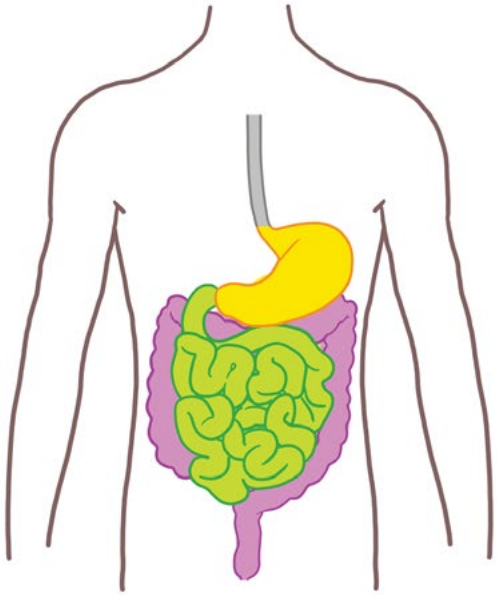
How Nobel used Biorelevant Media to achieve Bioequivalence for an Oral Generic Formulation

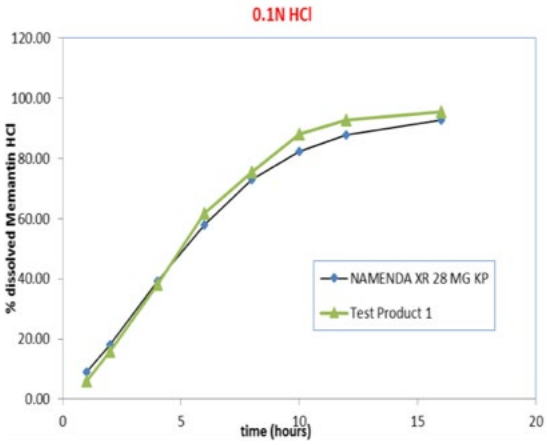
- Testing in Biorelevant Media was key to identify a bioequivalent formulation of Namenda XR 28 mg Extended Release Capsules BCS Class 1 for treatment of Alzheimers

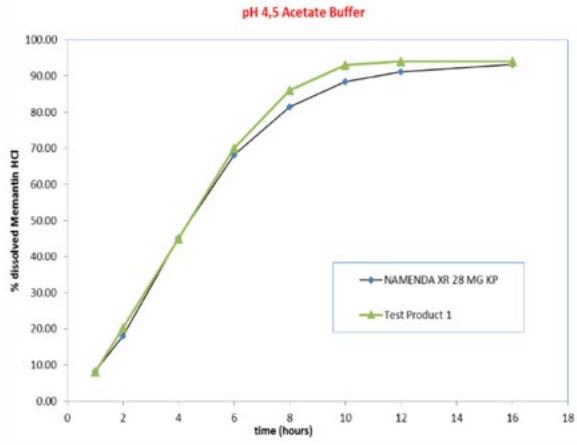


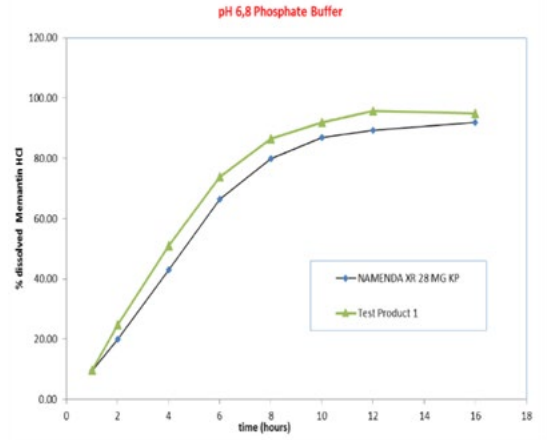
Testing in Standard Buffers

- Nobel Pharma's team used standard buffers 0.1 N HCl, pH 4.5 acetate buffer and pH 6.8 phosphate buffer to compare their generic "Test Product 1" to the originator Namenda XR 28 mg Extended Release Capsules

