Physical Instability of Uncoated and Coated Tablets Containing Tartaric Acid (TA)

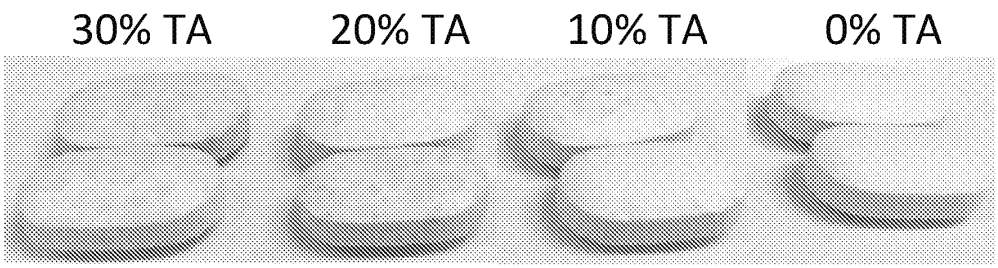


FIG. 1A

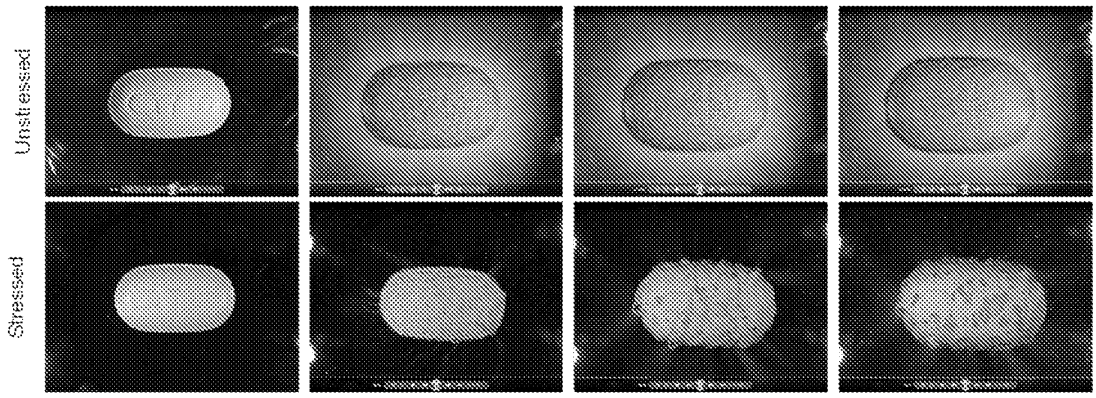
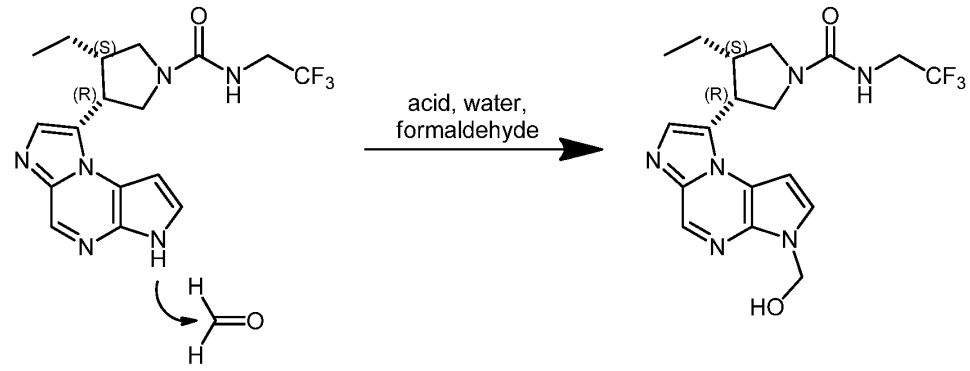


FIG. 1B

Generation of UHM Impurity Degradation Product



Upadacitinib

"Upadacitinib hydroxymethyl impurity" (UHM Impurity)

FIG. 2

Dissolution Profiles of RINVOQ (30 mg Upadacitinib) 500 mg Tablet and Smaller Sized (200 mg) Formulations with Tartaric Acid (T1; 30 mg Upadacitinib) and without Tartaric acid (A1; 15 mg Upadacitinib) at pH 1.1 and 6.8

