3PC-019 EVALUATION OF THE IMPACT OF MACHINE-AIDED DEBLISTERING IN UNIT DOSE BLISTER PRODUCTION ON THE FUNCTIONALITY OF TABLET COATING

T Steindl-Schönhuber*, G Gittler. *Konventhospital der Barmherzigen Brüder Linz, Hospital Pharmacy, Linz, Austria*

10.1136/ejhpharm-2022-eahp.43

Background and importance Deblistering of medication is a critical step in unit dose blister production. In our setting, large quantities of push-through packs are processed by manually operated deblistering machines. Visibly damaged drugs are removed. However, it has not been investigated whether mechanical stress by deblistering machines can cause minimal, hardly identifiable damage with negative effects on functional coating.
Aim and objectives The influence of machine-aided versus manual deblistering on drugs with modified release was studied to rule out negative effects on functionality of coating. Purposely damaged tablets with tiny superficial defects served as positive controls. Enteric coating and extended release were investigated in tablets chosen for their high deblistering volume and critical active agent, respectively.
Material and methods Thrombo ASS 100 mg (acetylsalicylic acid; enteric coating) and Quilonorm retard 450 mg (lithium carbonate; retardation of release) were deblistered (A) manually, (B) with deblistering machines and (C) manually and then minimally damaged on the surface with a pointed item. Ten tablets of each group were analysed in two ways. (1) Disintegration testing was performed based on the methods of the European Pharmacopoeia. (2) Tablets were immersed into a methylene blue dye bath to visualise intactness of coating as well as damaged areas.
Results Manually and machine deblistered Thrombo ASS tablets met the required 2 hours of acid stage duration in 0.1 N HCl. The minimally damaged fraction started to disintegrate within seconds. When transferred to neutral buffer solution, manually and machine deblistered tablets showed identical disintegration behaviour. All three groups of Quilonorm retard tablets showed acid stability and disintegrated the same way in a pH-neutral environment. Cavities and grooves were visible on damaged tablets immersed into the dye bath. Tablets deblistered by hand and machine showed identical, even dying of their surfaces.
Conclusion and relevance Although minimal damage can lead to a loss of coating functionality, machine-aided deblistering showed no negative effects on coated tablets. Neither differences in disintegration tests nor in the dye bath were detected compared with manually deblistered tablets. These results were examined during a good manufacturing practice (GMP) inspection by the Austrian authority, support machine qualification and the validation of this important step in the unit dose blister process and may therefore be of interest for other production sites.

REFERENCES AND/OR ACKNOWLEDGEMENTS

Conflict of interest No conflict of interest

3PC-020 CHEMICAL STABILITY AND PHYSICAL COMPATIBILITY OF INSULIN EYE DROPS USED IN CLINICAL PRACTICE

MA Martínez Gómez, P Martínez Albaladejo*, I Ricoy Sanz, C Bravo Crespo, J Polo Durán, A Llopis Alemany, S Giménez Giner, AC Cercós Lletí, M Climente Martí. *Doctor Peset University Hospital, Pharmacy, Valencia, Spain*

