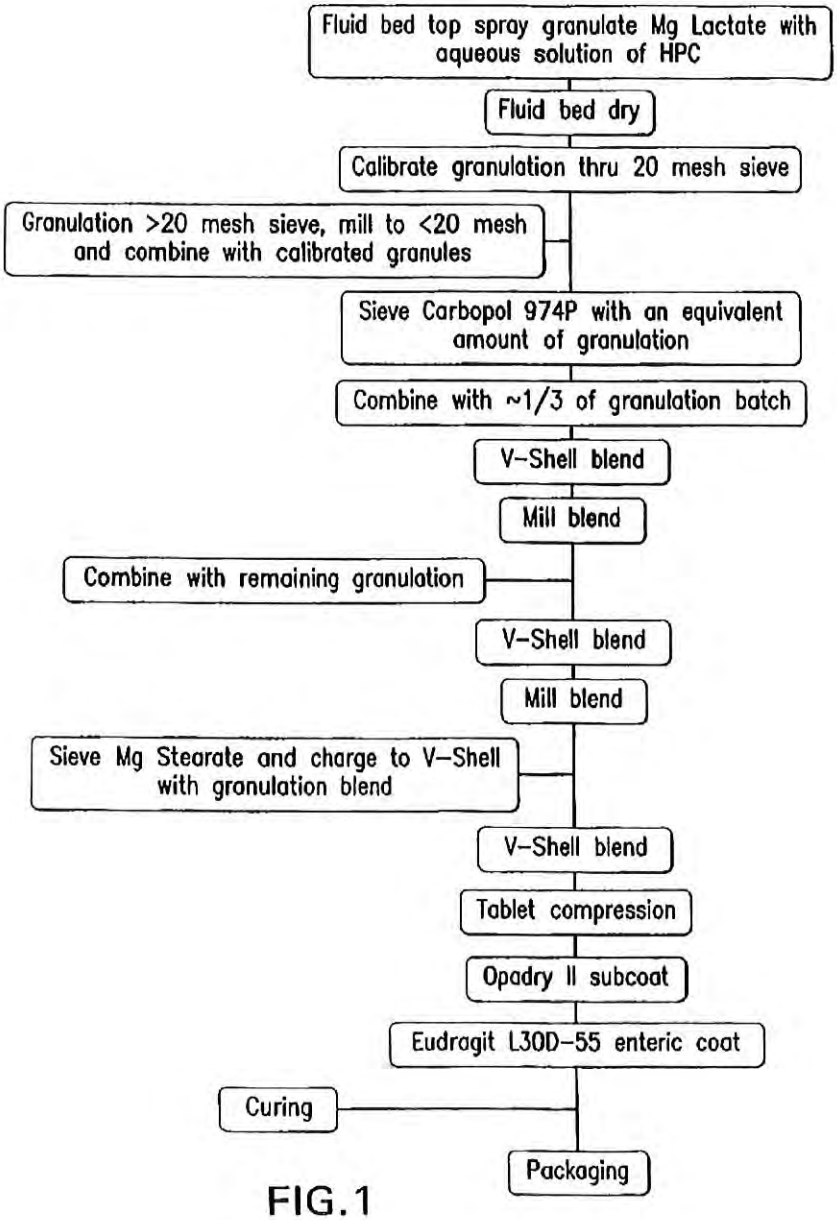

Fluid bed top spray granulate Mg Lactate with aqueous solution of HPC
Fluid bed dry
Calibrate granulation thru 20 mesh sieve
Granulation >20 mesh sieve, mill to <20 mesh and combine with calibrated granules
Sieve Carbopol 974P with an equivalent amount of granulation
Combine with ~1/3 of granulation batch
V-Shell blend
Mill blend
Combine with remaining granulation
V-Shell blend
Mill blend
Sieve Mg Stearate and charge to V-Shell with granulation blend
V-Shell blend
Tablet compression
Opadry II subcoat
Eudragit L30D-55 enteric coat
Curing
Packaging

