Development of HPLC Method for Determination of Colistimethate Sodium

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Introduction. Colistin (polymyxin E) is a polypeptide antibiotic, an effective treatment of infections caused by multi-drug resistant (MDR) Gram negative bacteria, such as MDR *Pseudomonas aeruginosa, Klebsiella pneumonia* and *Acinetobacter baumanii*. Colistin is commercially available in two forms as the sulfomethate sodium salt and as sulfate. Colistin is administered intravenously in the form of colistimethate sodium (CMS). *In vivo* the CMS is converted to colistin sulfate by hydrolysis. Hydrolysis of colistin sulfomethate sodium to colistin provides the drug antimicrobial activity. Colomycin is medicinal drug product what contains CMS and it is used in Pauls Stradins Clinical University Hospital (PSCUH) as a last resort agent for treatment of infections caused by multi-drug resistant (MDR) Gram negative bacteria. The main adverse effects of colomycin are nephro- and neurotoxicity; therefore, careful monitoring of plasma colistin levels could be beneficial.

Aim, Materials and Methods. The aim of the study was to develop a method for determination of CMS in medicinal drug product Colomycin using high performance liquid chromatography.

In this review were included articles from PubMed database published in 1981–2018. The searching keywords were (Determination of Colistin using liquid chromatography), and only articles published in English were included.

Results. According to the literature data, colistin has a very weak ultraviolet absorption and absence of native fluorescence. Additionally, taking into account that CMS is a polypetide, it consists of two major components Colistin A (Polymyxin E1) and Colistin B (Polymyxin E2) that means the sum of both peaks required for precise quantification. Therefore, it provides difficulties with the determination of CMS. During the method development, the mobile phase included water and acetonitrile (ACN) in different proportions and as the stationary phase were tried three different columns – Thermo BDS Hypersil C18 150 × 4.6 mm 5 μ, BEH C18 50 × 2.1 mm 1.7 μ and Symmetry C18 100 × 4.6 mm 5 μ. The UV detector was set to 215 nm after taking spectra of stock solution. A mixture of 0.05 % v/v aqueous trifluoroacetic acid (TFA) and ACN was finally chosen as the preferred mobile phase and BEH C18 as stationary phase because it produced the desired separation. The separation of Colistin A and Colistin B was performed only after applying gradient of 0.05 % v/v aqueous TFA acid and ACN for elution.

Conclusion. Colistimethate sodium has both *polar* and hydrophobic regions, the molecule is amphiphilic and thereby able to distribute well in both polar and non-polar environments. It also consists of two major components Colistin A (Polymyxin E1) and Colistin B (Polymyxin E2). Consequently, analysis requires stationary phase with small particle size and gradient conditions for separation and quantification of medicinal drug product.