ISSN: 2754-4761

Journal of Pulmonology Research & Reports

SCIENTIFIC Research and Community

Review Article

Open Access

Pulmonary Delivery of Aerosol Biologics for the Treatment of Eosinophilic Asthma

Nightingale Syabbalo

Professor of Physiology and Medicine, Nabanji Medical Centre P. O. Box 30243 Lusaka Zambia

***Corresponding author**
Nightingale Syabbalo, Professor of Physiology and Medicine, Nabanji Medical Centre P. O. Box 30243 Lusaka Zambia.

Received: December 28, 2021; **Accepted:** January 22, 2026; **Published:** January 30, 2026

Abbreviations

AATD, Alpha-1 antitrypsin deficiency
AHR, Airway hyperresponsiveness
AIC, Allergen inhalation challenge
ALI, Acute lung injury
ARDS, Acute respiratory distress syndrome
BOOP, Bronchiolitis obliterans organizing pneumonia
COPD, Chronic obstructive pulmonary disease
COVID-19, Coronavirus Disease 19
Dae, Aerodynamic diameter
DPI, Dry powder inhaler
AER, Early asthmatic response
FeNO, Fractional exhaled nitric oxide
FEV1, forced expired volume in one second
IgE, Immunoglobulin E
IL, Interleukin
LAR, Late asthmatic response
mAb, monoclonal antibody
PAP, Pulmonary alveolar proteinosis
pMDI, Pressure metered dose inhaler
RSV, Respiratory syncytial virus
SARS-CoV-2, Severe acute respiratory syndrome coronavirus 2
SMI, Soft mist inhaler
Th2, T helper type 2 lymphocytes
TNF-α, Tumor necrosis factor-α
TSLP, thymic stromal lymphopoietin

Pulmonary Delivery of Aerosol Biologics

Biological drugs (synonymous known as biologics) are a diverse group of therapeutic agents which are large and complex molecules produced through sophisticated biotechnology [1,2]. The biologics currently used to treat severe asthma are monoclonal antibodies (mAb), and antibody fragment which are administered subcutaneously, or intravenously (reslizumab). Injection of drugs is painful and inconvenient, especially when the drugs are for the treatment of chronic diseases, such as asthma, and cystic fibrosis [3,4]. Moreover, 10% of the patients worldwide suffer from needle phobia leading to poor compliance [5]. Pulmonary delivery of biologics to the lungs improves pharmacokinetics, and toxicity profiles of proteins [6]. It is a non-invasive route, and allows for self-administration, which could improve patient compliance [6,7].

Pulmonary delivery of biologics is an attractive route of administration for the treatment of respiratory diseases, such as asthma, cystic fibrosis, alpha-1 antitrypsin deficiency (AATD), pulmonary alveolar proteinosis (PAP), lung cancer, ARDS [NCT03368092, NCT02595060], and SARS-CoV-2 [8-27]. Pulmonary delivery of biologics is also an alternative route for administering biologics for the treatment of non-respiratory systemic diseases, including diabetes mellitus, anaemia, and multiple sclerosis [28-32]. The development of inhalation biologics, and design of methods of inhalation technology are outside the scope of this manuscript, but detailed comprehensive information can be found in references 8-11. Table 1 shows preclinical and clinical trials of aerosol biologics for the treatment of respiratory diseases, and non-respiratory diseases.

The large surface area, and the extensive vascularization of the lungs, and a thin alveolar-capillary membrane enable rapid absorption, and fast onset of action of drugs delivered to the lungs [33,34]. Pulmonary delivery also offers the advantage of delivering biologics at high concentration in the lungs, and directly to inflammatory cells, and has the potential to achieve high blood levels of the biologics. Additionally, there is a lower level of proteolytic enzymatic activity in the lung, and minimal first-pass metabolism, hence higher concentrations of the biologics in the airways, and lung parenchyma to target respiratory diseases [3,35]. Furthermore, protein biotherapeutics delivered through the airways are poorly absorbed from the lungs into the circulation, thus minimizing systemic toxic effects [6,23].

