DRUG ANALYTICAL RESEARCH - *ISSN: 2527-2616*
XIII MEETING OF Pharmaceutical Sciences Graduate Program of UFRGS, 2021 – Brazil
www.seer.ufrgs.br/dar

Development and Stability Assessment of Oral Liquid Pharmaceutical Forms Containing Baclofen for Hospital Use

Elisa de Saldanha Simon*[a]; Gabriele Primieri[a]; Caren Gobetti[a]; Nathalie Wingert[b]; Nádia Volpato[a]; Martin Steppe[a].

[a]*Laboratório de Controle de Qualidade Farmacêutico, Faculdade de Farmácia, Universidade Federal do Rio Grande do Sul, Porto Alegre, Brazil;* [b]*Núcleo de Pesquisa e Análise de Medicamentos, Faculdade de Farmácia, Universidade Federal da Bahia, Salvador, Brazil.*
**Doctoral's student since 2017*

Research area: Development, quality evaluation and use of pharmaceutical and cosmetic services, raw materials and produtcts (A1)
Subject area: Quality control
Keywords: baclofen; liquid oral formulation; quality by design; stability; chiral drug.

Introduction

The lack of oral liquid pharmaceutical forms suitable for use in pediatric and adult patients with swallowing difficulties is a public health problem, especially in the hospital context (1-2). The chiral drug baclofen is marketed in Brazil only in the tablets form containing its racemate, which highlights the need to develop liquid formulations to facilitate dose adjustment, administration and swallowing (3). This study aimed to develop oral liquid formulations containing the raw material of the drug baclofen, free or not of sugar, as a therapeutic alternative for hospitalized pediatric or adults patients with swallowing difficulties, optimizing them through the quality by design approach (QbD) and assess its stability.

Experimental section

Preliminary stability studies were carried out with twelve pre-formulations containing baclofen (5 $mg.mL^{-1}$) stored at room temperature for 28 days, evaluating aspect, color, odor, pH, viscosity and sedimentation volume after preparation and every seven days. With the aid of the MOODE® 12.1 software, the QbD methodology was applied through experimental screening and optimization designs. High performance liquid chromatography analytical method (HPLC) was developed for the quantitative determination of baclofen in formulations. The formulations were stored in amber glass bottles at room temperature, refrigerated and in an oven and their physical-chemical and microbiological stability was evaluated 14 days after preparation.

Results and Discussion

The analytical method presented selectivity, linearity, detection and quantification limits, precision, accuracy and robustness, in addition to an indicative character of stability, being adequate for the intended purpose. In preliminary stability studies, the preformulations presented variations within the specified limits for the evaluated parameters. The QbD study led to two formulations that met the pre-defined critical quality attributes, one containing glycerin, potassium sorbate, citric acid, liquid flavor, purified water and simple syrup as a vehicle, and the other containing the same excipients, sucralose and sodium carboxymethylcellulose solution as a vehicle. Both formulations presented aspect, color, odor, pH, viscosity, contente and microbiological stability in accordance with the established limits, for 14 days, at the three temperatures evaluated.

Conclusions

The optimized formulations remained stable for a period of 14 days, when stored at room temperature, refrigerated and in an oven. Such formulations have a simplified composition and production process and may serve as a contribution to the preparation of liquid oral formulations containing baclofen in hospital routine, in addition to collaborating with the safety and adherence to the treatment of adult and pediatric patients.

Acknowledgments

Financial support from CNPq/Brazil, doctoral scholarship from CAPES/Brazil and Hospital de Clínicas de Porto Alegre.

References

1. L. A. Ferreira *et al*., *Rev. Assoc. Med Bras*. 58, 82 (2012).

2. J. Magalhães *et al*., *Eur. J. Clin. Pharmacol.* 71, 1 (2015).
3. Bula Lioresal® Comprimidos 10 mg (NOVARTIS, São Paulo, 2020), https://portal.novartis.com.br/upload/imgconteudos/2796.pdf Acessed in 08.10.2021.