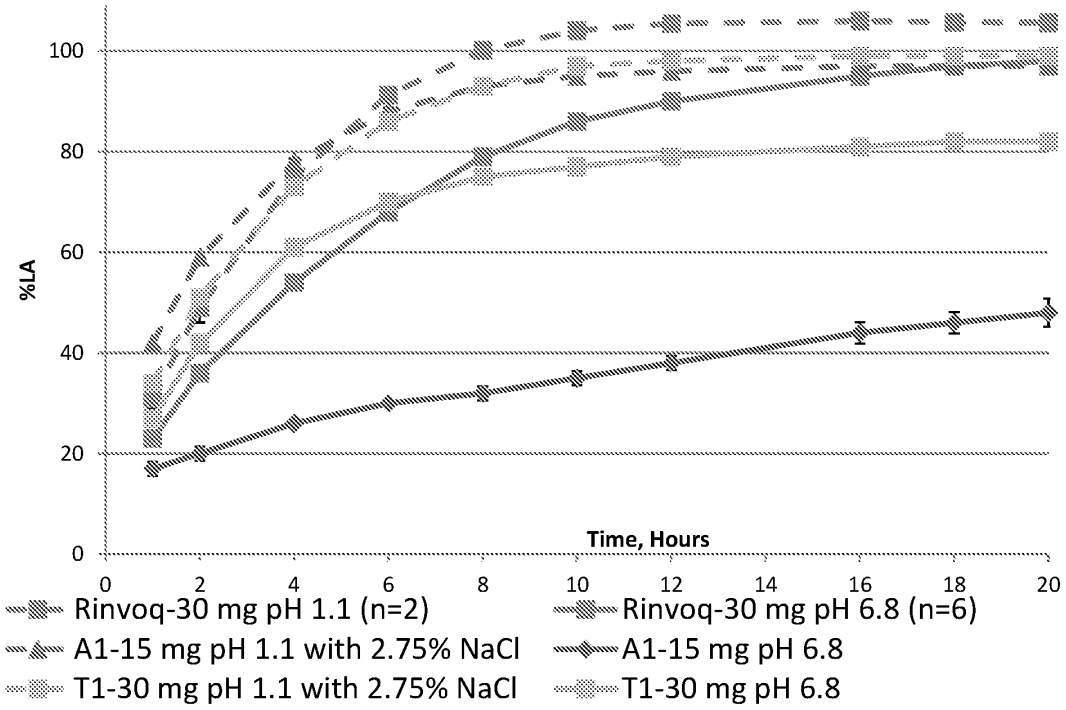


FIG. 3

Dissolution Profiles of RINVOQ (30 mg Upadacitinib) 500 mg Tablet and Formulation AS1 (250 mg tablet; 30 mg Upadacitinib) at pH 1.1 and 6.8

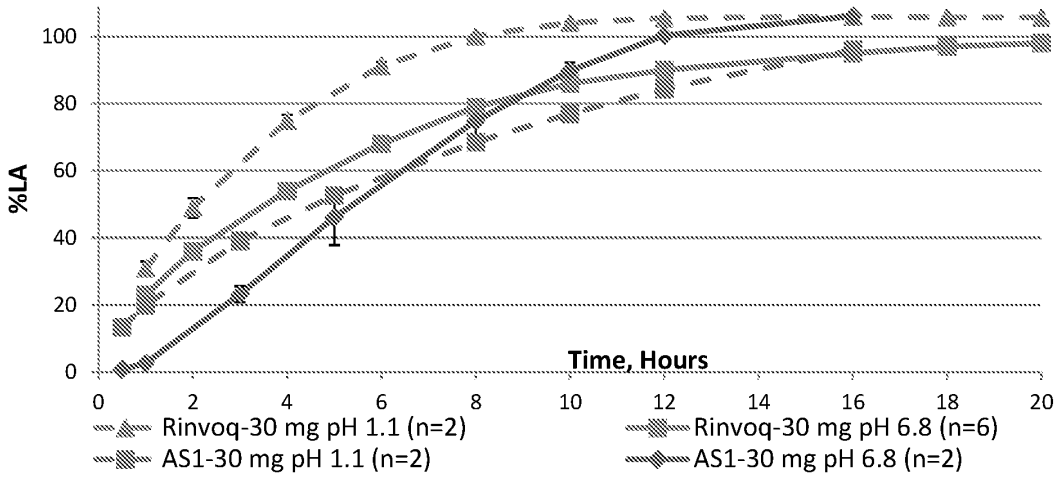


FIG. 4

Dissolution Profiles of RINVOQ (30 mg Upadacitinib) 500 mg Tablet and Formulation AS2 (200 mg tablet; 15 mg Upadacitinib) at pH 1.1 and 6.8

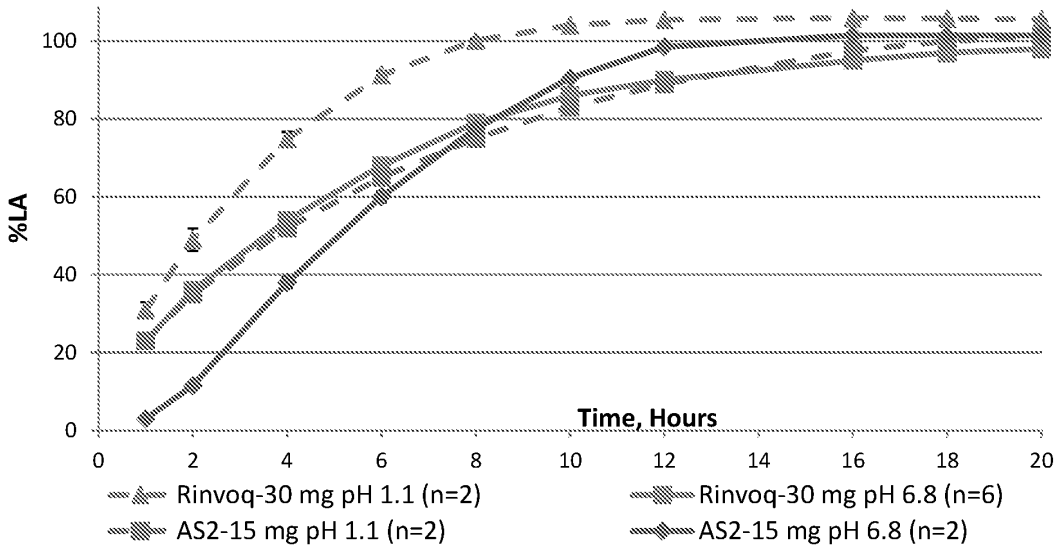


FIG. 5

Dissolution Profiles of RINVOQ (30 mg Upadacitinib) 500 mg Tablet and Formulation AS3 (150 mg tablet; 30 mg Upadacitinib) at pH 1.1 and 6.8