However, despite the beneficial effects of pulmonary delivery of biologics, it requires innovative biotechnology to develop biologics, and inhaler devices to propel the biologics to the tracheobronchial tree, and lung parenchyma [8-11]. Furthermore, there are anatomical, physiological, and immunological factors that affect the pharmacodynamics, and biotherapeutic efficacy, and safety of inhaled biologics [36]. The other obstacle is the formulation of biologics for delivery into the lungs [8,9,37]. Three methods have been applied to modify the structure, aerodynamic diameter (Dae), shape, hydroscopicity, and density of biologics to enhance their absorption through the mucociliary blanket, pharmacokinetics, and bioavailability [38,39]. They include antibody fragment development, Fc engineering, and pegylation [40,45].

Structural simplification is a vital strategy to improve the delivery of biologics to the tracheobronchial tree, and lung parenchyma [11]. Small fragments of mAbs expressed by bacterial or yeast cultures, or obtained by digestion of full-length antibodies with proteolytic enzymes are the most suitable biologics for delivery to the lungs [41,40]. Antibody fragments have a smaller molecular mass, and have the advantage of enhanced tissue diffusion, and are easy and inexpensive to produce. However, because they lack the Fc piece, they are rapidly degraded, and have a short half-life [11]. The pharmacological active receptor, or antigen-binding region of antibody fragments is the Fab region [12].

Pegylation protects proteins from renal clearance and proteolytic degradation, thus prolongs protein local residence time, and bioavailability in the body [44]. Pegylation has been shown to be an effective method for extending the retention time of biologics in the lung, such as human alpha 1 proteinase inhibitor (α1-PI), IFN-α, and antibody fragments [46-49].

The type of inhaler has critical importance for the delivery of biologics, because 75% of inhaled protein formulations in clinical research are produced as liquids [8]. There are four main types of inhalers for the delivery of orally inhaled proteins, peptides, and cytokines, such as pressure metered dose inhalers (pMDI), dry powder inhalers (DPI), soft mist inhalers (SMI), and nebulizers [9,11,50-55].

Most biologics in clinical trial for the treatment of asthma have been delivered to the lung by DPIs. However, SMIs are novel multidose propellant-free, handheld inhalers, and are more suitable for delivery of biologics than pMDI, and DPIs [9]. The most experience of pulmonary delivery of biologics with DPI has been the Exubera®, and Technosphere® insulin (Afrezza®), for the treatment of diabetes mellitus [56]. Currently, three DPIs have been utilized in clinical trials for the delivery of biologics to the lungs for the treatment of eosinophilic asthma. They include the F1P for administration of the anti-IL-13 monoclonal antibody fragment VR942 (Abrezekimab) Cyclohaler® (single dose, PB Pharma GmbH, Meerbusch, German) for the administration of DAS181 (Fludase®) and Concept1 (single dose, Norvatis, Basel, Switzerland) (NCT4410523) for administration of the anti-thymic stromal lymphopoietin (TSLP) monoclonal antibody Fab fragment CSJ117 [36,57,16,58]. Biotechnological modification of proteins and peptides, and proper inhaler devices can be successfully used to deliver biologics which are effective, and immunologically safe for the treatment of airway diseases, pulmonary diseases, and systemic diseases.

The precise mechanism by which mAb, and antibody fragments exert their immunotherapeutic effects is by inhibiting surface receptors on immune and inflammatory cells, thus preventing these cells from secreting cytokines, chemokines, and adhesion molecules. Several mAb and antibody fragments are in currently preclinical and clinical trials for the treatment of respiratory diseases, and non-respiratory diseases (Table 1).

