# Enhanced Formulations

## CASE STUDY


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# Enhanced Formulations

## *Successful Formulation Strategies*

Modifying the micro-environment to improve dissolution rate

### THE CHALLENGES

- Solubility is a problem in the development of formulations of poorly soluble drugs.
- Limited solubility can lead to formulations with inadequate oral bioavailability.

### THE SOLUTION

- Option 1: Use a spray drying process to form an amorphous solid dispersion. The process can be tricky and typically results in longer project timelines and higher costs.
- Option 2: Make water soluble salts of poorly soluble (BCS II or IV) acidic or basic drugs. However, upon contact with water in GI fluids, these salts can undergo dissociation and spontaneous precipitation if the pH generated during dissolution is not sufficient to maintain solubility of the free acid or free base.
- Option 3: Use excipients to modify the pH or solubility conditions at the surface of the dissolving salt to minimize precipitation. This approach utilizes conventional methods of manufacture, i.e., a high shear granulation and compression process.

### THE RESULTS

- Option 3 was selected and an increase in dissolution rate was achieved by modifying the micro-environment with acidic excipients. The diffusion layer was modified by granulating and/or co-compressing the drug salt form with an excipient designed to alter the diffusion layer properties, e.g., citric acid, sodium citrate, sodium bromide.

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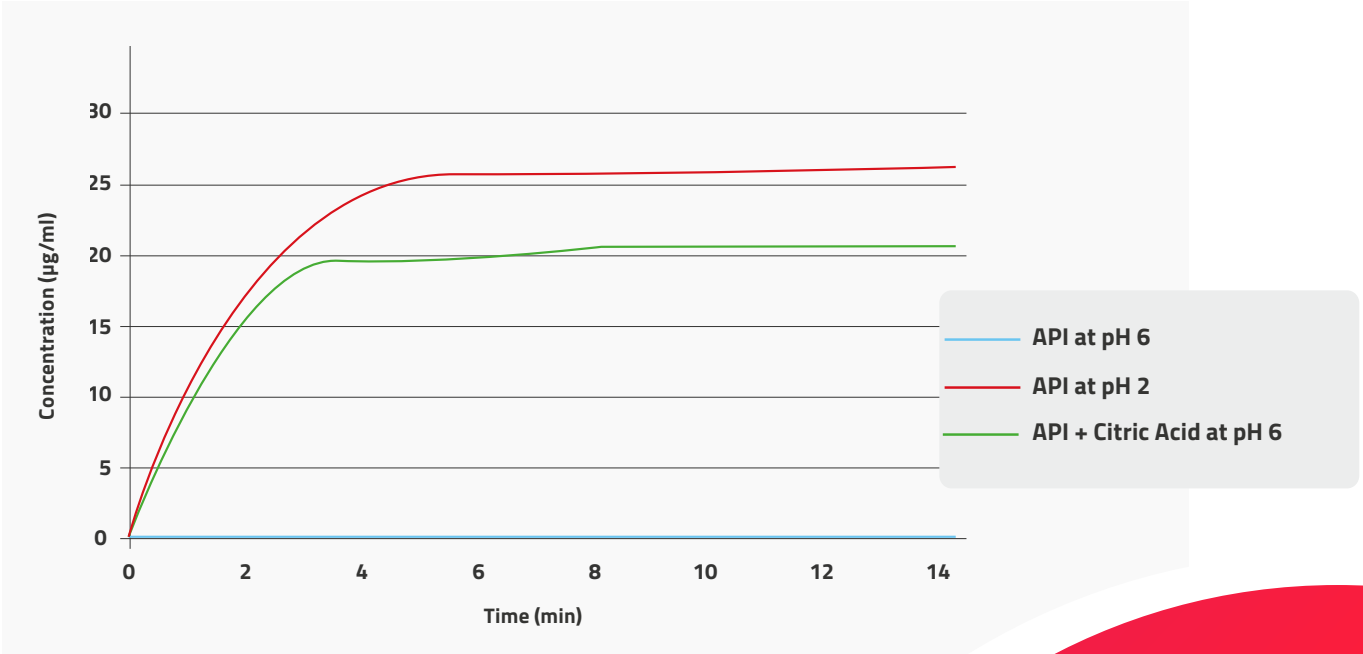
## *Example #1: Acidic Micro-Environment*

- The API was a soluble salt of a poorly soluble basic drug.
- Tablets were made using drug and citric acid in a 2:1 weight ratio.
- The citric acid was used to decrease the diffusion layer pH in order to prevent the precipitation of free base on the surface of the dissolving salt.
- Focus beam reflectance measurements (FBRM) were used for real-time monitoring of particles as they dissolved from tablets.
- FBRM monitored changes in particle dimension, particle count, and particle shape. This allowed for quick screening of formulations and processing parameters.

### SUCCESSFUL FORMULATION WITH MODIFIED DIFFUSION LAYER

Dissolution profiles of drug prepared with and without citric acid at pH 6 and pH 2

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