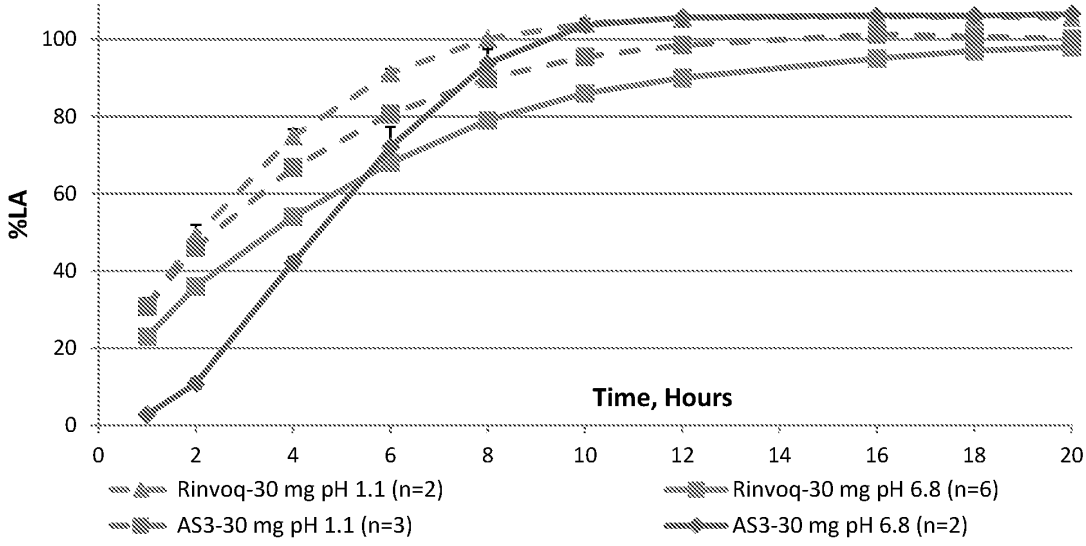


FIG. 6

Dissolution Profiles of RINVOQ (30 mg Upadacitinib) 500 mg Tablet and Formulation AS4 (200 mg tablet; 30 mg Upadacitinib) at pH 1.1 and 6.8

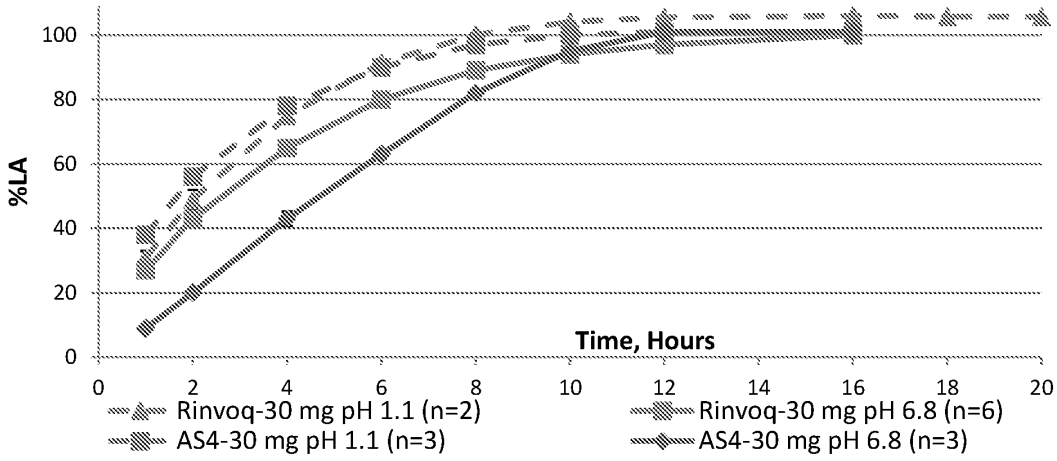


FIG. 7

Dissolution Profiles of RINVOQ (30 mg Upadacitinib) 500 mg Tablet and Formulation AS5 (200 mg tablet; 30 mg Upadacitinib) at pH 1.1 and 6.8

