

# Mixture of morphine and clonidine at high and low concentrations: evaluation of physical stability



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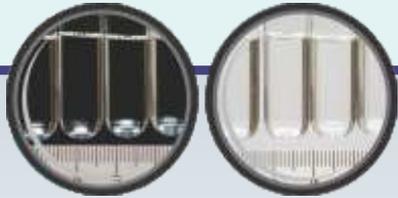
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## Background

- 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 aim of this study was to evaluate the physical stability of this analgesic combination at high and low concentrations in 14 mL and 48 mL plastic syringes.



## Material and methods

- Physical stability of low concentration was evaluated on five syringes of mixture clonidine (Catapressan® 0.15 mg/mL, Boehringer Ingelheim, Germany) and morphine (morphine hydrochloride 40mg/mL, Sterop, Belgium) at 0.003 and 0.417mg/L, respectively, in 48mL of NaCl 0.9%.
- The high concentration corresponding at 0.032 mg/mL of clonidine and 4.286 mg/mL of morphine was performed in five syringes of 14 mL NaCl 0.9%.
- All samples were visually examined immediately after the production and after 1 h, 4 h, 8 h, 24h, 48 h and 72h, on black and on white background.
- In addition, the apparition of turbidity was checked by spectrophotometric measurements (Genesys 10 series, USA) at three wavelengths (350, 410 and 550 nm) and pH was monitored with glass electrode pH-meter (Inolab level 1, WTW Weilheim, Germany with biotrode electrode, Hamilton, Bonaduz, Switzerland) throughout the period test.
- The crystal formation has been microscopically verified after centrifugation of each sample.



## Résultats

- During the 72 h period, syringes at low and high concentrations have evolved in the same way.
- There were no changes in color or appearance of opacity, turbidity or precipitation.
- Spectrophotometric measurements and pH were not significantly affected.
- The microscopic analysis did not detect any aggregate or crystal formation.

## Conclusions

- The mixture of clonidine and morphine hydrochloride at low and high concentrations in plastic syringes is physically stable for at least 72 hours at 4°C and at room temperature.
- These results paved the way for a subsequent study of chemical stability by Ultra Performance Liquid Chromatography.

