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Validated univariate and multivariate spectrophotometric methods for the determination of pharmaceuticals mixture in complex wastewater

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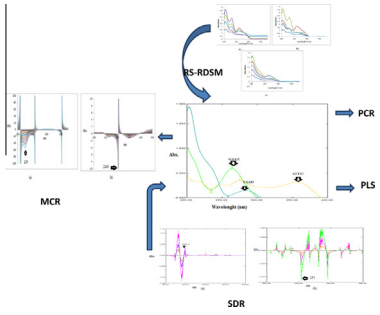
HIGHLIGHTS

- Five simple univariate and multivariate spectrophotometric methods were successfully applied.
- They are used for simultaneous analysis of complex ternary mixtures and do not require sophisticated techniques.
- They could be easily applied in wastewater analysis in case of lacking liquid chromatographic instruments.

GRAPHICAL ABSTRACT



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ABSTRACT

Five, accurate, precise, and sensitive univariate and multivariate spectrophotometric methods were developed for the simultaneous determination of a ternary mixture containing Trimethoprim (TMP), Sulphamethoxazole (SMZ) and Oxytetracycline (OTC) in waste water samples collected from different cites either production wastewater or livestock wastewater after their solid phase extraction using OASIS HLB cartridges. In univariate methods OTC was determined at its λ_{max} 355.7 nm (^{0}D), while (TMP) and (SMZ) were determined by three different univariate methods. Method (A) is based on successive spectrophotometric resolution technique (SSRT). The technique starts with the ratio subtraction method followed by ratio difference method for determination of TMP and SMZ. Method (B) is successive derivative ratio technique (SDR). Method (C) is mean centering of the ratio spectra (MCR). The developed multivariate methods are principle component regression (PCR) and partial least squares (PLS). The specificity of the developed methods is investigated by analyzing laboratory prepared mixtures containing different ratios of the three drugs. The obtained results are statistically compared with those obtained by the official methods, showing no significant difference with respect to accuracy and precision at $p = 0.05$.

Introduction

Since 1997, interest in the occurrence and behavior of pharmaceuticals in the aquatic environment has significantly increased although they are expected to occur in trace concentrations, because of their continuous use and bacterial resistance attributed to their action, they represent a particular problem [1]. Several investigations have shown some evidence that substances of pharmaceutical origin are often not eliminated during wastewater treatment and also not biodegraded in the environment [2].

In industrialized countries, most human use antimicrobials and other pharmaceuticals reach the aquatic environment, unchanged or transformed, mainly via discharge of effluents from municipal

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wastewater treatment plants (WWTPs). The residual concentrations of these bioactive compounds in the treated effluents depend on their removal during wastewater treatment. They can potentially pose a hazard for aquatic organisms if the removal is incomplete. In addition, exposure via sewage sludge disposal on land could represent a hazard for soil organisms [3].

The environmental persistence, rate of spread and bioaccumulation ability of biologically active substances differ depending on their chemical properties and on the environmental conditions. The continuous input of these compounds into the environment may lead to ecotoxicological effects [4–6]. In particular, antimicrobials are one of the most important groups of pharmaceuticals, employed in both human and veterinary medicine. These compounds have been used in large quantities for decades, and the emergence of antimicrobial resistance has prompted researchers to investigate their presence in the environment [7,8]. Such active compounds are frequently detected in environmental water samples.

Sulfonamides and tetracyclines are classes of antibiotic widely used in both human and veterinary medicine, Oxytetracycline (OTC) is from tetracycline (TCs) compound class, used to treat infections of the respiratory and urinary tracts, skin, ear, eye and Gonorrhoea. The drug is particularly useful when penicillins and/or macrolides cannot be used due to allergy. Trimethoprim (TMP) is of diaminopyrimidine compound class. It is a dihydrofolate reductase inhibitor, commonly prescribed with sulfonamides antimicrobial agents as synergist and mainly used in the prophylaxis and treatment of urinary tract infection. Sulfamethoxazole (SMZ) is one of the sulfonamides used for treatment of urinary tract infections they are also frequently used for the treatment of otitis, bronchitis, sinusitis and pneumocystis pneumonia [9].

The chemical structure of the selected drugs was shown in Fig. 1.

A number of papers described analytical methodologies for the determination of SMZ individually or combination in waste water such as HPLC-UV [10], HPLC-DAD [11], DLLME-UHPLC [12], and for OTC individually or in combination with other TCs such as UPLC-FD – tandem MS [13], HILIC-UV [14], and for TMP individually in waste water using LC–MS/MS [15].

