Determination of Cefadroxil Antibiotic by an Analytical Method

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Abstract
This paper includes the most relevant analytical methodology used for the determination of Cefadroxil antibiotic. Cefadroxil is an orally active semi-synthetic β-lactam antibiotic from the cephalosporin group, characterized by its prolonged action. This compound is effective against susceptible bacteria causing infections of the urinary tract, skin and soft tissue as well as pharyngitis and laryngitis. A variety of analytical methods have been proposed for the determination of cefadroxil in biological fluids and pharmaceutical samples. The spectrophotometric method using oxidative coupling reaction has been performed in which chloranillic acid & MBTH has been used as reagent at 535 nm & 420 nm absorbance with linear range of 15-415 µg/ml & 1-12µg/ml. Speed of analysis has become of paramount importance in many application areas, such as in pharmaceutical and clinical analysis, in order to increase throughput and reduce costs. In this way, the recently invented methods offer new practical possibilities for increasing their efficiencies.
Keywords: Cefadroxil(CFL); Antibiotics; Biological and pharmaceutical samples;

1. Introduction

Cephalosporins are β-lactam antibiotics which are closely related in structure and in their anti-bactericidal mechanism of action to penicillin and cephamicin which are also β-lactam antibiotics. The main nucleus of cephalosporins is 7-amino cephalosporanic acid (7-ACA) which is a cephem derivative and is obtained from cephalosporin C which is formed as a fermentation product of the *Cephalosporium acremonium* type of fungus. Cephalosporins[1] which are used for therapeutic purposes are semi synthetic
products. They are divided in four generations (Table 1), based approximately on the time of their discovery and their antimicrobial properties. In general, progression from first to fourth generation is associated with a broadening of the Gram-negative antibacterial spectrum, some reduction in activity against Gram-positive organisms, and enhanced resistance to β-lactamases. β-Lactam antibiotics, *i.e.*, penicillins and cephalosporins, are probably the most widely used class of medicines to treat respiratory tract infections, prostatitis,
urinary tract infections, skin, and soft tissues infections that are often caused by sensitive bacteria. Cefadroxil (CFL), represented in Fig. 1, is chemically designated as 8-[2-amino-2-(4-hydroxyphenyl)-acetyl]amino-4-methyl-7-oxo-2-thia-6-azabicyclo[4.2.0] oct-4-ene-5-carboxylic acid. It has the formula $C_{16}H_{17}N_3O_5S$. CFL is a first generation cephalosporin antibacterial drug that is the para-hydroxy derivative of cefalexin, and is used in the treatment of mild to moderate susceptible infections. CFL is a broad spectrum antibiotic effective in Grampositive and Gram-negative bacterial infections; it is a bactericidal antibiotic. CFL is active against many bacteria, including *Staphylococcus aureus*, *Streptococcus pneumoniae*, *Streptococcus piogenes*, *Moraxella catarrhalis*, *Escherichia coli*, *Klebsiella* and *Proteus mirabilis*. CFL is almost completely absorbed from the gastrointestinal tract and is generally well tolerated. About 20% of CFL is reported to be bound to plasma proteins and its plasma half-life is about 1.5 h. CFL is widely distributed in body tissues and fluids. More than 90% of a dose of CFL may be excreted unchanged in the urine within 24 h by glomerular filtration and tubular secretion. The most common side effects are diarrhoea or loose stools, nausea, abdominal pain and vomiting. Rarer side effects include abnormal liver function tests and allergic reactions. A wide variety of analytical methods have been reported for the determination of CFL in pure form, in pharmaceutical preparations and in biological fluids. These methods mainly involve spectrophotometry, atomic absorption spectrophotometry (AAS), fluorometry, chemiluminescence (CL), polarography, high performance liquid chromatography (HPLC), and capillary electrophoresis (CE). In this work, we have the method for the determination of CFL alone and in combination with other similar drugs through spectrophotometry.

2. Spectrophotometric method

2.1. Pharmaceutical analysis

2.1.1. ***Cefadroxil***

Various analytical procedures have been adopted for the determination of this drug, such as colorimetric methods[2-3], and also, fluorimetry, polarography, and liquid chromatography. In general, the colorimetric methods require a preliminary treatment of the samples such as alkaline or acid hydrolysis of the antibiotic and the use of a complexing agent. Moreover, the method has the disadvantage of not distinguishing between cephalosporins and other sulphide-producing degradation products.

Spectrophotometric method[4,9] using oxidative coupling reactions has been performed. As CFL possesses a p-substituted phenol group, the suitability of 3-methyl-2-benzothiazolinone hydrazon hydrochloride (MBTH) in conjunction with different oxidants(ferric chloride, potassium dichromate,sodium metaperiodate, chloramines-T,potassium hexacyanoferrate (III) and ceric ammonium sulphate) for the determination of CFL was examined and Ce(IV) was found to be the best with respect to sensitivity, speed and stability of the coloured product formed. In the second procedure, CFL was allowed to react with

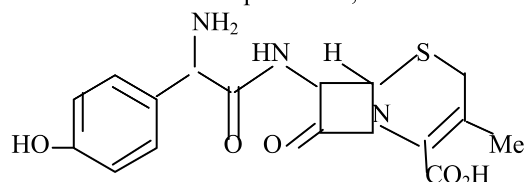

Fig. 1. Chemical structure of cefadroxil.

