

Figure 1: X-Ray Powder Diffraction (XRPD) of the Monohydrate Form of 3-(3-methoxy-4-((4-methoxybenzyl)oxy)benzyl)-6-(1-methyl-1H-pyrazol-4-yl)-3H-imidazo[4,5-b]pyridin-2-amine, 4–40 °2θ

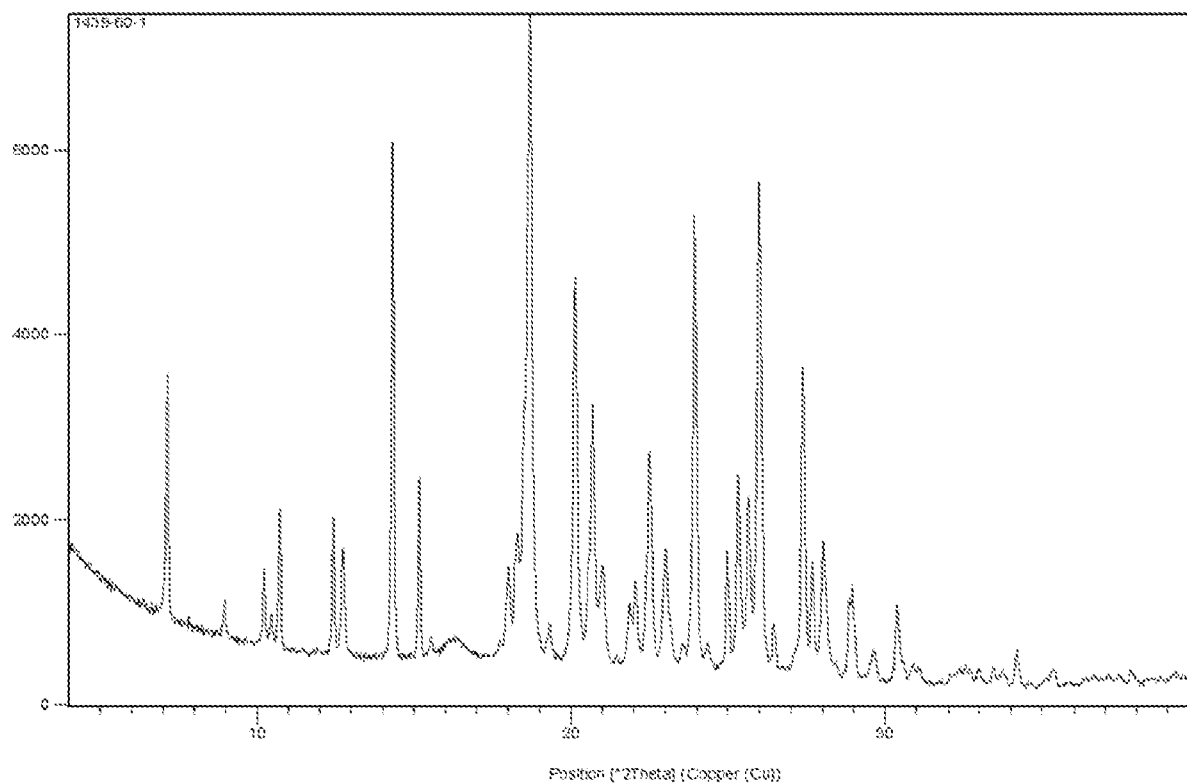


Figure 2: Differential Scanning Calorimetry (DSC) and Thermal Gravimetric Analysis (TGA) Thermogram of the Monohydrate Form of 3-(3-methoxy-4-((4-methoxybenzyl)oxy)benzyl)-6-(1-methyl-1H-pyrazol-4-yl)-3H-imidazo[4,5-b]pyridin-2-amine, Heated at 10°C/min

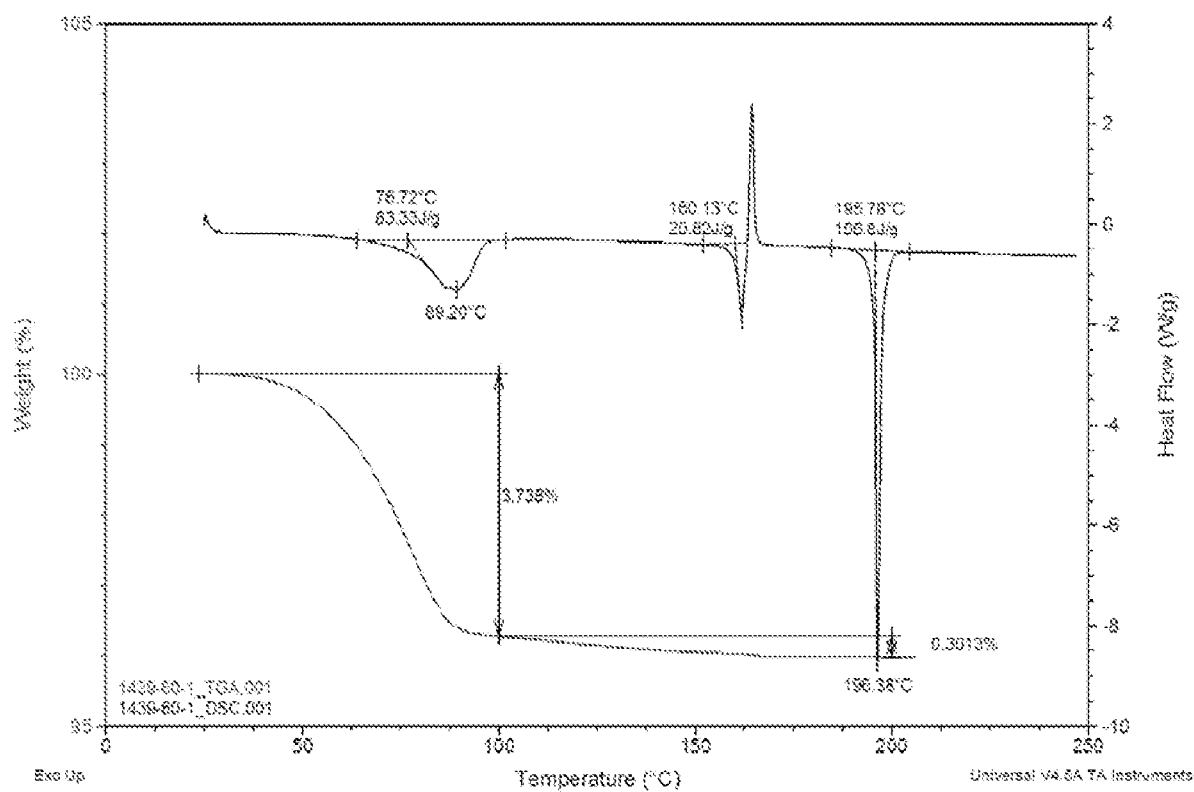


Figure 4: Overlay of Experimental XRPD Pattern with the XRPD Pattern Calculated from the Single Crystal Structure

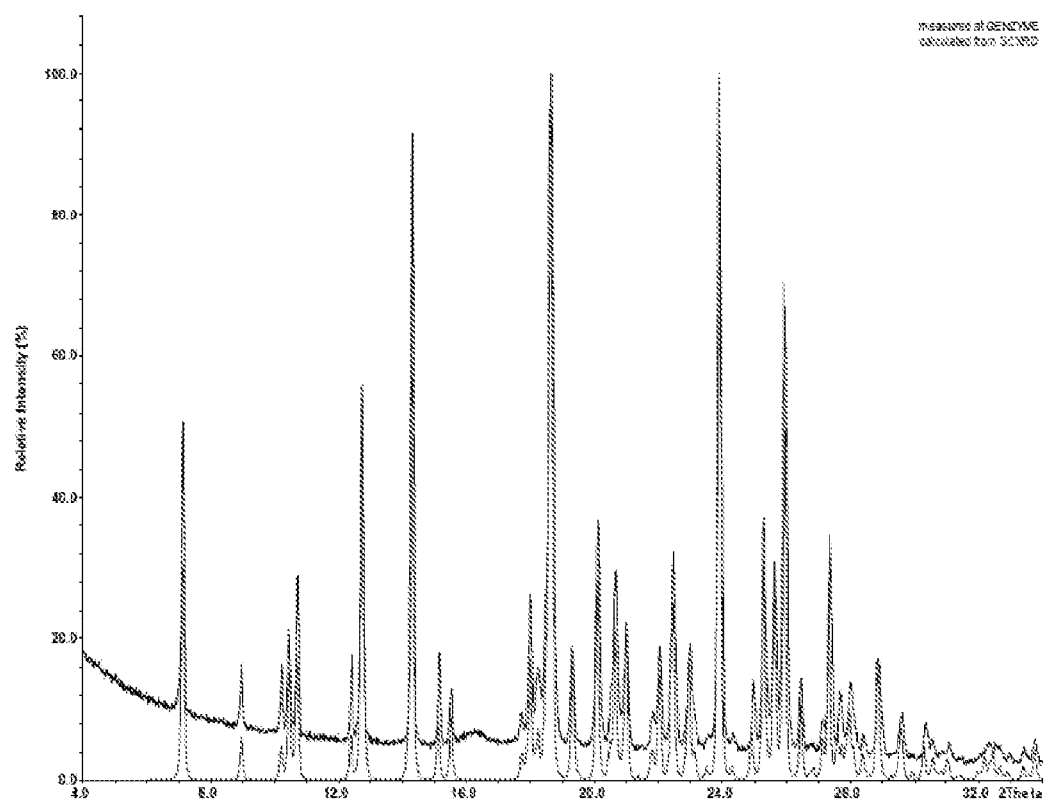


Figure 5: Effect of API Loading on IVR Profile – 12% API/9:1 R202H:752H, 16% API/9:1 R202H:752H and 20% API/9:1 R202H:752H Microspheres

