

# PH STABILITY OF TETRACAINE SOLUTIONS FOR SURFACE ANAESTHESIA

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## Background

Tetracaine hydrochloride is a local anaesthetic agent commonly used for surface anaesthesia, typically used in concentrations of 2-4 % for anaesthesia of the nose and throat. The substance is an ester – a functional group sensitive to pH – and over time it slowly degrades. Over the same time, the solution, in our experience, also discolours. For this reason tetracaine solutions have been made extemporaneously in our pharmacy – with a limited shelf life.

## Purpose

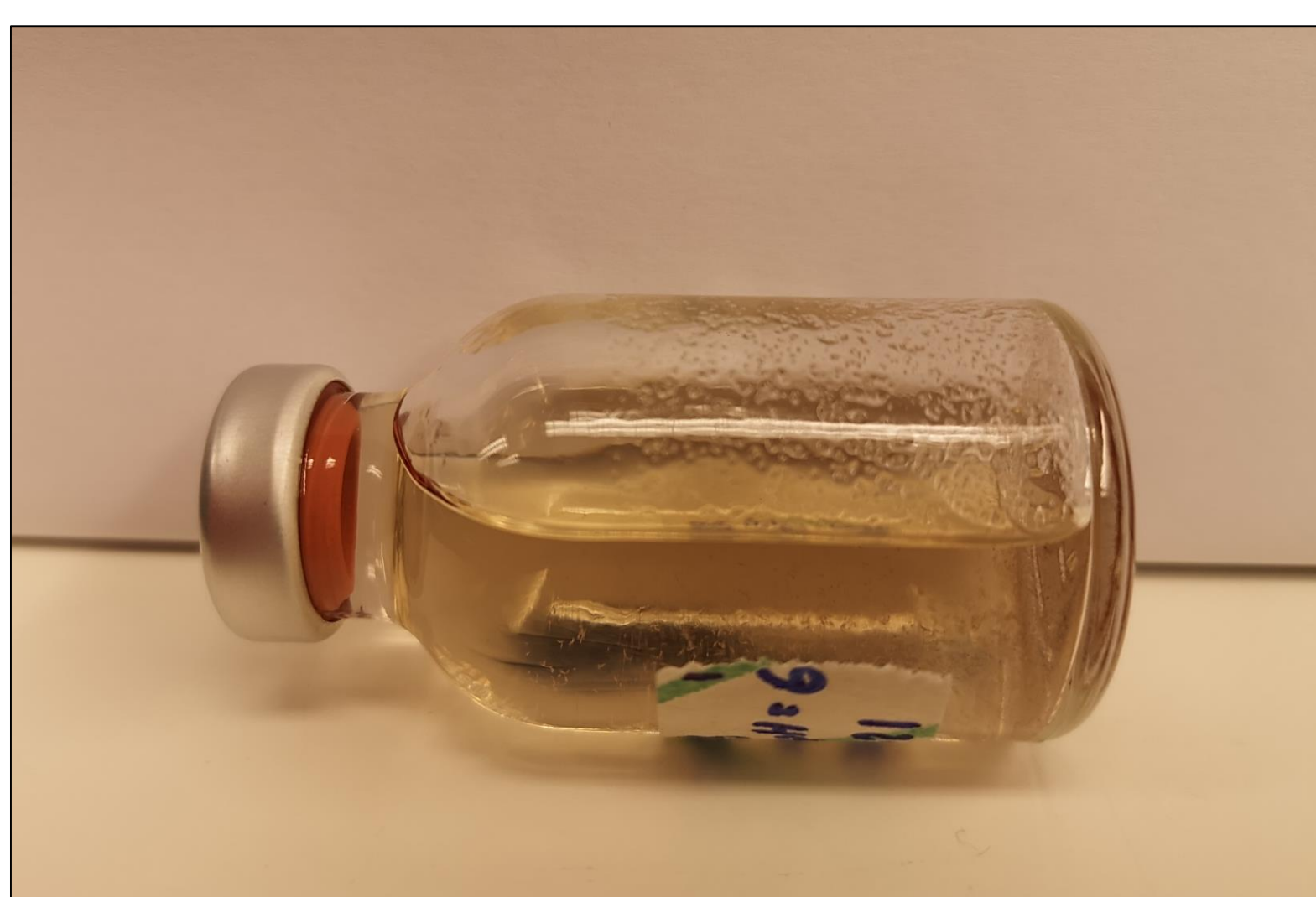
- To investigate the stability of a concentrated tetracaine solution (20.0 mg/mL), conserved with methylparaben
- To investigate the relation between pH and stability
- To investigate the relation between stability, degradation and appearance

