Annals of Clinical Pharmacology & Toxicology

ISSN: 2642-9233

Editorial

Chronic Obstructive Pulmonary Disease and Therapeutic Agents: Analytical Methods of Determination of these Agents in Biological Fluids

*Chika J Mbah**

Department of Pharmaceutical and Medicinal Agents, University of Nigeria, Nigeria

Editorial

Chronic Obstructive Pulmonary Disease (COPD) is a preventable and treatable lung disease characterized by chronic obstruction of lung airflow that interferes with normal breathing and may be punctuated by periods of acute worsening of respiratory symptoms [1]. The major diseases implicated in COPD are (i) chronic bronchitis (a chronic, inflammatory condition of the bronchi characterized by coughing and expectoration of sputum), (ii) emphysema (a respiratory disorder characterized by enlargement and eventual destruction of the air sacs (alveoli) in the lungs), (iii) bronchiectasis (characterized by inflamed and easily collapsible airways and obstruction to airflow). Chronic obstructive pulmonary disease may be caused by tobacco smoking, significant exposure to noxious particles or gases, genetic abnormalities and accelerated aging. Some of the symptoms of COPD are dyspnoea, productive cough with altered sputum, wheezing and fever. Other nonspecific symptoms include depression, fatigue, insomnia or sleepiness and malaise. Chronic obstructive pulmonary disease is currently diagnosed by spirometry (a simple breathing test that provides the severity of COPD) and post-bronchodilator forced expiratory volume at 1 second (FEV1) to forced vital capacity/ (FVC) ratio value [2]. A ratio value of less than 70% (<0.70) confirms the presence of persistent airflow limitation and consistent with the diagnosis of COPD.

According to Global Initiative for Chronic Obstructive Lung Disease (GOLD), severity of COPD is classified into (i) mild COPD (stage 1: FEV1 value of 80% or more of predicted value), (ii) moderate COPD (stage 2: FEV1 value of 50% to 79% of predicted value), (iii) severe COPD (stage 3: FEV1 value of 30% to 49% of predicted value) and (iv) very severe COPD (stage 4: FEV1 value of less than 30% of predicted value). The use of post-bronchodilator values shows that the obstruction is not fully reversible.

Citation: Mbah CJ. Chronic Obstructive Pulmonary Disease and Therapeutic Agents: Analytical Methods of Determination of these Agents in Biological Fluids. Ann Clin Pharmacol Toxicol. 2019; 1(2): 1011.

Publisher Name: Medtext Publications LLC

Manuscript compiled: September 13th, 2019

***Corresponding author:** Chika J Mbah, Department of Pharmaceutical and Medicinal Agents, Faculty of Pharmaceutical Sciences, University of Nigeria, Nsukka, Enugu State, Nigeria, E-mail: chika.mbah@unn.edu.ng

The management of COPD involves prevention and treatment [3,4]. Prevention deals with smoking cessation, elimination of environmental pollutants and vaccination. Treatment may involve use of therapeutic agents (drugs), physical activity training, pulmonary rehabilitation and oxygen treatment. Using therapeutic agents in the management of COPD, the GOLD guidelines recommend either long-acting inhaled β_2-agonists or anti cholinergic agents as first line drug therapy. With worsening lung function, GOLD guidelines also recommend combination therapy [5]. Combination therapy may involve combination of long-acting inhaled β_2-agonists and corticosteroids or long-lasting inhaled β_2-agonists and long-lasting anti cholinergic agents.

These therapeutic agents when placed in their pharmacological classes include:

(i) β2-agonists: short-acting ones are albuterol (salbutamol), fenoterol, levulbuterol, terbutaline while the long-acting ones are arformoterol, formoterol, indacaterol, olodaterol and salmeterol.

(ii) Anticholinergic agents: short-acting ones are ipratropium bromide, oxitropium bromide while long-acting ones are glycopyrronium bromide, tiotropium and umeclidinium.

(iii) Methylxanthines: typical examples are aminophylline and theophylline.

(iv) Corticosteroids: they include beclomethasone, budesonide, fluticasone furoate, mometasone.

(v) Phosphodiesterase-4-inhibitors: typical example is roflumilast.

These drugs are given as oral, parenteral and inhalation dosage forms respectively. Inhalation involves the use of Metered Dose Inhaler (MDI), Dry Powder Inhaler (DPI) and Soft Mist Inhaler (SMI) respectively.

As the strength of the administered drugs is very low, accurate, precise, selective, sensitive and specific analytical methods are needed in order to accurately quantify the drugs in biological fluids. Biological fluids are very important to life and assist in maintaining body homeostasis. Biological fluids most often used include blood (whole blood, serum or plasma); urine; Cerebrospinal Fluid (CSF) and saliva. However, occasionally other biological fluids namely amniotic fluid; ocular fluid; pleural fluid (from the sac surrounding the lungs); pericardial fluid (from the sac surrounding the heart); peritoneal fluid (also called ascitic fluid, from the abdomen) and synovial fluid (fluid that is found in joint cavities) could be analyzed.

Analytical methods that have been reported in literature for the analysis of these therapeutic agents are capillary electrophoresis, chromatographic, spectroscopic and immunoassay methods. Amongst the methods, chromatographic methods namely liquid chromatography (high performance liquid chromatography or ultra performance liquid chromatography) and gas chromatography are mostly used either as hyphenated or non-hyphenated systems. Hyphenation is an on-line combination of a chromatographic technique and one or more spectroscopic detection techniques.

In the present article, we present some hyphenated and non-hyphenated chromatographic techniques that have been used to determine these therapeutic agents in biological fluids.

They include:

(i) β_2-agonists: In human whole blood [6], human plasma [7-11], human serum [12,13], human urine [14-16].

(ii) Anticholinergic agents: in human plasma [17-20].

(iii) Corticosteroids: in human plasma [21-23], human urine [24].

(iv) Xanthine derivatives: in human serum [25-27], human urine [28], human saliva [29].

(v) Phosphodiesterase-4-inhibitors: in human plasma [30].

The bio analytical methods presented in this article are not exhaustive, however they do depict that therapeutic agents used in the management of COPD can accurately be determined in biological fluids.

Conclusion

The chronic airflow limitation that characterized chronic obstructive pulmonary disease is caused by a mixture of small airways disease such as obstructive bronchiolitis and emphysema. β_2-agonists, anti cholinergic agents, methylxanthines, corticosteroids and phosphodiesterase-4-inhibitors are classes of therapeutic agents widely used in the management of COPD. Due to low systemic concentrations of these therapeutic agents, accurate, precise, selective and sensitive analytical methods are used to determine them in biological fluids. Chromatographic hyphenation has provided a very significant increase in sensitivity and accuracy for their analyses and therefore currently the analytical techniques of interest.

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