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EURAMET

MEDD II

The effect of drugs rheological properties in the flow accuracy and uncertainty of infusion systems in the microflow range

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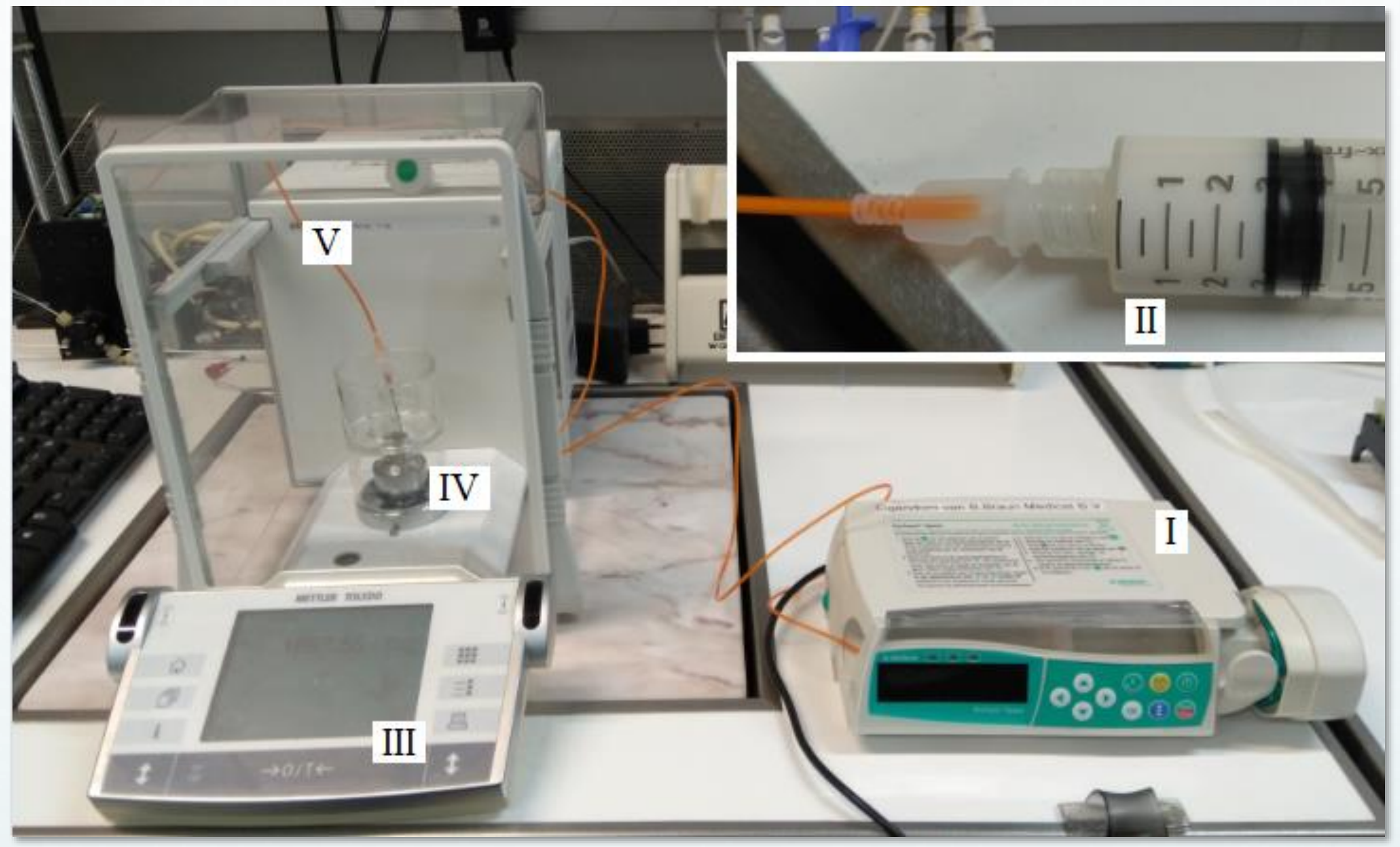
In clinical treatments most of the drugs used in infusion systems are water-based solutions, behaving like ideal viscous liquids, and therefore behaving as Newtonian liquids when under flow. However, when the infusion occurs within the µL/h flow range, some of the drugs, with more complex composition, such as protein or particle-based, shown viscoelastic flow behaviour, meaning they behave as non-Newtonian liquids when under flow. Even though these infusion systems are widely used in therapeutics to infuse a multitude of drugs, few are the published studies about the influence of drugs physical properties, namely rheological, on the accuracy and uncertainty of the flow rate of these instruments. With the purpose of providing new information concerning this topic the European joint research project entitled "Metrology for Drug Delivery" (MeDD II) [1] is focused on the study of the effect of drugs rheological properties in the flow accuracy and uncertainty of infusion systems for low flow rates, among other related topics, such as mixing behaviour and occlusion phenomena in multi-infusion systems.

