical and effective alternative to the pressurized MDI, *Aerosol Sci Technol*, 1995, 22, 335-345.
41. Silvasti M, Sormunen H, Laurikainen K, Lahelm S, Toivanen P, Easyhaler, a novel multidose powder inhaler—comparison with metered dose inhaler. *Drugs Today*, 1996, 32, 353-363.
42. Crowder TM, Louey, MD, Sethuraman VV, Smyth HDC, Hickey AJ, An odyssey in inhaler formulations and design. *Pharm Technol*, 2001, 25, 99-113.
43. Brown BAS, Rasmussen JA, Becker DP, Friend DR, Apiezo-electric inhaler for local and systemic application. *Drug Deliv Technol*, 2004, 4, 90-93.
44. Young PM, Cocconi D, Colombo P, Bettini R, Price R, Steele DF, Tobyn MJ, Characterization of a surface modified dry powder inhalation carrier prepared by particle smoothing, *J. Pharm. Pharmacol*, 2002, 54, 1339-1344.