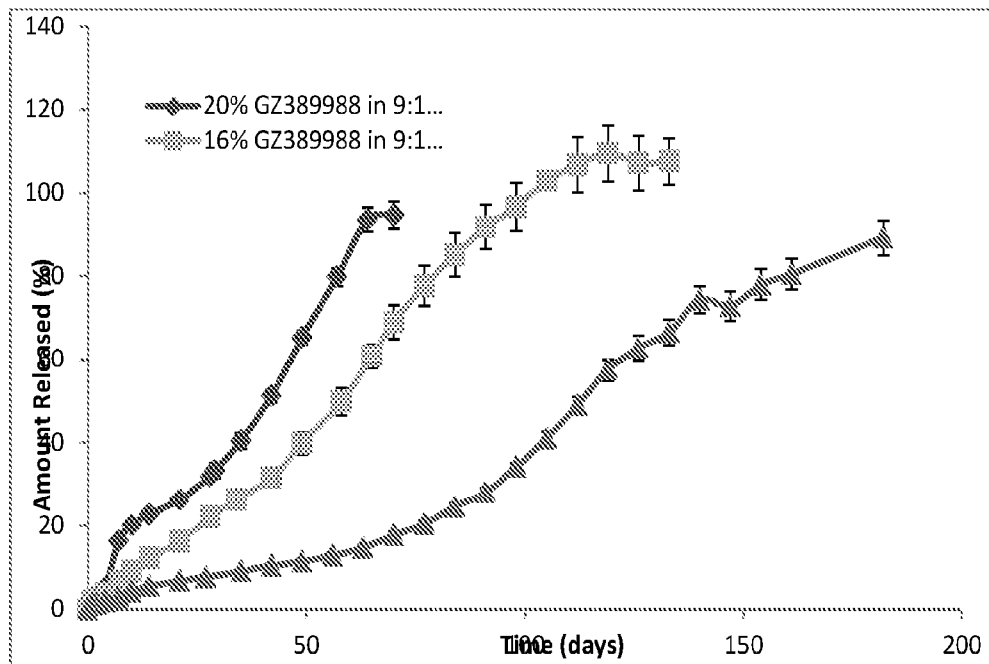
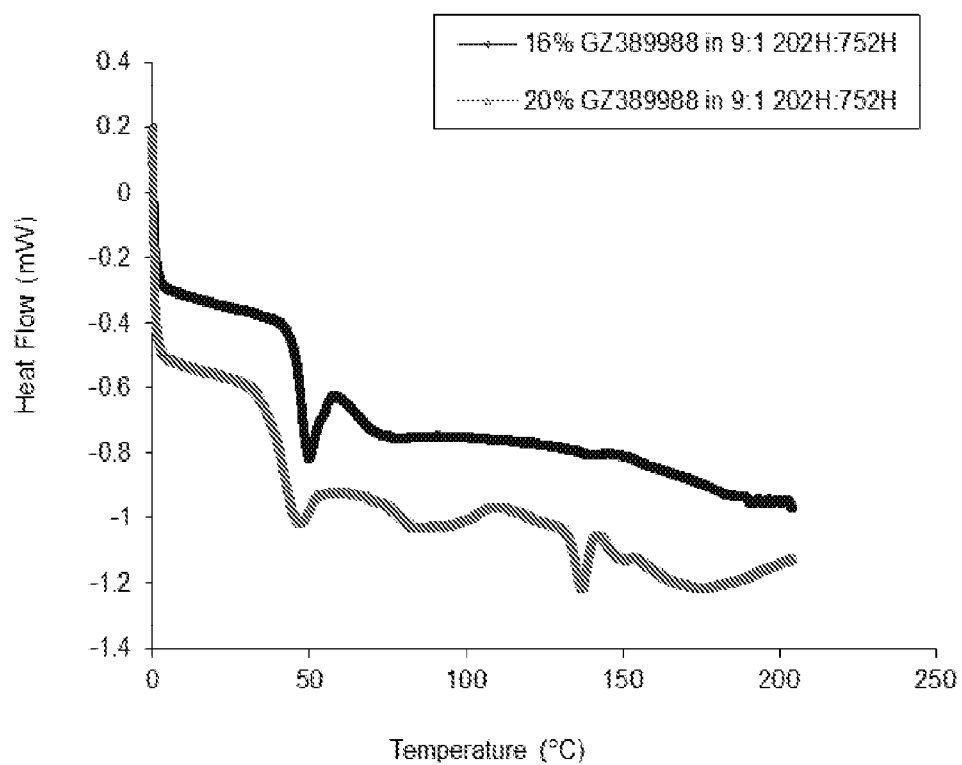
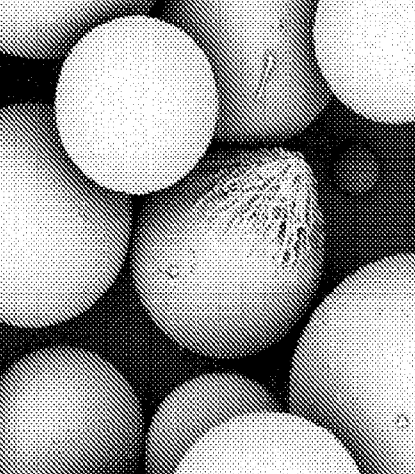


Figure 6: DSC Thermograms of 16% API/9:1 R202H:752H and 20% API/9:1 R202H:752H Microspheres





This SEM image shows a collection of spherical particles. Most are smooth and uniform in size, but one particle in the center-right is notably textured and irregular, possibly representing a different phase or a defect. The particles are densely packed against a dark background.

**Figure 8: Scanning Electron Microscopy (SEM) View of
20% API/9:1 R202H:752H Microspheres (1500X)**

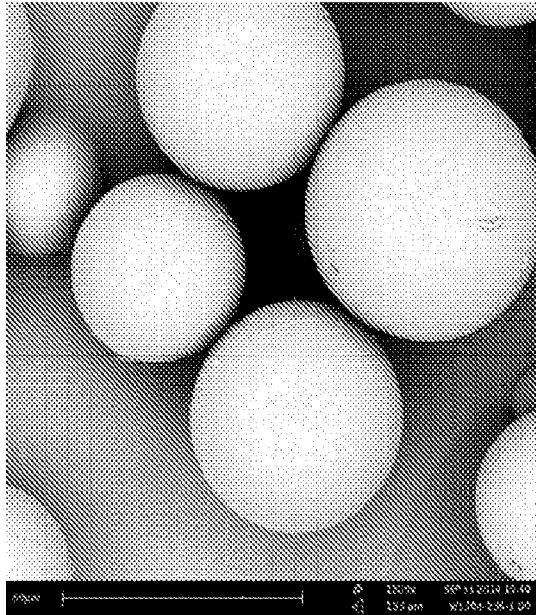


Figure 9: Effect of API Loading on IVR Profile – 15% API/R202H, 17% API/R202H and 19% API/R202H Microspheres

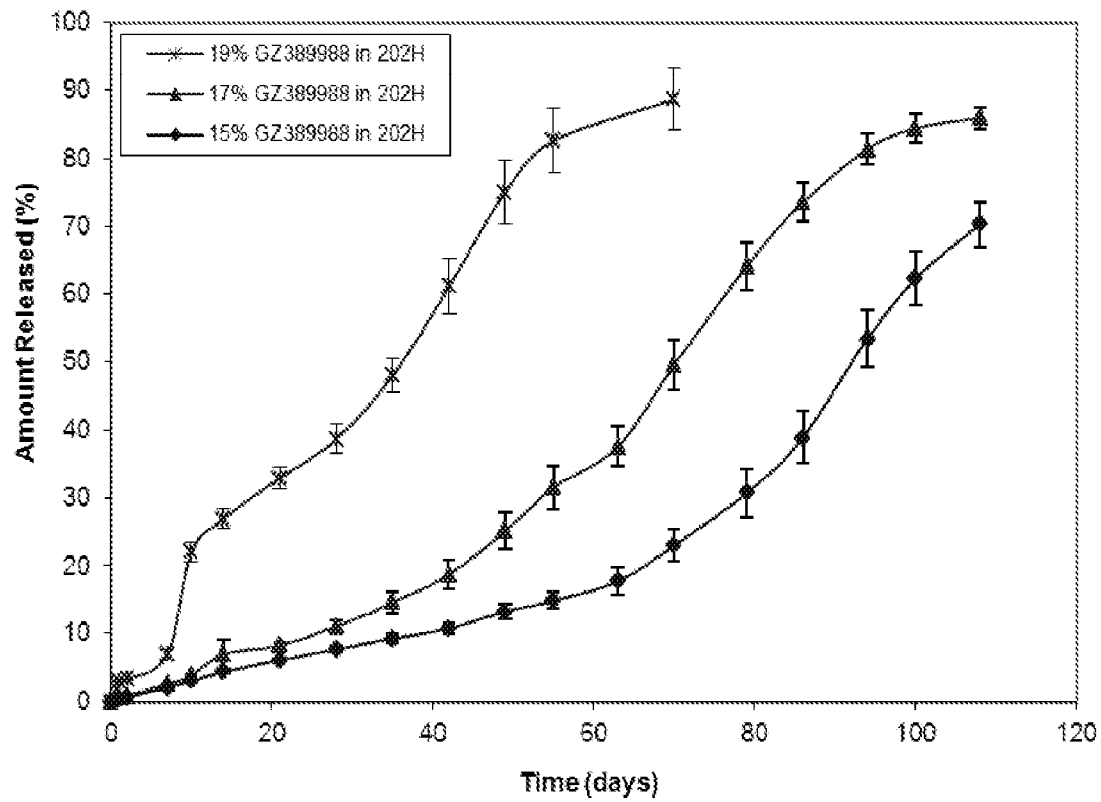


Figure 10: Effect of API Loading on IVR Profile – 16% API/9.5:0.5 R202H:752H, 18% API/9.5:0.5 R202H:752H and 20% API/9.5:0.5 R202H:752H Microspheres

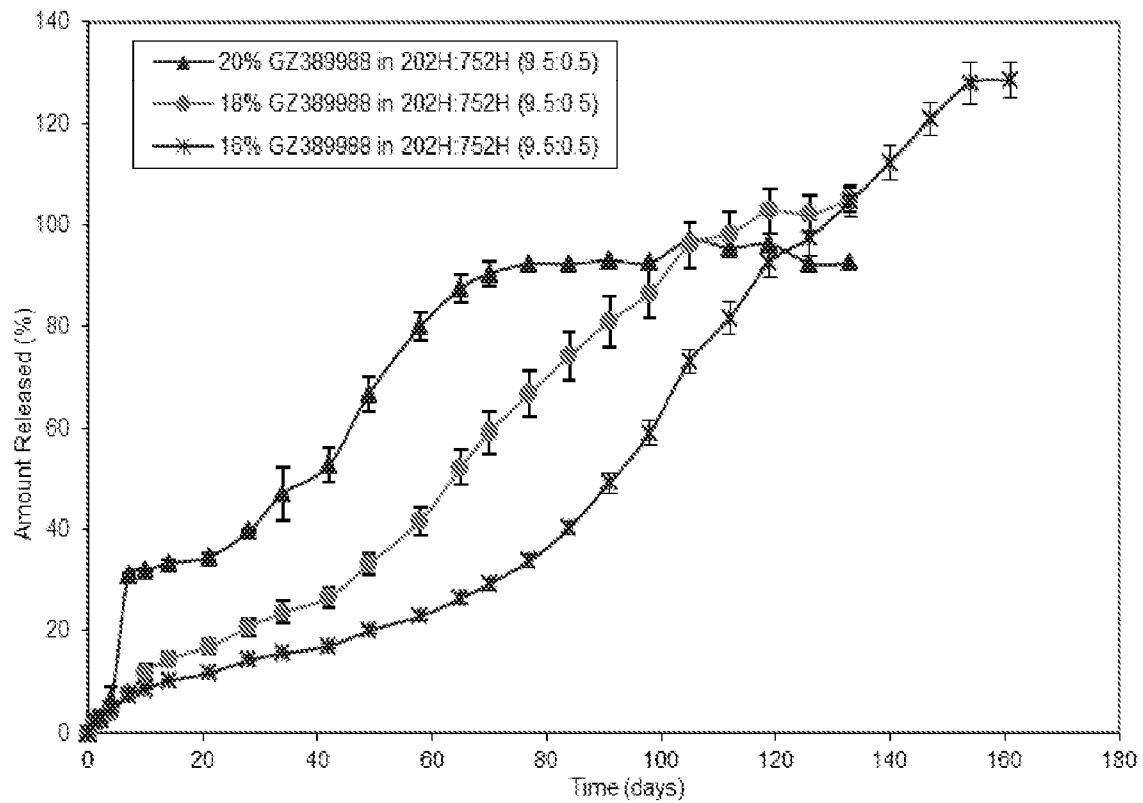


Figure 11: Effect Polymer Blend on IVR Profile – 16% API/R202H, 16% API/9.0:0.5 R202H:RG752H and 16% API/9:1 R202H:RG752H Microspheres

