Development of Child-Friendly Oral Formulations Containing Celecoxib: Biopharmaceutical Considerations for Formulation Scientists

Ramzi Shawahna[1,2*], Ahed Zyoud[3], Aseel Haj-Yahia[1], Raheek Taya[1]

[1] Faculty of Medicine & Health Sciences, An-Najah National University, Nablus, Palestine
[2] An-Najah BioSciences Unit, Center for Poison Control, Chemical and Biological Analyses, An-Najah National University, Nablus, Palestine.
[3] Faculty of Science, An-Najah National University, Nablus, Palestine.

DOI: https://doi.org/10.35516/jjps.v16i2.1496

ABSTRACT

Purpose: Recently, different international regulatory agencies and task forces have encouraged the pharmaceutical industry to develop child-friendly oral dosage forms. The biopharmaceutical classification system (BCS) has emerged as a tool that facilitates the development of traditional, reformulated, and novel oral dosage forms. Little research was conducted to evaluate the applicability of the BCS in developing child-friendly oral dosage forms. This study was conducted to assess the effects of age-related developmental changes in the composition and volume of gastrointestinal fluids on the solubility and performance of oral formulations containing celecoxib.

Methods: Solubility studies were conducted at 37 ºC in the pH range of 1.2 to 6.8 in 13 different age-appropriate biorelevant media that reflected the gastric and proximal small environments in fasted and fed states for adults and pediatric populations. Quantities of celecoxib were determined using a validated HPLC method. The permeability class of celecoxib was determined using *in vivo* pharmacokinetic parameters, and experimental and computational molecular descriptions.

Results: The solubility of celecoxib in the adult fed-state simulated gastric fluid was lower than that in the pediatric fed-state gastric media representative of neonates (birth to 28 days) fed soy-based formula. Similarly, the solubility of celecoxib in adult fasted-state simulated intestinal media was lower than that in the pediatric fasted-state intestinal media formulated with bile salt concentrations 50% of the adult levels. However, solubility values of celecoxib were lower in the other pediatric media compared to adult media. The age-appropriate pediatric to adult solubility ratios were outside the 80 to 125% range in 3 and was borderline in 1 out of 9 pediatric to adult solubility ratios.

Conclusions: The solubility ratios of celecoxib exhibited significant variability in about 44.4% of the media. This indicated that significant age-related variability could be predicted for oral formulations containing celecoxib intended for pediatric use. Formulation scientists should consider the significant biopharmaceutical considerations when developing child-friendly oral formulations.

Keywords: BCS, initial gastric volume, pediatric, permeability, solubility.