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# Stability of Extemporaneously Prepared Sodium Benzoate Oral Solution

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# Stability of Extemporaneously Prepared Sodium Benzoate Oral Solution

## **Abstract**

**Purpose:** Sodium benzoate ( $\text{NaC}_7\text{H}_5\text{O}_2$ ), a common food preservative, is the salt form of benzoic acid. It is used as an alternative treatment in patients with hepatic encephalopathy or urea cycle disorders as it is believed help stimulate ammonia removal via a non-urea cycle based pathway. Despite its use, sodium benzoate is not an FDA approved medication and has no commercially available oral formulations, although an IV formulation is available in combination with sodium phenylacetate (Ammonul®). The objectives of this study were to prepare a sodium benzoate solution and determine the stability of an extemporaneously prepared oral solution over a 90-day period.

**Methods:** An oral solution of sodium benzoate was prepared and a 1 ml sample was withdrawn from each bottle immediately after preparation and at 7 and 14 days and assayed for drug concentration by stability-indicating high performance liquid chromatography. Stability of sodium benzoate solution will be defined as maintenance of greater than or equal to 90 percent of the initial concentration.

**Results:** The sodium benzoate maintained 96% and 93% of the initial concentration at 7 and 14 days, respectively. Therefore, sodium benzoate oral solution in cherry syrup is stable for a minimum of 14 at room temperature.

## **Keywords**

fsc2016

## **Disciplines**

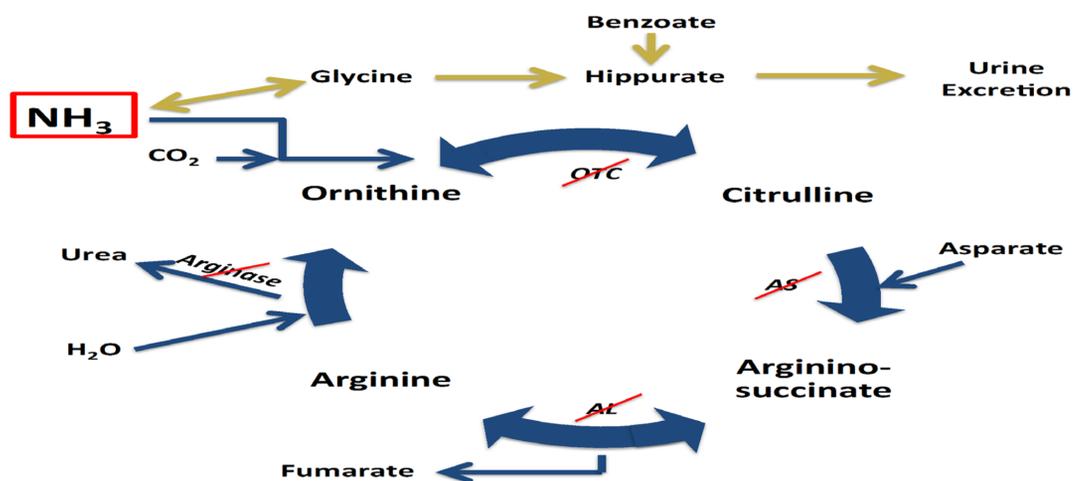
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## **Comments**

Presented at American Society of Health Systems Pharmacy Midyear Clinical Meeting in New Orleans, Louisiana, December 2015.

## Background

- Urea cycle disorders (UCD) occurs in 1: 8500 births and leads to an accumulation of ammonia due to a deficiency of the enzyme(s) utilized in the urea cycle
- Depending on the severity, UCD can lead to growth suppression, neurologic changes, seizures, coma, and death
- Sodium benzoate is believed to stimulate ammonia removal via the Hippurate pathway, independent of the urea cycle
- Sodium benzoate/sodium phenylacetate (Ammonul®) is an FDA approved IV formulation approved for the treatment of UCD
- There is currently no FDA approved oral formulation of sodium benzoate commercially available; although many pediatric patients utilize compounded solutions for chronic therapy



**The Urea Cycle**  
 AL – Argininosuccinate Lyase AS - Argininosuccinate Synthase OTC – Ornithine Transcarbamylase  
 / - Potential enzyme deficiency present in urea cycle disorders

## Objectives

- Determine the 90-day stability of sodium benzoate oral solution, defined as the retention of at least 90% of the initial concentration

## Methods

### Sample Preparation:

- Twenty five grams of sodium benzoate was added to a beaker containing 50 ml of sterile water and stirred until dissolved
- The resulting solution was filtered via Whatman filter paper and added to a 4-oz amber bottle pre-calibrated to 100 ml
- The beaker which contained the sodium benzoate solution was rinsed with cherry syrup and added to the amber bottle until final volume of solution was 100 ml
- Final solution concentration was 250 mg/ml