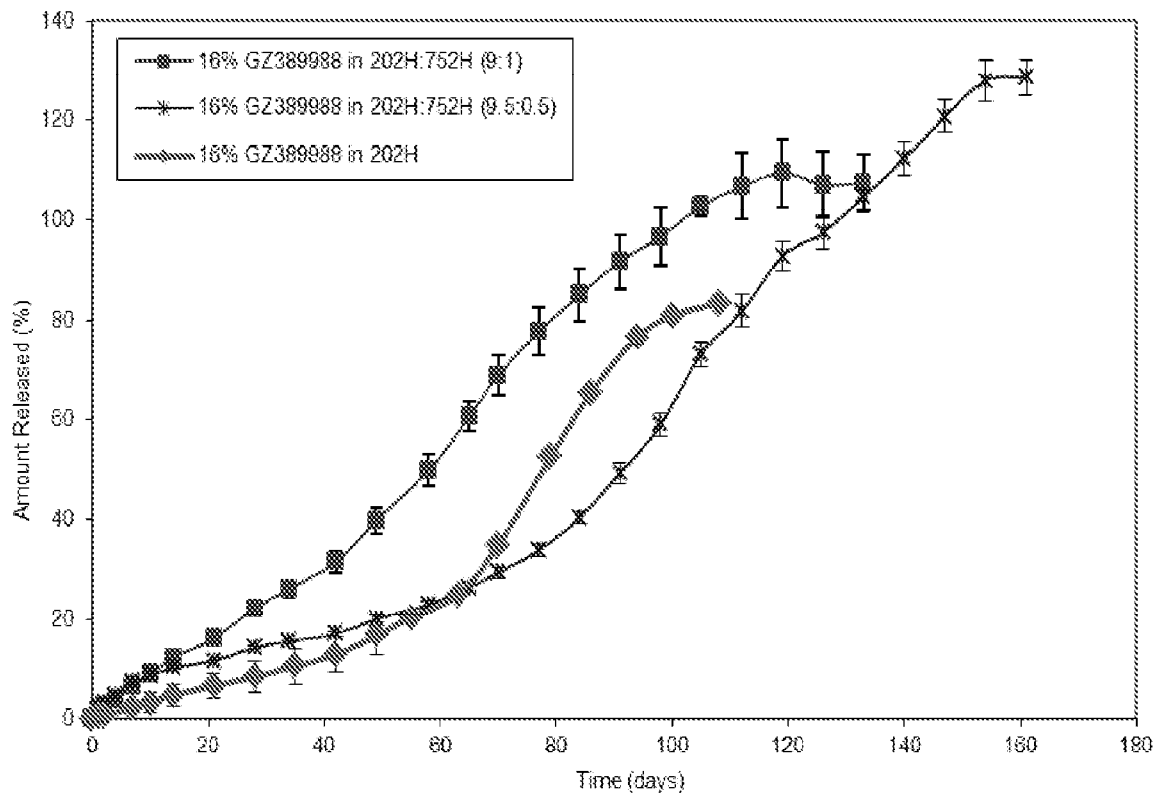


Figure 12: Effect Polymer Blend on IVR Profile – 16% API/R202H, 16% API/9.5:0.5 R202H:RG502H and 16% API/9:1 R202H:RG502H Microspheres

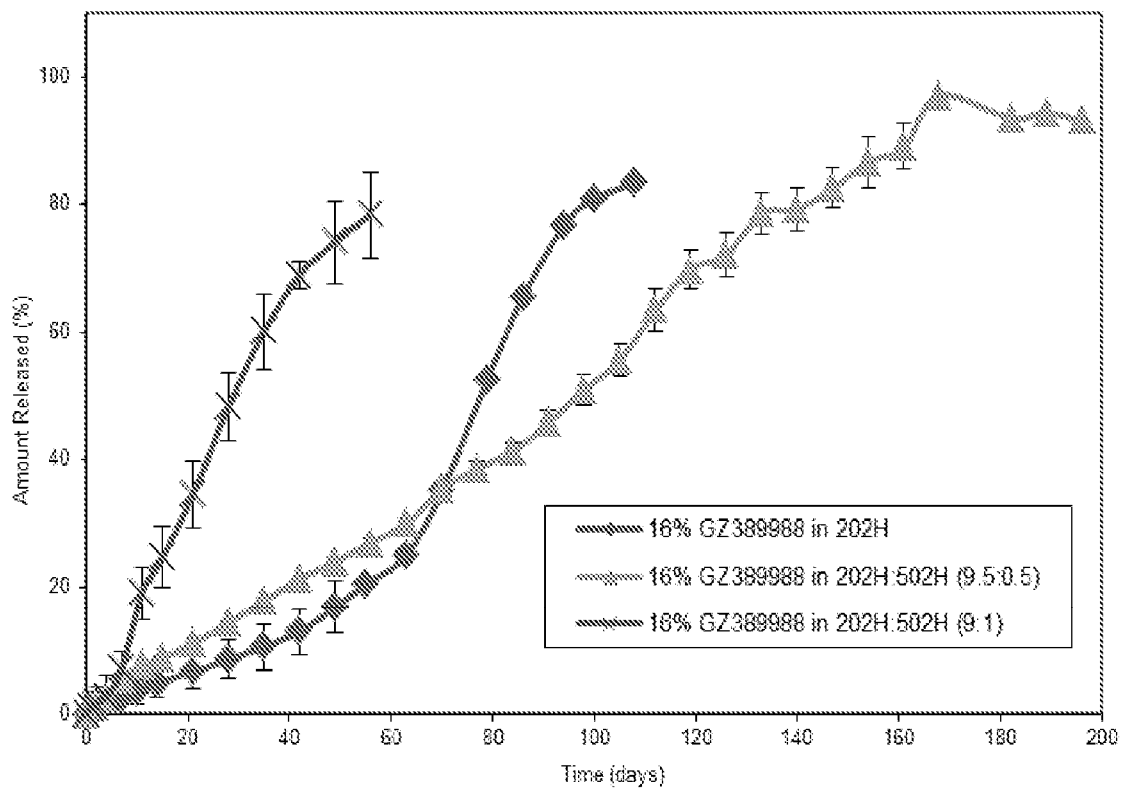


Figure 13: Formulations Showing Zero-Order IVR Profile for 180 Days – 15% API/9:1 R203H:RG752H and 16% API/9.5:0.5 R202H:RG502H Microspheres

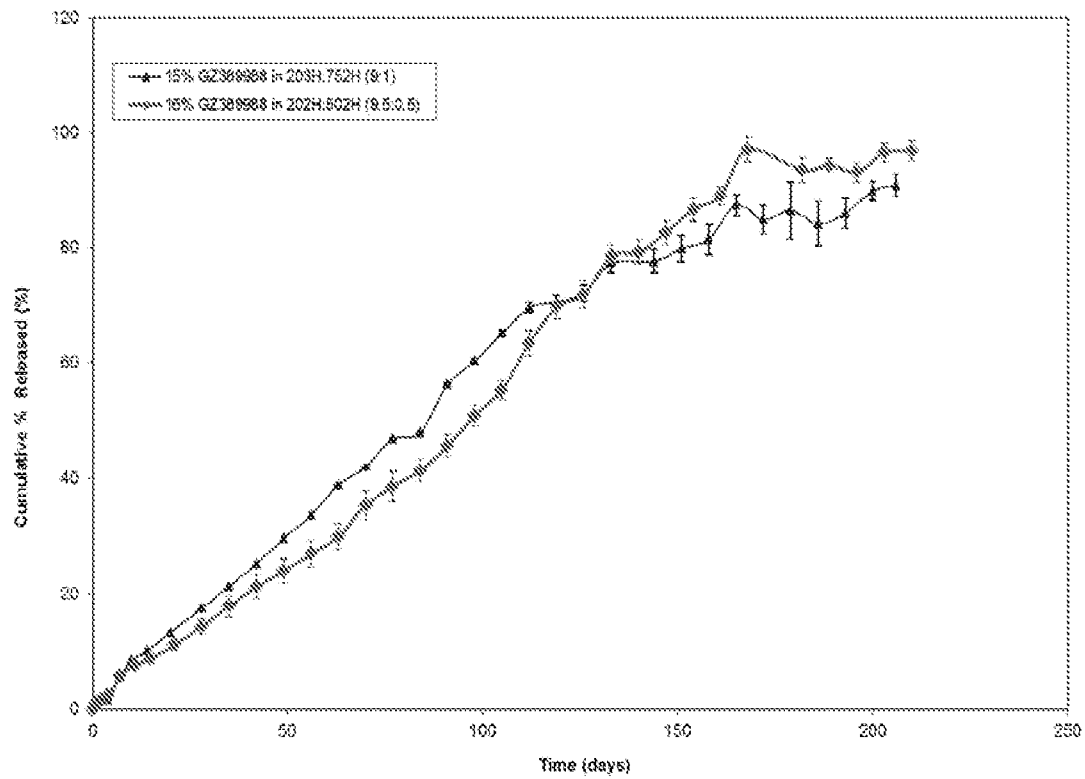


Figure 14: Effect of Co-Solvent Systems in Preparation on IVR Profile – 16% API/9:1 R203H:RG752H Microspheres – 9:1 DCM:MeOH, 9:0.5:0.5 DCM:MeOH:BA, 9.5:.05 DCM:BA, 9:1 DCM:BA

