Introduction

Biorelevant in vitro dissolution testing is an essential requirement for an accurate prediction of oral drug absorption. Current biorelevant dissolution methods were developed to simulate gastrointestinal (GI) conditions in the Western healthy adult population. Appropriate in vitro methods for estimating oral drug absorption in children of different age groups, ethnicities and prandial states have not yet been described. Since particularly in very young children GI physiology and nutrition is significantly different from adults, these differences should be addressed when developing biorelevant in vitro dissolution methods. The aim of the present study was to establish in vitro models that allow simulating gastrointestinal conditions after drug administration with typical children’s breakfasts around the world.

Materials and Methods

Step 1:

a) Literature screen to identify typical breakfasts of children around the world.

b) Preparation, homogenisation of different breakfasts (figure 1) and determination of the physicochemical properties, i.e. pH, buffer capacity, osmolality and surface tension.

c) Documentation of specific product information, such as the fat:protein:carbohydrate ratios and caloric contents from the product label for further evaluation.

Step 2:

Development of simulated paediatric breakfast media with a focus on the breakfast composition with regard to the content of:

- calories
- proteins
- fat
- carbohydrates

Results

Table 1 shows the composition of the paediatric breakfasts and the corresponding simulated breakfast media. All breakfasts are carbohydrate-based, but differ in fat- and protein content. While cassava porridge does not contain any fat, the American breakfast is characterised by a high fat- and protein content. Figure 3 displays the mean pH-values, buffer capacities, surface tensions and osmolalities of the different paediatric breakfasts and the simulated paediatric breakfast media. Results show that we were able to adjust both the composition and the physicochemical properties of the paediatric breakfast meals. Dissolution profiles of the fenofibrate mini-tablets are shown in figure 4 and clearly indicate the impact of breakfast composition and properties on drug release.

Conclusion

Simulated paediatric breakfast media that resemble composition and physicochemical properties of typical children’s breakfasts around the world were designed and applied in a first set of in vitro dissolution experiments. Results clearly indicate the impact of breakfast composition and properties on drug release. The novel media are thus a promising tool for better estimating the variability of in vivo drug release after drug administration with a typical paediatric breakfast in different parts of the world.

Figure 1: Typical breakfasts of children around the world

Figure 2: Dissolution test design

Figure 3: Physicochemical properties of homogenised paediatric breakfast meals (left column) and simulated paediatric breakfast media (right column) at 23 °C, mean of n=3 ± S.D.

Figure 4: Furosemide dissolution in gastric (0-30 min) and small intestinal (35-90 min) conditions when simulating tablet co-administration with different breakfast meals (mean of n=3 ± S.D.).

References

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