ABSTRACT NUMBER 1207

Taste-Masked Coating of Sodium Phenylbutyrate (ACER-001) Improves the Palatability of Sodium Phenylbutyrate for Treatment of Urea Cycle Disorders

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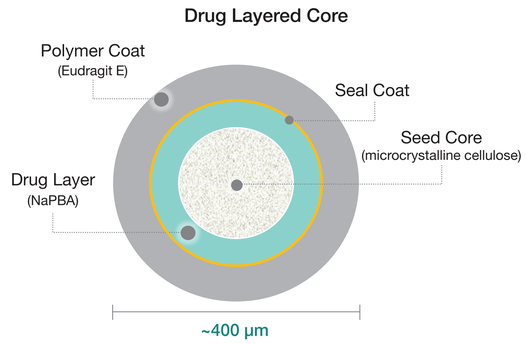
BACKGROUND

- The primary urea cycle disorders (UCDs) result from an inherited defect in one of the 6 enzymes or 2 transporters of the urea cycle[1]
- A defect in any of the urea cycle enzymes leads to the accumulation of ammonia, resulting in deleterious effects on the central nervous system, including brain damage, coma, and death[2,3]
- Treatment of UCDs includes the use of nitrogen-scavenging agents, such as sodium phenylbutyrate (salt of 4-phenylbutyric acid; NaPBA) and glycerol phenylbutyrate, which provide an alternative pathway for nitrogen disposal through the urinary excretion of phenylacetylglutamine[3]
- While these treatments are effective, treatment with NaPBA may be limited in some patients by its unpleasant bitter taste, which can compromise patient compliance, potentially reducing its effectiveness[4,5]
- ACER-001 is a novel formulation of NaPBA designed for tolerability and is currently being developed as a treatment option for patients with UCDs
- ACER-001 is designed to be ingested within 5 minutes as polymer-coated granules in suspension, to briefly mask the unpleasant bitter taste of NaPBA in the mouth, after which, the polymer-coated granules break down and release NaPBA (**Figure 1**)

Figure 1. ACER-001 is a polymer-coated granule formulation



OBJECTIVE

- To identify and quantify the intensity of perceived flavor attributes of ACER-001 relative to NaPBA powder in two taste assessment studies that enrolled trained healthy panelists

METHODS

- Studies 1 and 2 were Phase 1, open-label, repeated measures, taste assessment studies of 1) ACER-001 5-g active pharmaceutical ingredient (API, NaPBA) suspended in room temperature water containing Thick-It and 2) NaPBA powder dissolved in room temperature water
- The studies included healthy panelists (Study 1, N=10; Study 2, N=9) who were required to complete a training program for a minimum of 6 months that educated panelists on the identification, description, and quantification of sensory attributes of products
- ACER-001 was either tasted immediately (time=0) or after the preparation was allowed to sit for 1, 2, 3, 4, 5, and 10 minutes after mixing the preparation (hold times)
- As NaPBA powder is readily soluble in water, NaPBA was only evaluated at hold times of 1, 5, and 10 minutes
- Each sample was swished in the mouth for 10 seconds, tasted, and subsequently expectorated, and panelists cleansed their palates with spring water and unsalted crackers before evaluating the next sample

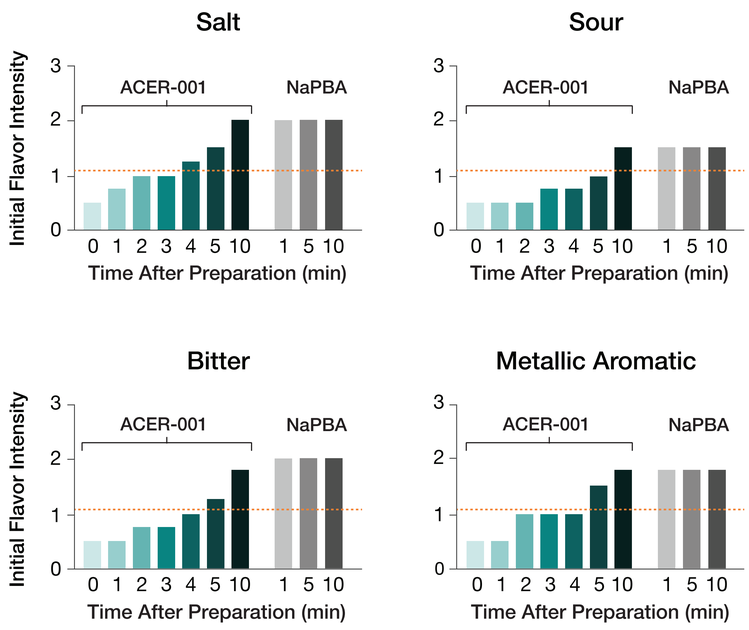
METHODS *(continued)*

- Panelists assessed and recorded taste perceptions on a paper test instrument immediately after swishing at each hold time interval (initial taste assessment) as well as at 1-, 3-, 5-, 10-, 15-, and 20-minutes following tasting (aftertaste assessment)
  - Perceived flavors and intensities for basic tastes, aromatics, mouthfeels, and texture were graded using the American Society for Testing and Material (ASTM) approved Flavor Profile method of sensory analysis on a scale of 0 to 3, with higher values associated with poor taste quality and values >1 clearly perceptible and above the aversive threshold[6] (specific results for select flavors are reported in this poster)
  - As flavors of the samples were not known a priori, the panelists identified and quantified all perceived attributes unaided by a pre-populated questionnaire