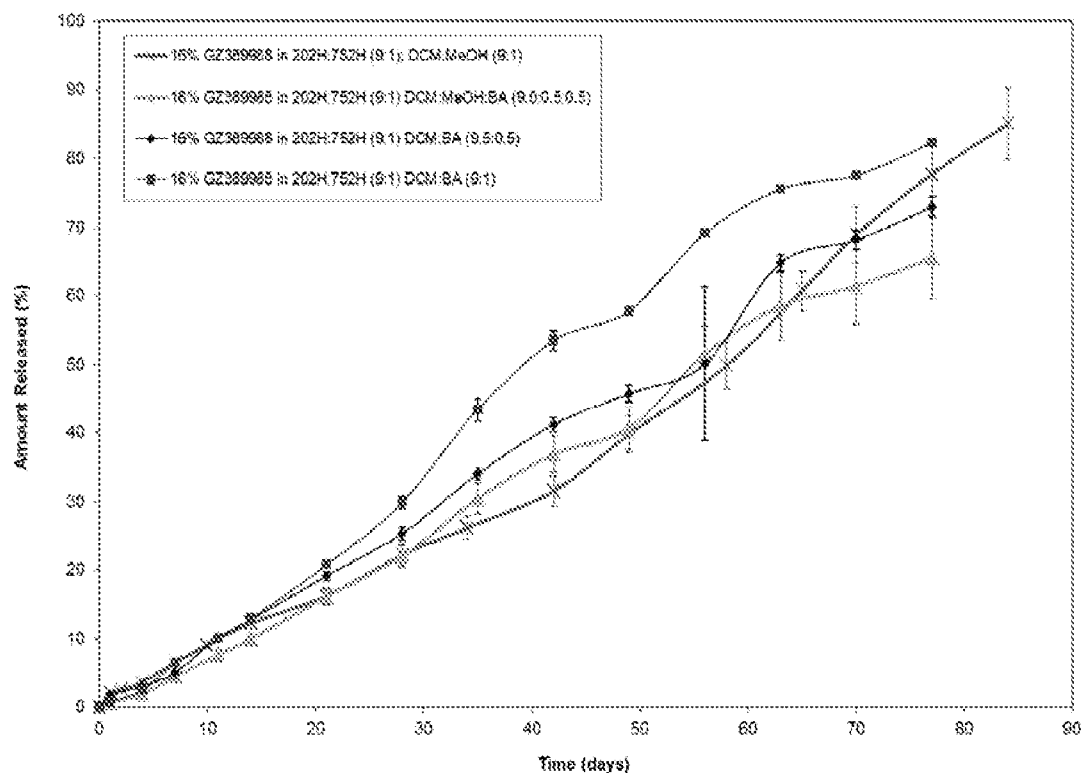


Figure 15: Effect of DCM:BA Co-Solvent System to Increase API Loading on IVR Profile
 – 16% API/9:1 R202H:RG752H, 25% API/9:1 R202H:RG752H, 30% API/R202H, 40%
 API/R202H, 25% API/R203H, 30% API/R203H, 40% API/R203H, 50% API/R203H
 Microspheres

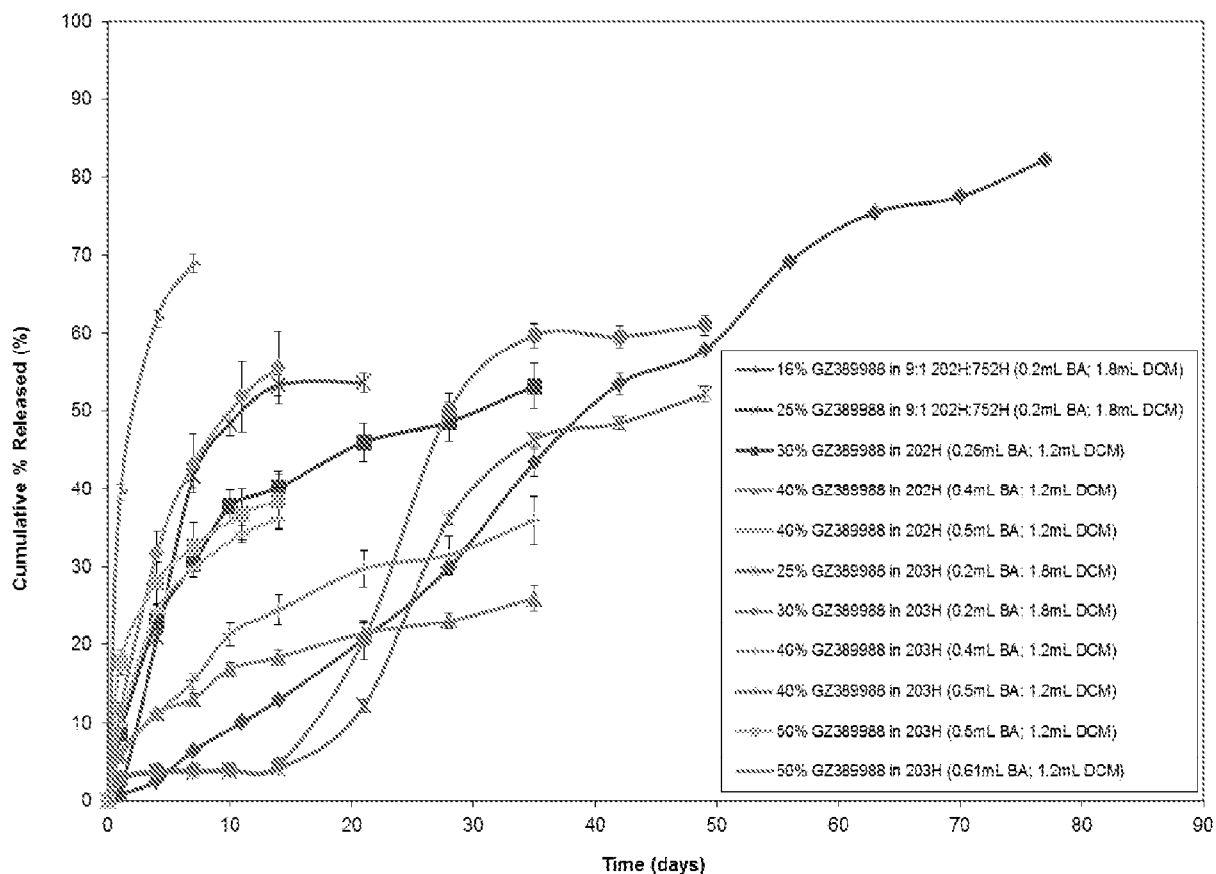


Figure 16: Scanning Electron Microscopy (SEM) View of Microspheres Prepared with Micronized Suspension Microencapsulation Process (1500X)

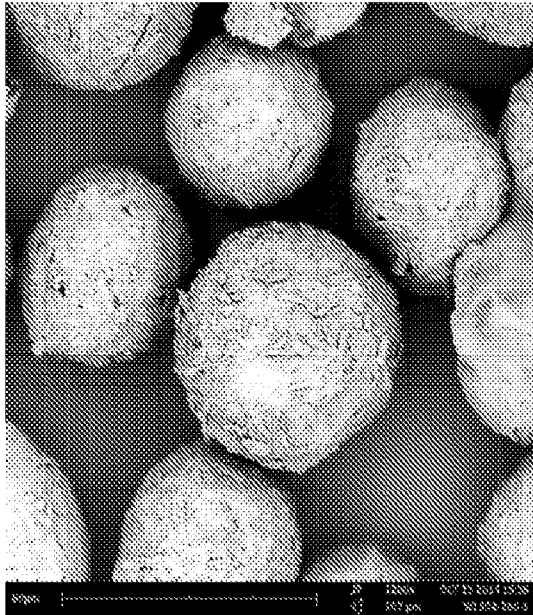


Figure 17: Effect of Micronized Suspension Microencapsulation Process on IVR Profile –
25% API/9:1 R202H:RG752H 39 mL 5% PVA + 2.6 mL EA, 25% API/9:1
R202H:RG752H 39 mL 5% PVA + 3.25 mL EA, 25% API/R203H 39 mL 5% PVA + 2.0
mL EA, 30% Microfluidized API/9:1 R202H:RG752H 39 mL 5% PVA + 2.0 mL EA, 40%
Microfluidized API/9:1 R202H:RG752H 39 mL 5% PVA + 2.0 mL EA, 30%
Microfluidized API/9:1 R202H:RG752H 39 mL 5% PVA + 2.0 mL EA, 30%
Microfluidized API/9:1 R202H:RG752H 39 mL 5% PVA + 2.3 mL EA, 30%
Microfluidized API/R202S 39 mL 5% PVA + 2.0 mL EA, 30% Microfluidized API/R203S
39 mL 5% PVA + 2.0 mL Microspheres

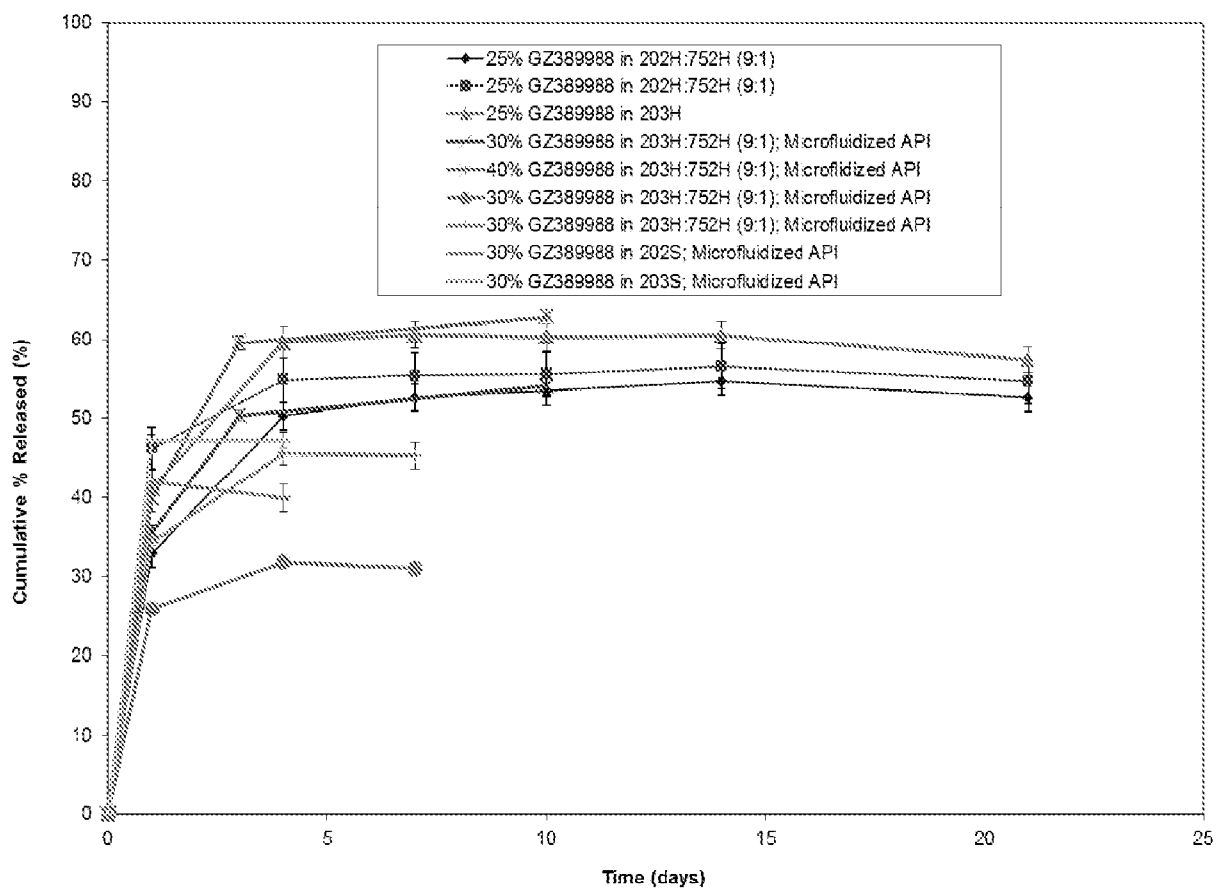


**Figure 18: Scanning Electron Microscopy (SEM) View of
16% API/9:1 R202H:RG752H Microspheres, Solvent Extraction (1000X)**