A number of analytical methods were reported for TMP and SPM in either binary or multi-component mixtures using HPLC–MS [16,17], HPLC-DAD [18], UPLC–MS [19–21], capillary electrophoresis – UV [22], for TMP and OTC using HPLC-DAD [23], HPTLC-video densitometry[24], SMZ and OTC using UPLC and MS–MS [25], HPLC–MS [26,27], RRLC-MS [28].

Few methods have been reported for the determination of three selected antibiotics in wastewater by LC–MS [29–31].

Sample preparation is necessary to isolate the desired components from complex matrices, because most analytical instruments cannot handle the matrix directly [32]. Classical extraction procedures consume large amounts of solvent, and thus themselves create environmental and occupational hazards, and are often of very low selectivity. Analysts have responded to this challenge by increasing research on sorbent traps, solid-phase extraction (SPE), solid-phase microextraction (SPME), and stir bar sorptive extraction (SBSE) as alternatives to charcoal tube, liquid–liquid, and Soxhlet extraction which consume less solvent.

El-Bardicy et al. [33] introduced ratio subtraction (RS) method for the determination of binary mixtures where the spectrum of one component is extended than the other. Recently, RS method is used as a resolution method for solving the spectra of multi component dosage forms whether ternary or more [34,35], or as mixtures with their degradation products. In successive resolution technique the interference of one or more components in the mixtures was eliminated by applying stepwise ratio subtraction. After subtraction the constants of the interfering substances other spectra could be resolved as a binary mixture by conventional spectrophotometric methods (e.g. direct absorbance, derivative, derivative ratio, ratio difference. . ..etc.) could be used.

The aim of this work was to provide an accurate and a cost effective spectrophotometric methods, alternative to the use of HPLC in the simultaneous determination of selected pharmaceuticals: SMZ, TMP and OTC in complex production wastewater matrices. The method involved sample pre-treatment by solid-phase extraction (SPE) and analytical determination by several spectrophotometric methods. Then the developed spectrophotometric methods involved three univariate methods: successive spectrophotometric resolution technique (SSRT), which starts with the ratio subtraction method followed by ratio difference method, successive derivative ratio technique (SDR) and mean centering of the ratio spectra (MCR); and two multivariate methods: principle component regression (PCR) and partial least squares (PLS).

Theories of the novel univariate spectrophotometric methods

Successive spectrophotometric resolution technique (SSRT)

Successive spectrophotometric resolution technique starts with ratio subtraction method [33] for the ternary mixture of (*X*), (*Y*) and (*Z*) followed by ratio difference for the obtained binary mixture, where *Z* shows extended absorption spectrum than *X* and *Y*. (*X* + *Y*) can be determined by dividing the spectrum of the mixture (*X* + *Y* + *Z*) by a known concentration of *Z* as a divisor (*Z*′). The

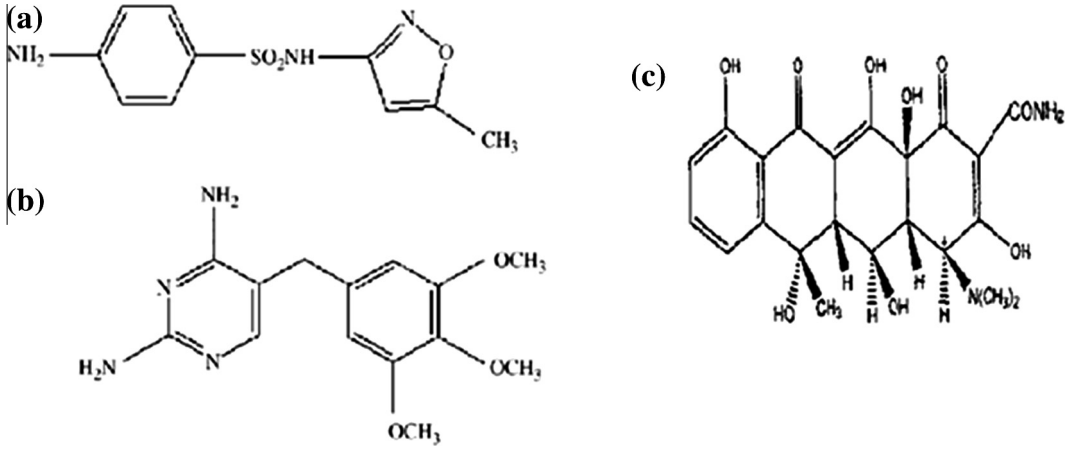

Fig. 1. Chemical structure of (a) Sulphamethoxazole (SMZ), (b) Trimethoprim (TMP) and (c) Oxytetracycline (OTC).