FIG.1

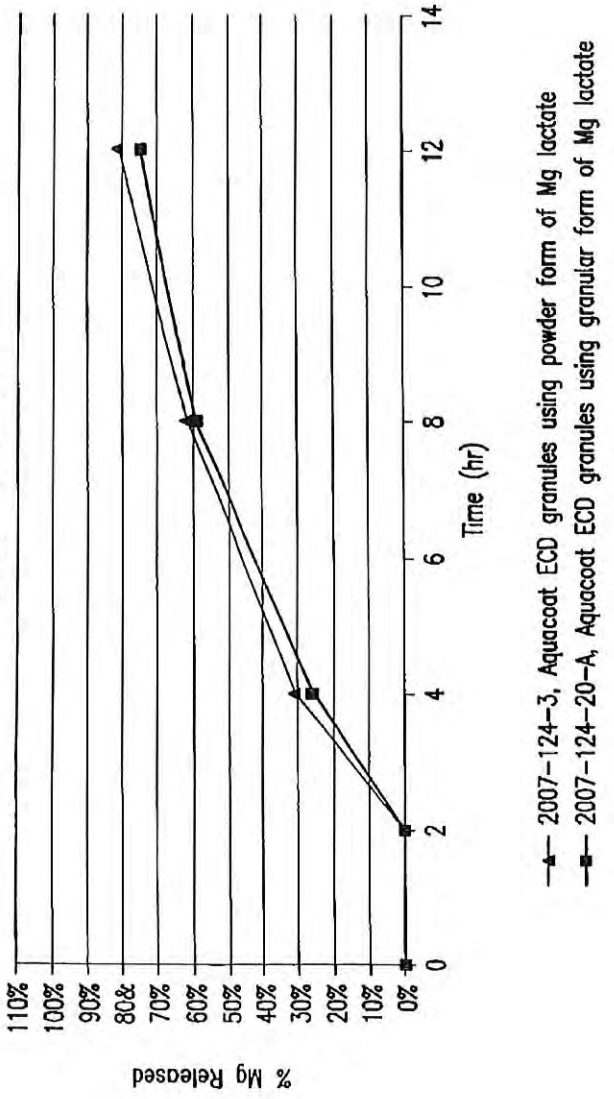

Lots 2007-124-3 & 20-A
% Mg Released
110%
100%
90%
80&
70%
60%
50%
40%
30%
20%
10%
0%
0
2
4
6
8
10
12
14
Time (hr)
2007-124-3, Aquacoat ECD granules using powder form of Mg lactate
2007-124-20-A, Aquacoat ECD granules using granular form of Mg lactate

FIG.2

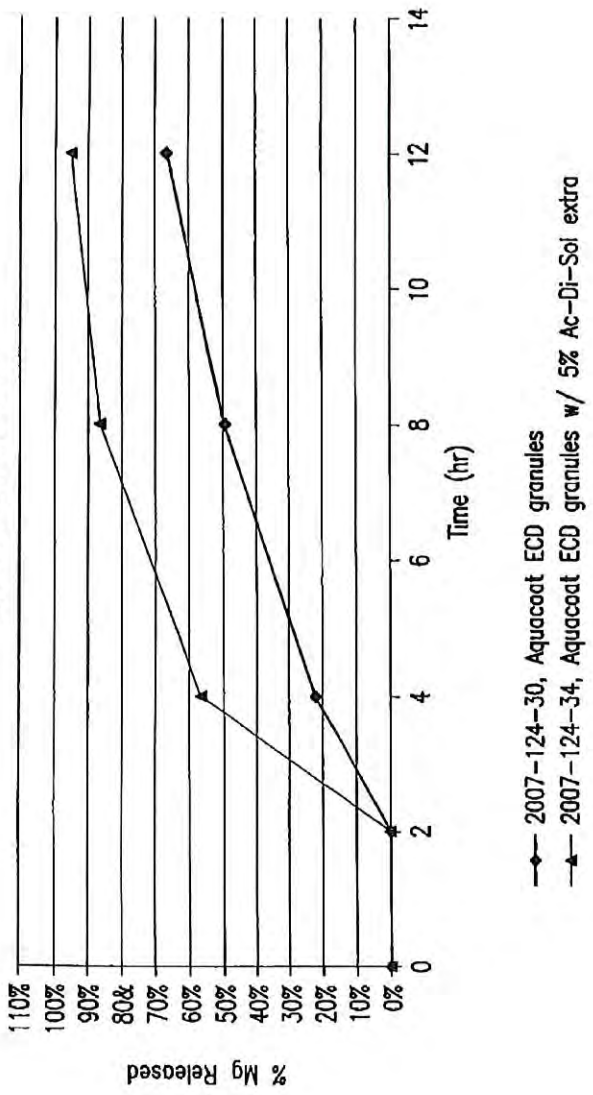

Lots 2007-124-30 & 34
% Mg Released
110%
100%
90%
80&
70%
60%
50%
40%
30%
20%
10%
0%
0
2
4
6
8
10
12
14
Time (hr)
2007-124-30, Aquacoat ECD granules
2007-124-34, Aquacoat ECD granules w/ 5% Ac-Di-Sol extra