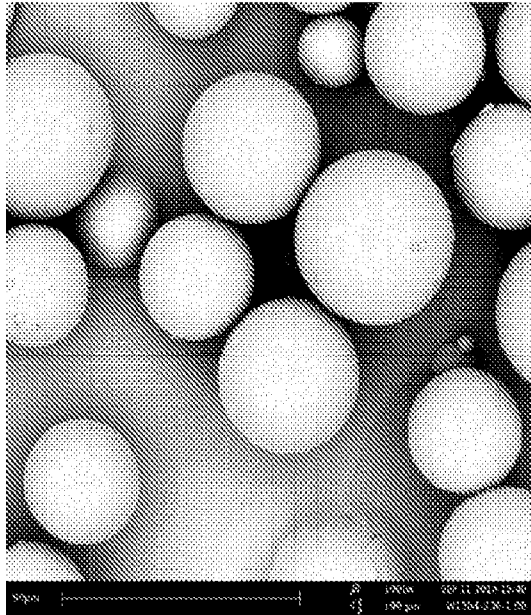


**Figure 19: Scanning Electron Microscopy (SEM) View of
16% API/9:1 R202H:RG752H Microspheres, Spray Drying (1000X)**

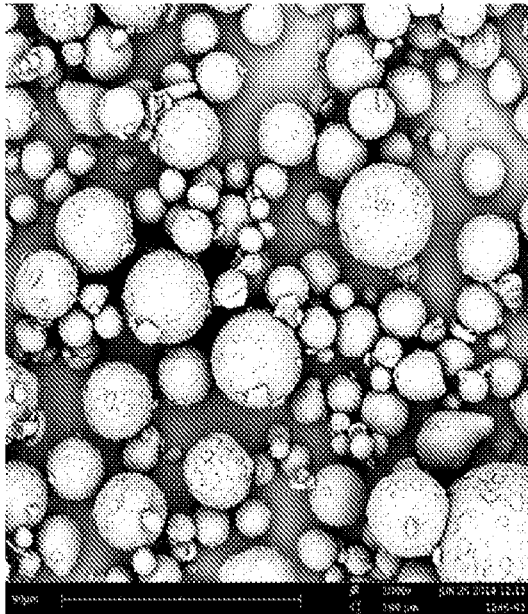


Figure 20: Effect of Microencapsulation Process on IVR Profile – 16% API/9:1 R202H:RG752H Microspheres by Solvent Extraction (OW), 16% API/9:1 R202H:RG752H Microspheres by Spray Drying (20% and 22.5% Polymer) and 16% API/9:1 R203H:RG752H Microspheres by Spray Drying (22.5% Polymer)

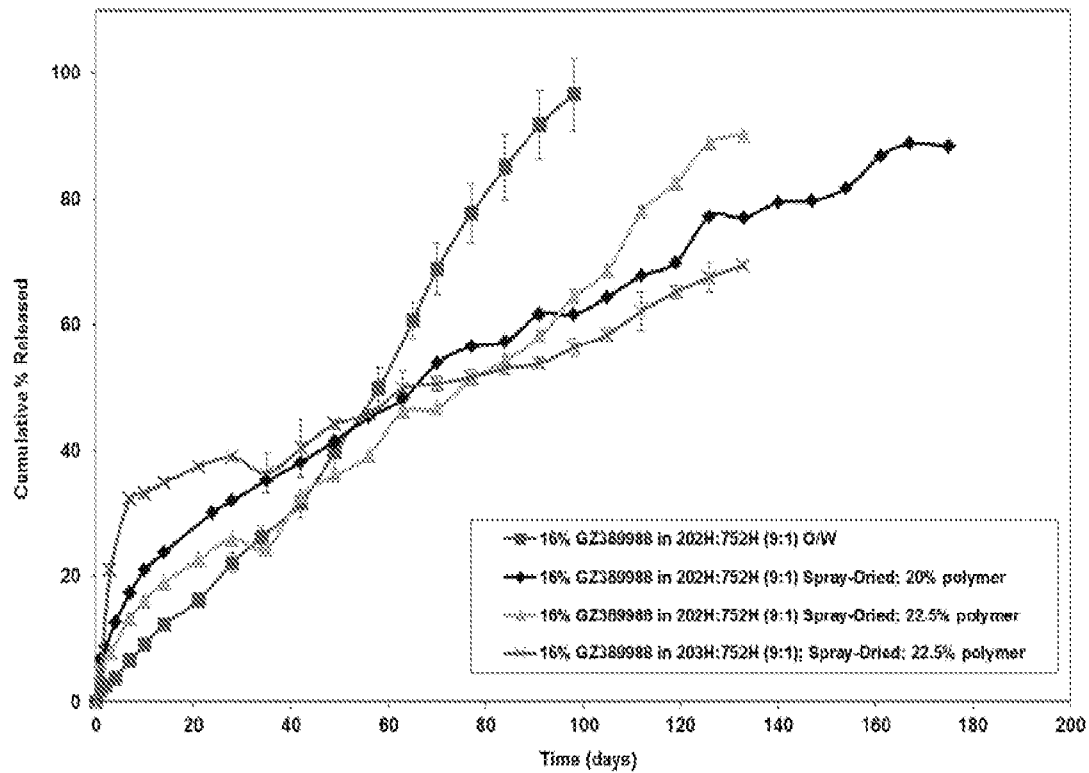


**Figure 21: Scanning Electron Microscopy (SEM) View of
16% API/1:1 R202H:R203H/No Additive Microspheres, Spray Dried (1000X)**

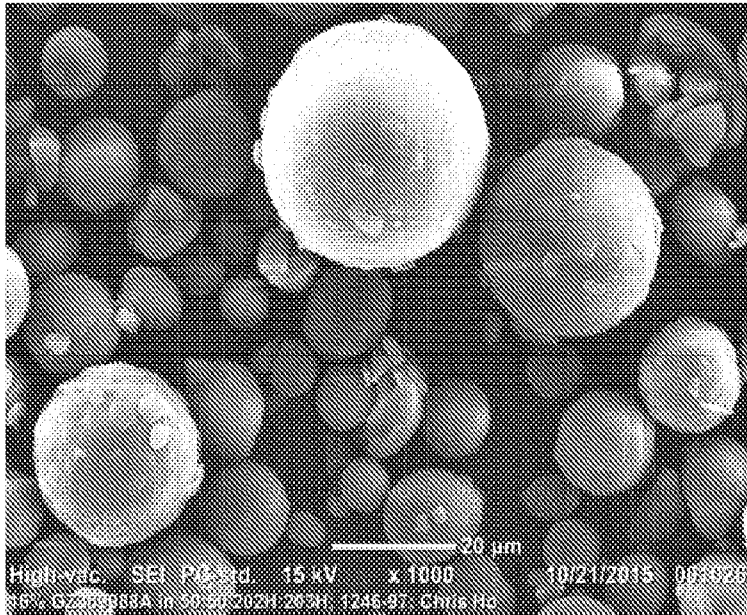


**Figure 22: Scanning Electron Microscopy (SEM) View of
16% API/1:1 R202H:R203H/31.25 mg PEG Microspheres, Spray Dried (1000X)**

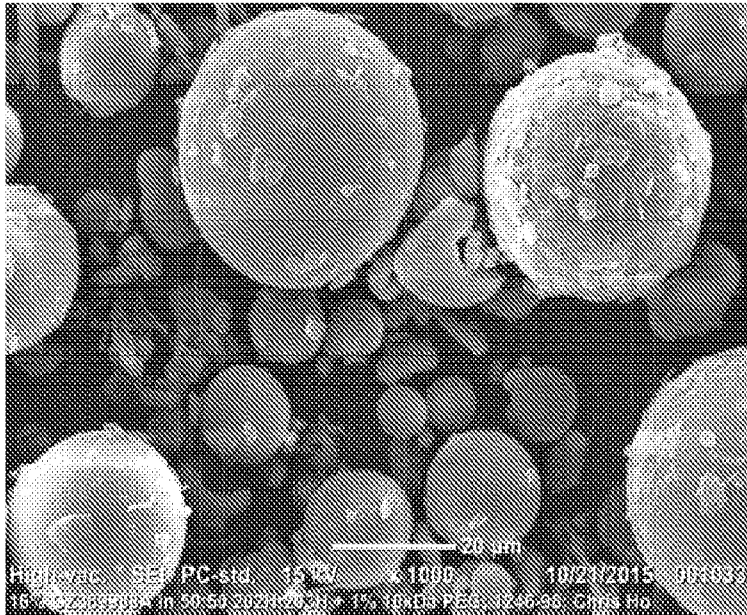


**Figure 23: Scanning Electron Microscopy (SEM) View of
16% API/1:1 R202H:R203H/31.25 mg Poloxamer 407 Microspheres, Spray Dried (1000X)**

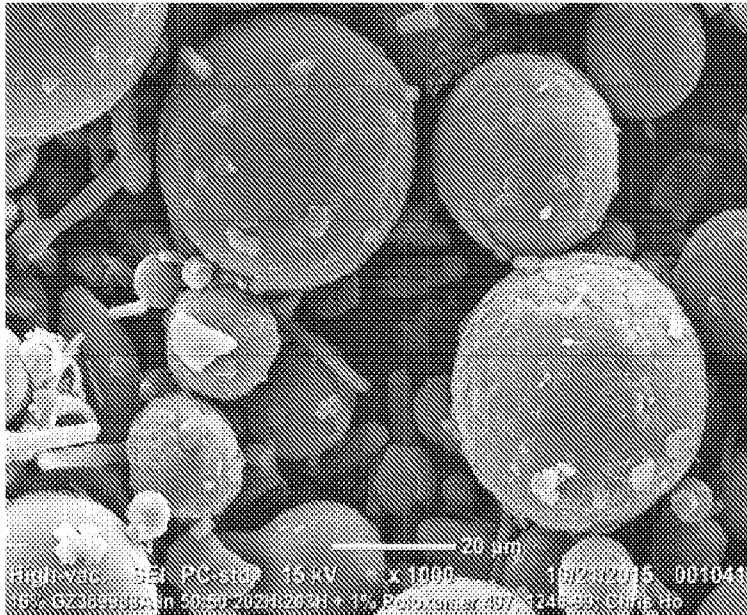


Figure 24: Effect of % 10kDa PEG or 1% Poloxamer 407 on IVR Profile – 16% API/1:1 R202H:R203H/No Additive, 16% API/1:1 R202H:R203H/31.25 mg PEG, 16% API/1:1 R202H:R203H/31.25 mg Poloxamer 407

