On the basis of the Resolution 189/2018 published by our City Health Counseling, our hospital pharmacy service was entrusted with the centralization of the procedure for the acquisition, compounding, distribution and dispensing of methadone to drug addicts integral attention centers. In order to improve and increase the beyond use date (BUD) of methadone oral solutions, we will carry out a physicochemical stability study.

**BACKGROUND AND IMPORTANCE**
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**AIM AND OBJECTIVES**
To perform an analytical method development and validation to carry out a physicochemical stability study of two oral solutions of methadone to increase their BUD. Method development should be made in an effective and reproducible manner.

**MATERIAL AND METHODS**
The study was carried out on two formulations of methadone 10 mg/mL, which were prepared with and without parabens as preservatives.

- First, we carried out the analytical method development to achieve the analytical performance characteristics.
- Then, we accomplished the analytical method validation obtaining the linearity; instrumental intra-assay, and inter-assay precision; accuracy and recovery percentage.

**RESULTS**

**Chromatographic conditions**
- **Flow rate**: 1.6 mL/min
- **Mobile phase**:
  - A: Water (phosphate buffer: 25 mM, pH=10);
  - B: Organic (Acetonitrile)
    - B: 55%
    - A: 45%
- **Injection volume**: 5 µl
- **Temperature** in the column: 40°C
- **Column**: Xterra C18 (because methadone pKa =8.3)
- **Retention times**:
  - Methadone: 4.10 minutes
  - Methylparaben 0.67 and propylparaben 0.82 minutes

The final methadone determination method was validated for a standard of 10 mg/mL and applied for the determination of methadone with two parabens.

**CONCLUSION**
Analytical method development and validation procedures are vital in the discovery and development of drugs and pharmaceuticals to ensure performance of the method. The proposed HPLC conditions to determine methadone have been proved to be valid and reproducible for carrying out physicochemical stability studies of different methadone oral solutions. According to ICH, robustness should be assessed as well.

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