FIG.3

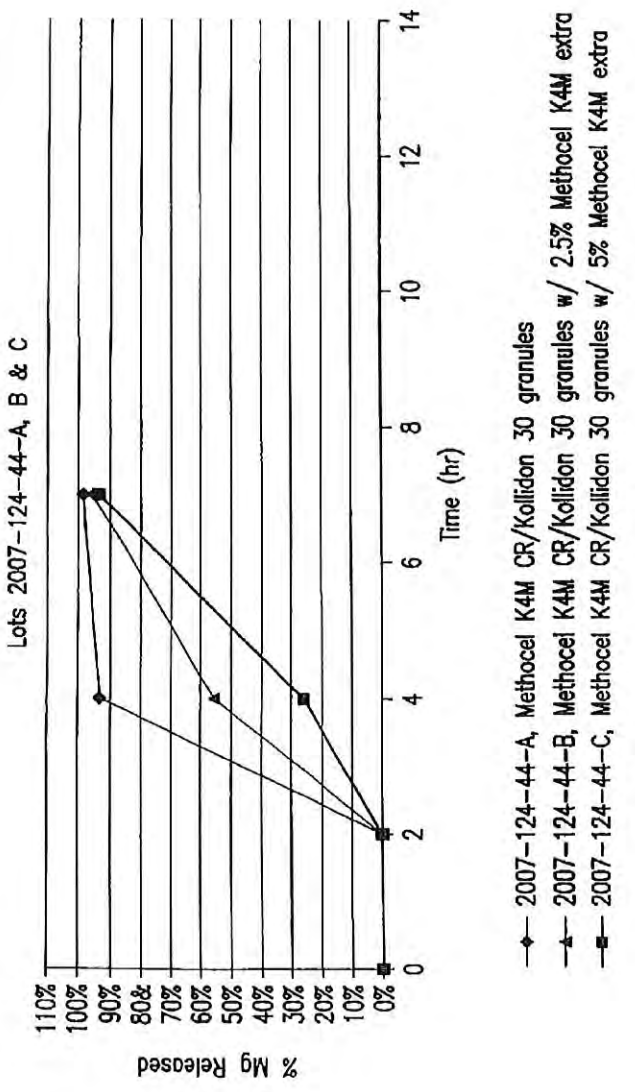

Lots 2007-124-44-A, B & C
% Mg Released
110%
100%
90%
80&
70%
60%
50%
40%
30%
20%
10%
0%
0
2
4
6
8
10
12
14
Time (hr)
2007-124-44-A, Methocel K4M CR/Kollidon 30 granules
2007-124-44-B, Methocel K4M CR/Kollidon 30 granules w/ 2.5% Methocel K4M extra
2007-124-44-C, Methocel K4M CR/Kollidon 30 granules w/ 5% Methocel K4M extra