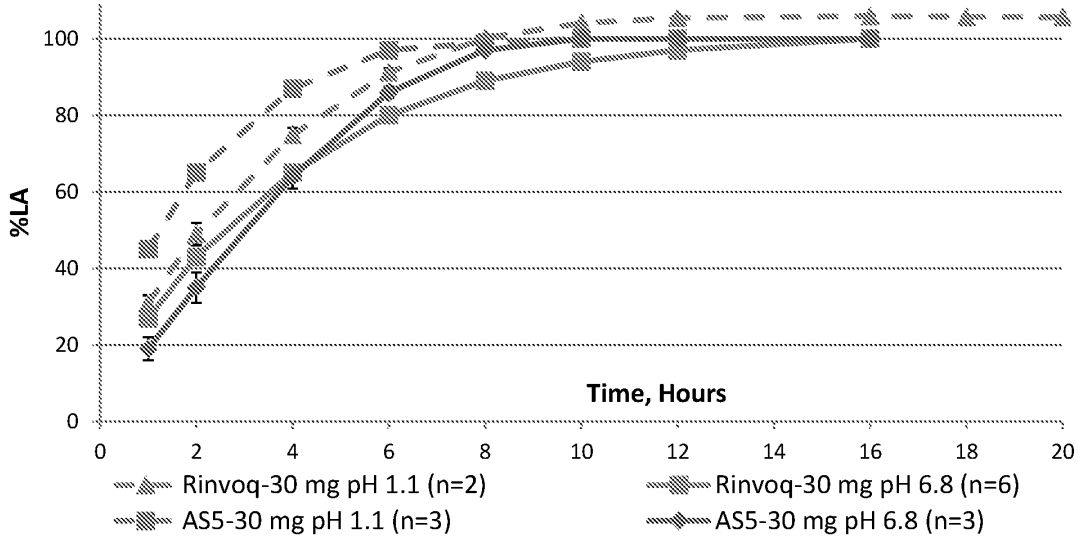


FIG. 8

Dissolution Profiles of RINVOQ (30 mg Upadacitinib) 500 mg Tablet and Formulation AL1 (200 mg tablet; 30 mg Upadacitinib) at pH 1.1 and 6.8

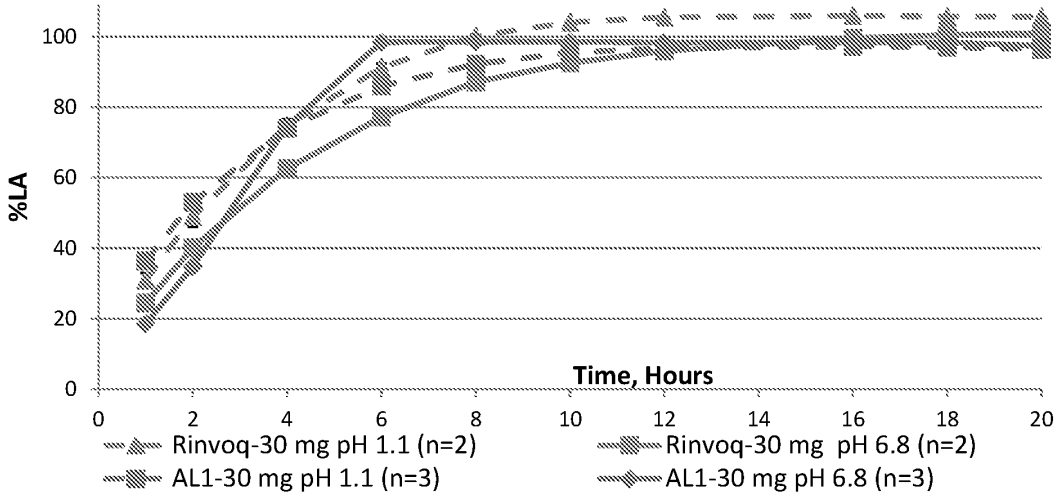


FIG. 9

Dissolution Profiles of RINVOQ (30 mg Upadacitinib) 500 mg Tablet and Formulation AL2 (200 mg tablet; 15 mg Upadacitinib) at pH 1.1 and 6.8

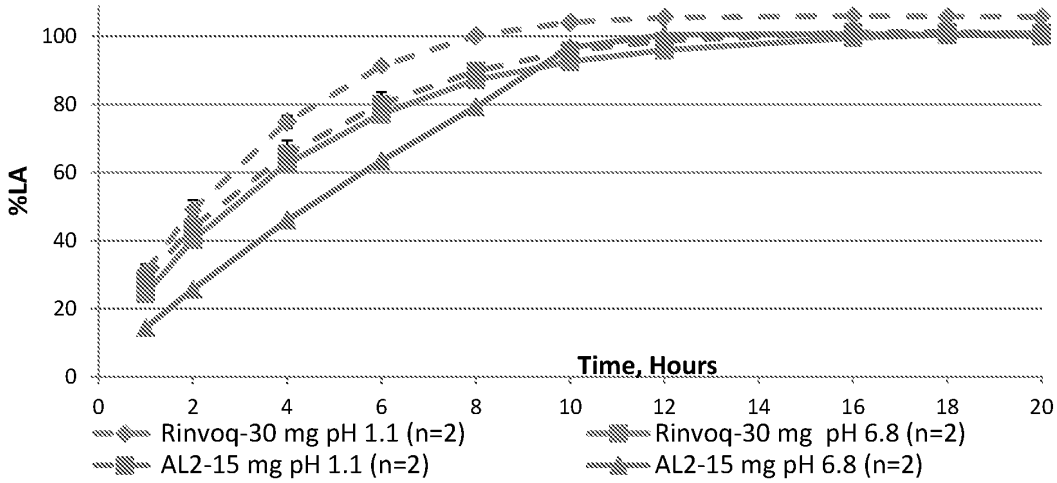


FIG. 10

Dissolution Profiles of RINVOQ (30 mg Upadacitinib) 500 mg Tablet and Formulation AL3 (200 mg tablet; 15 mg Upadacitinib) at pH 1.1 and 6.8