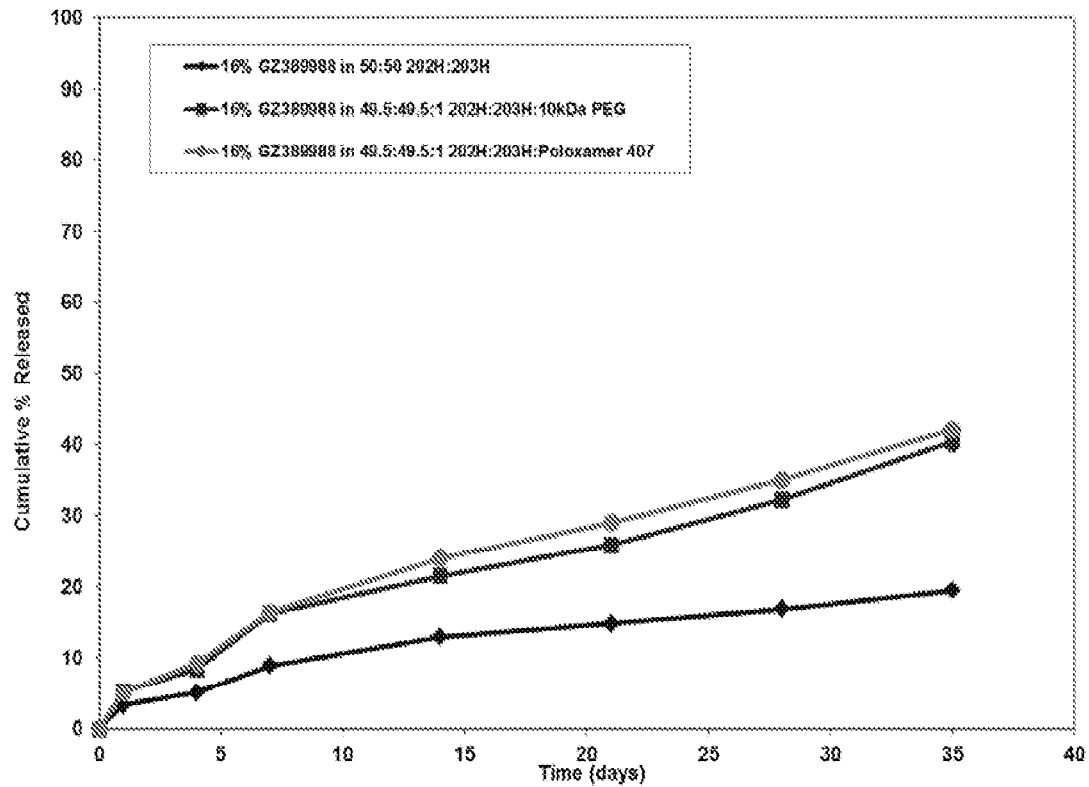


Figure 25: *In vivo* (Rat) IVR Profile – 16% API/9:1 202H:RG502H and 15% API/9:1 R203H:RG752H Microspheres

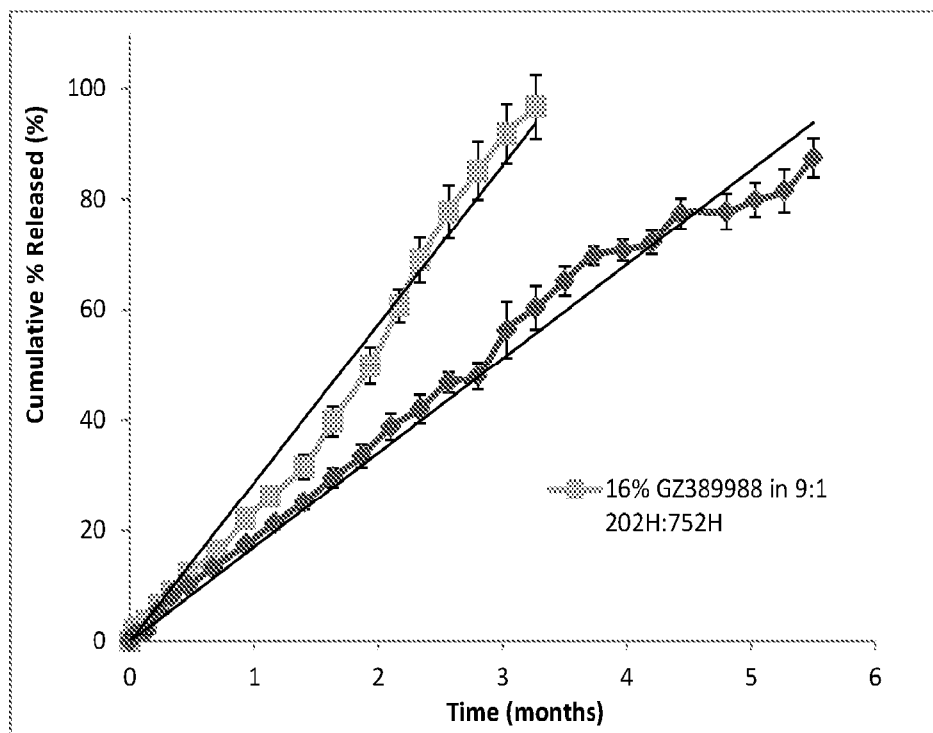


Figure 26: [¹⁴C] 3-(3-methoxy-4-((4-methoxybenzyl)oxy)benzyl)-6-(1-methyl-1H-pyrazol-4-yl)-3H-imidazo[4,5-b]pyridin-2-amine Remaining Over Time (Rat Knee Joint) – 16% API/9:1 202H:RG502H and 15% API/9:1 203H:RG752H Microspheres

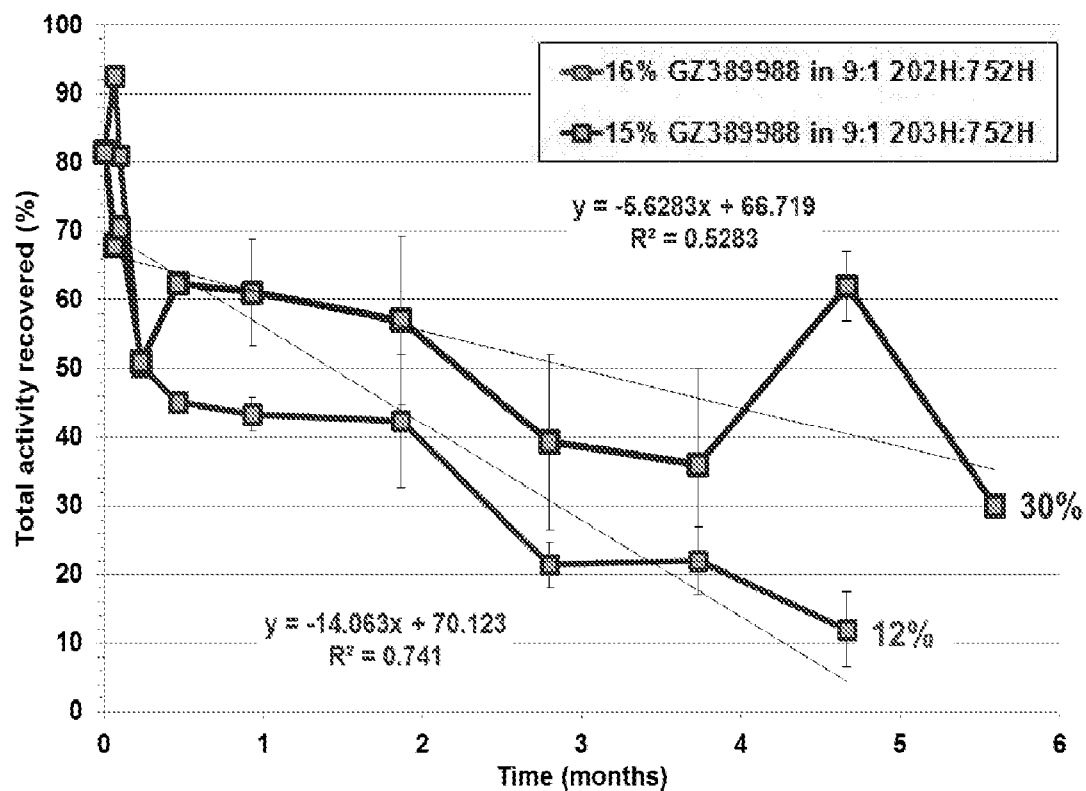
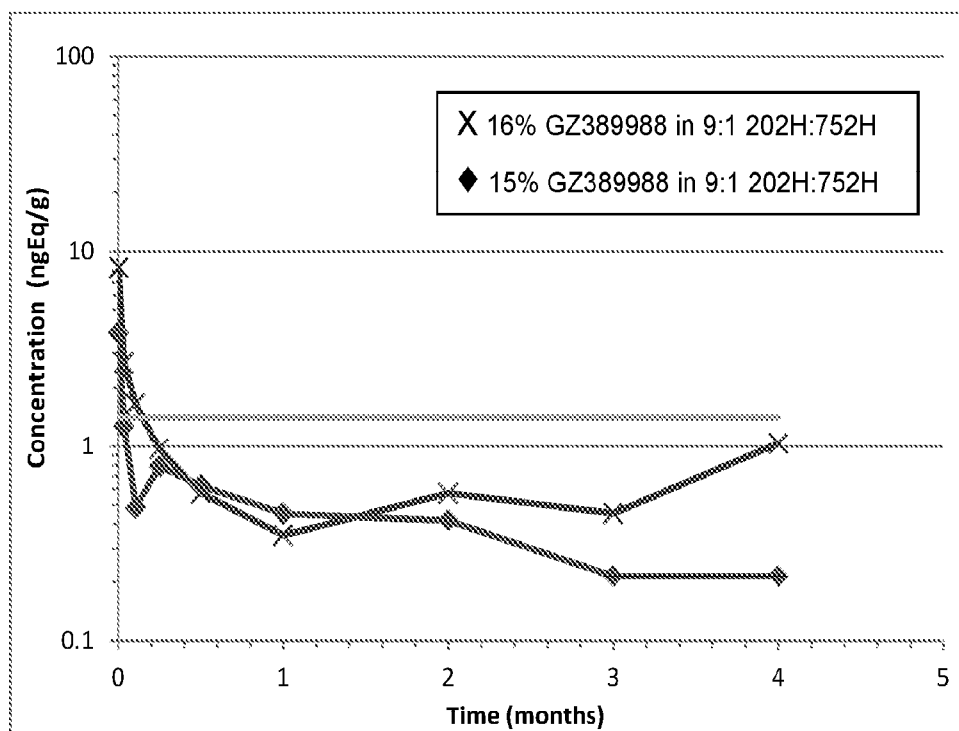