The first biologic administered as inhalation to be approved by the Food and Drug Administration (FDA) was Pulmozyme® in 1993 for the treatment of cystic fibrosis [59]. Inhaled insulin formulation Exubera® was approved by the FDA in 2006, but was withdrawn in 2007 due to a large inhalation device size, high cost, and safety concerns [60]. Consequently, Afrezza®, another DPI, marketed as an ultra-rapid-acting inhaled insulin was approved by the FDA in 2014 for glycaemic control in adults with type 1 and 2 diabetes mellitus [61]. Afrezza® is less cumbersome than Exubera®, and offers better flexibility in dosing [62].

Pulmonary Delivery of Aerosol Biologics for the Treatment of Eosinophilic Asthma

The first documented clinical trial on pulmonary delivery of aerosol biologics for the treatment of asthma was self-administered omalizumab via nebulization in 1999. The study showed no change in serum immunoglobulin E (IgE) levels, and no improvement in airway hyperresponsiveness (AHR). Unfortunately, one patient developed anti-omalizumab antibodies, raising concerns about the immunogenicity of inhaled biologics compared to parenteral administered biologics [63].

Pitrakinra, and AZD1402/PRS-060 are inhaled IL-4 muteins that inhibit IL-4 receptor-α (IL-4Rα). Phase IIa clinical trial of Pitrakinra attenuated the late phase asthmatic response, and airway inflammation in asthmatic subjects after allergen challenge [64]. AZD1402/PRS-060 is another IL-4Rα antagonist with higher affinity and inhibitory effect to IL-4Rα than Pitrakinra in vitro [65]. Single inhaled dose of AZD1402/PRS-060 was well tolerated in healthy subjects [66]. A dose-ranging of AZD1402/PRS-060 in adult patients with mild asthma is ongoing, and the results are eagerly awaited [NCT03574805].

VR942 (UCB 4144) is a dry powder formulation containing CDP7766, a mAb fragment targeting IL-13. Inhalation of VR942 resulted in a rapid and sustained inhibition of fractional exhaled nitric oxide (FeNO) production, and was safe and well-tolerated by healthy and asthmatic subjects (NCT02473939 [36]. Table 2 shows monoclonal antibodies, and antibody fragments in preclinical and clinical trials for the treatment of eosinophilic asthma.

CSJ117 DPI for the Treatment of Eosinophilic Asthma

CSJ117 (Norvatis, NCT04410523) is a potent neutralizing antibody Fab fragment against TSLP with a molecular mass of 46 kDa. It is formulated as a PulmoSol TM engineered powder in hard capsules for delivery to the lungs by a dry powder inhaler. Phase 2 double-blind, placebo-controlled clinical trial evaluated the efficacy and safety of CSJ117 on the late asthmatic response (LAR), the early asthmatic response (EAR), and biomarkers of eosinophilic asthma after allergen inhalation challenge (AIC) [16,67]. CSJ117 significantly attenuated the LAR, and modestly reduced the EAR on day 84 of treatment. The maximum decrease in FEV1 from pre-AIC were significantly lower in the CSJ117 group compared to placebo (9.28% versus 17.70%; P = 029), during the LAR. Similarly, during the EAR, the maximum decrease in FEV1 pre-AIC was lesser in the CSJ117 group compared with the placebo arm (25.48% versus 30.90%; P = 0.105). CSJ117 also significantly reduced fractional exhaled nitric oxide before AIC on day 83; and significantly reduced the allergen-induced increase in % sputum eosinophil count after AIC on day 84 [16]. These encouraging results demonstrate the potential of inhaled biologics, particularly those targeting the alarmin cytokines in the treatment, and prevention of eosinophilic asthma responses.