### Preparation for Analysis:

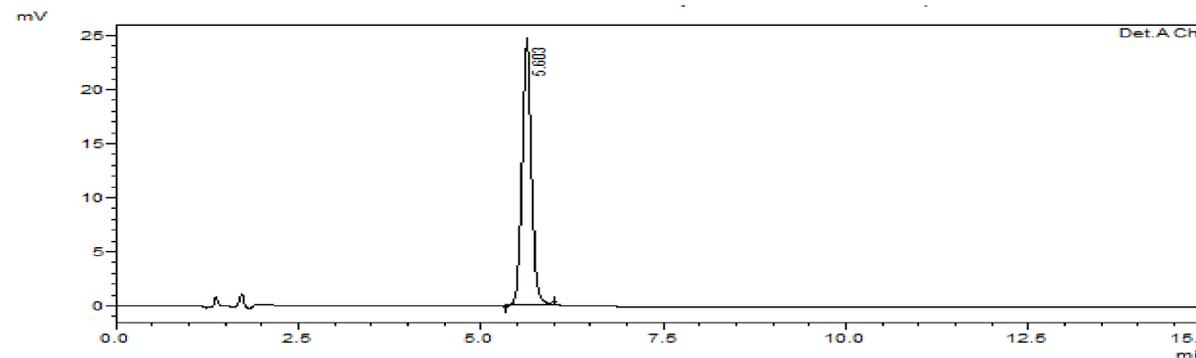
- Prepared samples for shaken for 1 minute before sampling
- A 1 ml aliquot was removed from each sample and diluted to 100 ml with diluent (50:50 mixture of sterile water and acetonitrile) for a concentration of 2.5 mg/ml
- A 0.1 ml aliquot of the 2.5 mg/ml solution was further diluted to 100 ml with diluent for a final concentration of 2.5 mcg/ml
- Samples were filtered through a 45-micron filter
- Samples were analyzed at days 0, 7, and 14

### Analysis:

- Samples were analyzed via a Shimadzu HPLC with a C18 column and mobile phase of 30:70 acetonitrile and 20-mM monobasic potassium phosphate adjusted to pH of 2.5 with phosphoric acid
- A 15 uL sample was injected and analyzed with the detector set at 230 nm
- The samples were run for 15 minutes with a mobile phase rate of 1 ml/min
- The chromatogram was analyzed using LC solutions version 1.25

## Results

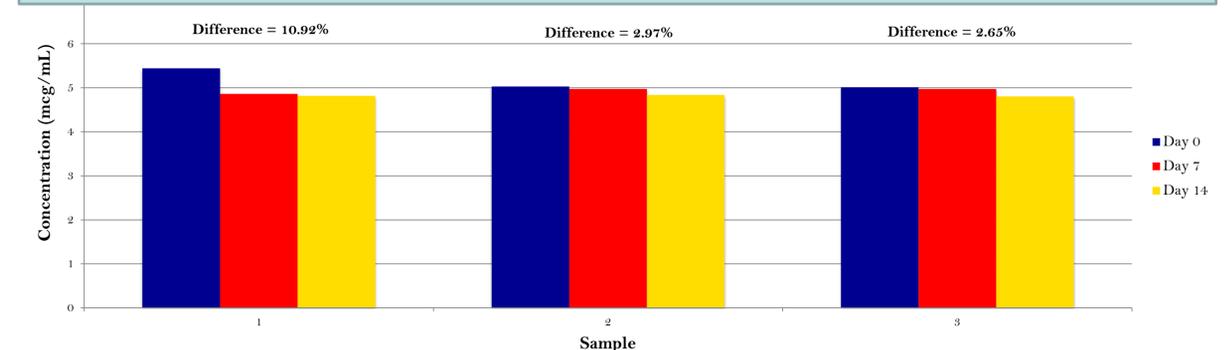
### Day 0 Chromatogram



### Peak Summary

	Sample 1			Sample 2			Sample 3		
	Day 0	Day 7	Day 14	Day 0	Day 7	Day 14	Day 0	Day 7	Day 14
<b>Retention time (min)</b>	5.620	5.606	5.661	5.620	5.603	5.642	5.622	5.605	5.369
<b>Maximum Intensity (mV)</b>	26751	23251	24460	24726	24101	24468	24438	24108	24202
<b>Area</b>	215016	213917	211816	219287	218913	219817	221916	220093	219824

### Sodium Benzoate Concentration



## Conclusion

- Sodium benzoate oral solution in cherry syrup appears to be stable for at a minimum of 14 days at room temperature.
- Further stability analysis will be conducted at days 30, 60, and 90.
- A forced degradation analysis will also be conducted by exposing the samples to acidic and basic pH, hydrogen peroxide, direct sunlight, and prolonged exposure to 60°C.

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### DISCLOSURE:

Authors of this project have nothing to disclose concerning possible financial or personal relationships with commercial entities that may have a direct or indirect interest in the subject matter of this presentation: Andrew S. Decker: Nothing to disclose; Melinda E. Lull: Nothing to disclose; David J. Hutchinson: Nothing to disclose. a