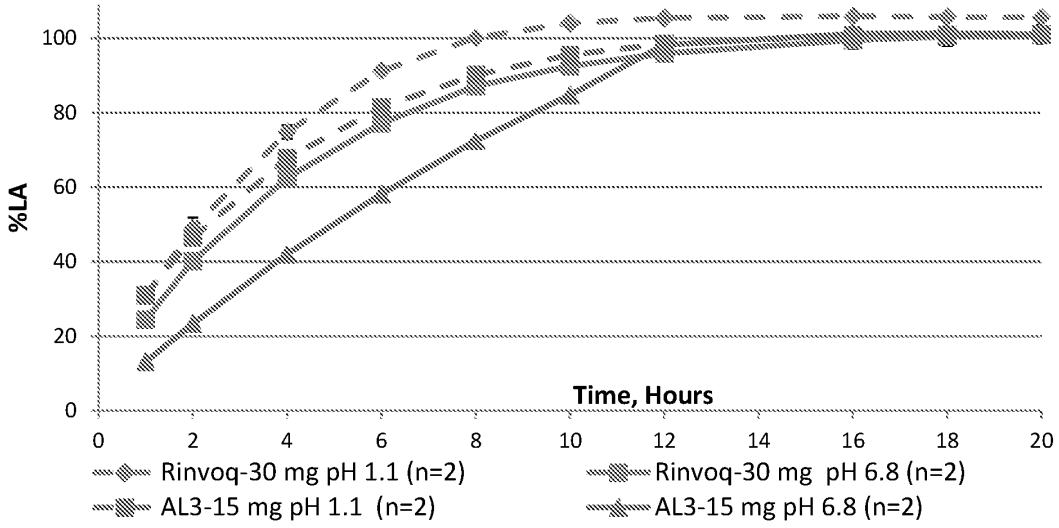


FIG. 11

Dissolution Profiles of RINVOQ (30 mg Upadacitinib) 500 mg Tablet and Formulation T2 (200 mg tablet; 30 mg Upadacitinib with HPMC-AS, HPMC, and TA) at pH 1.1 and 6.8

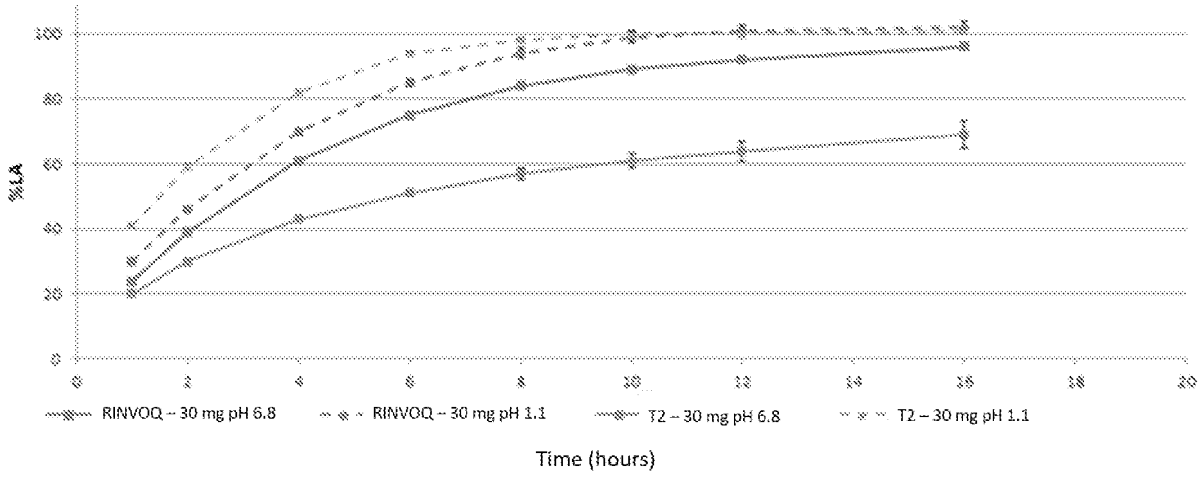


FIG. 12

Dissolution Profiles of RINVOQ (30 mg Upadacitinib) Tablet and Formulation E1 (15 mg Upadacitinib) Tablet in 0.1N HCl and pH 6.8 Buffer

