

Flavor Profile Method of Descriptive Sensory Analysis Guided Development of a Solithromycin Pediatric Powder for Oral Suspension Formulation

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Background/Purpose: Current solithromycin development is focused on treatment of community-acquired bacterial pneumonia and uncomplicated gonorrhea. A solithromycin pediatric suspension formulation is desired for providing dosing flexibility to pediatricians. Therefore, development of a pediatric powder for oral suspension was initiated and it was necessary to mask the bitter taste of solithromycin to achieve a more palatable formulation.

Methods: The Flavor Profile Method of descriptive sensory analysis was used by Senopsys (Woburn, MA) to measure sensory attributes of formulations prototypes developed by Toyama Chemical Company, LTD (Japan) and to guide the development of palatable formulations. The method evaluates taste on a scale of 0 to 3 for initial overall perception of balance and fullness (Amplitude), character notes (basic tastes, aromatics, texture and mouthfeel) and aftertaste. For formulation optimization, a three step sensory-directed process was followed to improve palatability: (1) development of a mimetic system using Bitrex® to model solithromycin bitterness and minimize human exposure during optimization; (2) development of a neutral-tasting base by balancing (reducing) the bitterness with complementary basic taste excipients – sweet, sour and salty and (3) identify and select flavoring aromatics to reduce the aromatic off-notes of solithromycin. Relevant portions of the taste evaluation were conducted under a Clinical Trial Protocol (CE01-124; IRB# 13-450).

Results: The results indicated that solithromycin in pH 8 phosphate buffer represents a multi-dimensional taste masking challenge due to a strong lingering intensity bitterness and secondary aromatic off-notes (soapy, cardboard) and mouthfeel effects (soapy, tannin, tongue sting and drying) that are above a patient-perceptible intensity(>1). The formulation prototypes evaluated exhibited initial flavor quality (Amplitude) ranging from ½ to 1½. A formulation suitable for phase I pediatric studies was identified. For formulation optimization studies, Bitrex® at 1.5 ppm most closely approximated the overall solithromycin bitterness and was selected as an appropriate mimetic for solithromycin. Five high intensity sweeteners, acesulfame potassium, sodium saccharin, neotame, aspartame and sucralose were evaluated. Aspartame and sucralose were found to be the most effective in reducing mimetic bitterness. The evaluation of bulk sweeteners indicated that sucrose was effective in reducing mimetic bitterness and although it was less effective alone than either aspartame or sucralose it provided a beneficial effect on the fullness and blend of the formulation. Binary sweetener blends consisting of sucrose 50% w/v with either aspartame or sucralose provided slightly more reduction in mimetic bitterness than the high intensity sweeteners alone, however ternary system blends did not provide additional benefits. The bitterness reduction effects of the binary system with sucralose were somewhat greater than with aspartame. The addition of sodium chloride for saltiness and citric acid for sourness improved sucrose/sucralose system while the taste modifier, MagnaSweet® produced a beneficial effect in mimetic bitterness in the sucrose/aspartame-sweetened system. Formulations developed with a mimetic were confirmed with solithromycin in the formulation and the sucrose/aspartame/MagnaSweet® formulation and the sucrose/Sucralose/Sodium chloride/Citric acid formulation both reduced the intensity of the aversive solithromycin attributes (bitterness, aromatic off notes and mouthfeel) below the typical patient perception levels (1>).

Conclusion: The studies demonstrated that the Flavor Profile Method of descriptive sensory analysis is a usefully tool to guide the development of a solithromycin pediatric powder for oral suspension formulation.