DEVELOPMENT OF A NEW ORAL SUSPENSION OF MORPHINE AT 1 MG/ML FOR NEONATAL AND PEDIATRIC USE IN A READY-TO-USE LIQUID VEHICLE

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INTRODUCTION

Background: Lack of dosage adapted to newborns to treat pain and neonatology abstinence syndrome at hospital → **Hospital compounding Morphine at 1 mg/mL**

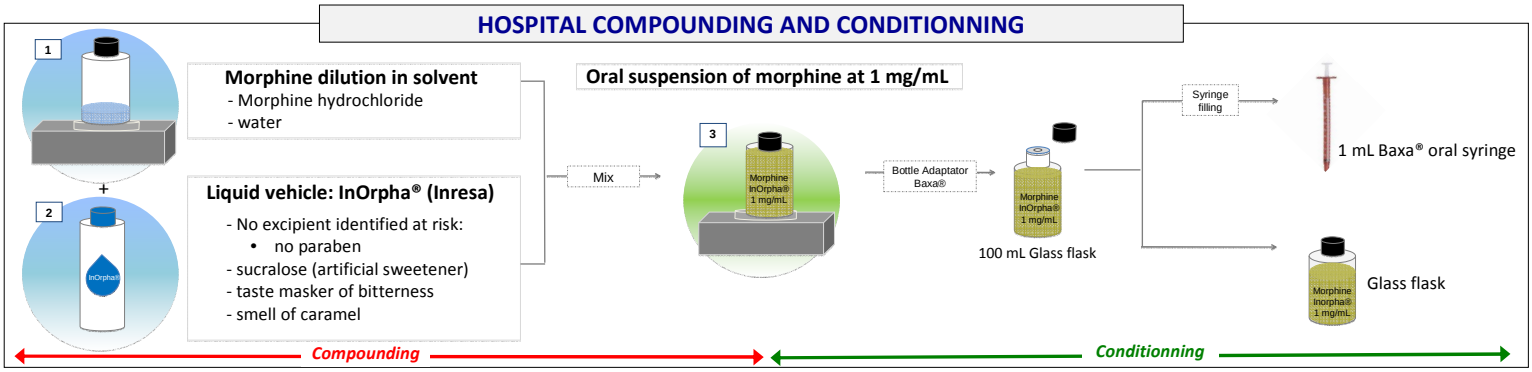
Current pratice: Morphine syrup dispensed in a glass flask

- ☺ Paraben free - alcool free
- ☹ High viscosity - high osmolality - stability limited to 1 month

Aim

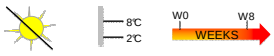
- A new oral morphine formulation adapted to newborns
- easier to prepare and to dispense at hospital
- with a longer stability period

HOSPITAL COMPOUNDING AND CONDITIONNING



STABILITY STUDY

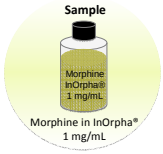
A stability study was led on syringes placed with the proximal site downward and on a glass flask, both stored at 2-8°C, out of light and for eight weeks.



PHYSICAL PROPERTIES

Organoleptic properties

The liquid suspension of morphine has and keeps:
- ➢a yellow colour
- ➢a sweet smell of caramel



pH measurement

pH was determined by a pH strip indicating.
- ➢An acid value was obtained (5 units)
- ➢pH is in agreement with the good morphine stability in acid conditions

➢ After eight weeks of storage, the yellow colour, the smell of caramel and the acid pH (5 units) of the suspension of morphine were maintained for syringes and the glass flask.

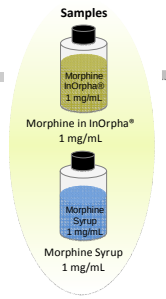
Relative viscosity

- **Rotational viscometer**

- Contraves – Mettler Rheomat 115
- Couette geometry : MS DIN 125
- Sample temperature : 20 °C
- Shear rate: 100 s^{-1}
- Recording time: 1 min

- **Viscosity:**

	Morphine syrup 1 mg/mL	Morphine in InOrpha® 1 mg/mL
Viscosity (mPa.s^{-1})	11	5.6



➢ Viscosity of morphine in InOrpha® is twice less that morphine syrup, making easier the syringe administration.

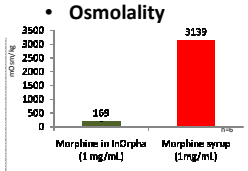
Osmolality

- **Osmometer (freezing point depression)**

- Advanced Micro-Osmometer Model 3300
- volume sample : 20 µL
- Recording time: 1 min

➢ Mean viscosities of Morphine in InOrpha® and in syrup are close to 200 and 3000 mOsm/kg, respectively.

- **Osmolality**

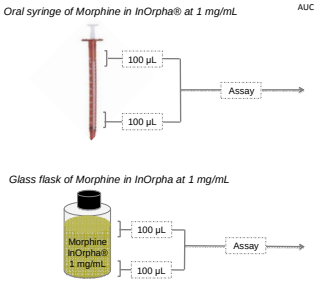


➢ Osmolality of morphine in InOrpha® is fifteen less that the morphine syrup, decreasing risk of enterocolities for neonate and abdominal pain.

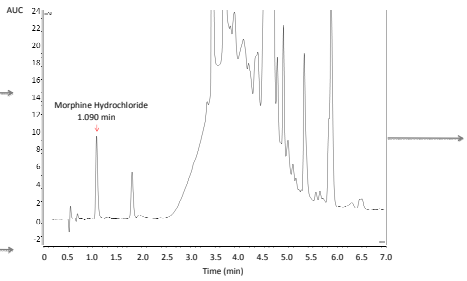
CHEMICAL STABILITY

Drug content and Homogeneity

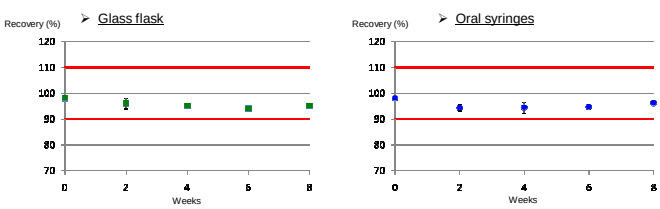
Sampling



HPLC/UV



Recovery and Homogeneity



➢ Each experiment day, two aliquots were withdrawn and analysed with a HPLC/UV method

➢ After 8 weeks, morphine recoveries in the glass and oral syringes are both between 90 and 110%, in agreement with our validation criterias.

➢ Homogenities between the proximal and distal sides have been checked and approved by the Wilcoxson test (p-values > 0.05).

➢ **After 8 weeks, physico-chemical stability was maintained with no degradation products observed and with acceptable recoveries.**

CONCLUSION

After 8 weeks of storage at 2-8°C out of light, morphine in InOrpha® vehicle at 1 mg/mL remains stable in both pre-filled syringes and volumetric flasks. This ready-to-use excipient appears to be a suitable vehicle to compound and deliver morphine to children. Currently, the stability study is still ongoing to assess the maximum stability period.

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