Conclusion

Pulmonary delivery of biologics to the lungs is a non-invasive route of administration, and improves pharmacokinetics, bioavailability, and toxicity profiles of mAb, and antibody fragments. The large surface area, and the extensive vascularization of the lungs, and a thin alveolar-capillary membrane enable rapid absorption, and fast onset of action of drugs delivered to the lungs. Currently, there are several biologics in preclinical and clinical trials for the treatment of respiratory diseases, such as asthma, cystic fibrosis, and SARS-CoV-2; and non-respiratory diseases, including diabetes mellitus, and anaemia. CSJ117 is a potent neutralizing antibody Fab fragment against TSLP, formulated as a PulmoSol TM engineered powder for delivery to the lungs by a DPI. CSJ117 aerosol has been shown to significantly attenuate the LAR, and modestly reduce the EAR on day 84 of treatment. Additionally, CSJ117 has been demonstrated to significantly reduce FeNO before AIC on day 83; and significantly reduce the allergen-induced increase in % sputum eosinophil count after AIC on day 84. Aerosol CSJ117 by acting topically, and blocking the immunopathological effects of TSLP may become the first precise biologic for the treatment of eosinophilic asthma in the nearby future.

Conflict of Interest

The author declares that the publication was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest. ORCID ID: https://orcid.org/0000-0002-94355456.

