 International Standard Serial Number (ISSN): 2319-8141

International Journal of Universal Pharmacy and Bio Sciences 9(3): May-June 2020

INTERNATIONAL JOURNAL OF UNIVERSAL PHARMACY AND BIO SCIENCES

IMPACT FACTOR 4.018***

ICV 6.16***

Pharmaceutical Sciences

REVIEW ARTICLE……!!!

DRY POWDER INHALER DEVICES FOR PULMONARY DRUG DELIVERY

Amine Ousaid*, Jaouad Akrim, Youssef Khayati

Laboratory of Drug Sciences, Biomedical and Biotechnological Research, Faculty of Medicine and Pharmacy, Hassan II University. Casablanca. Morocco.

KEYWORDS:

Devices; Dry Powder Inhaler; Pulmonary Drug Administration.

FOR CORRESPONDENCE:

Amine Ousaid *

ADDRESS:

Laboratory of Drug Sciences, Biomedical and Biotechnological Research, Faculty of Medicine and Pharmacy, Hassan II University. Casablanca. Morocco.

ABSTRACT

The dry powder inhalers are highly efficient systems for pulmonary drug delivery and has become widely known as a very attractive platform for drug delivery. They are being used for the treatment of asthma, chronic obstructive pulmonary disease and cystic fibrosis by many patients. There are over 20 devices presently in the DPI market. DPIs are preferred over nebulizers and conventional metered dose inhalers. However, they are also complicated systems, some of the challenges of DPI are dependence on inspiratory flow, systemic absorption due to deposition of drug in deep lung, and increase in upper airway deposition of a large fraction of coarse particles. This article reviews DPI devices currently available, their advantages and disadvantages, the design of the different inhalers.

INTRODUCTION:

A dry-powder inhaler (DPI) is a device that delivers medication to the lungs in the form of a dry powder. DPIs are commonly used to treat respiratory diseases such as asthma, bronchitis, emphysema and chronic obstructive pulmonary disease.

They offer an alternative delivery system to patients who are unable to synchronize the discharge and inhalation of metered dose inhalers.

They are bolus drug delivery devices that contain solid drug, suspended or dissolved in a non polar volatile propellant or in dry powder inhaler that is fluidized when the patient inhales. Many factors affect the device performance. Some of the factors include mouth piece configuration, grid structure and mouthpiece length, impaction angle of the powder with devices and air inlet size. Due to the complexity and various configurations of the device, there are numerous device designs.

This review is to give a brief summary of the currently available devices and highlights some new developments. DPI devices can be categorized as capsule based, blister based, cartridge based and other types.

DRY POWDER INHALER

Dry powder inhaler (DPI) is a vehicle that is used to transfer drug into body. The efficient delivery of drug into the lungs depends on performance of drug delivery system and powder formulation. DPI and drug chemistry needs to fulfill safety, efficacy, bio-equivalence and reliability for product approval.

DPIs provide alternative to metered-dose inhaler(MDI). DPI require a measured dose of powder ready to use by patient use. The drug may be held either in capsule for manual loading or installed in device and ready to use.

Once loaded the patient puts mouth piece of inhaler into their mouth and take a deep inhalation holding the amount of dose delivered is less than few tens of milligrams in a single push. Larger powder may cause cough.

Most DPIs depends on the force of patient to inhale powder from DPI. For this reason, particles that are small that are unable to reach lungs any lead to reduced drug delivery. Due to various design and configuration there are number of devices.

Some categories of DPI devices are described in Figure 1.

Fig. 1. Some of currently available DPI devices.

A:Inspiromatic device; B:Twisthaler; C:Nexthaler; D:Handihaler ; E:Turbohaler; F:Easyhaler

KEY PHYSICAL ATTRIBUTES FOR AN INHALER DELIVERY SYSTEM

- Easy to use (Simple operation, dose counter, dose-ready indicator, patient feedback of dose administration).
- Discreet, compact and portable.
- Easy dose loading (Uniform dose through life).
- Clean and hygienic.
- Separate doses.

