

## Human Diseases and Therapeutic Agents: The Role of Ion Pair Liquid Chromatography in the Analysis of Therapeutic Agents in Biological Fluids

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### Abstract

Human disease is a deviation from normal mental, physical and social well-being leading to disruption or loss of homeostasis. Human diseases can be classified as congenital, hereditary, degenerative, inflammatory, metabolic and neoplastic etc [1]. Various methods utilized to diagnose diseases and conditions may be invasive or noninvasive. Such methods include clinical laboratory tests, cytologic or histologic tests, electrical activity tests, endoscopy, laparoscopy, computer tomography (CT), magnetic resonance imaging (MRI), positron emission tomography (PET), radioisotope tests, ultrasound tests and X-ray examination etc. Following diagnosis, best treatment options for the patient are considered and one of those options very often will involve the use of therapeutic agents (drugs).

**Keywords:** *Computer Tomography (CT); Magnetic Resonance Imaging (MRI); Positron Emission Tomography (PET)*

Although demonstration of a clinically significant effect, quantification of pharmacologic effect have been used to predict the therapeutic potential of a drug, however, because of their limitations, the current method to assess the clinical performance of a drug involves measurement of the drug concentrations in the biological fluids [2]. Biological fluids are very vital to life and help maintain body homeostasis. Such biological fluids include blood (whole blood, serum or plasma); urine; cerebrospinal fluid (CSF); 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); saliva and synovial fluid (fluid that is found in joint cavities). Out of these fluids, the biological fluid of choice is mostly blood and is based on the assumption that there is a direct relationship between the concentration of drug in blood or plasma and the concentration of drug at the site of action. Thus, by monitoring the drug concentration in the blood, it is possible to obtain an indirect measure of drug response.

Drug concentrations are determined in biological fluids mostly by clinical laboratory tests involving the use of instrumental methods such as spectroscopic and chromatographic methods. Ion pair chromatography (IPC) is one of the chromatographic methods that effectively and efficiently separate organic and inorganic ions using ion-pair reagents. The method enables the control of selectivity in the separation of ionic samples and has increased retention of weakly retained ionized acids and bases. The stationary phase could be normal or reverse. In normal phase operation, the pairing-ion is coated as an aqueous solution onto a support and only elutes from the column when paired with solute ions. However, in reverse phase operation, the pairing-ion is always added to the mobile phase permitting the hydrophobic

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tail of the reagent to get retained by the stationary phase and resulting in an ion exchange group forming on the surface of the stationary phase. The mobile phase consists of water-rich eluent that may contain organic modifiers such as acetonitrile and/or methanol; additives such as ethylenediaminetetraacetic acid EDTA or potassium tetrakis (1H-pyrazolyl) borate. Some of the ion-pair reagents (IPR) include: alkyl sulfonates  $R-SO_3^- (R^-)$ ; tetraalkylammonium salts  $R_4N^+ (R^+)$ ; tetrabutylphosphonium salts  $R_4P^+ (R^+)$ ; tributylsulfonium salts  $R_3S^+ (H^+)$ ; strong carboxylic acids (trifluoroacetic acid, TFA; pentafluoropropanoic acid PFA; heptafluorobutyric acid, HBA); polarizable chaotropic anions (perchlorate  $ClO_4^-$ ; thiocyanate  $SCN^-$ ; iodide  $I^-$ ). Negatively charged reagent (IPR) can be used to retain positively charged ionic bases while positively charged reagent can be used to retain negatively charged ionic acids. The retention mechanism of this analytical method has been explained mainly by partition model [3] and adsorption model [4] respectively.

In the present article, efforts were made to provide some of the therapeutic agents used in the treatment of human diseases that have been determined in biological fluids by ion pair chromatography. A number of such determinations include:

- (i) Quantification of amphetamine, methamphetamine in urine [5].
- (ii) Assay of methadone in human plasma [6].
- (iii) Pramipexole determination in plasma and urine [7].
- (iv) Analysis of quaternary ammonium anti-cholinergics drugs in whole blood [8].
- (v) Assay of cephamycins in human serum and urine [9].
- (vi) Neomycin and bacitracin determination in human serum [10].
- (vii) Anthracyclines antibiotics assay in plasma and urine [11].
- (viii) Oxomemazine determination in human plasma [12].
- (ix) Methotrexate determination in plasma [13].
- (x) Ceftriaxone and other cephalosporins assay (cefotaxime, cefoperaz) in serum, urine, cerebrospinal fluid [15].
- (xi) Ketanserin assay in plasma [16].

### Conclusion

Treatment of human diseases is very vital once diagnosis has been established. The use of therapeutic agents (drugs) is one the treatment options in disease management. The efficacy of the therapeutic agents against any disease state can be verified by determining its maximum plasma concentration. Ion pair chromatography is one of those analytical methods that can be employed in such determinations. Ion pair chromatography is an accurate, reliable, selective and sensitive analytical method. It is a technique of choice for most analysts because of its versatility in analyzing both polar and non-polar chemical compounds, usefulness for the analysis at low concentrations, the determination of analytes in a wide concentration range and the ease of hyphenation with other spectroscopic methods. Finally, in addition to the analytical qualities in terms accuracy, precision, sensitivity, selectivity, ion pair chromatography is one of the most analytical techniques to offer substantial retention and versatile detection to ionizable analytes.

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