Chemical and physical stabilities of admixture of Morphine HCl and Clonidine at high and low concentrations

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INTRODUCTION

- Clonidine, an alpha2-adrenoreceptor agonist, is frequently combined to opioids (i.e., morphine hydrochloride) for the management of chronic pain.
- In the palliative care, the mixture of clonidine and morphine is preconized in front of rapid increasing doses when a tolerance effect is suspected.
- The study aimed to evaluate the physical and chemical stabilities of this analgesic admixture at high and low concentrations in 14 mL and 48 mL polypropylene syringes.

MATERIAL AND METHODS

- Stability of low concentration was evaluated on five syringes of admixture clonidine (Catapressan® 0.15 mg/mL, Boehringer Ingelheim, Germany) and morphine (morphine hydrochloride 40 mg/mL, Sterop, Belgium) at 0.003 and 0.417 mg/L, respectively, in 48 mL of NaCl 0.9%.
- The high concentration with 0.032 mg/mL of clonidine and 4.286 mg/mL of morphine was evaluated on five syringes of 14 mL NaCl 0.9%.
- All syringes were stored for 30 days at 5±3°C.
- Periodic samples were visually and microscopically examined to observe any particle appearance or colour change.
- pH and absorbance at 3 wavelengths (350, 410 and 550nm) were measured.
- The concentrations were measured by Ultra-High Performance Liquid Chromatography (UHPLC) – photodiode array detection.

RESULTS

- During the 30 days, syringes at low and high concentrations have evolved in the same way. There was no change in color or appearance of opacity, turbidity or precipitation and pH remained stable.
- The low and high admixtures were considered as chemically stable since the lower one-sided prediction limit at 95 % remains superior to 90 % of the initial concentration.
- Concentration measurements demonstrated that degradation rate was less than 1 % per 10 days for each component in both admixtures.

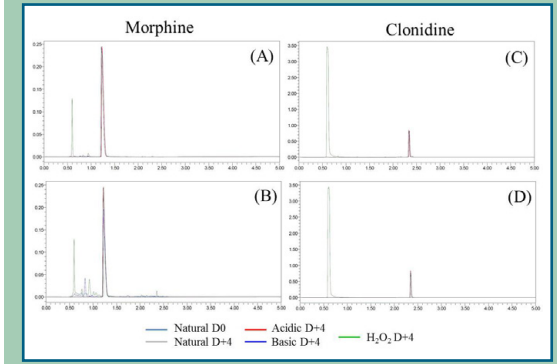

Figure 1: Evaluation of stability-indicating capability of the method by forced degradation at day 4 in different conditions. Morphine at room temperature (A) and at 60°C (B). Clonidine at room temperature (C) and at 60°C (D). Chromatogram in black was in natural condition at Day 0, in grey was natural condition at day four, and in red was acidic condition at day four, in blue basic condition at day four and in green oxidative condition at day four.

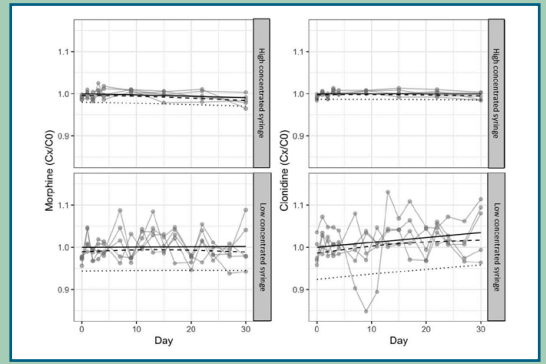

Figure 2 : Relative concentration evolution over time for Morphine (A) and Clonidine (B). Grey lines represent observations for each studied syringe. Black line represents the mean estimated by the linear regression. Dashed line represents the lower limit of the one-sided 95% CI and Dotted line represents the lower limit of the one-sided 95% prediction interval.

Reference
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CONCLUSION

- The admixture of clonidine and morphine HCl at low and high concentrations in polypropylene syringes appeared to be physically and chemically stable throughout the studied period of 30 days at 5±3°C.
- In conclusion, the admixture can be prepared in advance under aseptic condition by a centralized intravenous additive service in the department of pharmacy.

Possible conflict of interest : nothing to disclose.