FIG. 4

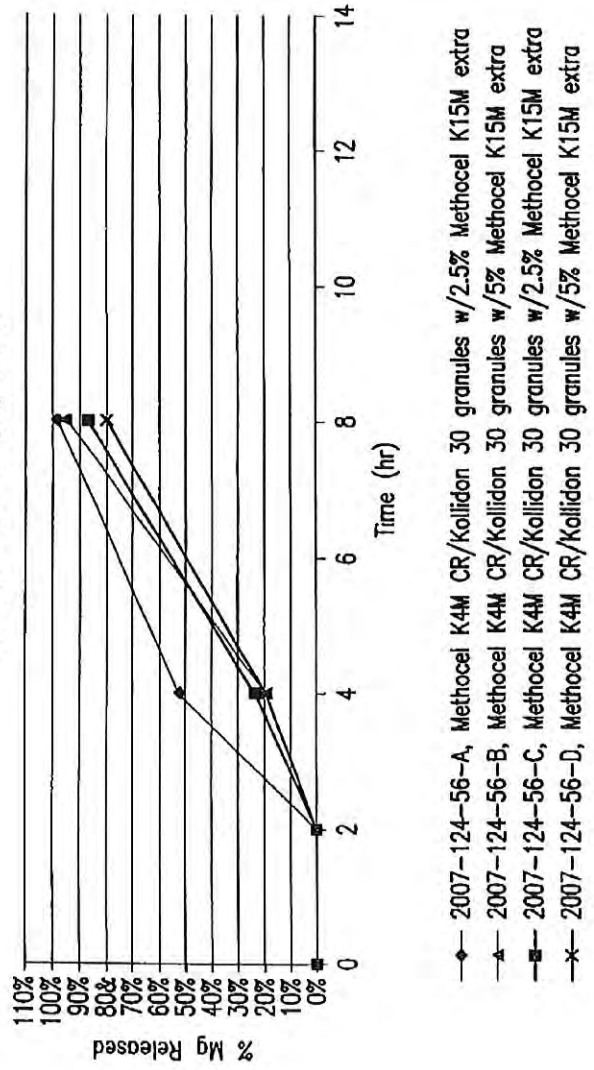

Lots 2007-124-56-A, B, C & D
% Mg Released
110%
100%
90%
80%
70%
60%
50%
40%
30%
20%
10%
0%
0
2
4
6
8
10
12
14
Time (hr)
2007-124-56-A, Methocel K4M CR/Kollidon 30 granules w/2.5% Methocel K15M extra
2007-124-56-B, Methocel K4M CR/Kollidon 30 granules w/5% Methocel K15M extra
2007-124-56-C, Methocel K4M CR/Kollidon 30 granules w/2.5% Methocel K15M extra
2007-124-56-D, Methocel K4M CR/Kollidon 30 granules w/5% Methocel K15M extra

FIG.5

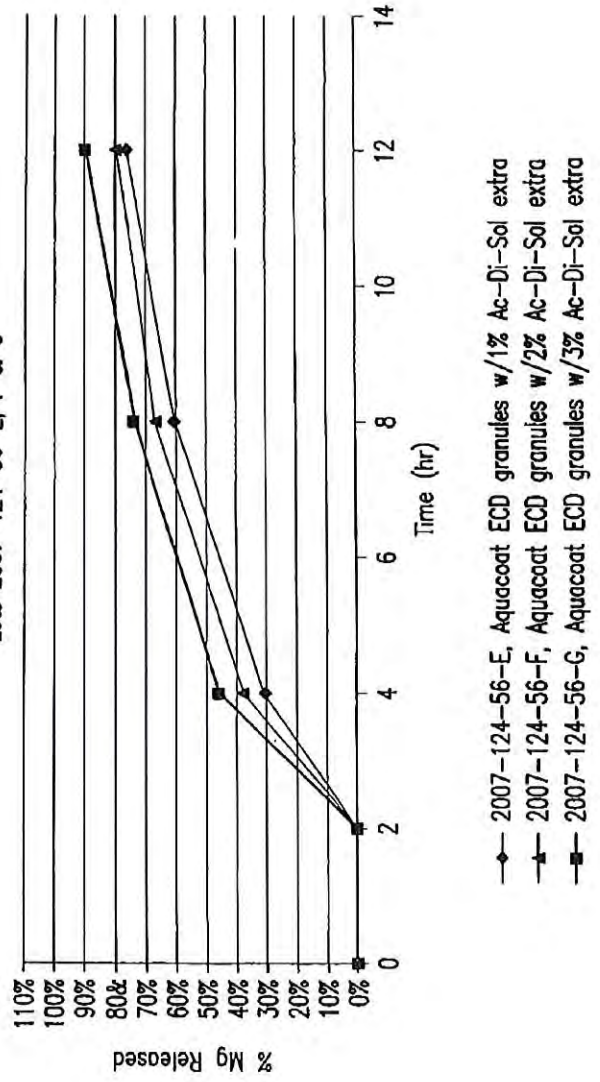

Lots 2007-124-56-E, F & G
% Mg Released
110%
100%
90%
80&
70%
60%
50%
40%
30%
20%
10%
0%
0
2
4
6
8
10
12
14
Time (hr)
2007-124-56-E, Aquacoat ECD granules w/1% Ac-Di-Sol extra
2007-124-56-F, Aquacoat ECD granules w/2% Ac-Di-Sol extra
2007-124-56-G, Aquacoat ECD granules w/3% Ac-Di-Sol extra