10.1136/ejhpharm-2022-eahp.44

Background and importance Insulin eye drops are an effective treatment for corneal neurotrophic ulcers due to the action of insulin as a tissue growth factor. Owing to the lack of studies on the stability of this eye drops, in clinical practice it is not possible to give them for more than 7 days of use. The purpose of this study was to assess whether the stability could be increased, making the preparation and dispensing by the Pharmacy Service easier, as well as making it more comfortable for the patient.
Aim and objectives The objective was to study the chemical stability and physical compatibility of eye drops of human insulin (Humulina and Actrapid) at 1 UI/mL, diluted in Systane, Liquifilm or 0.9% sodium chloride (0.9% NaCl), in polyethylene bottles, protected from light, at 24°C or 4.5°C, for 30 days.
Material and methods Three preparations were prepared for each condition. At the time of analysis, one sample for each preparation was analysed by high performance liquid chromatography. The time at which human insulin retained 90% of the initial concentration (T90) was obtained for each preparation. The method was validated according to the International Conference on Harmonisation Q2 (R1). Physical stability was evaluated by visual inspection, gravimetric analysis and pH measurement.
Results Humilina preparations, T90 was: (a) with Systane: 9 days at 4.5°C, 7 days at 24°C; (b) with Liquifilm: 9 hours at 4.5°C, 10 hours at 24°C; (c) with 0.9% NaCl: 1 day at 4.5°C, 15 hours at 24°C. Actrapid preparations, T90 was: (d) with Systane: 10 days at 4.5°C and 24°C; (e) with Liquifilm: 17 hours at 4.5°C, 6 hours at 24°C; (f) with 0.9% NaCl: 4 days at 4.5°C, 3 days at 24°C. During the study, neither changes in colour nor losses of weight were observed in the preparations assayed: variations of pH were higher than 5% from day 2 in all preparations with Humulina and Actrapid in 0.9% NaCl.
Conclusion and relevance Eye drops of human insulin (Humulina or Actrapid) at 1 UI/mL diluted in Systane, in polyethylene bottles and protected from light, can be used in clinical practice.

REFERENCES AND/OR ACKNOWLEDGEMENTS

Conflict of interest No conflict of interest

3PC-021 DESIGN AND ELABORATION OF METRONIDAZOLE 1% TOPICAL SOLUTION FOR TREATMENT OF ULCERS INFECTED BY ANAEROBIC BACTERIA

EA Álvaro Alonso*, N Barrueco Fernandez, L De Agustín Sierra, E Izquierdo García, B Montero Pastor, A Garrido Dorao, R Vara San Pedro, I Moron Mesa, I Escobar Rodríguez. *Hospital Universitario Infanta Leonor, Pharmacy, Madrid, Spain*

10.1136/ejhpharm-2022-eahp.45

Background and importance The scientific literature was reviewed in order to investigate metronidazole 1% topical solution for treatment of ulcers infected by anaerobic bacteria, and whether refrigerated storage is recommended. However, the samples formulated in the Hospital Pharmacy Department presented a crystalline precipitate, which could not be redispersed. Therefore, a compounding improvement was necessary.
Aim and objectives Design and analyse, by galenic validation, different compounding improvement to increase the solubility of metronidazole in water in three storage environments.

Material and methods A bibliographic search found that metronidazole base solubility in water is 10.5 mg/mL (25°C) and 17 mg/ml (20°C) in propyleneglycol. The 1% solution in water is a saturated solution that initially presents an oversaturation stage whose intensity and duration are determined by solid particle size and its solubility increases progressively over the time.

Thereby, we formulated three metronidazole solutions in different vehicles: water (M1), water+glycerin (M2) and water +propyleneglycol (M3). They were stored in refrigeration, room temperature (RT) and T^a>25°C conditions. A galenic validation was carried out, monitoring organoleptic characteristics, sedimentation time, redispersability, homogeneity, crystal growth and pH on days 0, 1, 5, 7, 11, 14, 18, 30 in a 30-day follow-up.

Results The three solutions had a pH=5.5 and showed neither colour nor odour throughout the 30-day analysis.

With refrigeration, in less than 24 hours, the three solutions crystallised and could not be resuspended. Therefore, follow-up was stopped and refrigeration was discarded.

At RT, M1 and M2 presented crystals and vigorous hand shaking and heating for several minutes was necessary to resuspend them. M3 maintained the physical characteristics and was no longer oversaturated from day 18.

At T^a>25°C, the three solutions started as oversaturated solutions (no crystals were observed at any time). Subsequently, M3 became a saturated solution on day 4 and M1/M2 on day 7.

Conclusion and relevance Metronidazole base in solution cannot be stored in a refrigerator due to an irreversible crystallisation. Glycerin as a humectant does not provide any advantage compared with water as a single vehicle. Propyleneglycol allows a compounding improvement because it increases the solubility of metronidazole in water, allowing the solution to be preserved at RT without crystal formation and to reach the saturation phase quickly at T^a>25°C. The hospital pharmacists' knowledge allows the resolution of compounding difficulties derived from the physicochemical characteristics of raw materials.