Figure 27: 3-(3-methoxy-4-((4-methoxybenzyl)oxy)benzyl)-6-(1-methyl-1H-pyrazol-4-yl)-3H-imidazo[4,5-b]pyridin-2-amine Concentration-Time Profiles (Rat Blood) – 16% API/9:1 202:H:RG502H and 15% API/9:1 R203H:RG752H Microspheres



— represents the EC₅₀ value (cell based) of 3-(3-methoxy-4-((4-methoxybenzyl)oxy)benzyl)-6-(1-methyl-1H-pyrazol-4-yl)-3H-imidazo[4,5-b]pyridin-2-amine of 1.4 ng/mL

Figure 28: IVR Profile – 16% API/9:1 202:H:RG752H, 15% API/9:1 R203H:RG752H and 40% API/203H Microspheres

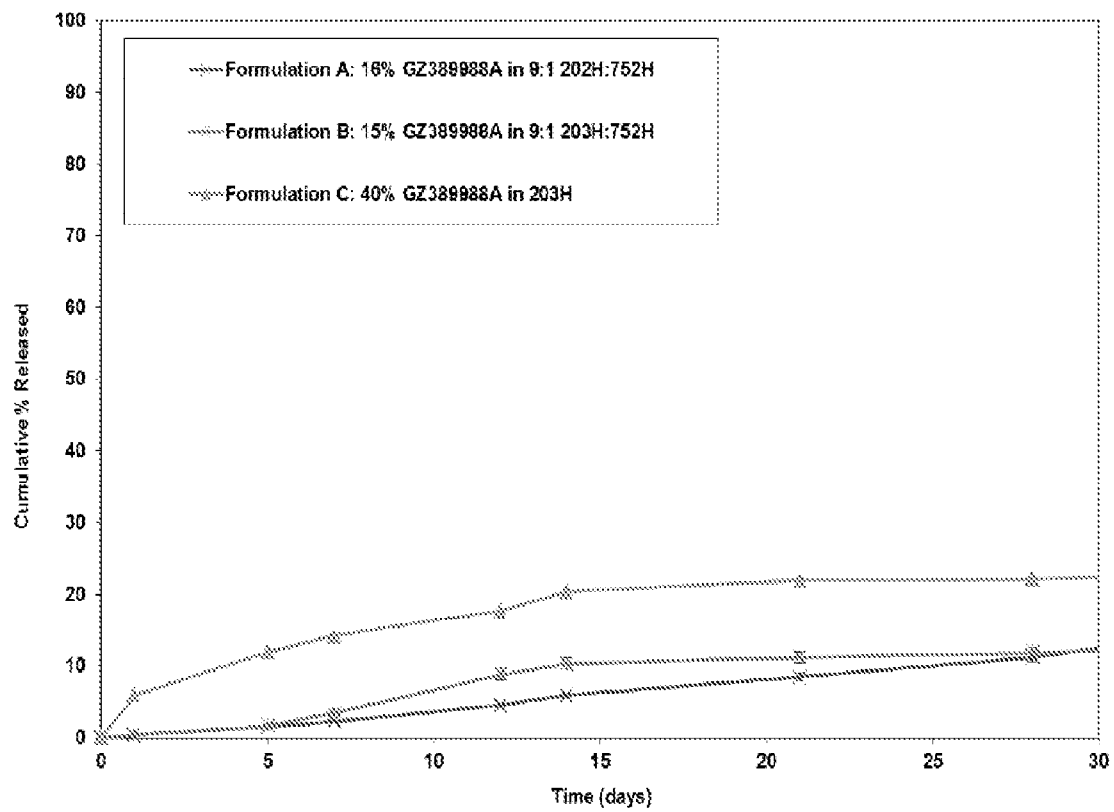


Figure 29: 3-(3-methoxy-4-((4-methoxybenzyl)oxy)benzyl)-6-(1-methyl-1H-pyrazol-4-yl)-3H-imidazo[4,5-b]pyridin-2-amine Concentration-Time Profiles – 16% API/9:1 202:H:RG752H, 15% API/9:1 R203H:RG752H and 40% API/203H Microspheres

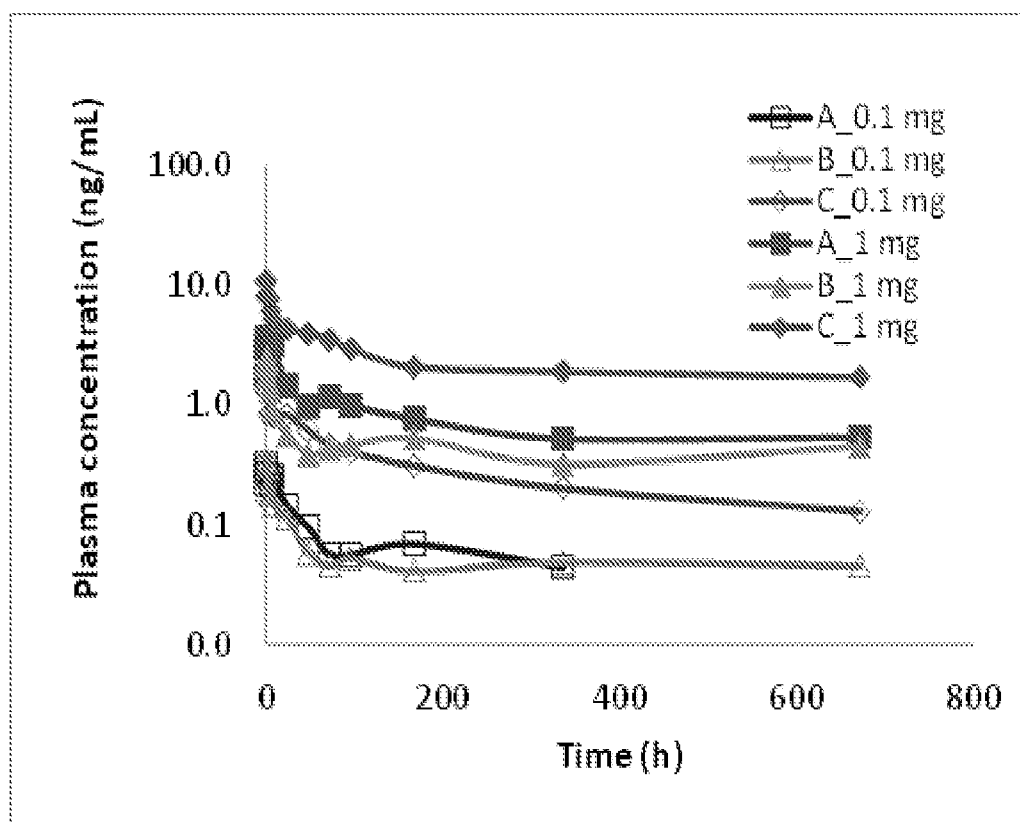


Figure 30: Measured or Simulated XRPD of Forms 1 to 4 (Anhydrous and Hydrate)

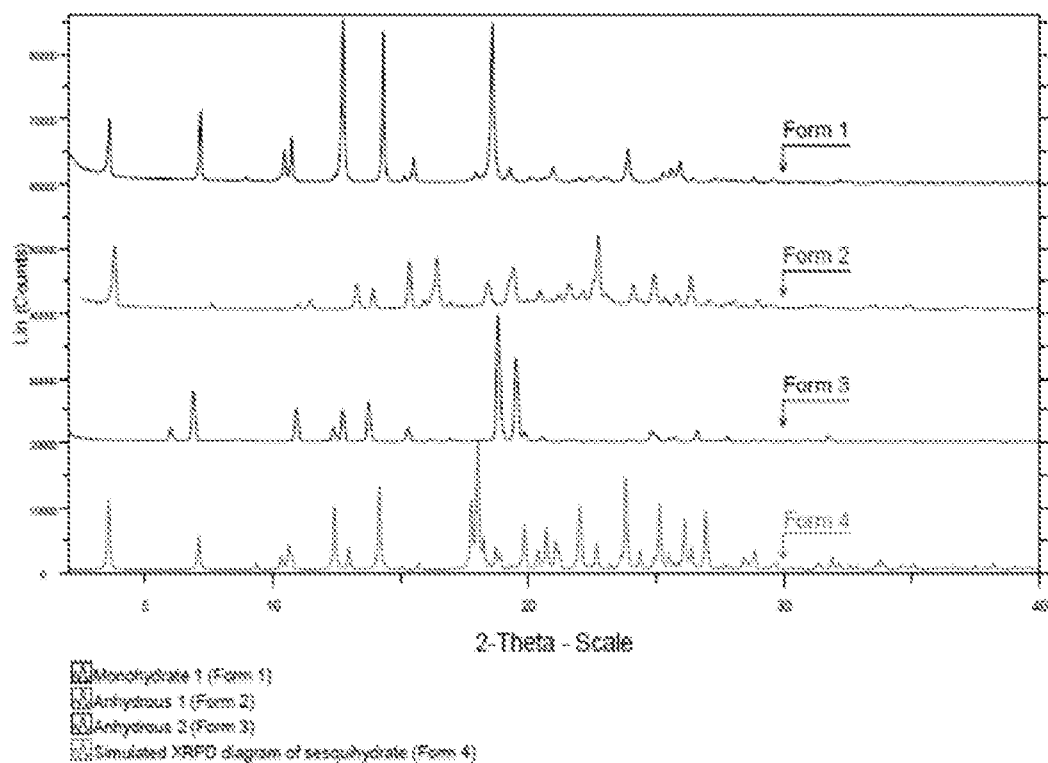


Figure 31: XRPD of Form 5 (Ethanol)