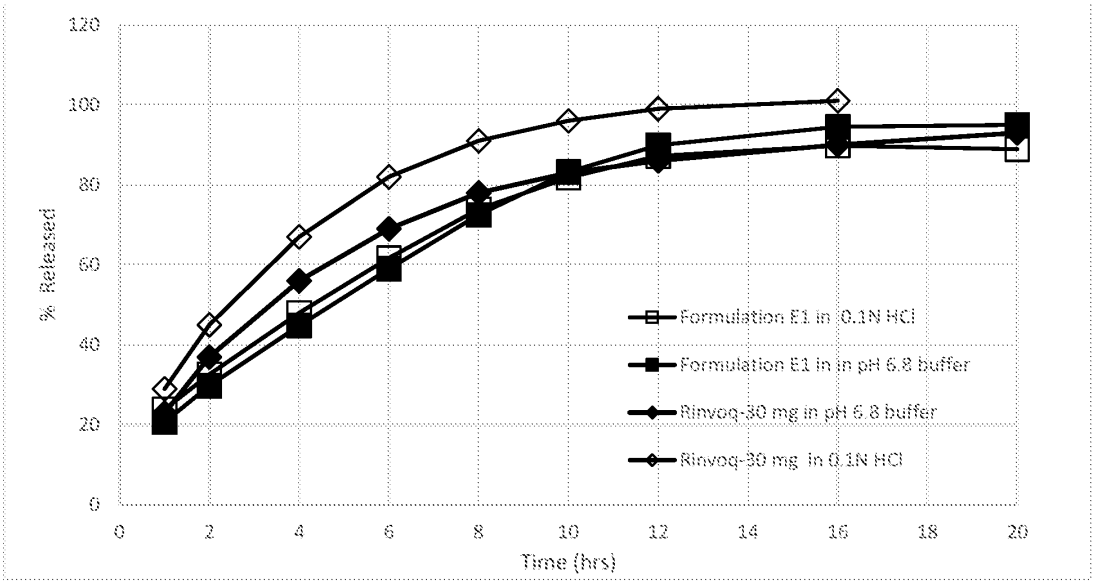


FIG. 13

Dissolution Profiles of Formulation E2, E3, and E4 (30 mg Upadacitinib) Tablets in 0.1N HCl and pH 6.8 Buffer

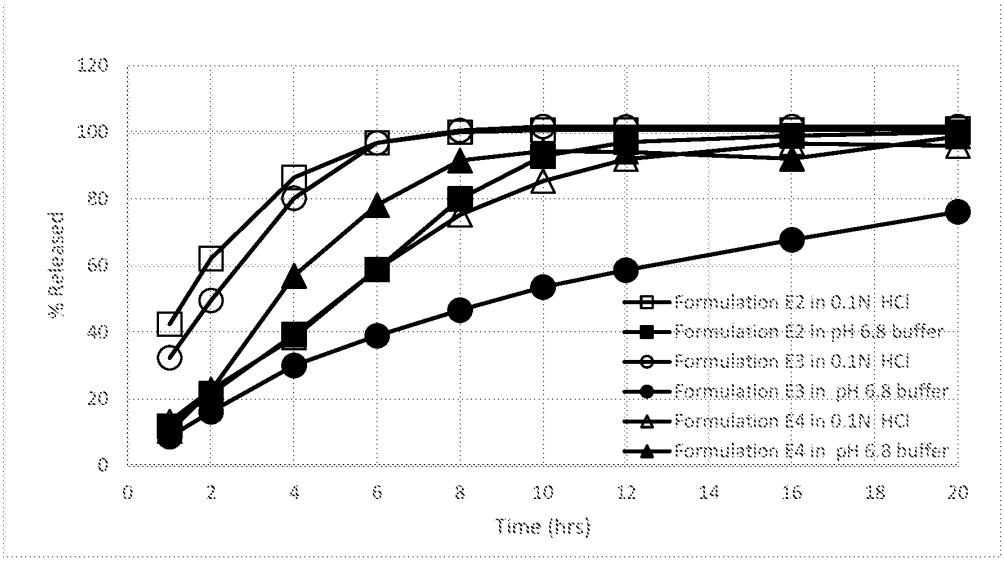


FIG. 14

Dissolution Profiles of Formulation E4 and E5 (30 mg Upadacitinib) Tablets in 0.1N HCl and pH 6.8 Buffer

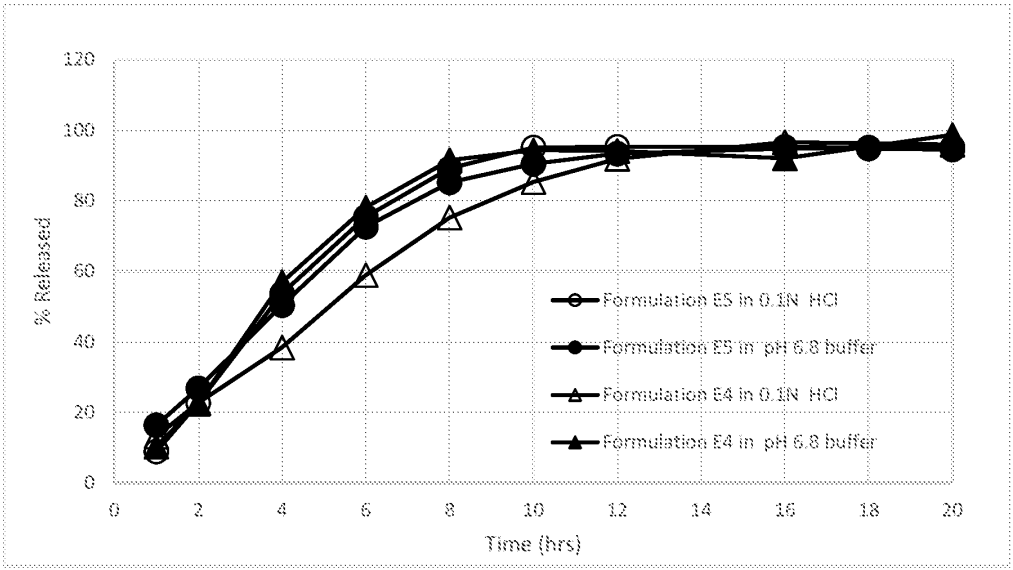


FIG. 15

Dissolution Profiles of Formulation E6 and E7 (30 mg Upadacitinib) Tablets in 0.1N HCl and pH 6.8 Buffer

