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Review

A review on development of analytical methods to determine monitorable drugs in serum and urine by micellar liquid chromatography using direct injection

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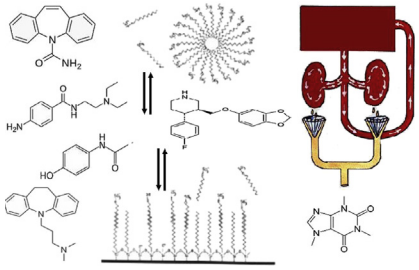
HIGHLIGHTS

- Therapeutic drug monitoring is a daily practice in clinical laboratories of the Hospitals.
- Micellar liquid chromatography is used to perform the monitoring, and the use of this technique has been here reviewed.
- The studied groups are: anticonvulsants, antiarrhythmics, tricyclic antidepressants, analgesics and bronchodilators.
- Detection techniques includes UV absorbance or amperometry, and samples are serum and urine.
- All methods has been optimized and validated.

GRAPHICAL ABSTRACT



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ABSTRACT

Therapeutic drug monitoring is a common practice in clinical studies. It requires the quantification of drugs in biological fluids. Micellar liquid chromatography (MLC), a well-established branch of Reverse Phase-High Performance Liquid Chromatography (RP-HPLC), has been proven by many researchers as a useful tool for the analysis of these matrices. This review presents several analytical methods, taken from the literature, devoted to the determination of several monitorable drugs in serum and urine by micellar liquid chromatography. The studied groups are: anticonvulsants, antiarrhythmics, tricyclic antidepressants, selective serotonin reuptake inhibitors, analgesics and bronchodilators. We detail the optimization strategy of the sample preparation and the main chromatographic conditions, such as the type of column, mobile phase composition (surfactant, organic solvent and pH), and detection. The finally selected experimental parameters, the validation, and some applications have also been described. In addition, their performances and advantages have been discussed. The main ones were the possibility of direct injection, and the efficient chromatographic elution, in spite of the complexity of the biological fluids. For each substance, the measured concentrations were accurate and precise at their respective therapeutic range. It was found that the MLC-procedures are fast, simple, inexpensive, ecofriendly, safe, selective, enough sensitive and reliable. Therefore, they represent an excellent alternative for the determination of drugs in serum and urine for monitoring purposes.

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Contents

1. Introduction

1.1. Role of therapeutic drug monitoring in medical care

Nowadays, the population is subjected to suffer a broad spectrum of diseases. Most of them cause symptoms that can strongly diminish the quality of life of the patient, and may have lethal consequences [1]. In order to cure them or palliate their symptoms, many drugs have been developed by the pharmaceutical industry. Physicians have established treatments based on them by selecting the most adequate medication, and adjusting the dose, frequency and route of administration, as well as the expected duration. Although these therapies usually have a high degree of success, some cases of failure, adverse side effects, weak clinical effects or relapse have been noticed. Therefore, a useful strategy to straighten these situations must be applied [2].

The beneficial effects of a drug are maximized when the plasmatic concentration remains in its therapeutic range. At higher values, adverse effects due to overdose can appear, and under the low value, the drug is ineffective and the patient may develop tolerance, as well as long-term negative side effects. Both cases can lead to an early interruption of the treatment. However, the blood concentration of a drug depends on diverse features, such as bioavailability, gastrointestinal absorption, drug interactions with other medications or endogenous compounds, metabolization, liver and renal activity, and elimination kinetics, which are related to a large number of personal factors, such as genetics, drug tolerance, immunology, environment, physiology, age, ethnicity, diet, health and lifestyle, among others. These factors strongly vary for each patient, and even for a same patient through time. As a consequence, the prescription of the same dose to diverse patients or at several stages of the therapy for the same patient can lead to different plasmatic concentrations and clinical results, complicating the success of the therapy. The implementation of therapeutic drug monitoring can help to resolve these situations [3,4].

Therapeutic drug monitoring (TDM) is a clinical practice, consisting on the determination of the biological behaviour of a prescribed drug in the human body through time. It is carried out through the quantification of the drug and its main metabolites in physiological fluids (mainly plasma, serum and urine) at several times after the ingestion of the pharmaceutical formulation, and at several stages of the treatment. It can be used to establish the pharmacokinetics for a specific patient and understand the influence of the personal characteristics. In addition, this would be useful to explain and predict the clinical effects. The medical staff can use the information provided by TDM to adjust the prescription (dose, frequency and route of administration) for each patient at each stage of the treatment, in order to maximize the beneficial activity and limit the side effects, by maintaining the plasmatic concentration in the therapeutic range. Besides, it can be applied to detect noncompliance or chronic abuse, as well as in medical research, to investigate the influence of the personal factors in the pharmacokinetics. In fact, the main goal of TDM is the improvement of the medical assistance for chronic and acute pathologies [4–7].

It is unnecessary to apply TDM for the majority of the