FIG.6

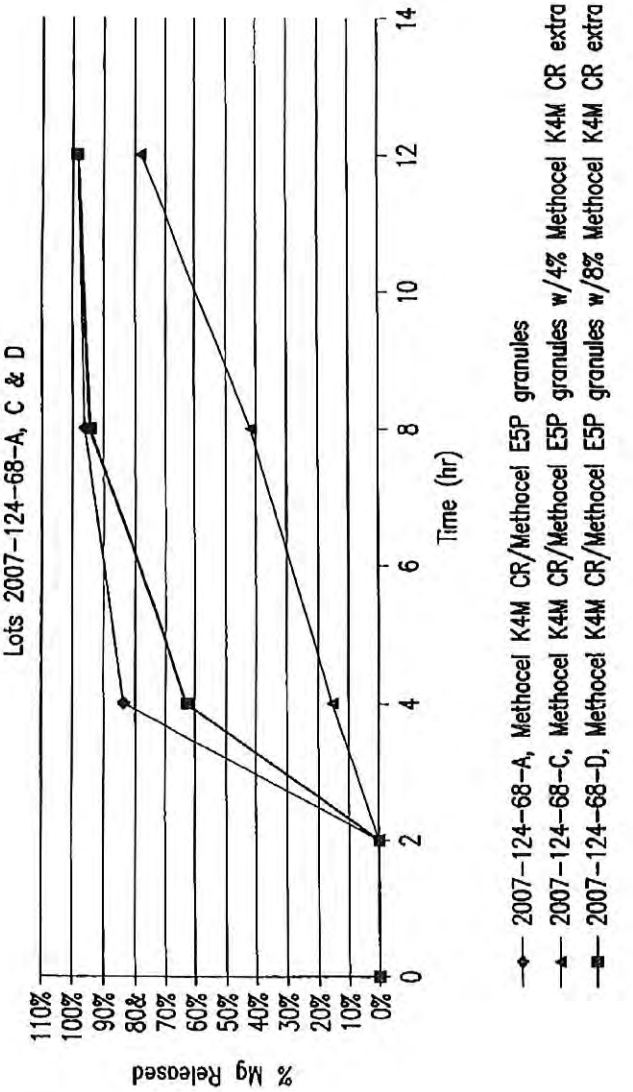

Lots 2007-124-68-A, C & D
% Mg Released
110%
100%
90%
80%
70%
60%
50%
40%
30%
20%
10%
0%
0
2
4
6
8
10
12
14
Time (hr)
2007-124-68-A, Methocel K4M CR/Methocel E5P granules
2007-124-68-C, Methocel K4M CR/Methocel E5P granules w/4% Methocel K4M CR extra
2007-124-68-D, Methocel K4M CR/Methocel E5P granules w/8% Methocel K4M CR extra

FIG. 7

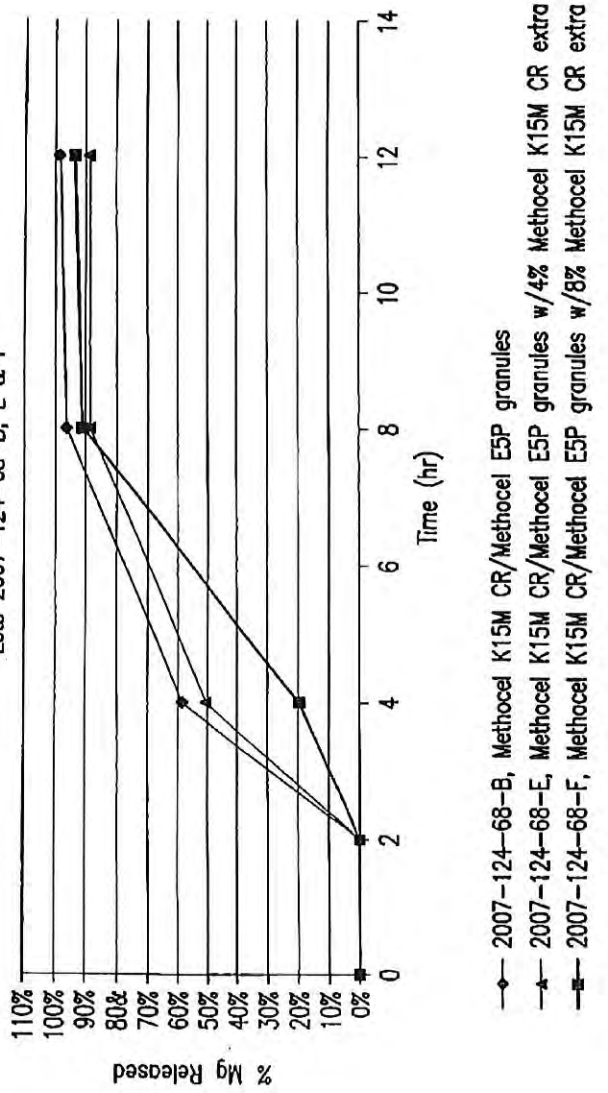

Lots 2007-124-68-B, E & F
% Mg Released
110%
100%
90%
80%
70%
60%
50%
40%
30%
20%
10%
0%
0
2
4
6
8
10
12
14
Time (hr)
2007-124-68-B, Methocel K15M CR/Methocel E5P granules
2007-124-68-E, Methocel K15M CR/Methocel E5P granules w/4% Methocel K15M CR extra
2007-124-68-F, Methocel K15M CR/Methocel E5P granules w/8% Methocel K15M CR extra