ADVANTAGES AND LIMITS OF DPI

ADVANTAGES	DISADVANTAGES
No coordination required	Forceful inhalation needed to aerosolize particles
Not to be used with spacer	More expensive than MDIs
Portable and compact; multi-dose devices available	Only used with drug that is dispensed with the device
Single-dose devices with doses kept separately in sealed packs	Must be kept upright or horizontal during inhalation
Breath actuated	Patients not to exhale into device once prepared

Chrystyn & Price. Prim Care Resp J 2009; Laube et al. Eur Respir J 2011

Table 1. Advantages and disadvantages of DPI

PRINCIPLES OF OPERATION AND TECHNOLOGY OF DISPERSION

Figure 2 shows the principles of DPI design. Most DPIs contain micronized drug blended with larger carrier particles, which prevents aggregation and helps flow.

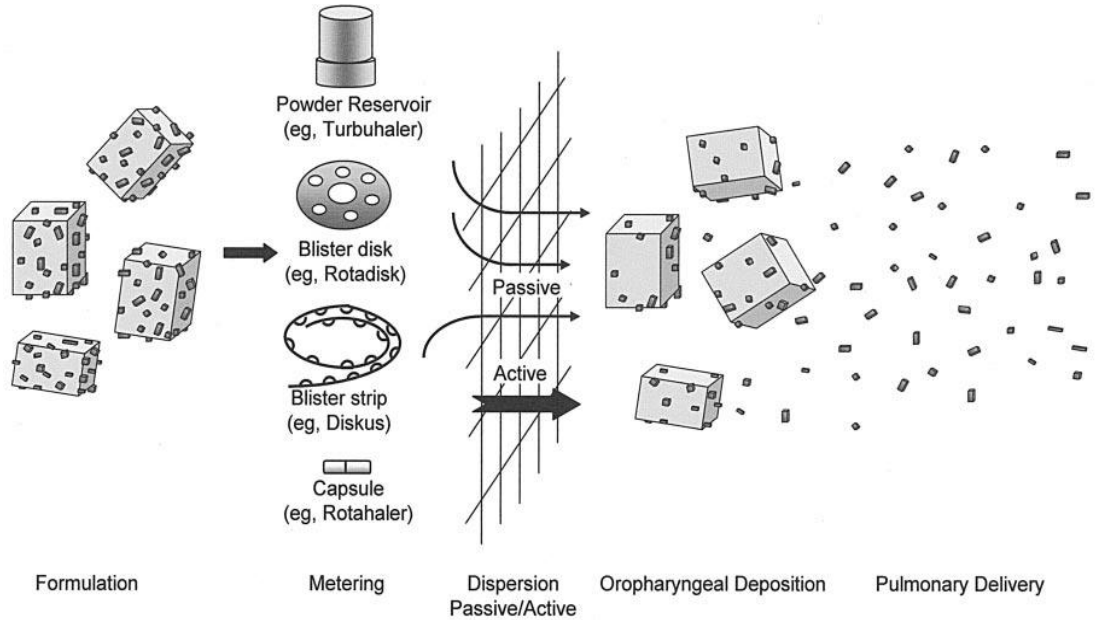

Fig. 2. Schematic diagram of dry powder inhaler formulations and dispensing powder mechanisms.

IDEAL CHARACTERISTICS FOR DPI DEVICE

- Device should be easy to use.
- Convenient to carry.
- Contain multiple doses
- Protect the drug from moisture.
- Indicate the doses remaining i.e. audiovisual.
- Accurate and uniform delivery of doses over wide range of inspiratory flow rate.
- Consistent dose delivery throughout the life of the inhaler.
- Optimal particle size of drug for deep drug lung delivery
- Suitability for a wide range of drugs and doses.
- Minimum adhesion between drug formulation and devices.
- Product stability in the device.
- Cost effectiveness.