This communication gives further insight regarding the flow accuracy and uncertainty of an infusion system operating at 1000 µL/h with two non-Newtonian drugs (propofol, used to induced general anaesthesia and gelaspan®, a colloidal plasma substitute).

The obtained results show that with the tested fluids, whether Newtonian or non-Newtonian, both infusion pumps comply with the maximum permissible error established by IEC 60601-2-24 [2], i.e., 2%. Additionally, water appears to be a reliable fluid to carry out calibrations of infunsion pumps that work with viscoelastic fluids, since the sum of the modulus of the relative flow error and the expanded uncertainty ($|\delta'Q| + U'_Q$) obtained for water and for the non-Newtonian fluids is of the same magnitude.

FLOW RATE RELATIVE DEVIATION FROM THE NOMINAL VALUE AT 1000 µL/h



Measuring method: gravimetric method [4] at 20 ºC

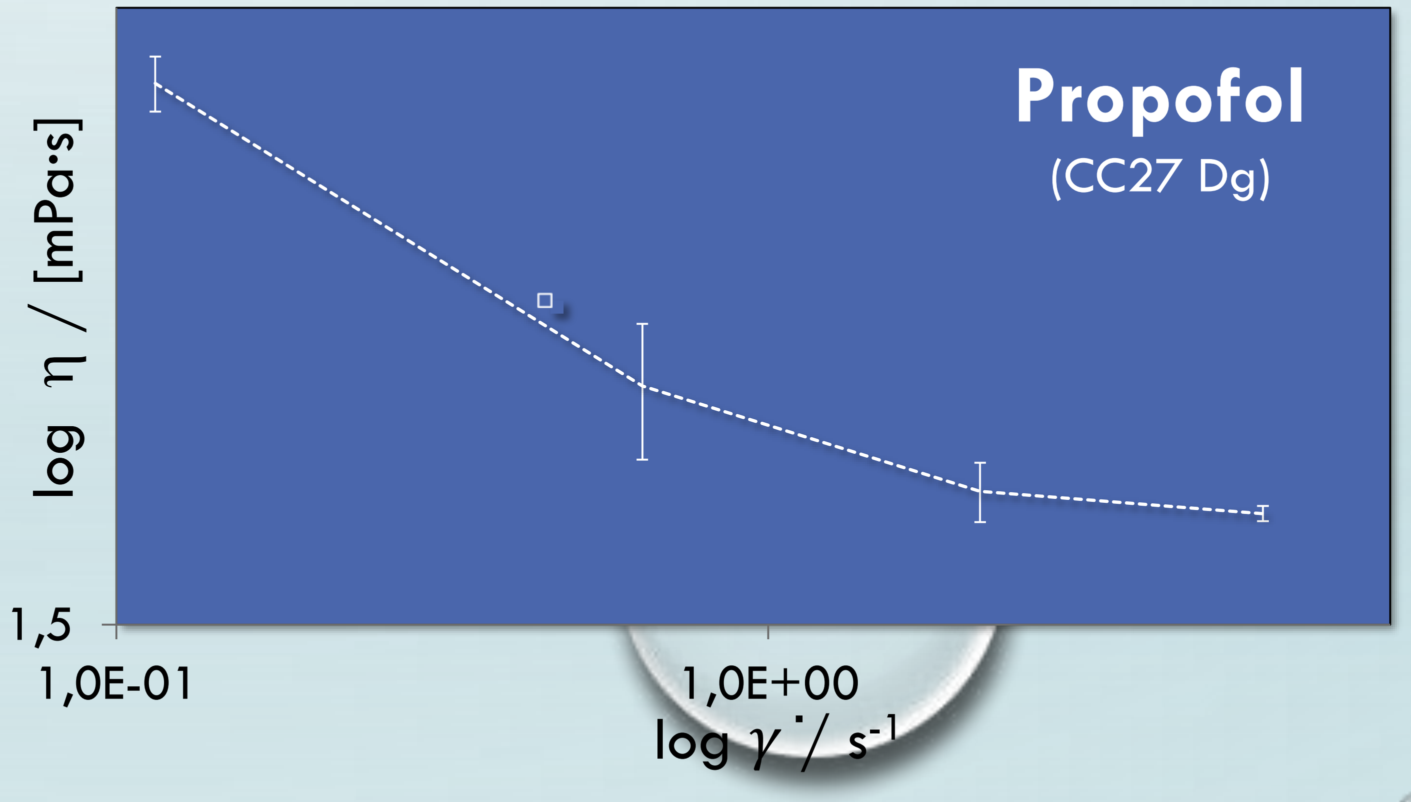
Measuring apparatus: the syringe of the tested infusion pump (Bbraun Perfusor Space, 49682 (I) is connected by teflon tubing ending in a needle (V) submerged in the liquid contained in the calibrating vessel inside the evaporation trap (IV) connected to a balance (Mettler Toledo) (III).