FIG.8

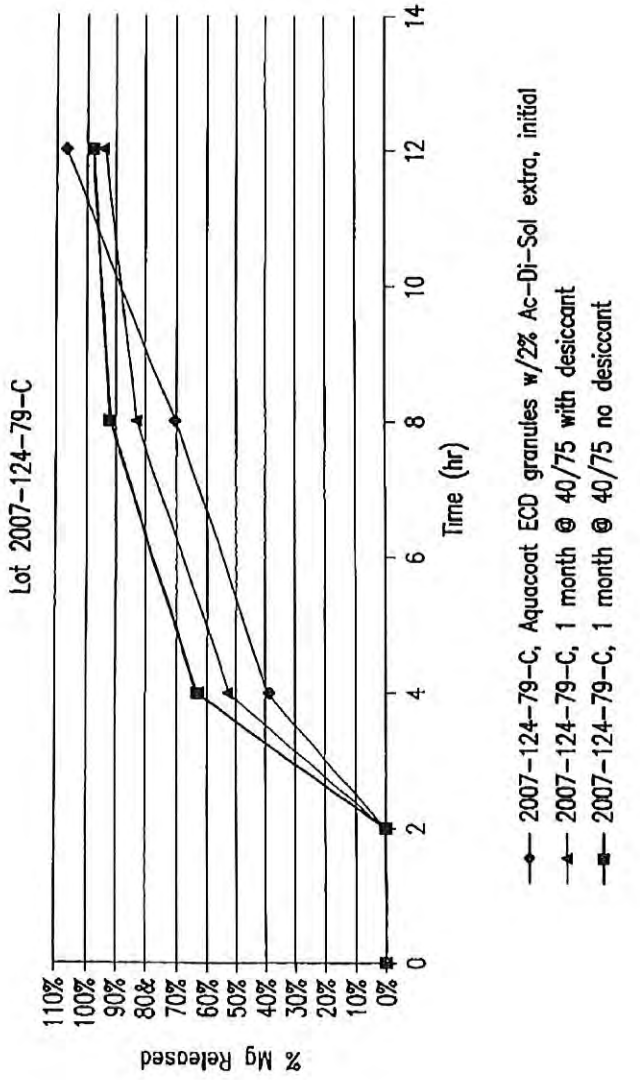

Lot 2007-124-79-C
% Mg Released
110%
100%
90%
80&
70%
60%
50%
40%
30%
20%
10%
0%
0
2
4
6
8
10
12
14
Time (hr)
2007-124-79-C, Aquacoat ECD granules w/2% Ac-Di-Sol extra, initial
2007-124-79-C, 1 month @ 40/75 with desiccant
2007-124-79-C, 1 month @ 40/75 no desiccant