CLASSIFICATION OF DPI DEVICE

Dry powder inhaler devices are mainly classified by dose type. (Fig. 3)

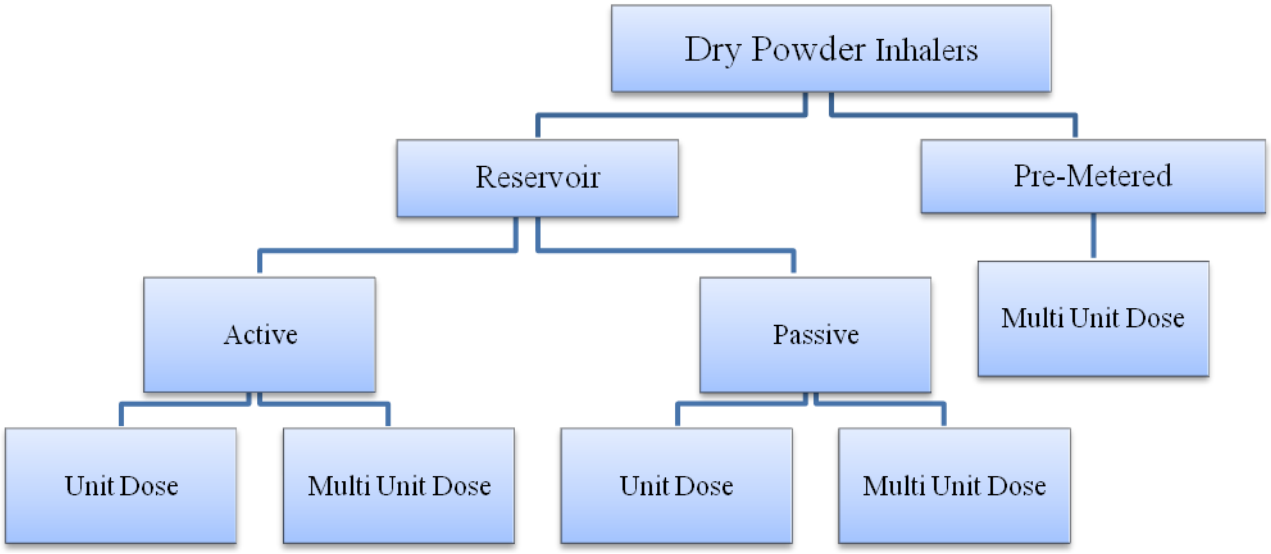

Fig. 3. Classification of DPI device

- **Capsule Based Devices**

Capsule based devices generally have a chamber where capsule is placed. The capsule is broken by external force by action of twist or pins. Powder is released from the capsule and inhaled by patient. Examples of Capsule based devices are listed in *Table 2.*

No	DEVICE NAME
1	Aerohaler
2	Aeroliser (Fig. 4)
3	Arcus
4	Breezhaler (Fig. 5)
5	DOTT DPI
6	FlowCaps
7	Handihaler
8	Podhaler
9	Redihaler
10	Spinhaler
11	XCaps

Table 2. Examples of capsule based inhaler devices

- Aerolizer (Fig. 4) consists of capsule chamber, air inlet, pins near the air inlet, grid in between the capsule chamber and the mouthpiece. The powder is released from capsule by piercing the capsule by the pins. It is usually used for asthma.

