

pH-measurement: Not as simple as we think? A case of sodium perchlorate injections

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BACKGROUND

- Ampoules with sodium perchlorate 100 mg/ml for injection are manufactured at the Hospital Pharmacy.
- pH measurements during quality control were between batches, resulting in out of trend/specification results and greater variation between in-process and release values.
- No data explaining these variations could be found in the literature.

AIM AND OBJECTIVE

Determine factors which could cause unstable pH measurements of sodium perchlorate solutions.

Determine if changing the pH electrode could solve the problem.

MATERIALS AND METHODS

- pH-meter: Mettler Toledo SevenExcellence S400-Bio
- pH-electrodes: (A) InLab Routine Pro-ISM (Reference electrolyte: potassium chloride (KCl) 3M); (B) InLab Science Pro-ISM (Reference electrolyte: KCl 3M); (C) InLab Expert Pro-ISM (Reference electrolyte: XEROLYT®-polymer).
- pH was measured over time in different types of vials (glass/plastic) with extended exposure of solution to air.
- pH was measured uninterrupted at regular intervals for 420 seconds (n=3).
- Raman spectra of the precipitates were acquired by using a WITec Alpha300 Apyron Confocal Raman Microscope.

RESULTS

Different type of vials as well as extended air exposure of solution did not result in significant change of pH values. Initial testing with electrode A resulted in a characteristic trend where the pH increased, stabilized, and then decreased, while electrode C remained stable. For electrode B the same trend was observed as for electrode A, but testing was aborted due to visible precipitation in the sample. Results from subsequent comparison is shown in Table 1.

The precipitates (Figure 1) were identified as Potassium perchlorate by Raman spectroscopy (Figure 2).

Table 1. Comparison between electrode A and C (mean±SD, n=3)

pH measurement	60 seconds	240 seconds	420 seconds
Electrode A	5.22±0.39	5.30±0.40	5.09±0.02
Electrode B	5.70±0.07	5.73±0.08	5.75±0.08