FIG.9

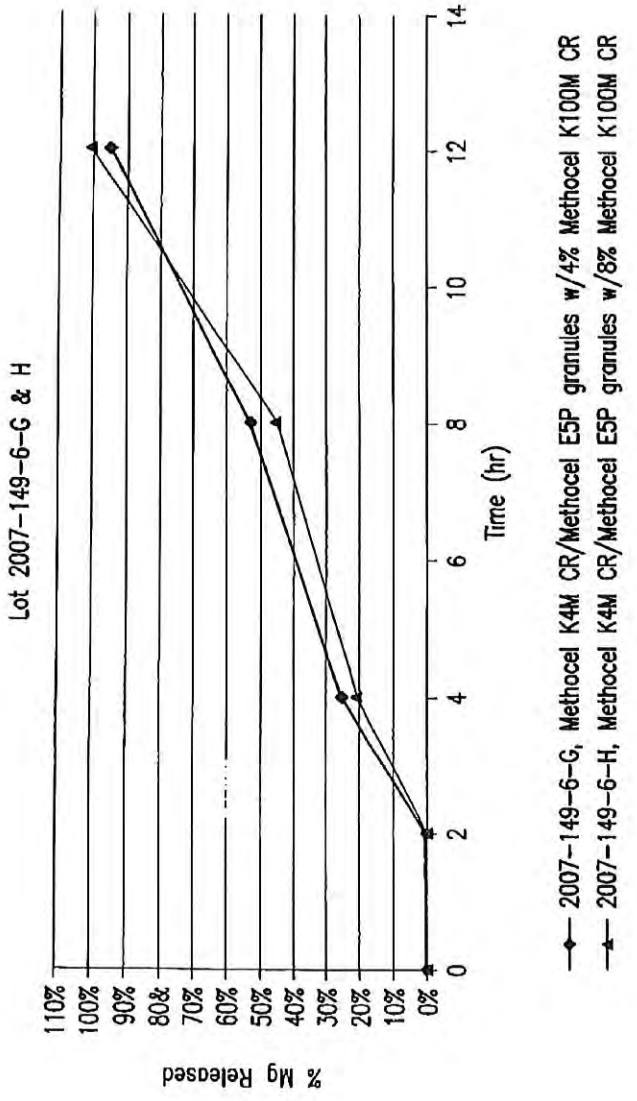

Lot 2007-149-6-G & H
% Mg Released
110%
100%
90%
80&
70%
60%
50%
40%
30%
20%
10%
0%
0
2
4
6
8
10
12
14
Time (hr)
2007-149-6-G, Methocel K4M CR/Methocel E5P granules w/4% Methocel K100M CR
2007-149-6-H, Methocel K4M CR/Methocel E5P granules w/8% Methocel K100M CR

FIG.10

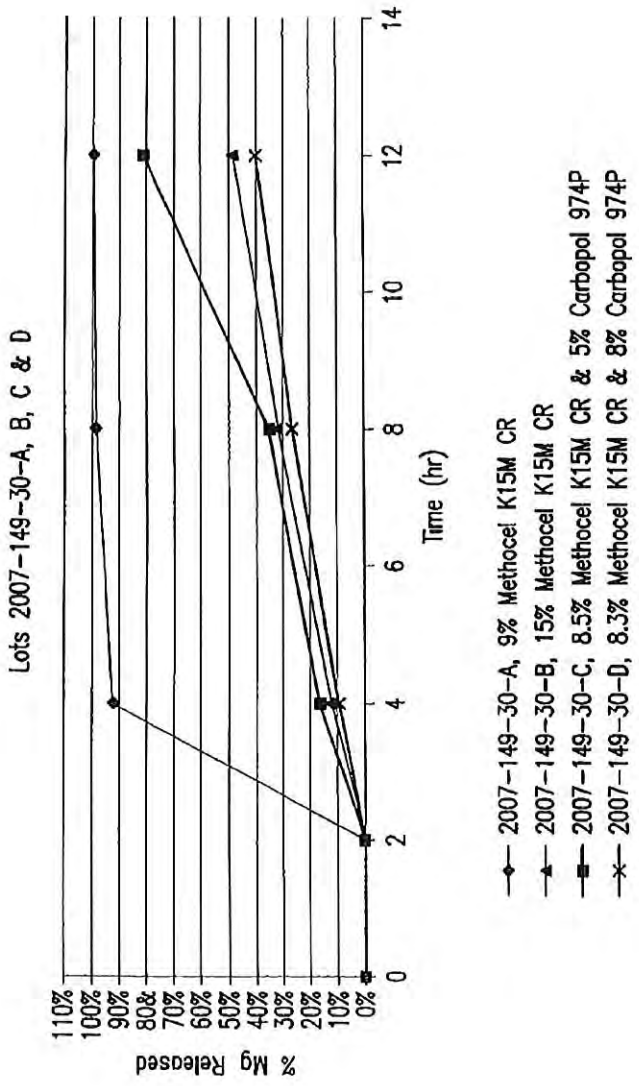

Lots 2007-149-30-A, B, C & D
% Mg Released
110%
100%
90%
80&
70%
60%
50%
40%
30%
20%
10%
0%
0
2
4
6
8
10
12
14
Time (hr)
2007-149-30-A, 9% Methocel K15M CR
2007-149-30-B, 15% Methocel K15M CR
2007-149-30-C, 8.5% Methocel K15M CR & 5% Carbopol 974P
2007-149-30-D, 8.3% Methocel K15M CR & 8% Carbopol 974P