REFERENCES AND/OR ACKNOWLEDGEMENTS
Conflict of interest No conflict of interest

3PC-022 PH STABILITY OF TETRACAINE SOLUTIONS FOR SURFACE ANAESTHESIA

[1]J Brustugun, [2]O Asphjell, [3]M Negård, [1]RH Svendsen*, [2]I Tho. *[1]Oslo Hospital Pharmacy, RandD, Oslo, Norway; [2]Section for Pharmaceutics and Social Pharmacy, Department of Pharmacy, Oslo, Norway; [3]Norwegian Medicines Agency, Safe Use, Oslo, Norway*

10.1136/ejhpharm-2022-eahp.46

Background and importance 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 and slowly degrades over time. 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.

Aim and objectives The aim of the study was to investigate the stability of tetracaine solutions as a function of pH, and from this determine the optimum stability as regards drug content and appearance.

Material and methods Tetracaine hydrochloride (Sigma-Aldrich, St Louis, Missouri, USA). Instrument: ultra-high performance liquid chromatography (UHPLC) system (Shimadzu Corp., Kyoto, Japan) with a Nexera *diode array detector* (DAD) detector. Analytical column: Ace Excel 2 C8, 2 µm 2.1 × 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 2–6. The samples were stored until visible discolouration was observed in all solutions: First for 3 days at 70°C, then at 3 days at 25°C at ambient humidity, and protected from light.

Results Upon heat stress, the drug content remained highest at pH 5: 20.5±0.1 mg/mL (97.2%) (n=3); the appearance, however, changed to yellowish brown, and the solution was unclear. The content decreased the most at pH 2: 18.2±0.0 (86.8%) (n=3); in appearance, this solution remained clear, but turned yellow.

Conclusion and relevance Using a validated UHPLC method the optimum stability for tetracaine hydrochloride is found at pH 4–5 as regards assay value. Paradoxically, however, this is not the pH at which the appearance is the most acceptable.

REFERENCES AND/OR ACKNOWLEDGEMENTS
Conflict of interest No conflict of interest

3PC-023 INVESTIGATION OF LEACHABLE COMPOUNDS IN WATER FOR INJECTION USED IN HOSPITAL PHARMACY

[1,2,3,4]W Bello*, [1]J Pezzatti, [2,3]S Rudaz, [1,2,3,4]F Sadeghipour. *[1]Lausanne University Hospital, Service of Pharmacy, Lausanne, Switzerland; [2]University of Geneva, School of Pharmaceutical Sciences, Geneva, Switzerland; [3]University of Geneva and University of Lausanne, Institute of Pharmaceutical Sciences of Western Switzerland, Geneva and Lausanne, Switzerland; [4]Lausanne University Hospital and University of Lausanne, Center for Research and Innovation in Clinical Pharmaceutical Sciences, Lausanne, Switzerland*

10.1136/ejhpharm-2022-eahp.47

Background and importance Industries have been manufacturing prepackaged water for injection (WFI) and other aqueous solutes to enable simpler and practical hospital pharmacy compounding. In hospitals, the preparation of total parenteral nutrition (TPN) or other intravenous (IV) treatments like antibiotics are often administered for continuous treatment. Industrially prepackaged WFI are frequently employed to reconstitute or dilute parenteral preparations. This proves convenient due to their large volume variety availability in the market and stocking capabilities before being used in hospital compounding.

Aim and objectives However, prepackaged aqueous products could potentially leach plastic additives over time. These compounds could influence active substance stability through different physical–chemical interactions, which in turn could affect treatment efficacy. Furthermore, the patient, receiving continuous IV treatments, could get affected with potential endocrine disrupting (ED) compounds, leading to probable latent health effects.

Material and methods The Quality Control laboratory of the Pharmacy of the Lausanne University Hospital (Switzerland) has developed an analytical method using liquid