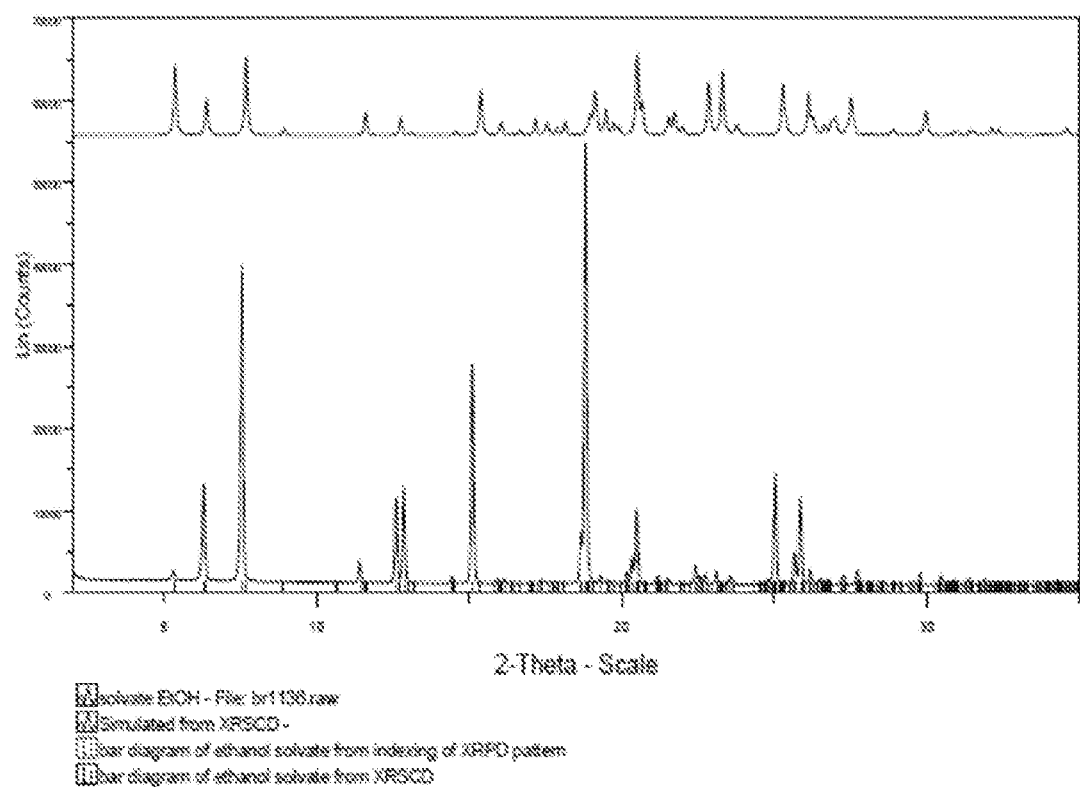


Figure 32: XRPD of Form 9 (Acetone)

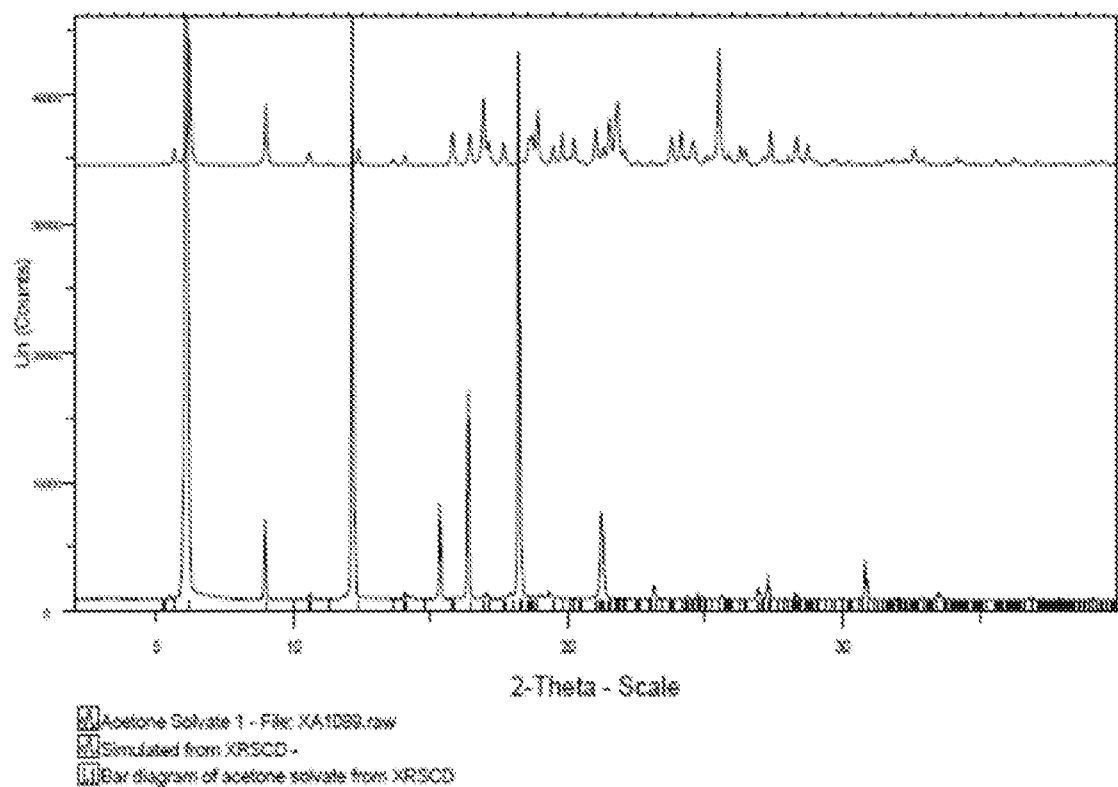


Figure 33: XRPD Comparison of Form 10 (Acetone) and Form 9 (Acetone)

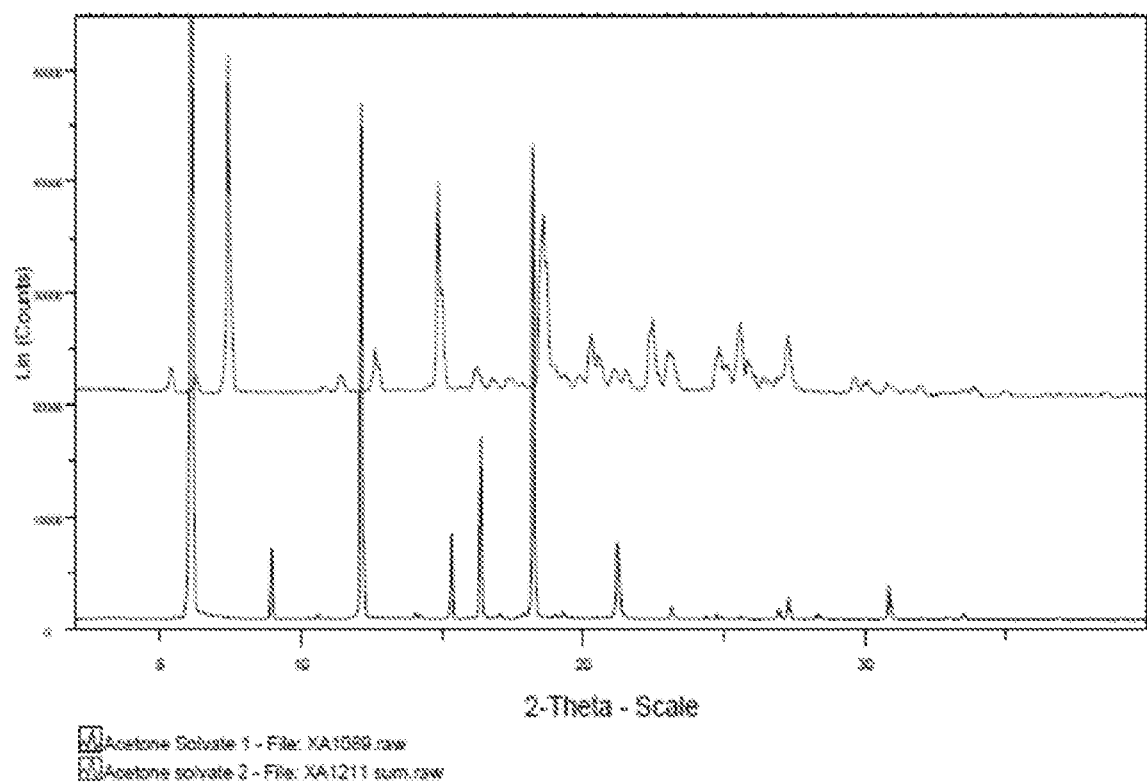


Figure 34: XRPD of Form 11 (Acetonitrile)

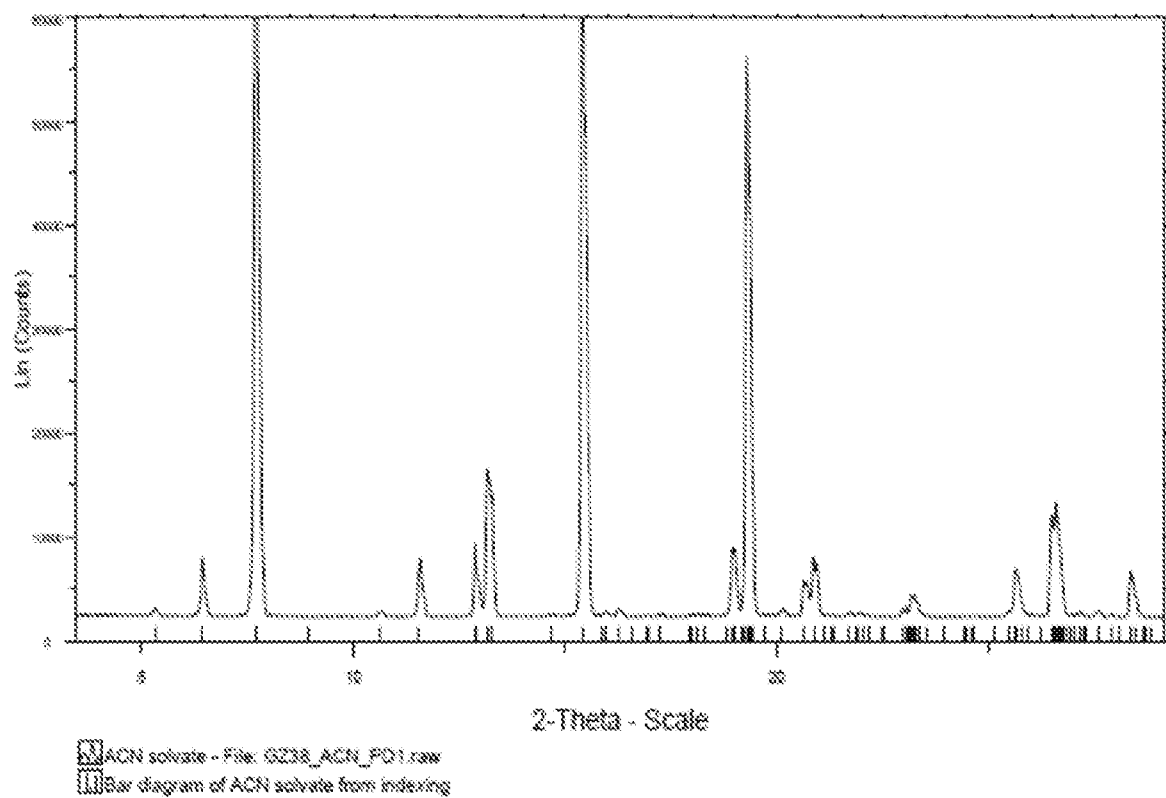


Figure 35: Solid Crystalline Phases of 3-(3-methoxy-4-((4-methoxybenzyl)oxy)benzyl)-6-(1-methyl-1H-pyrazol-4-yl)-3H-imidazo[4,5-b]pyridin-2-amine

