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Multiple response optimization applied to the development of a capillary electrophoretic method for pharmaceutical analysis

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Abstract

Multiple response simultaneous optimization by using the desirability function was used for the development of a capillary electrophoresis method for the simultaneous determination of four active ingredients in pharmaceutical preparations: vitamins B_6 and B_{12}, dexamethasone and lidocaine hydrochloride. Five responses were simultaneously optimized: the three resolutions, the analysis time and the capillary current. This latter response was taken into account in order to improve the quality of the separations. The separation was carried out by using capillary zone electrophoresis (CZE) with a silica capillary and UV detection (240 nm). The optimum conditions were: 57.0 mmol l^{-1} sodium phosphate buffer solution, pH 7.0 and voltage = 17.2 kV. Good results concerning precision (CV lower than 2%), accuracy (recoveries ranged between 98.5 and 102.6%) and selectivity were obtained in the concentration range studied for the four compounds. These results are comparable to those provided by the reference high performance liquid chromatography (HPLC) technique.

Keywords: Multiple response optimization; Desirability function; Capillary electrophoresis; Lidocaine; Dexamethasone; Vitamins B_6 and B_{12}

1. Introduction

The analysis of complex preparations in the pharmaceutical field calls for very powerful separation techniques. The simultaneous determination of a large number of components can be performed by high performance liquid chromatography (HPLC). On the other end, due to its high efficiency, capillary electrophoresis (CE) appears as an appropriate technique for the analysis of complex formulations, as demonstrated in several published papers in this area, in which CE has been shown as a valuable alternative technique for their separation [1–4].

In developing a CE method, optimization is usually applied to reduce the analysis time, without losing the resolution between the peaks originated by the analyte migration. The need of taking into account different aspects of the analysis at the same time calls for the use of multicriteria optimization. In order to carry out the latter type of optimization, experimental design is a valuable tool, specifically surface response analysis [5]. In addition, when different objective functions have to be optimized, the so-called Derringer's desirability function is a valuable tool [6]. This function requires to define which results are acceptable for each individual response and which results are not be acceptable at all. Then a continuous function between these two conditions should be fitted. Remarkably, though this methodology presents considerable advantages in chemical analyses, few applications can be found in the literature [7–11].

The mixture of vitamin B_6 (pyridoxine hydrochloride), vitamin B_{12} (hydroxocobalamin), dexamethasone and lidocaine hydrochloride is usually present in several pharmaceutical preparations (injection and tablets). This association is used in human medicine as analgesic, anti-inflammatory, myorelaxant and antineuritic. It produces a rapid and effective response in the treatment of many diseases such as articular rheumatism, post-traumatism of the local motion system, osteoarthritis, ankylosing spondylitis, musculoeskeletal disorders, postpartum pain and sport injuries. The most important side effects that have been reported are of gastrointestinal origin (ulcer, bleeding ulcers, etc.) [12–14]. Fig. 1 shows the structure of the four studied analytes.

Different monographs were introduced in the USP XXVI for the separate determination of dexamethasone, lidocaine, vitamin B_6 and B_{12} in injections, by using high performance

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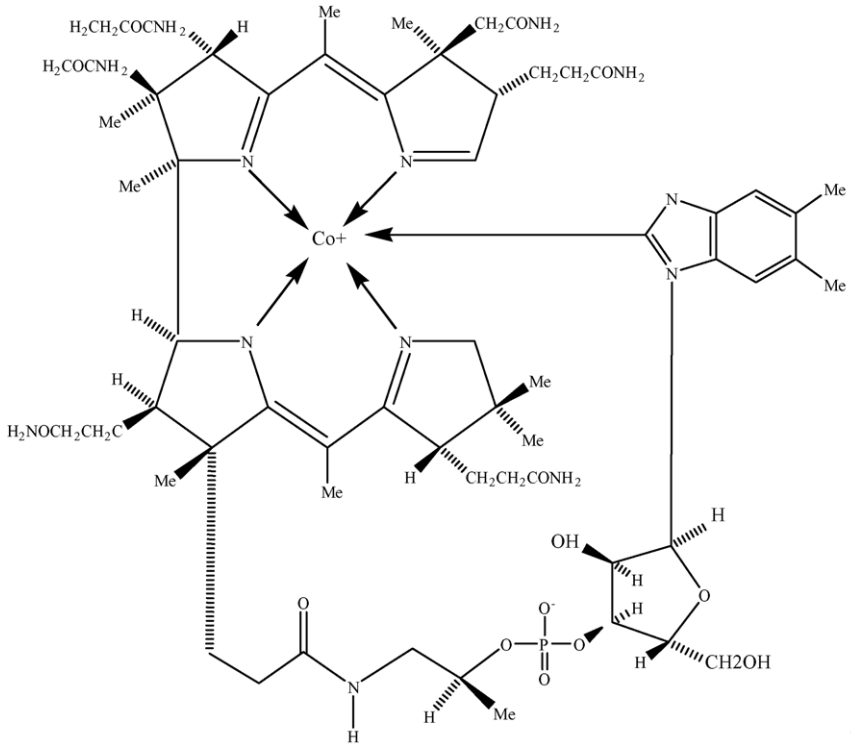
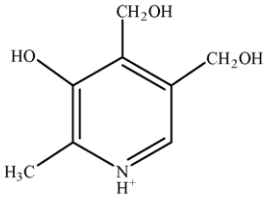
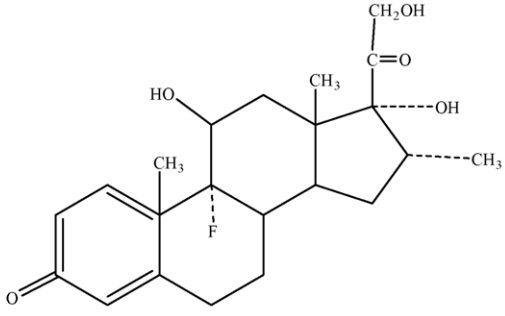


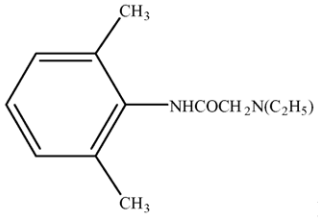
Vitamin B12



Vitamin B_6



Dexametasone



Lidocaine

Fig. 1. Structures of the four studied analytes.