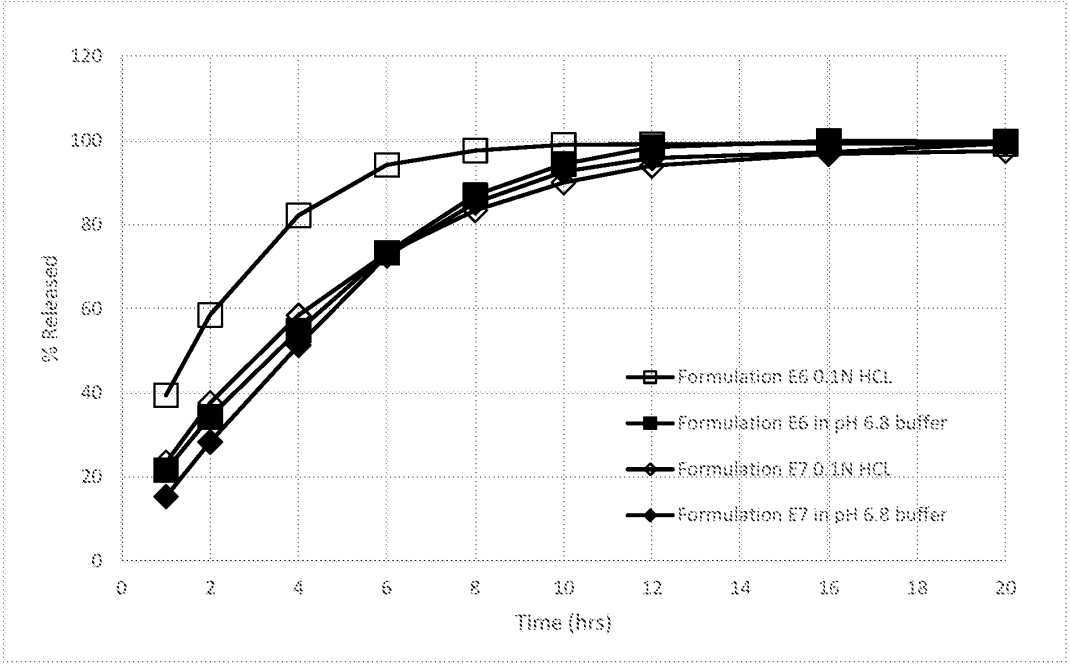


FIG. 16

Dissolution Profiles of Formulation E6 and E8 (30 mg Upadacitinib) Tablets in 0.1N HCl and pH 6.8 Buffer

