Study on the migration behaviour of DEHP versus an alternative plasticiser, Hexamoll® DINCH, from PVC tubes into enteral feeding solutions

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Introduction

PVC is a commodity polymer widely used in medicinal applications. For these purposes, PVC is typically plasticised with substances like di-(2-ethylhexyl) phthalate (DEHP). The functional characteristics of plasticised PVC makes it very suitable for the construction of a wide variety of medical devices, some of which are crucial to the delivery of care to critically or chronically ill patients. On the other hand, a plasticiser has to be a low molecular weight compound, because it has to be mobile within the molecular structure of the polymer. As an unavoidable consequence, this leads to a significant migration of the plasticiser into contact media provided their solubility for the plasticiser is high enough. In the case of enteral feeding solutions, which usually have some fat content, this migration leads to a significant consumer (patient) exposure with plasticisers from the feeding set. These effects are especially for new born individuals more pronounced and of higher concern. Therefore the contribution of plasticisers to the health care of the patients and neonates has to be taken into account.
Due to the fact that there are hints that DEHP may have an unfortunate toxicology the EU Scientific Committee on Food (SCF) has recommended a tolerable daily intake (TDI) for DEHP of 50 µg kg^{-1} [1]. On the other hand the EU Scientific Committee on Medicinal Products and Medical Devices (SCMPMD) came to the conclusion that for DEHP no tolerable intake value in medical devices can be recommended and rather emphasizes to consider the balance between achievable benefits and possible risks [2].
Regarding this background, technically equivalent but toxicologically unsuspicious alternatives for DEHP are automatically of great interest. A recently proposed, new alternative for DEHP is di-(isononyl)-cyclohexane-1,2-dicarboxylate (Hexamoll® DINCH) which has been reported with tremendously better toxicological properties [3]. Whereas DEHP was recently assigned to a NOAEL of 4.8 mg kg^{-1} b.w. per day for testicular and developmental toxicity [4], the NOAEL for DINCH from different reproduction toxicity studies was concluded to be higher than 1000 mg kg^{-1} b.w. per day [3]. Moreover, DINCH has recently been approved by the German BfR for food contact materials with a migration restriction of 5 mg kg^{-1} food [5].
Considering these facts, an important missing link for the evaluation of the new alternative to DEHP for applications in clinical nutrition was the migration behaviour of DINCH into realistic contact media. Therefore, the aim of this study was to measure comparatively the migration of DINCH versus DEHP from soft PVC tubes into an enteral feeding solution under realistic application conditions.

Results

The commercial enteral feeding solution for neonates was tested with two feeding sets one time based on DEHP and the other set based on the alternative plasticiser DINCH. The total time in both experiments was 24 h, which is the maximum application duration of one feeding set. The results are given in Figure 1 as the fractional mass transfer and in Figure 2 as the cumulated effect of plasticisers migration into the feeding. It can be recognised from Figure1 that within a relatively short time an equilibration under the applied flow rate takes place leading to a timely constant release of plasticiser. When cumulating the migrated mass (Figure 2) then a typical migration curve is obtained. As a direct result from both figures it can be found that the migration of DINCH is by a factor of approximately 8 lower than that of DEHP. This result is in the first place an effect of the different plasticisers contents of the tubes and at a minor degree also of the different molecular weights. Both effects determine finally the observable migration behaviour.

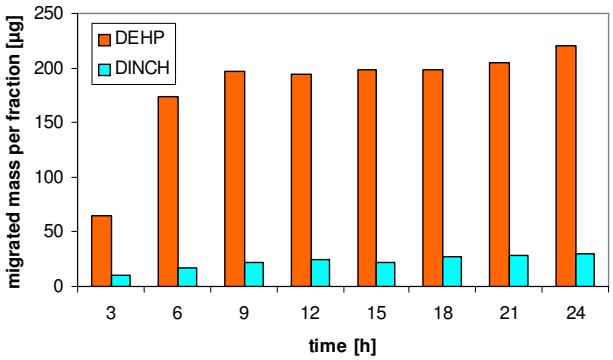

Figure 1: Mass plasticiser migrated into enteral feeding solution per 3 hours (15 ml fraction) at room temperature and a flow rate of 5 ml h^{-1} (realistic application conditions)

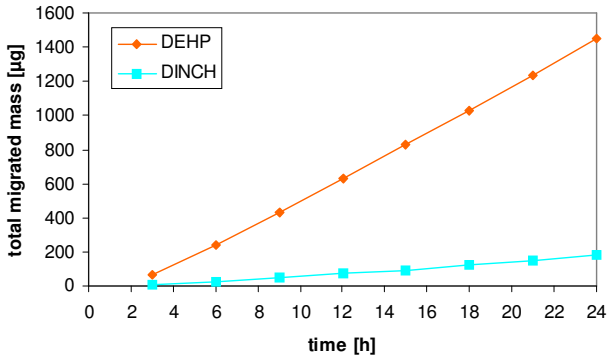

Figure 2: Cumulated mass plasticiser migrated into enteral feeding solution under realistic application conditions (24 h, 5 ml h^{-1})

Conclusions

Under realistic application conditions, the alternative DINCH PVC system shows compared to the standard DEHP PVC tube a reduced plasticiser migration by a factor of approx. 8. In addition to the lower migration the alternative compound offers an advantageous toxicological profile.
Concerning exposure after 24 hours of a patient or neonate when fed with both systems the following figures can be derived: A standard 60 kg person would be exposed to 0.024 mg kg^{-1} b.w. per day with the DEHP PVC system and to only 0.003 mg kg^{-1} b.w. per day with the alternative system. For a 2 kg neonate 0.726 and 0.094 mg kg^{-1} b.w. per day, respectively, would be obtained.
In comparison to these figures, the food contact material relevant "specific migration limits" for both plasticisers when translated into values expressed in mass per kg b.w. per day would be for DEHP (in this case the TDI is set) 0.05 mg kg^{-1} b.w. and 0.083 mg kg^{-1} b.w.. For the alternative substance DINCH this means that the 60 kg person would be exposed only to 0.036 SML equivalents whereas the neonate would have an exposure in the range of the currently accepted SML equivalent.

References

[1] European Commission DG SANCO D3: Doc. INT/SYNOPTIC DOCUMENT (04/2003) updated to 13 May 2003.
[2] European Commission DG SANCO: Doc. SANCO/SCMPMD/2002/0010 Final – Opinion on Medical devices containing DEHP plasticised PVC; neonates and other groups possibly at risk from DEHP toxicity (adopted 26 September 2002).
[3] Otter R. and Goth H.: Hexamoll® DINCH – our response to the plasticiser challenge. Presentation at the Conference Plasticisers 2004, Brussels, September 2004.
[4] European Commission DG SANCO: Doc. C7/GF/csteeop/DEHP/080104 D(04) – Opinion on the results of a second risk assessment of DEHP Human health part (adopted by CSTEE 8January 2004).
[5] Recommendations of the German Plastics Commission of BfR, Berlin.

Acknowledgements

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