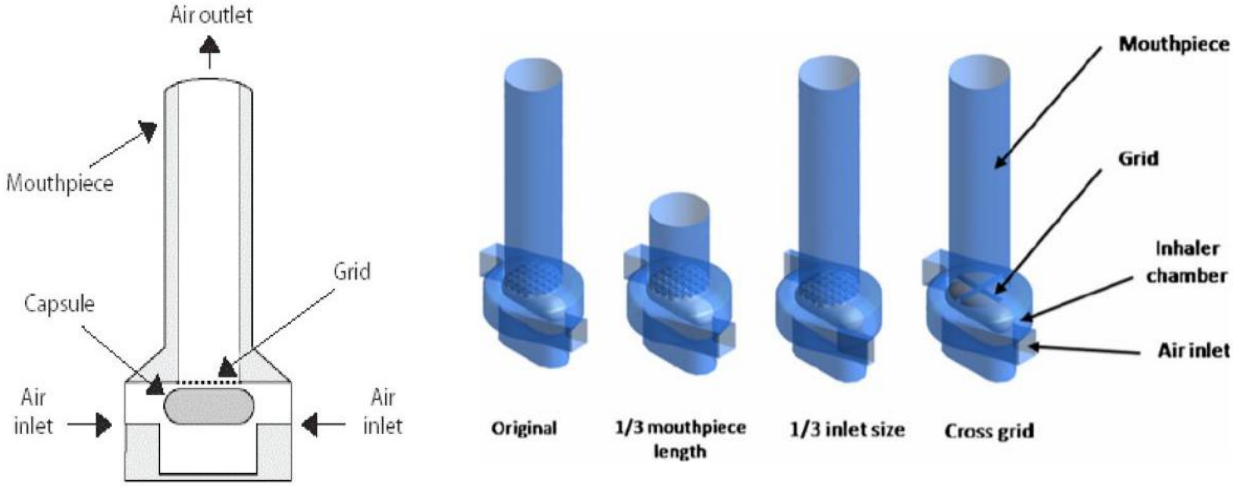

Fig. 4. Illustration of Aerolizer

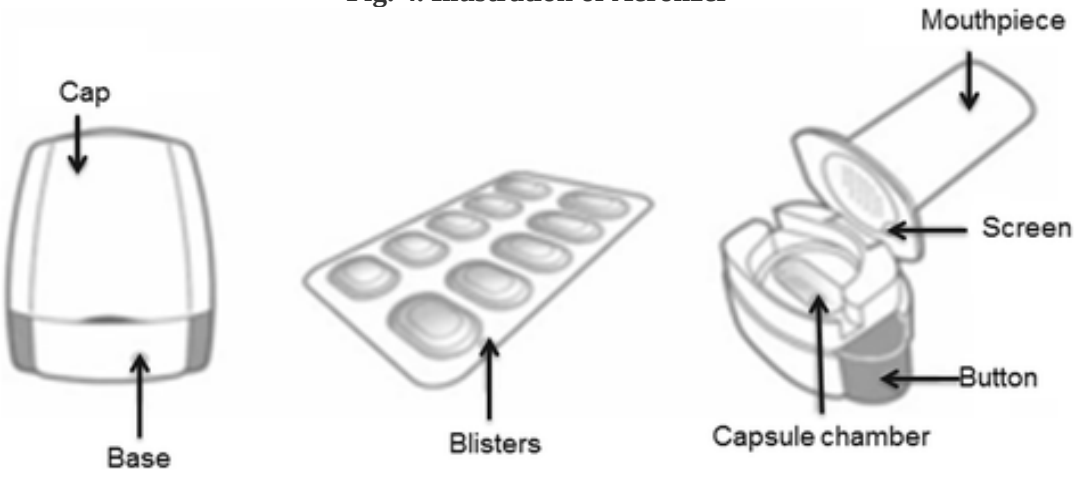

Fig. 5. The Breezhaler capsule-based dry powder inhaler

- Rotahaler (*Fig.* 6) The device has a barrel-shaped cap and body shell. The cap has two holes, one for capsule insert and the other one is for air inlet during aspiration. The body serves as a mouthpiece to be inserted into mouth. There is a grid between the cap and the body. The grid has many functions, it generates small eddies and allows high speed collisions for the drug particles. The space between cap and grid is the capsule chamber. When in use, the patient inserts the capsule prefilled with the drug into the cap. The drug powder is released from the capsule into the device chamber by twisting the cap and body. Powder will fluidize when the patient breathes through the mouthpiece. Drug particles pass through the grid and eventually deposit in the lung following the air stream.