RESULTS

- Initial taste scores (time 0) and scores following initial assessment (aftertaste) are presented in **Figures 2** and **3**, respectively
  - The taste quality of ACER-001 was numerically lower (better) than NaPBA powder at hold times up to 5 minutes
  - For ACER-001, at hold times of 0 to 3, taste scores for all flavors were below the aversive threshold (taste score ≤1)
  - For ACER-001, hold times of 4 and 5 minutes had a maximum taste flavor score of 1.25 (salt, bitter) and 1.5 (salt, metallic aromatic), respectively
  - ACER-001 had a similar taste score as NaPBA powder at a hold time of 10 minutes
  - NaPBA powder had similar taste scores at all hold times (1, 5, and 10 minutes)
- The initial and after taste scores were highly correlated, and showed that ACER-001 has a better flavor quality than NaPBA powder (**Figure 4**)
- There were no adverse events reported during the studies

Figure 2. Graded flavor intensity for ACER-001 and NaPBA powder at initial taste (time 0) by hold time (initial taste assessment)



Dotted orange line represents the aversive threshold. Taste scores for other sensory profiles, such as serum-like mouthfeel, oily mouthfeel, tongue sting mouthfeel, and soapy mouthfeel were ≤1 for both ACER-001 and NaPBA powder at all times after preparation.

Figure 3. Graded flavor intensity for ACER-001 and NaPBA powder by time after initial taste (aftertaste assessment)

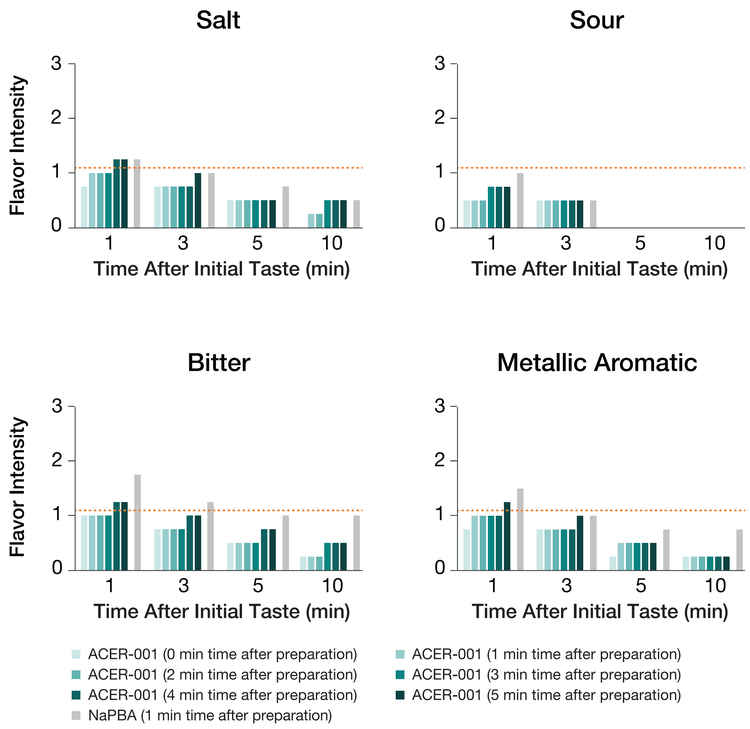
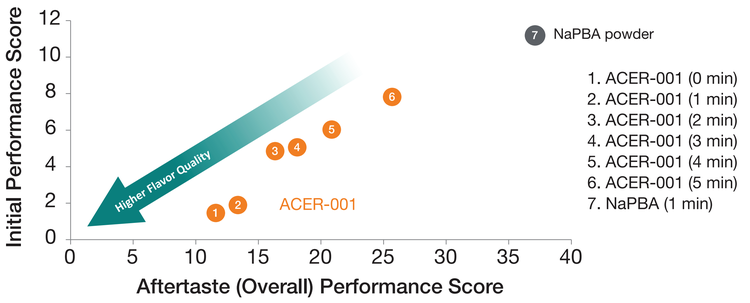


Figure 4. Correlation of initial and aftertaste flavor quality



To facilitate comparison across samples, the intensity of "aversive" flavor attributes (including bitter, salt, metallic aromatic, soapy, sulfite aromatic, serum-like mouthfeel, tongue sting mouthfeel, and throat burn mouthfeel) were summed across time intervals to create "Performance Scores." Initial Performance Score represents the aversive attributes measured in the initial flavor (ie, time 0). Aftertaste (Overall) Performance Score represents the aversive attributes in both the initial flavor and aftertaste (ie, sum of time = 0, 1, 3, 5, 10, 15, 20 minutes). Lower scores indicate less negative flavor impact, ie, high flavor quality.

CONCLUSION

- ACER-001 was shown to have overall lower flavor intensity scores than NaPBA powder when administered within 5 minutes of preparation

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