## Materials and Methods

- Tetracaine hydrochloride from Sigma-Aldrich, St. Louis, Missouri, USA.
- **Instrument:** UHPLC-system from Shimadzu Corp, Kyoto, Japan (with a Nexera DAD-detector).
- **Analytical column:** Ace Excel 2 C8, 2 µm 2.1 x 100 mm (Advanced Chromatography Technologies Ltd, Aberdeen, GB).
- **The analytical method** was validated for linearity, precision, and specificity.
- **pH-stability study:** Samples were prepared containing tetracaine hydrochloride (20.0 mg/mL), methyl parahydroxybenzoate (1 mg/mL), and sodium chloride (5.5 mg/mL) with pH-values spanning approximately 2-6 (adjusted with 0.1M hydrochloric acid or 0.1M sodium hydroxide).
  - The samples were stored until visible discoloration was observed in all solutions: First for 3 days at 70 °C, then at 3 days at 25 °C at ambient humidity, protected from light.

## Tetracaine hydrochloride – appearance vs stability

- The potency of concentrated tetracaine solutions can not be gleaned from visual inspection: the optimum pH of stability was found at pH 4-5 (Figure 1), but these solutions became brownish and contained particles. The clear and yellow solution produced at pH 2.2 contained the least tetracaine.
- The production of a clear, yellow solution (with stable pH) at low pH – and brownish, unclear solution (with changing pH) at more neutral pH values (Figure 2), suggest that different degradation pathways are effective at different pH values.
- Although the assay-values may be acceptable for some of the solutions in Figure 1, the appearance to the user may not be. Further, neither the identity nor acceptability of degradation products are established.



**Figure 2:** Tetracaine solution (20 mg/mL), pH 5.8. Particles can be observed on the wall of the vial.

## Results

Upon heat stress, the drug content remained highest at pH 5.1: 20.5 ± 0.1 mg/mL (97.2 %) (n=3), the appearance, however, changed to yellowish brown, and the solution was unclear. The content fell the most at pH 2.2: 18.2 ± 0.0 mg/mL (86.8 %) (n=3); in appearance, this solution remained clear, but turned yellow.



pH (day 0-day 6)	pH 2.2 (2.1 – 2.2)	pH 3.3 (3.3 – 3.3)	pH 4.2 (4.2 – 4.2)	pH 5.1 (5.4 – 4.7)	pH 5.8 (6.3 – 5.2)
% at day 6 (low - high)	87 % (87 – 87)	92 % (90 – 94)	97 % (95 – 97)	97 % (97 – 98)	96 % (96 – 96)

**Figure 1:** Effect of pH on tetracaine hydrochloride stability (initial concentration: 20 mg/mL). Per cent of initial concentration remaining upon exposure to 3 days at 70 °C, then 3 days at 25 °C at ambient humidity given. Sample to the far left: Water, for comparison.

## pH adjustment

The pH-values were instilled using 0.1 M hydrochloric acid or 0.1 M sodium hydroxide. No buffer was added to the test-solutions. This, to allow the pH to change dynamically, and to prevent any artificial interference with the appearance of the solutions.

## Conclusions

Using a validated UHPLC-method the optimum stability for preserved tetracaine hydrochloride solution (20 mg/mL) is found at pH 4-5 with regards to assay value. Paradoxically, however, this is not the pH at which the appearance is the most acceptable.