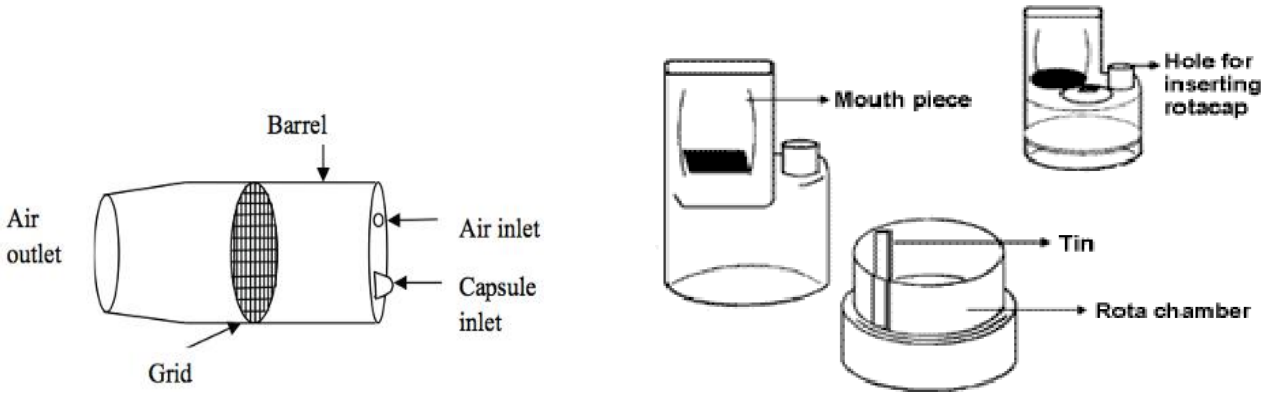

Fig. 6. Illustration of Rotahaler

- **Blister Based Devices**

The blister based DPIs have a ring of aluminum blister inside the DPI device. Each blister contains one dose of drug pre-dispensed. Dose is indicated by a dose counter installed in DPI. Drug powder is released by piercing the blister before inhalation. The drug powder is carried away by the air stream created by the patient's inhalation.

No	DEVICE NAME
1	Acu Breathe
2	Aspirair
3	Diskhaler
4	Diskus
5	Forspiro
6	Gyrohaler
7	Meadwest Vaco
8	Microdose DPI
9	Pro haler
10	Votran DPI

Table 3. Exemple of Blister based inhaler devices

- Microdose DPI is an example of blister based devices. It has a piezo electric vibrator that converts electrical energy to mechanical motion. A blister is burst before patient breathe. Activation of this vibrator depends on threshold level of air flow inhaled by patient.

  The vibrator pierced the blisters and release the drug to be inhaled by patient. Micro dose has been developed specially for pulmonary delivery of drugs (Fig. 7).

Inhaled atropine is being developed as a systemic and pulmonary treatment for the extended recovery period after chemical weapons exposure. Micro dose DPI is used for delivery of Atropine.