4-AP in the presence of alkaline $[Fe(CN)_6]^{3-}$Other oxidising agents, such as potassium persulphate, sodium metaperiodate and potassium iodate, were tried and found to be inferior with respect to sensitivity. CFL was determined in dosage forms through the reaction with Folin reagent to form a blue coloured chromogen. formaldehyde reagent, which gives a yellow chromogen. CFL was determined kinetically by measuring the absorbance at 470 nm after hydrolysis with NaOH at 80˚C over the suitable concentration range. Validation[5] of the method has been performed by assay of CFL in commercial capsules and tablets.

Table 1

Classification of cephalosporins.

Generation	Compounds
First	Cefadroxil, Cefacetrile, Cefalexin, Cefaloglycin, Cefaloridine, Cefalotin, Cefapirin, Cefatrizine, Cefazedone, Cefazolin, Cefradine,Cefroxadine,Ceftezole
Second	Cefaclor, Cefamandole, Cefmetazole, Ceforanide, Cefotiam, Cefprozil, Cefuroxime
Third	Cefdinir, Cefditoren, Cefetamet, Cefixime, Cefmenoxime, Cefodizime, Cefoperazone, Cefotaxime, Cefpiramide, Cefpodoxime, Cefsulodin, Ceftazidime, Ceftibuten, Ceftizoxime, Ceftriaxone, Latamoxef
Fourth	Cefepime, Cefpirome, Cefquinome

In contrast to other methods using sophisticated instruments, this method is simple to implement with relatively inexpensive instrumentation and fewer operators are required since the method is almost fully automated. The speed of analysis and the precision make this method also suitable for the quality controls of most industrial products, such as pharmaceuticals, food, and beverages.

Table 2
Spectrophotometric method for the determination of cefadroxil in the pure state & in pharmaceutical dosage form.

Reagent	Experimental conditions	Analytical characteristics
Chloranillic acid[6-7]	In a mixture of methanol and ethanol at 50˚C for 15 min; at 535 nm	Linear range 15−415 µg/ml; RSD 1.4%; recoveries 99.0%−100.8%
Diazonium salt of sulfanilic acid[8]	At 420 nm	Linear range 1−12 µg/ml recoveries 94.8%−98.2%
MBTH in presence of ceric ammonium sulphate[9]	25 ml calibrated flasks, with aliquots of CFL, added 2 ml of 3-methyl-2-benzothiazolinone hydrazon hydrochloride (MBTH) and kept for 2 min at room temperature. Then 2 ml of Ce(IV) added, kept for 15 min and diluted to the mark with water; at 410 nm	Linear range 1.0−6.0 µg/ml; recoveries 98.0%−100 %; RSD 1%
4-aminophenazone[9] in presence of potassium hexacyanoferrate(III)	25 ml calibrated flasks with aliquots of CFL, 0.6 ml of sodium carbonate, 1 ml of 4-AP and 1 ml of $K_3[Fe(CN)_6]$ added successively and total volume brought to 9 ml with water, solutions set aside for 5 min and diluted with water; at 510 nm	Linear range 1.5−24.0 µg/ml; recoveries 96.0%−100.1%; RSD 1%
2,6-dichloroquinone-4-chlorimide[9] (Gibb's reagent, DCQC)	25 ml calibrated flasks with CFL, 1.5ml of borate buffer solution (pH 9.4) and 2.5 ml of DCQC added successively and the total volume brought to 10 ml with water, after 10 min the flasks were made up to the mark with water; at 620 nm	Linear range 1.2−4.2 µg/ml; recoveries 98.0%−100.5%; RSD 1%

Table 3
Spectrophotometric method: procedure and analytical characteristics for CFL.

Procedure	Linear range (µg/ml)	Detection limit (DL, µg/ml)	RSD (%)
1−5 ml of stock solutions placed in 10 ml calibrated flasks. Distilled water added to give volumes of 5 ml. Fresh ascorbic acid reagent (1 ml) was then added to each flask before heating at 100˚C for 20 min. After cooling, the volume was completed to 10 ml with water, mixed well before reading at 410 nm	2−12	0.6	< 1%
1 ml of *o*-nitroaniline and 2.5 ml of sodium nitrite mixed and left to stand 10 min. Accurately measured aliquots of standard drug added followed by 1.5 ml of sodium hydroxide. Mixture allowed to stand 5 min and then treated with 5 ml of copper sulfate, 6 ml of 0.5 mol/l sulphuric acid and extracted three times with a total volume of 25 ml of chloroform. Extracts collected in a 25 ml calibrated flask; absorbance measured at 415 nm	3−7	0.067	0.02

5. Conclusion

As can be seen that, several methods for analyzing CFL in pharmaceuticals and biological fluids[10] have been performed, including spectrophotometry. Compared with other techniques, spectrophotometry is very simple, rapid, non-destructive and less expensive. In addition to this, spectrophotometers are commonly available in all laboratories. Most of these detectors have been coupled with flow injection analysis (FIA). In recent years, it is becoming a powerful analytical tool for pharmaceuticals in general and also for CFL determination because of the low detection
limit and wide linear dynamic range. The combination of determination[11] and detection has been developed rapidly bringing together the advantages of both techniques in rapid and simple instrumentation and allowing improvements in sensitivity, selectivity and precision. Speed of analysis has become of paramount importance in many application areas of this method, such as in pharmaceutical and clinical analysis[12], in order to increase throughput and reduce costs. In this way, the recently developed method offer new practical possibilities for increasing efficiencies.

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