References

1. Zelikin AN, Healy CEAM (2016) Materials and methods for delivery of biological drugs. Nat Chem 8: 997-1007.
2. Durán Lobato M, Niu Z, Alonso MJJAM (2020) Oral delivery of biologics for precision medicine. Adv Mater 32: 1901935.
3. Chung SW, Hil Lal TA, Byun Y (2012) Strategies for non-invasive delivery of biologics. J Drug Target 20: 481-501.
4. Griese M, Scheuch G (2016) Delivery of Alpha-1 Antitrypsin to Airways. Ann Am Thorac Soc 13: 346-351.
5. Sokolowski CJ, Giovannitti JA, Boynes SG (2010) Needle Phobia: Etiology, Adverse Consequences, and Patient Management. Dent Clin 54: 731-744.
6. Respaud R, Vecellio L, Diot O, Heuzé Vourc HN (2015) Nedulization as a delivery method for mAbs in respiratory diseases. Expert Opin Drug Deliv 12: 1027-1039.
7. Osman N, Kaneko K, Carini V, Saleem I (2018) Carriers for the targeted delivery of aerosolized macromolecules for pulmonary pathologies. Expert Opin Drug Deliv 15: 821-834.
8. Montagutelli EB, Mayor A, Vecellio L, Respaud R, Vourch NH (2018) Designing inhaled protein therapeutics for topical lung delivery: what are the next steps? Expert Opin Drug Del 15: 729-736.
9. Mathews A, Ee PLR, Ge R (2020) Developing inhaled protein therapeutics for lung diseases. Mol Biomed 1: 11.
10. Fröhlich F, Behzadi SS (2021) Oral inhalation for delivery of proteins and peptides to the lung. Eur J Pharmaceutics Biopharmaceutics 163: 198-211.
11. Liang W, Pan HW, Vllasaliu D, Lam JKW (2020) Pulmonary delivery of biological drugs. Pharmaceutics 12: 1025.
12. Hacha J, Tomlinson K, Maertens L, Paulissen G, Rocks N, et al. (2012) Nebulized anti-IL-13 monoclonal antibody Fab0 fragment reduces allergen-induced asthma. Am J Respir Cell Mol Biol 47: 709-717.
13. Gozzard N, Lightwood D, Tservistas M, Zehentleitner M, Sarkar K, et al. (2017) Novel inhaled delivery of anti-IL-13 MAb (Fab fragment): Preclinical efficacy in allergic asthma. In Proceedings of the European Respiratory Society Annual Congress, Milan, Italy 9-13.
14. Bruns I, Fitzgerald M, Mensing G, Tsung M, Pardali K, et al. (2019) Late Breaking Abstract – Multiple ascending dose study of inhaled IL-4Ra antagonist, AZ1402/PRS-060, in mild asthmatics demonstrates robust FeNO reduction and a promising clinical profile for the treatment of asthma. Eur Respir J PA3709.
15. Faghihi H, Najafabadi AR, Daman Z, Ghasemian E, Montazeri H, et al. (2019) Respiratory administration of Infliximab powder for local suppression of inflammation. AAPS PharmSciTech 20: 128.
16. Gauvreau G, Hohlfeld J, Grant S, Jain M, Cabanski M, et al. (2020) Efficacy and safety of an inhaled anti-TSLP antibody fragment in adults with mild atopic asthma. Am J Respir Crit Care Med 201: 4207.
17. Kerem E, Blau H, Shteinberg M, Efrati O, Alon S, et al. (2017) WS01.2 phase II clinical trial results of alidornase for the treatment of cystic fibrosis. J Cystic Fibros 16: 1-16.
18. Nanus M (2017) Protalix BioTherapeutics announces phase II clinical trial results for alidornase alfa in cystic fibrosis presented at the 40th European Cystic Fibrosis Society Conference. Protalix BioTherapeutics https://protalixbiotherapeutics.gcs-web.com/news-releases/news-release-details/protalix-biotherapeutics-announces-phase-ii-clinical-trial.
19. Sorrells S, Camprubi S, Griffin R, Chen J, Ayguasanova J (2015) SPARTA clinical trial design: Exploring the efficacy and safety of two dose regimens of alpha 1-proteinase inhibitor augmentation therapy in alpha 1-antitrypsin deficiency. Respir Med 109: 490-499.
20. Strnad P, McElvaney NG, Lomas DA (2020) Alpha 1-Antitrypsin Deficiency. N Engl J Med 382: 1443-1455.
21. Campo I, Mariani F, Paracchini E, Kadija Z, Zorzetto M, et al. (2016) Inhaled sargramostim and whole lung lavage (WLL) as therapy of autoimmune pulmonary alveolar proteinosis (aPAP). Eur Respir J 48: PA3870.
22. Tazawa R, Ueda M, Abe M, Tatsumi K, Eda R, et al. (2019) Inhaled GM-CSF for pulmonary alveolar proteinosis. N Engl J Med 381: 923-932.
23. Maillet A, Guilleminault L, Lemarié E, Lerondel S, Azzopardi N, et al. (2011) The airways: a novel route for delivering monoclonal antibodies to treat lung tumors. Pharm Res 28: 2147-2156.
24. Guilleminault L, Azzopradi N, Arnoult C, Sobilo J, Hervé V, et al. (2014) Fate of inhaled monoclonal antibodies after deposition of aerosolized particles in the respiratory system. J Control Release 196: 344-354.
25. Hanke L, Perez LV, Sheward DJ, Das H, Schulte T, et al. (2020) An alpaca nanobody neutralizes SARS-CoV-2 by blocking receptor interaction. Nat Commun 11: 4420.
26. Konwarh R (2020) Nanobodies: Prospects of Expanding Gamut of Neutralizing Antibodies Against the Novel Coronavirus, SARS-CoV-2. Front Immunol 11: 1531.
27. (2020) Ansun Biopharma enrols first patient in proof-of-concept trial of DAS181 for the treatment of COVID-19. BioSpace https://www.biospace.com/ansun-biopharma-enrolls-first-patient-in-proof-of-concept-trial-of-das181-for-the-treatment-of-covid-19.
28. White S, Bennett DB, Cheu S (2005) Exuberafi: Pharmaceutical Developmant of a Novel Product for Pulmonary Delivery of Insulin. Diabetes Technol Ther 7: 896-906.
29. Cassidy JP, Amin N, Marino M, Gotfried M, Meyer T, et al. (2011) Insulin Lung Deposition and Clearance Following TechnospherefiInsulin Inhalataion powder Administration. Pharm Res 28: 2157-2164.
30. Klonoff DC (2014) Afrezza inhaled insulin: The fastest-acting FDA-approved insulin on the market has favourable properties. J Diabetes Sci Technol 8: 1071-1073.
31. Dumont JA, Bitonti AJ, Clark D, Evans S, Pickford M, et al. (2005) Delivery of an Erythropoietin-Fc Fusion Protein by Inhalation in Humans through an Immunoglobulin Transport Pathway. J Aerosol Med 18: 294-3003.
32. Vallee S, Rakhe S, Reidy T, Walker S, Lu Q, et al. (2012)

