STABILITY OF A TRIPLE-COMPONENT SOLUTION containing ropivacaine, ketorolac and adrenaline

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BACKGROUND
The ambition for The Pharmacy Department at Aarhus University Hospital is to provide drugs that are ready-to-use, to minimize errors and enhance drug safety for patients and to assure the quality of the handling of drugs.

The Department of Orthopaedic Surgery uses a triple-component solution containing ropivacaine, ketorolac and adrenaline for local and intraarticular infiltration. Use of triple-component solution during total hip arthroplasty significantly reduces consumption of narcotics, reduces occurrence of side effects, reduces length of hospital stay and also improves early mobilisation (1,2). The clinical staff on the ward used to prepare the solution themselves.

However in accordance with the ambition of the Pharmacy, the triple-component solution is now produced at the Pharmacy. This is possible because of cooperation between The Department of Orthopaedic Surgery, the departments for Clinical Pharmacy, Quality Assurance (QA) and the Production Unit at the Pharmacy.

METHODS
3 batches of ready-to-use infusion solutions were produced aseptically by adding 1 ml ketorolac (Toradol, Roche A/S) 30 mg/ml and 0.5 ml adrenaline (Adrenalin DAK, Nycomed A/S) 1 mg/ml to a 100 ml ropivacain (Naropin, AstraZeneca A/S) 2 mg/ml infusion bag. The infusion bags were stored in the dark at 2-8 °C. After 20 days the bags were transferred and stored at room temperature (approximately 22 °C) for 48 h. The bags were protected from light in plastic bags. Each infusion bag was analysed by High-Performance Liquid Chromatography (HPLC) just after preparation and after 1 and 20 days storage at 2-8 °C and again at the end of the experiment. The pH of the infusion solution was measured at the same time points.

HPLC ANALYSIS
HPLC analysis was performed by using an Elite LaChrom system employing an UV detector; see figure 2 and 3. Each sample and standard was injected in duplicate; pH was measured with a PHM210 from Radiometer. Both HPLC methods were validated in accordance to linearity and precision.

RESULTS / DISCUSSION
After 20 days of storage at 2-8 °C and 48 h at the room temperature, the average concentration of adrenaline remained within 92% of initial average concentration (Table 1). The concentration of ropivacaine and ketorolac remained within 99% and 98% of their respective initial concentration. The solution in the beginning was 5.0-5.2 and remained within specified range of 4.0-6.5 during the experiment. These results demonstrate small differences less than 10% in concentration between start and end of experiment. The triple-component solution is chemically stable for up to 20 days at 2-8 °C and 48 h at room temperature.

CONCLUSION
The triple-component solution is stable for 20 days at 2-8 °C followed by 48 hours below 25 °C. As the stability of the triple-component solution is depend on pH, temperature and light exposure a shelf life of 20 days at 2-8 °C followed by 48 hours below 25 °C is recommended.

It is expected that the use of infiltrationanalgesia can be used in other types of surgeries and in other hospitals. Currently the pharmacy manufactures 7 different preparations, differing in size, dispensing form and drug combinations to several clinical wards at different hospitals.