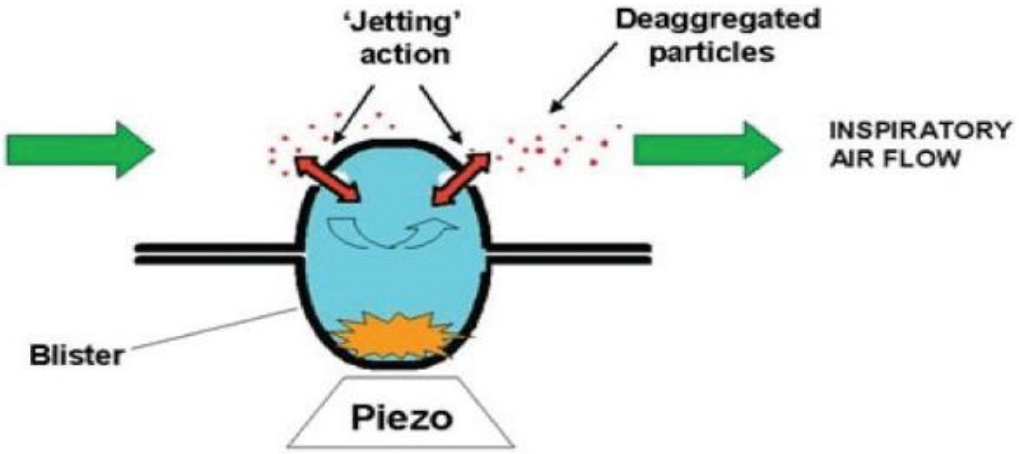

Fig. 7. Illustration of Microdose DPI.

- **Cartridge Based Device**

The cartridge based device has a powder chamber to store drug powder. The device has a mechanism to dispense the powder each time during inhalation. This Multiple use device has a dosing meter. *Table 4* summarizes some examples of cartridge based devices.

No	DEVICE NAME
1	E flex
2	NEXThaler
3	PADD
4	Pulmojet
5	Spiromax
6	Swinghaler
7	Ultrahaler
8	VIP inhaler
9	Xectovair

Table 4. Exemple of Cartridge based inhaler devices

- The Novolizer is example of cartridge based device. It has a button connected with a lever. The push lever is connected with a bar that is linked with the powder chamber. It can be used multiple times (Figure 8).

  A Metered amount of drug powder is stored in a metering cavity besides the sliding bar. The metered drug powder is then moved to powder channel through the sliding bar when the button is

pressed. Drug powder in the powder channel is then inhaled into the lung through the cyclone based mouthpiece.

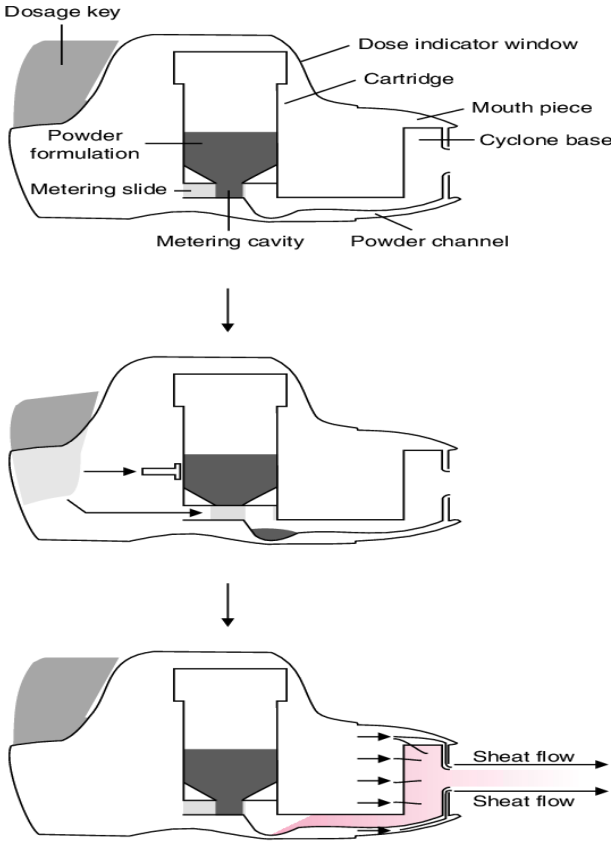

Fig. 8. Illustration of Rotahaler

CONCLUSION

Drug powder inhalation is fast growing area. These devices play key role in efficient inhalation of drug and provide quick intake of drug. This review summarizes basic information regarding DPIs, types of devices and their mechanism.

ACKNOWLEDGEMENTS

I would like to thank Pr. Khayati and Pr. Akrim, for their valuable contributions and timely advice that shaped this work.

DECLARATION OF INTEREST

The authors report no declarations of interest.