- In these three media, the dissolution profiles between the generic test product and the originator seemed identical and non-discriminating

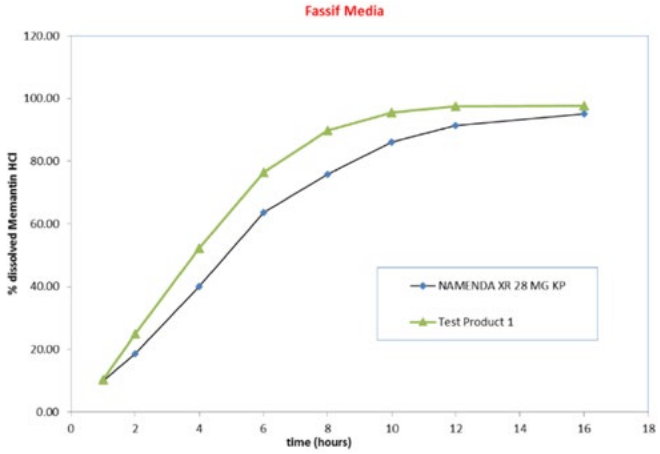


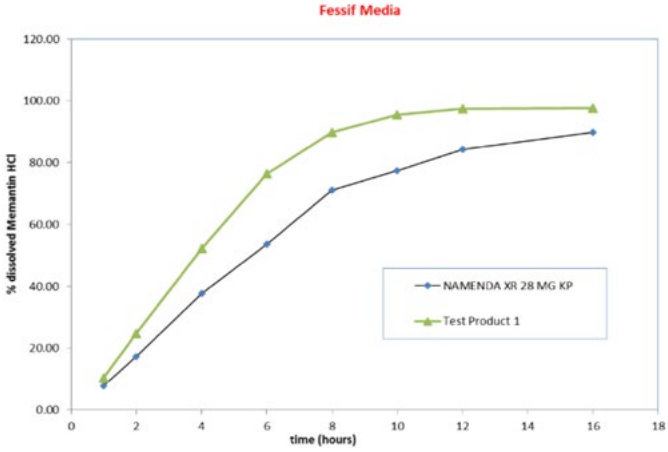




Testing in Biorelevant Media

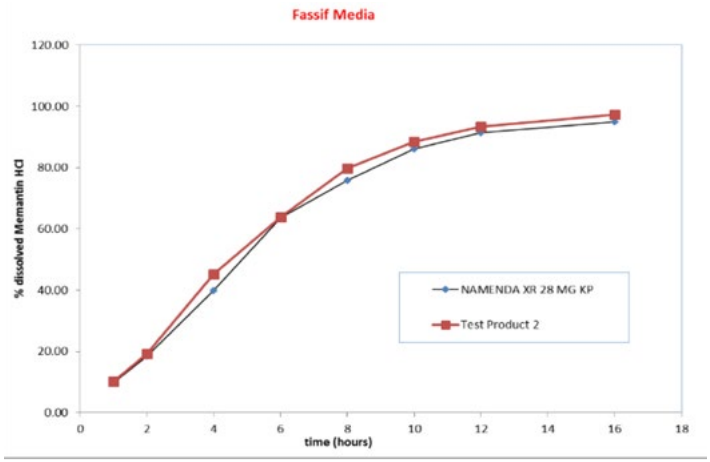
- Nobel Pharma's development team decided to use Biorelevant Media (from biorelevant.com) before sending the product off for a bioequivalence study
- Surprising results were obtained from testing in FaSSIF (fasted small intestine) and FeSSIF (fed small intestine) Biorelevant Media
- Test Product 1 and Namenda XR biorelevant dissolution profiles were very different from those tested in standard buffers

