

## The effect of food and co-medication on amoxicillin bioaccessibility as studied in the in vitro GI model TIMpediatric

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### **Purpose**

To investigate amoxicillin availability in the TIMpediatric dynamic in vitro system mimicking the daily practice in relation with age-relevant food and chronic proton pump inhibitor (PPI) co-medication.

In daily practice amoxicillin is the number 1 prescribed drug to the pediatric population in the Netherlands in 2011 [SFK, 2012]. Additionally, proton pump inhibitors (PPI) are frequently used making combined drug therapy inevitable. For some antibiotic agents (amoxicillin, clarithromycin, penicillin G) degradation under low gastric pH conditions has been reported [Huang, 1953] [Erah 1997]. The type of meal and use of PPI's influence the gastric environment and may affect the pharmacokinetic profile of the compound.

### **Methods**

TIMpediatric is a dynamic computer controlled in vitro system of the stomach and small intestine mimicking age and maturation-related specific physiological parameters various pediatric age groups. TIMpediatric was programmed to simulate GI conditions for toddlers including age-related specific physiological parameters and post-prandial effects on transit time, pH and digestive fluid secretion. Age related foods (milk plus cereals (pH 6.7) and juice plus cereals (pH 3.2)) were prepared as test meals. Under simulation of chronically use of PPI, stomach HCl secretion was inhibited in the system. Oral amoxicillin (oral suspension Sandoz® Forte) in a dose of 25 mg/kg b.w. was given concomitant with the meal. Intestinal filtered fractions were collected 30 to 60 min aliquots. Amoxicillin samples were analyzed according HPLC-UV for calculation of in vitro the bioaccessibility profiles.

### **Results**

Concomitant amoxicillin administration with milk (pH 6.7) and juice (pH 3.2) did not result in differences in total amoxicillin bioaccessibilities. Simulation of chronically use of PPI, i.e. inhibition of gastric acid secretion, increased the stomach pH but did not affect amoxicillin bioaccessibility

### **Conclusion**

Under simulated pediatric daily practice conditions and co-administration of PPI in TIMpediatric, profiles for amoxicillin absorption did not change. These findings are in line with adult in vivo data where the use of PPI in combination with amoxicillin did not demonstrate a significant change in AUC [Cardaci, 1995] [Mainz, 2002].