

STABILITY STUDY OF 0.2% MORPHINE MOUTHWASHES FOR HIGH DOSE CHEMOTHERAPY INDUCED MUCOSITIS

Auteurs : **Marie Dubois**¹, **Kathleen Leger**¹, **Elina Wolff**¹, **Sophie Perriat**¹, **Anais Grand**¹, **Yann Cretu**¹, **Jean Marie Canonge**¹, **Coralie Guillemot**¹, **Florent Puisset**¹
Pharmacie IUCT-Oncopole, Toulouse, France

Introduction and objectives :

Treatment of pain of chemo-induced mucositis after high dose chemotherapy : unmet medical need et no gold standard.

Proposition of 0.2% morphine mouthwash for pain relief and limiting systemic opioid intake.

According to study in our facility : pain relief without increasing opioid intake in near than 50% of patients

Stop mouthwashes before using all preparations and destruction prepared mouthwashes

? Possibility of setting up a serial preparation ?

Objectives : Assess the physical, chemical and microbiological stability of 0.2% morphine mouthwashes to set up hospital preparations.

Method and materials:

✓ **Development** of a high performance liquid chromatography (HPLC) method using a photodiode array detector, a ProntoSIL® C18 column (150 x 4.6 mm, 5 µm), a mobile phase with a mixture of trifluoroacetic acid at 0 , 1% and acetonitrile in an 80:20 volumetric ratio, at a wavelength of 255 nm to measure the concentration of morphine.

✓ **Validation of HPLC method :**

Forced degradation of morphine in NaOH, HCl, H₂O₂ and heat

Linearity → correlation coefficient r = 0,999

Inaccuracy → [-2,6;2,7] – Precision → [0,05;0,39]

✓ **Preparations :**

1 batch of 48 mouthwashes kept at room temperature

1 batch of 48 mouthwashes kept between 2°C and 8°C

✓ **Measure at each time** (t0, week 1-2-3-4-6-8-10 and 12):

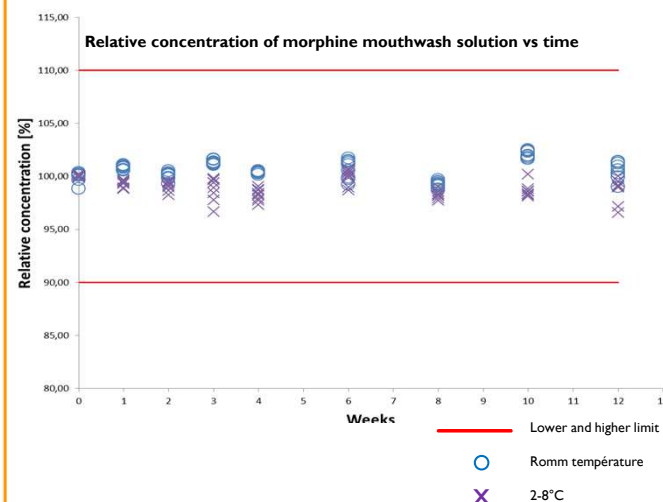
Visual control

Concentration measurement and emergence of degradation products by HPLC

pH measurement by pH meter

Bacteriological monitoring

Results:



→ Stability of morphine concentration from the 12th week

→ No formation of degradation product

→ No color change

→ Sterility of mouthwashes

BUT :

→ Elevation of pH from the 8th week

Conclusion : According to these results, the chemical and microbiological stability of 0.2% morphine mouthwashes stored at room temperature and between 2 and 8°C as well is proven for three months. Due to the physical stability, the shelf life of morphine mouthwash is capped to 2 months. Therefore, the stability is as long as enough to allow the preparation of morphine mouthwashes as serial preparation.