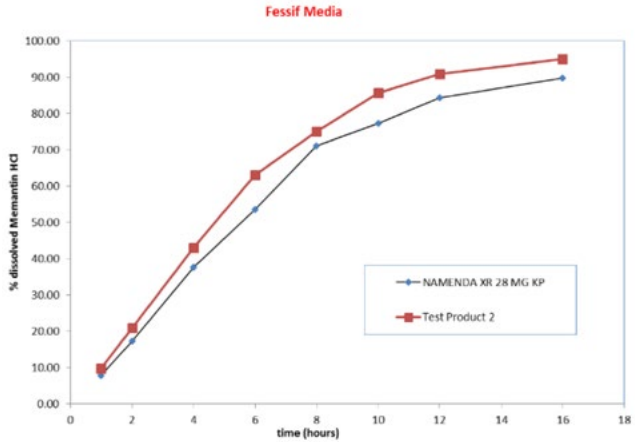




Formulation Optimization in Biorelevant Media

- The unexpected biorelevant dissolution result forced them to change the formulation of Test Product 1
- Nobel switched testing in standard buffers for Biorelevant Media “because of the discriminative power of that media”
- They tested Test Product 2 in FaSSIF and FeSSIF Biorelevant Media and achieved much improved results compared to Test Product 1

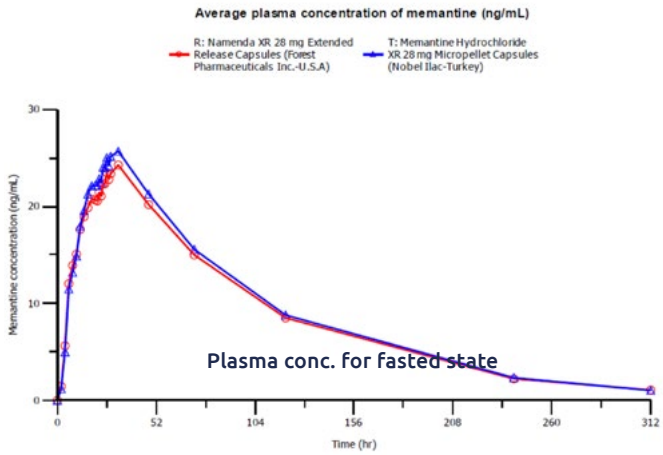


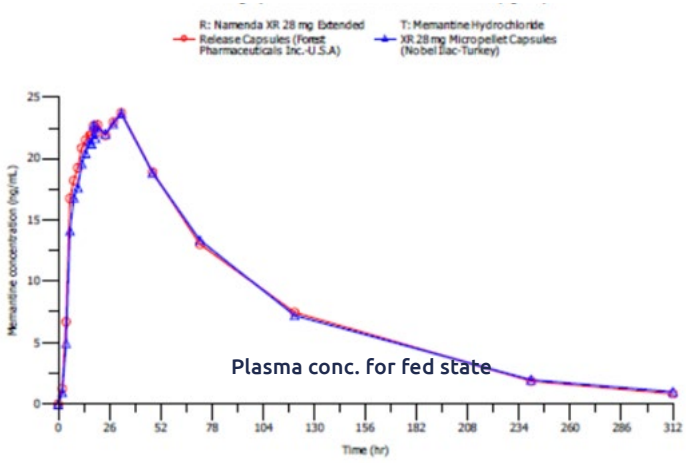


Clinical Study After Testing in Biorelevant Media

- After testing Test Product 2 in Biorelevant Media, Nobel sent the products to a CRO for a bioequivalence study under both fasted and fed states and obtained positive results and a bioequivalent drug product for both conditions

- The plasma concentration graphs for fasted and fed state are given here:





Results

- Standard buffers gave false positive results for Nobel's generic version of Namenda XR 28 mg Extended Release Capsules
- Biorelevant Media enabled their scientists to discriminate between drug product formulations
- This saved them time and money on clinical bioequivalence studies for a formulation that simply may not have been bioequivalent