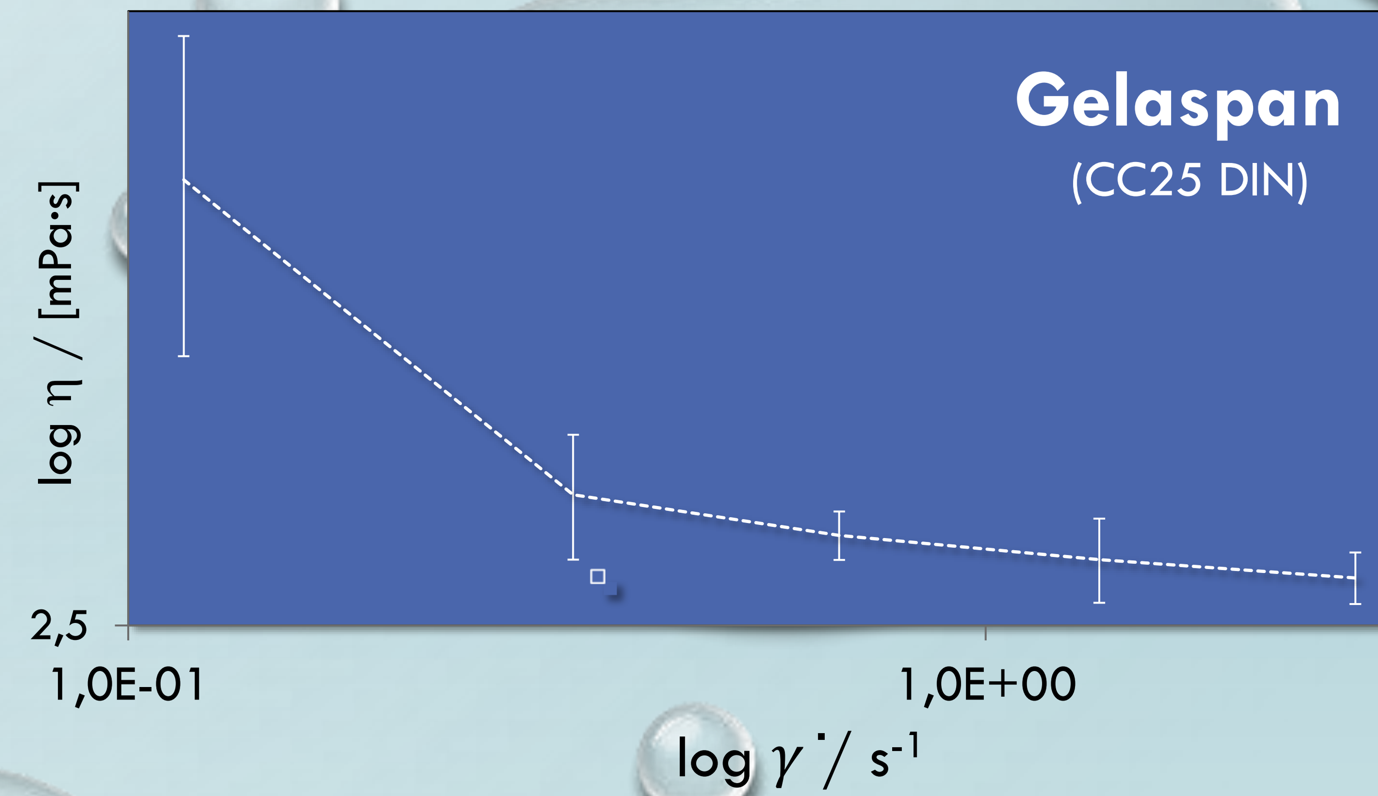
Infusion pump	Fluid	Q / (µL/h)	$\delta'Q^{(a)}$ / %	$U'_Q{}^{(b)}$ / %	$[|\delta'Q| + U'_Q]^{(c)}$ / %
I	water	997,39	-0,26	0,49	0,75
	propofol	998,90	-0,11	0,53	0,64
II	water	991,2	-0,88	0,72	1,60
	propofol	989,3	-1,07	0,43	1,50
	gelaspan	989,0	-1,10	0,49	1,59

Notes: (a) δQ - relative mean flow deviation from the nominal value (1000 µL/h); (b) $U'Q$ - relative expanded uncertainty of the flow is stated as the standard measurement uncertainty multiplied by the coverage factor k = 2, which for a t-distribution with $\nu_{ef} = y$ effective degrees of freedom corresponds to a coverage probability of approximately 95 %, calculated according to GUM [5]; (c) the maximum permissible error according to the standard IEC 60601-2-24 [2] is 2%.

VISCOSITY CURVES

Rotational rheometer (Mars III, HAAKE ThermoScientific) in controlled stress step mode





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