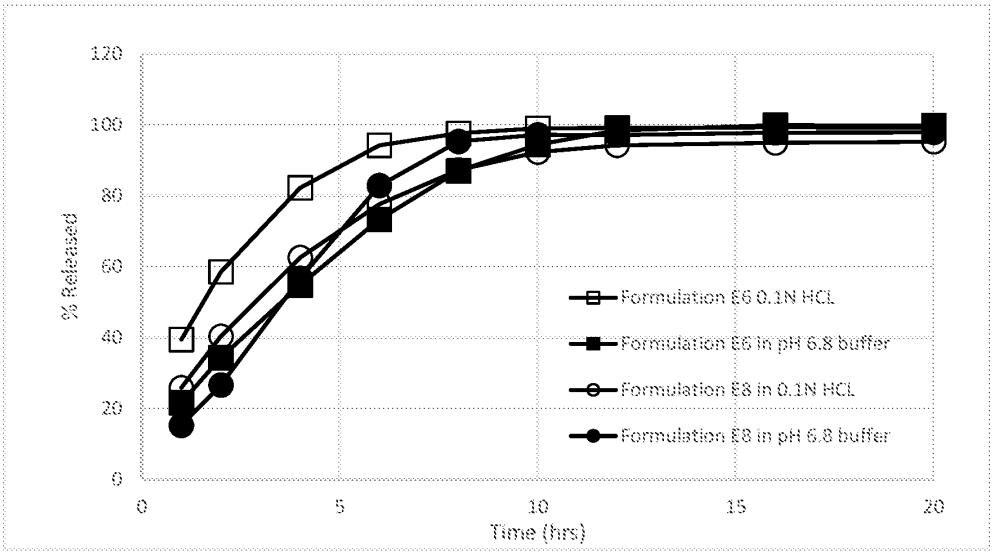


FIG. 17

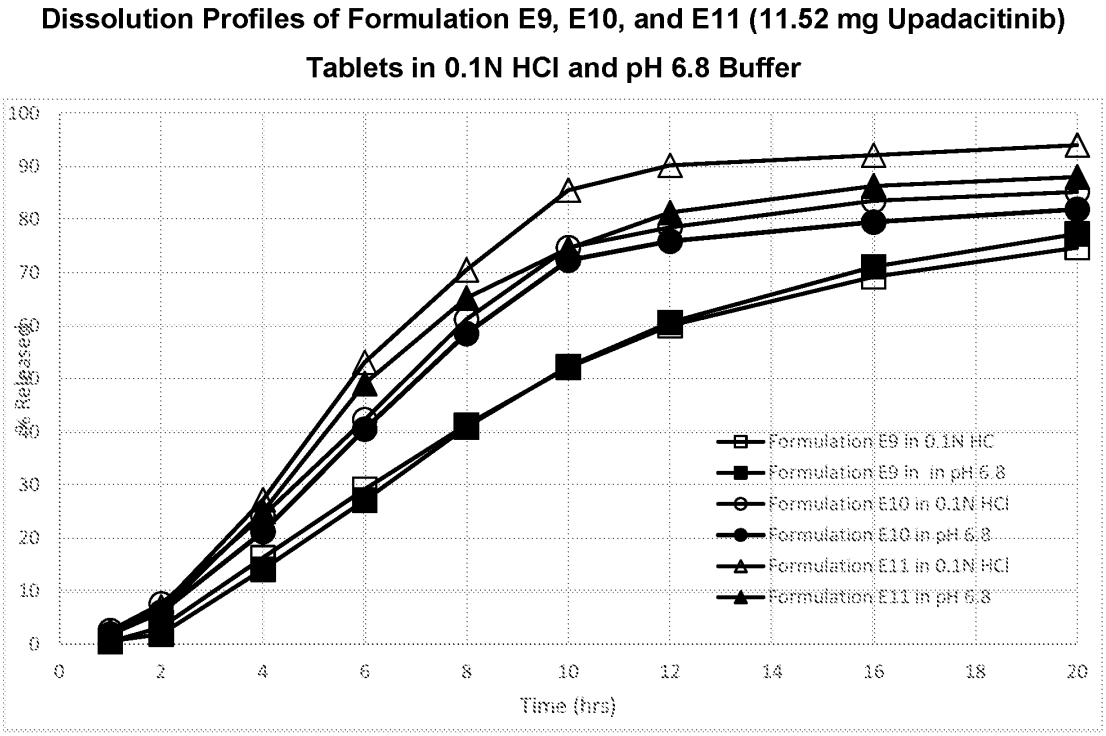

Dissolution Profiles of Formulation E9, E10, and E11 (11.52 mg Upadacitinib) Tablets in 0.1N HCl and pH 6.8 Buffer
% Released
Time (hrs)
Formulation E9 in 0.1N HC
Formulation E9 in in pH 6.8
Formulation E10 in 0.1N HCl
Formulation E10 in pH 6.8
Formulation E11 in 0.1N HCl
Formulation E11 in pH 6.8

FIG. 18

Dissolution Profiles of Formulation E10 and E12 (11.52 mg Upadacitinib) Tablets in 0.1N HCl and pH 6.8 Buffer

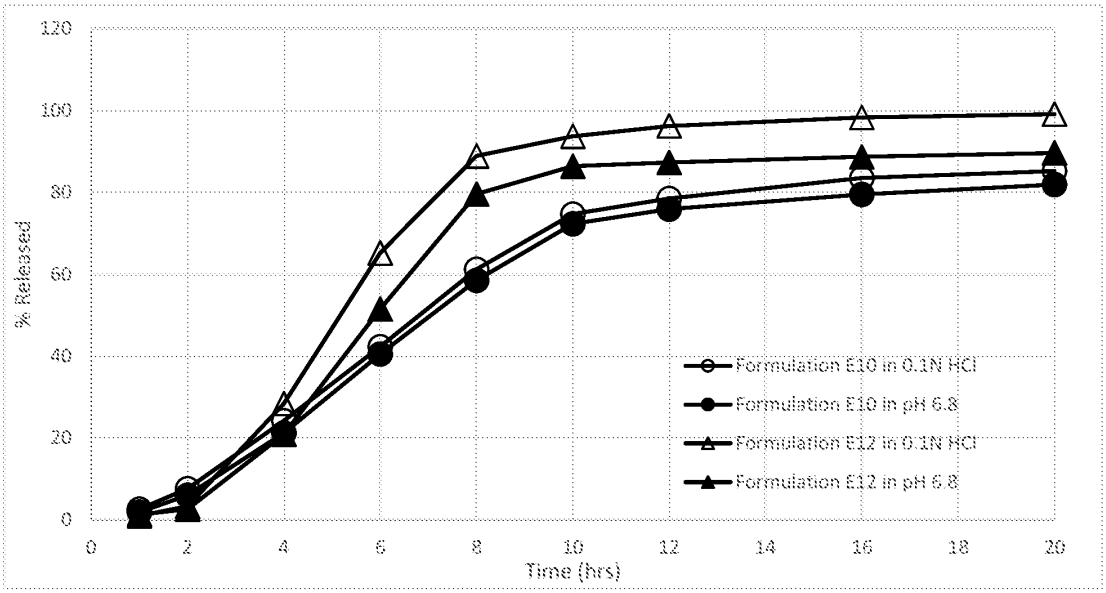


FIG. 19