Pulmonary Administration of Interferon Beta-1a-Fc Fusion Protein in Non-Human Primates Using an Immunoglobulin Transport pathway. J Interf Cytokine Res 32: 178-184.
33. Agu R, Ugwoke MI, Armand M, Kinget R, Verbeke N (2001) The lung as a route for systemic delivery of therapeutic proteins and peptides. Respir Res 2: 198-209.
34. Dhanani J, Fraser JF, Chan HK, Rello J, Cohen J, et al. (2016) Fundamentals of aerosol therapy in critical care. Crit Care 20: 269.
35. Lexmond A, Forbes B (2017) Drug Delivery Devices for Inhaled Medicines. Handb Exp Pharmacol 237: 265-280.
36. Burgess G, Boyce M, Jones M, Larsson L, Main MJ, et al. (2018) Randomized study of the safety and pharmacodynamics of inhaled interleukin-13 monoclonal antibody fragment VR942. EBioMedicine 35: 67-75.
37. Pilcer G, Amighi K (2010) Formulation strategy and use of excipients in pulmonary drug delivery. Int J Pharm 392: 1-19.
38. Carvalho TC, Peters JI, Williams RO III (2011) Influence of particle size on regional lung deposition – What evidence is there. Int J Pharm 406: 1-10.
39. Ibrahim M, Verma R, Garcia Contreras L (2015) Inhalation drug delivery devices: technology update. Med Devices 8: 131-139.
40. Jones RGA, Landon J (2003) A protocol for 'enhanced pepsin digestion': A step-by-step method for obtaining pure antibody fragments in high yield from serum. J Immunol Methods 275: 230-250.
41. Ma H, O'Kennedy R (2017) Recombinant antibody fragment production. Methods 116: 23-33.
42. Spiekerman GM, Finn PW, Ward ES, Dumont J, Dickison BL, et al. (2002) Receptor-mediated immunoglobulin G transport across mucosal barriers in adult life: Functional expression of FCRn in the mammalian lung. J Exp Med 196: 303-310.
43. Bitonti AJ, Dumont JA, Low SC, Peters RT, Kropp KE, et al. (2004) Pulmonary delivery of an erythropoietin Fc fusion protein in non-human primates through an immunoglobulin transport pathway. Proc Natl Acad Sci USA 101: 9763-9768.
44. Harris JM, Chess RB (2003) Effect of pegylation on pharmaceuticals. Nat Rev Drug Discov 3: 214-221.
45. Guichard MJ, Leal T, Vanbever R (2017) PEGylation an approach for improving the pulmonary delivery of biopharmaceuticals. Curr Opin Colloid Interface Sci 31: 43-50.
46. Cantin AM, Woods DE, Cloutier D, Dufour EK, Leduc R (2002) Polyethylene glycol conjugation at Cys 232 prolongs half-life of α 1 proteinase inhibitor. Am J Respir Cell Mol Biol 27: 659-665.
47. McLeod VM, Chan LJ, Ryan GM, Porter CJ, Kaminskas LM, et al. (2015) Optimal PEGylation can improve the exposure of interferon in the lungs following pulmonary administration. J Pharm Sci 104: 1421-1430.
48. Koussoroplis SJ, Paulissen G, Tyteca D, Goldansaz H, Todoroff J, et al. (2014) PEGylation of antibody fragments greatly increases their local residence time following delivery to the respiratory tract. J Control Release 187: 91-100.
49. Patil HP, Freches D, Karmani L, Duncan GA, Ucakar B, et al. (2018) Fate of PEGylated antibody fragments following delivery to the lungs: influence of delivery site, PEG size and lung inflammation. J Control Release 272: 62-71.
50. Pleasants RA, Hess DR (2018) Areosol delivery devices for obstructive lung diseases. Respir Care 16: 708-733.
