Compounding of suspension-type ointments with electric mixing systems and three roll mills – a comparative study

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ABSTRACT

Suspension-type ointments were compounded with two commercially available electric mixing systems and with three roll mills. The aim of this study was to compare these differently prepared ointments with regard to the quality of the manufactured formulations.

INTRODUCTION

As it is difficult to examine every individually prepared ointment formulation after the manufacturing process, automatic mixing systems used in pharmacies must guarantee the required quality. Due to the fact that automatic mixing systems have hardly been explored systematically [1], in this study different automatic electric mixing systems were investigated with regard to their impact on homogeneity, particle size distribution, rheological properties and stability of the manufactured ointments.

MATERIALS

Wool wax alcohols, cetylstearyl alcohol, white petrolatum, polyethylene glycol 300 and 1500 as well as salicylic acid were purchased from Caelo, Germany, methylene blue from Merck, Germany.

METHODS

Suspension-type ointments with the ointment bases wool wax ointment (DAB) and macrogol ointment (DAC) containing either 10% of salicylic acid or methylene blue were compounded with the electric mixing systems Cito-Unguator®, TopiTec® and three roll mills (Exakt 50, 50EC, and 80E) of different gap size. The manufacturing process was evaluated with regard to the time required for ointment preparation and ointment temperature. The quality of the ointments was examined with respect to formulation homogeneity [2], particle size distribution, rheological properties [2] and stability.

RESULTS & DISCUSSION

Formulation homogeneity:

All methylene blue formulations appeared to be homogeneous after visual assessment. However, the drug content of the investigated samples deviated more or less from the average value. The homogeneity of the ointments was best with the three roll mills and the TopiTec® mixing system leading to relative standard deviations between 1.7 and 2 % (Fig. 1).

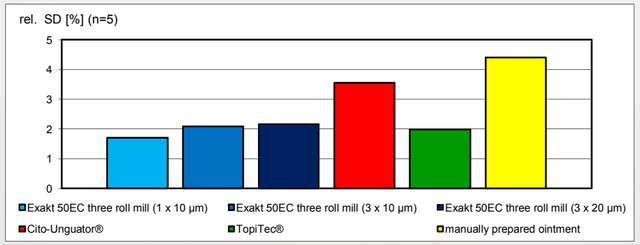

Fig. 1: Results of the homogeneity test with a formulation of 10% methylene blue in macrogol ointment

Particle size distribution:

Particle size distribution was best with the three roll mills leading to a particle size between 10 and 40 µm with the smallest gap size of 10 µm (Fig. 2). The Cito-Unguator® and the TopiTec® mixing systems led to broader particle size distributions and particles were larger (Fig. 3).

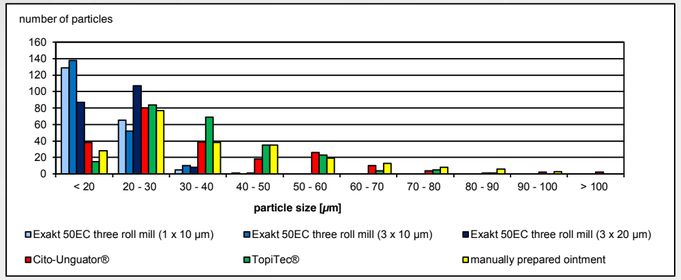

Fig 2: Wool wax ointment with 10% salicylic acid; the particle size distribution of 200 particles in each sample was determined microscopically

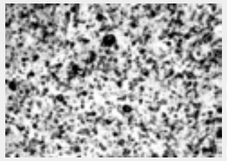

Fig. 3a: Microscopic picture (40x magnification) of wool wax ointment with 10% salicylic acid, manual preparation

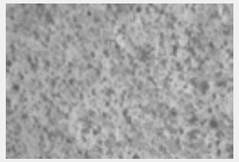

Fig. 3b: Microscopic picture (40x magnification) of wool wax ointment with 10% salicylic acid, homogenized with the three roll mill Exakt 50EC (3 x 10 µm)

Rheological properties:

The rheological properties of the ointments prepared with the three roll mills and the two mixing systems, respectively, differed significantly from each other (Fig. 4). Three roll mills led to a soft consistency of the ointments accompanied by low flow limits, whereas the consistency of the ointments prepared with the two electric mixing systems was hard and flow limits were high. This phenomenon may be explained by the significant temperature increase of the ointments during manufacture with the two mixing systems. The time required for preparation of the ointments was not significantly longer with the three roll mills. However, some product loss has to be expected.

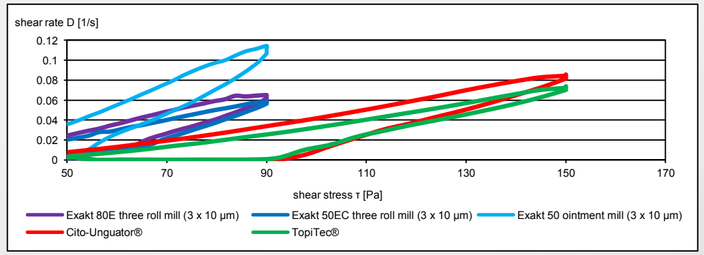

Fig. 4: Results of the rheological characterization of wool wax ointment with 10% salicylic acid (Haake RheoStress 1 Rheometer)

Stability:

After 5 weeks of storage at 21 °C and 47 % R.H., the manually prepared wool wax ointment showed the fastest particle growth. Particles up to 100 µm were detected. The formulations with the smallest particles and the most favorable stability were those homogenized with the three roll mills. The formulations with the Cito-Unguator® and the TopiTec® electric mixing systems showed only minor particle growth, and no particles over 90 µm were observed in these formulations (Fig. 5).

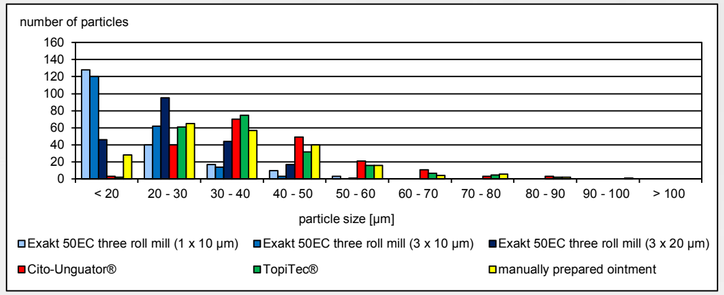

Fig. 5 : Results of the stability test of wool wax ointment with 10 % salicylic acid (21 °C and 47% R.H. over 5 weeks)

CONCLUSIONS

From the results of this study it may be concluded that the quality of suspension-type ointments homogenized with three roll mills is better than that of ointments prepared with the Cito-Unguator® and the TopiTec® electric mixing systems:

The particle size is smaller, particle size distribution is narrow, ointment stability is better, the temperature of the manufactured ointments does not increase significantly and the rheological properties are most favorable. Moreover, preparation of ointments with three roll mills allows quality control measures during the manufacturing process before transfer of the ointments into jars or tubes.

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