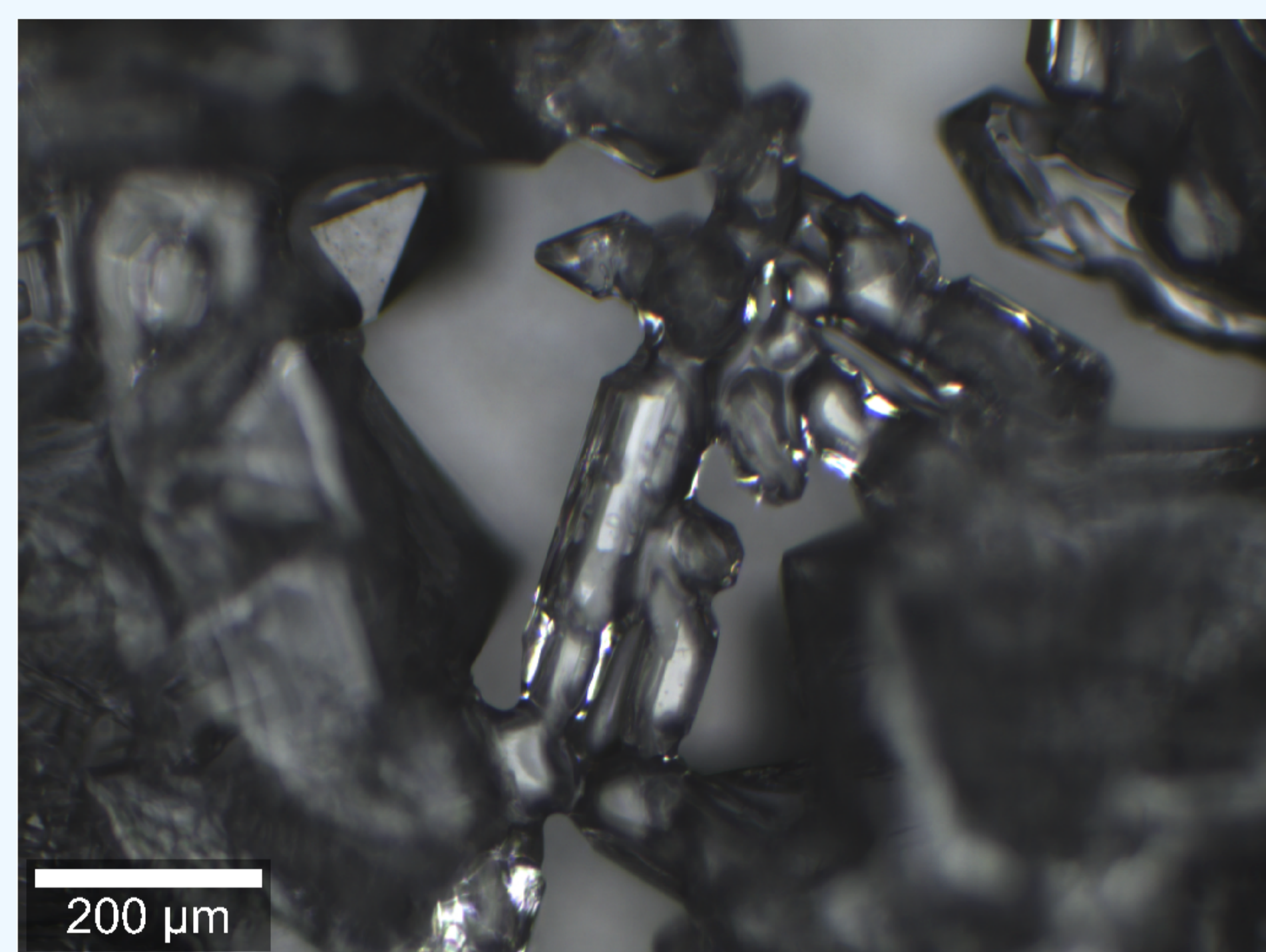


Figure 1. Microscopic image of the precipitate

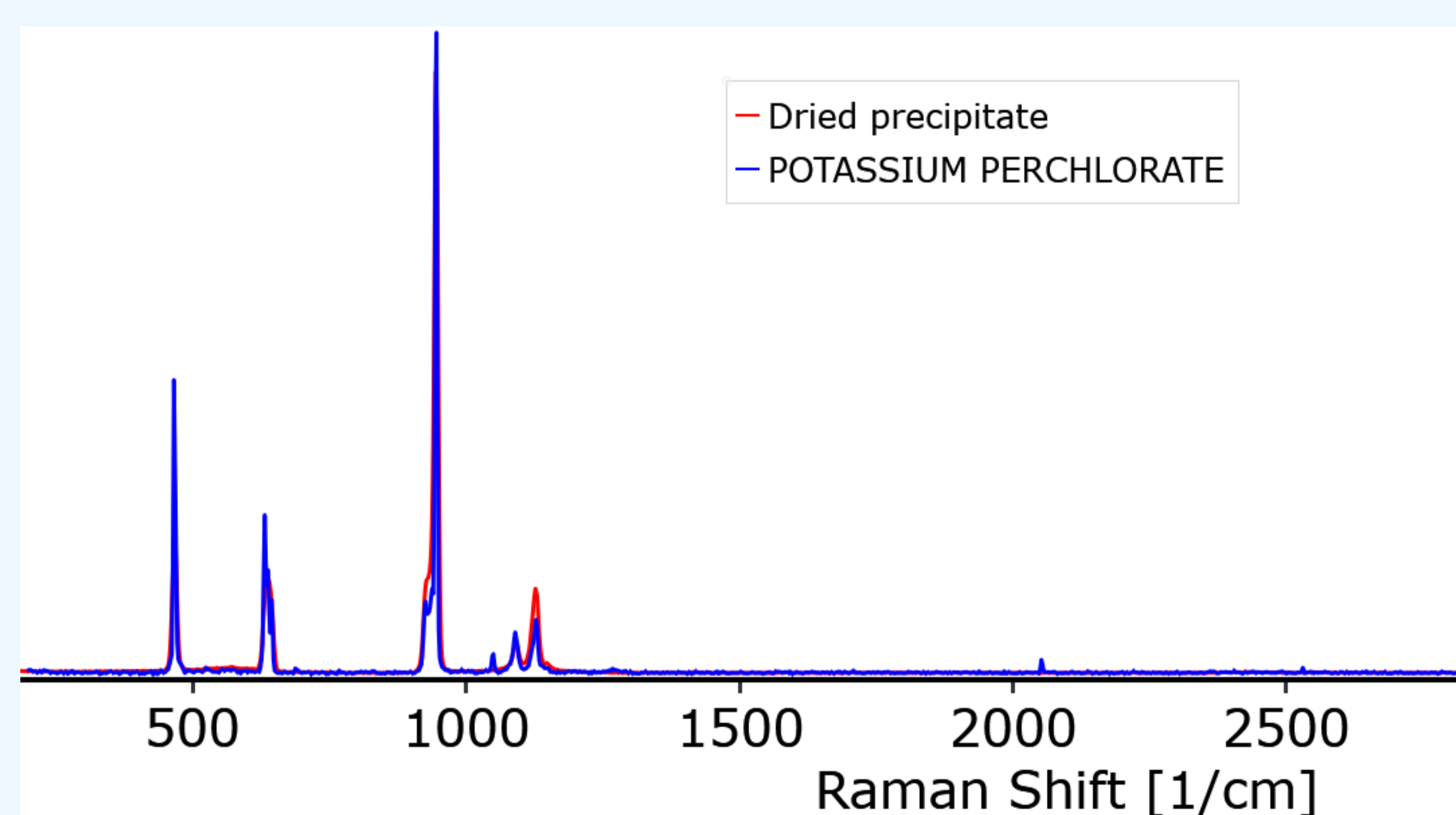


Figure 2. Raman spectra of the dried precipitate compared to database spectra of potassium perchlorate.

CONCLUSION

The unreliable results could be attributed to an interaction between Sodium perchlorate and KCl reference electrolyte. This also created a precipitation, more clearly visible in electrode B due to higher flow of reference electrolyte to the sample than electrode A. Electrode C with polymer electrolyte was the most stable, without the characteristic decrease in pH after the initial stabilization, and no precipitation.