REFERENCES:

1. Coates M, Chan HK, Fletcher D, Chiou H (2007) ,Influence of mouth piece geometry on the aerosol delivery performance of a dry powder inhaler. Pharm Res 24: 1450-1456.
2. Hak-Kim Chan, Paul M. Young, Daniela Traini, Matthew Coates. Dry powder inhalers: challenges and goals for next generation therapies

3. Coates MS, Fletcher DF, Chan HK, Raper JA (2004) Effect of design on the performance of a dry powder inhaler using computational fluid dynamics. Part 1: Grid structure and mouth piece length. J Pharm Sci 93: 2863-2876.
4. Adi S, Tong Z, Chan HK, Yang R, Yu A (2010) Impact angles as an alternative way to improve aerosolisation of powders for inhalation? Eur J Pharm Sci 41: 320-327.
5. Coates MS, Chan H-K, Fletcher DF, Raper JA (2006) Effect of design on the performance of a dry powder inhaler using computational fluid dynamics. Part 2: Air inlet size. J Pharm Sci 95: 1382-1392.
6. Barry PW, O'Callaghan C. The influence of inhaler selection on efficacy of asthma therapies. Adv Drug Deliv Rev 2003;55(7):879– 923.
7. Chan HK, Young PM, Traini D, Coates M (2007) Dry powder inhalers: Challenges and goals for next generation therapies. Pharma Tech Eur 19: 19-24
8. Islam N, Gladki E (2008) Dry powder inhalers (DPIs): A review of device reliability and innovation. Int J Pharm 360: 1-11.
9. Ashurst I., Malton A., Prime D., SumbyB.; Latest advances in the development of dry powder inhalers, reviews-research focus, July 2000, PSTT Vol. 3:7; 246-256.
10. Frijlink HW, de Boer AH (2005) Trends in the technology-driven development of new inhalation devices. Drug Discov Today Technol 2: 47-57.
11. Hoppentocht M, Hagedoorn P, Frijlink HW, de Boer AH (2014) Technological and practical challenges of dry powder inhalers and formulations. Adv Drug Deliv Rev 75: 18-31.
12. Drug Development and Delivery. A Piezo-electronic Inhaler for local & systemic applications. Accessed on April 09, 2017.
13. Kohler D (2004) He Novolizer®: overcoming inherent problems of dry powder inhalers. Respir Med 98: S17-S21.
14. Parisini I, Cheng SJ, Symons DD, Murnane D (2013) Potential of a cyclone prototype spacer to improve in vitro dry powder delivery. Pharm Res 31: 1133-1145.
15. Matida EA, Finlay WH, Rimkus M, Grgic B, Lange CF (2004) A new addon spacer design concept for dry-powder inhalers. J Aerosol Sci 35: 823-833.
16. Timsina MP, Martin GP, Marriott C, et al. Drug-delivery to the respiratory-tract using dry powder inhalers. Int J Pharm 1994;101(1): 1–13.
17. Aswania O, Ritson S, Iqbal SM, Bhatt J, Rigby AS, Everard ML. Intra-subject variability in lung dose in healthy volunteers using five conventional portable inhalers. J Aerosol Med 2004;17(3):231–238.

18. Cochrane MG, Bala MV, Downs KE, Mauskopf J, Ben-Joseph RH. Inhaled corticosteroids for asthma therapy: patient compliance, devices, and inhalation technique. Chest 2000;117(2):542 550.

19. Smyth HD, Hickey AJ. Carriers in drug powder delivery: implications for inhalation system design. Am J Drug Deliv 2005;3(2)117– 132.

20. Dolovich MB, Ahrens RC, Hess DR, Anderson P, Dhand R, Rau JL, et al. Device selection and outcomes of aerosol therapy: evidencebased guidelines: American College of Chest Physicians/American College of Asthma, Allergy, and Immunology. Chest 2005;127(1): 335–371.

21. Atkins PJ, Crowder TM. The design and development of inhalation drug delivery systems. In: Hickey A. Pharmaceutical inhalation aerosol technology, 2nd ed. New York: Dekker; 2004.