51. Lamche H, Meade C, Zierenberg B, Reimholz R (2002) Process for nebulizing aqueous compositions containing highly concentrated insulin. U.S. Patent US20030064032A1.
52. Morales JO, Fathe KR, Brunaugh A, Ferrati S, Li S, et al. (2017) Challenges and future prospects for the delivery of biologics: oral mucosal, pulmonary, and transdermal routes. AAPS J 19: 652-668.
53. Deller D, Thipphawong B, Otulana B, Caplan D, Ericson L, et al. (2003) Bolus inhalation of rhDNase with the AERx system in subjects with cystic fibrosis. J Aerosol Med 16: 175-182.
54. Sangwan S, Agosti JM, Bauer LA, Otulana BA, Morishige RJ, et al. (2001) Aerosolized protein delivery in asthma: gamma camera analysis of regional deposition and perfusion. J Aerosol Med 14: 185-195.
55. Zillen D, Beugeling M, Hinrichs WLJ, Frijlink HW, Grasmeijer F (2021) Natural and bioinspired excipients for dry powder inhalation formulation. Curr Opin Colloid Interface Sci 56: 101497.
56. Hollander PA, Blonde L, Rowe R, Mehta AE, Milburn JL, et al. (2004) Efficacy and safety of inhaled insulin (exubera) compared with subcutaneous insulin therapy in patients with type 2 diabetes: Results of a 6-month, randomized, comparative trial. Diabetes Care 27: 2356-2362.
57. Colombo RE, Fiorentino C, Dodd LE, Hunsberger S, Haney C, et al. (2015) A phase 1 randomized, double-blind, placebo-controlled, crossover trial of DAS181 (Fludasefi) in adult subjects with well-controlled asthma. BMC Infect Dis 16: 1-10.
58. Matera MG, Rogliani P, Calzetta L, Cazzola M (2020) TSLP inhibitors for asthma: current status and future prospects. Drugs 80: 449-458.
59. Borghardt JM, Kloft C, Sharma A (2018) Inhaled therapy in respiratory disease: the complex interplay of pulmonary kinetic processes. Can Respir J 2018: 1-11.
60. Anselmo AC, Gokarn Y, Mitragotri S (2018) Non-invasive delivery strategies for biologics. Nat Rev Drug Discov 18: 19-40.
61. Al Tabakha MM (2015) Future prospect of insulin inhalation for diabetic patients. The case of Afrezza versus Exubera. J Control Release 215: 25-38.
62. Mohanty RR, Das S (2017) Inhaled insulin - Current direction of insulin research. J Clin Diagn Res 11: 01-02.
63. Fahy JV, Cockroft DW, Boulet LP, Wong HH, Deschesnes F, et al. (1999) Effects of aerosolized anti-IgE (E25) on airway responses to inhaled allergen in asthmatic subjects. J Respir Crit Care Med 160: 1023-1027.
64. Wenzel S, Wilbraham D, Fuller R, Getz EB, Longphre M (2007) Effect of an interleukin-4 variant on late phase asthmatic response to allergen challenge in asthmatic patients. Results of phase 2a studies. Lancet 370: 1422-1431.
65. Matschiner G, Huang S, Constant S, Rattenstetter B, Gille H, et al. (2018) The discovery and development of AZD1402/PRS-060, an inhaled, potent and selective antagonist of IL-4 receptor alpha. Airway Pharmacol Treat 52: PA1047.
66. Bruns I, Fitzgerald MF, Pardali K, Gardiner P, Keeling D, et al. (2019) First-in-human data for the inhaled IL-4R antagonist AZD1402/PRS-060 reveals a promising clinical profile for the treatment of asthma. Am J Respir Crit Care Med 199: 7476.
67. Gauvreau G, Hohfeld J, Boulet LP, Cockcroft D, Davis B, et al. (2020) Late Breaking Abstract - Efficacy of CSJ117 on allergen-induced asthmatic responses in mild atopic asthma patients. Eur Respir J 56: 3690.