FIG.11

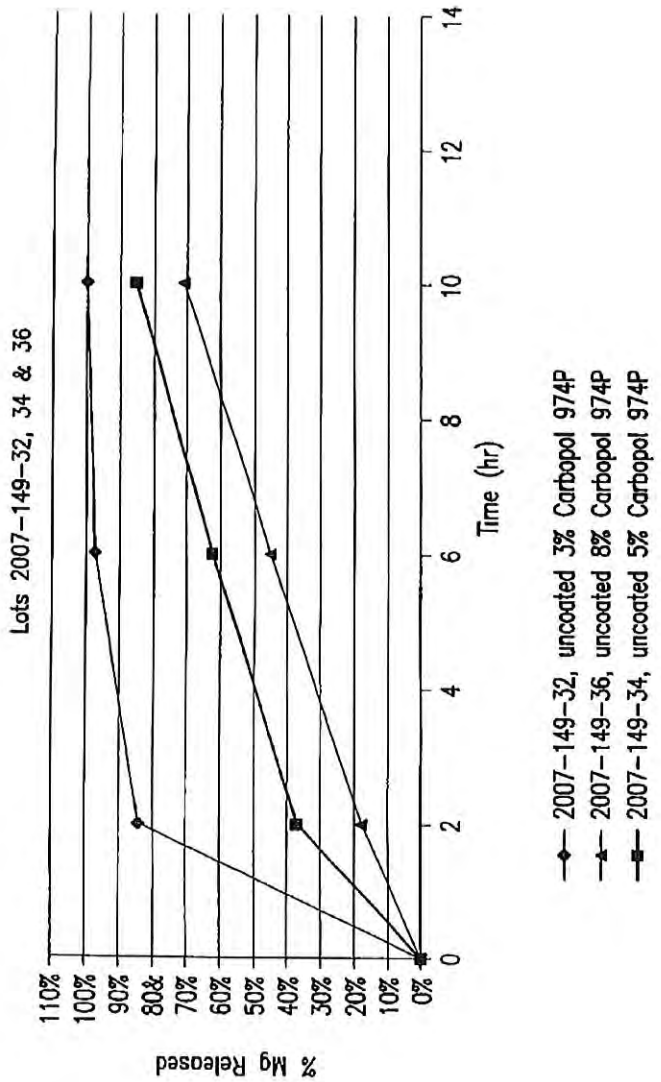

Lots 2007-149-32, 34 & 36
% Mg Released
110%
100%
90%
80%
70%
60%
50%
40%
30%
20%
10%
0%
0
2
4
6
8
10
12
14
Time (hr)
2007-149-32, uncoated 3% Carbopol 974P
2007-149-36, uncoated 8% Carbopol 974P
2007-149-34, uncoated 5% Carbopol 974P

FIG. 12

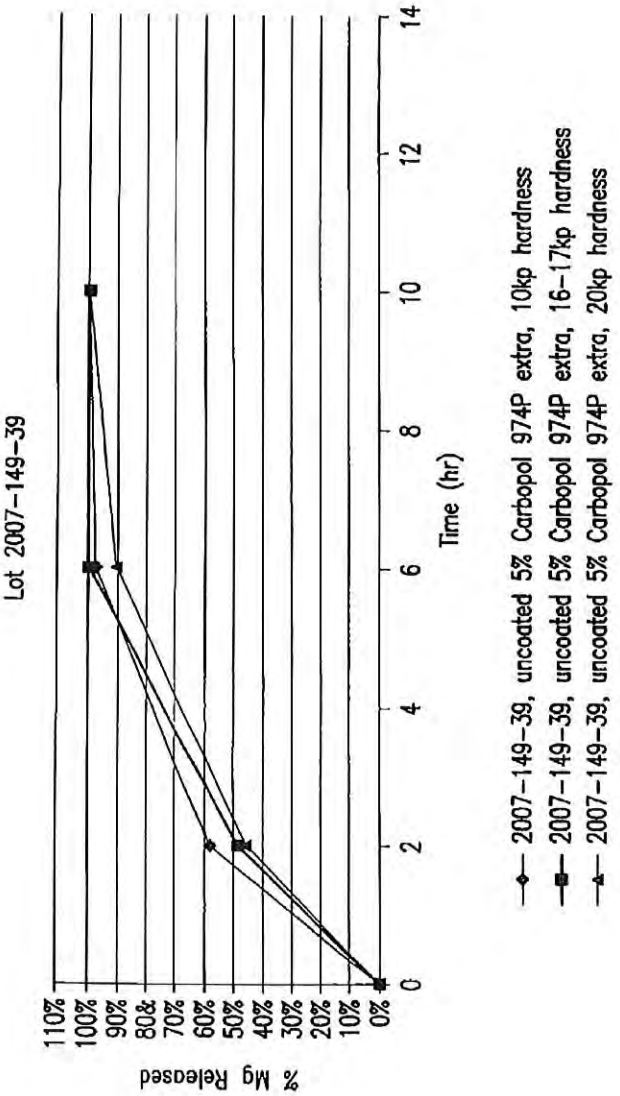

Lot 2007-149-39
% Mg Released
110%
100%
90%
80%
70%
60%
50%
40%
30%
20%
10%
0%
0
2
4
6
8
10
12
14
Time (hr)
2007-149-39, uncoated 5% Carbopol 974P extra, 10kp hardness
2007-149-39, uncoated 5% Carbopol 974P extra, 16-17kp hardness
2007-149-39, uncoated 5% Carbopol 974P extra, 20kp hardness

FIG. 13

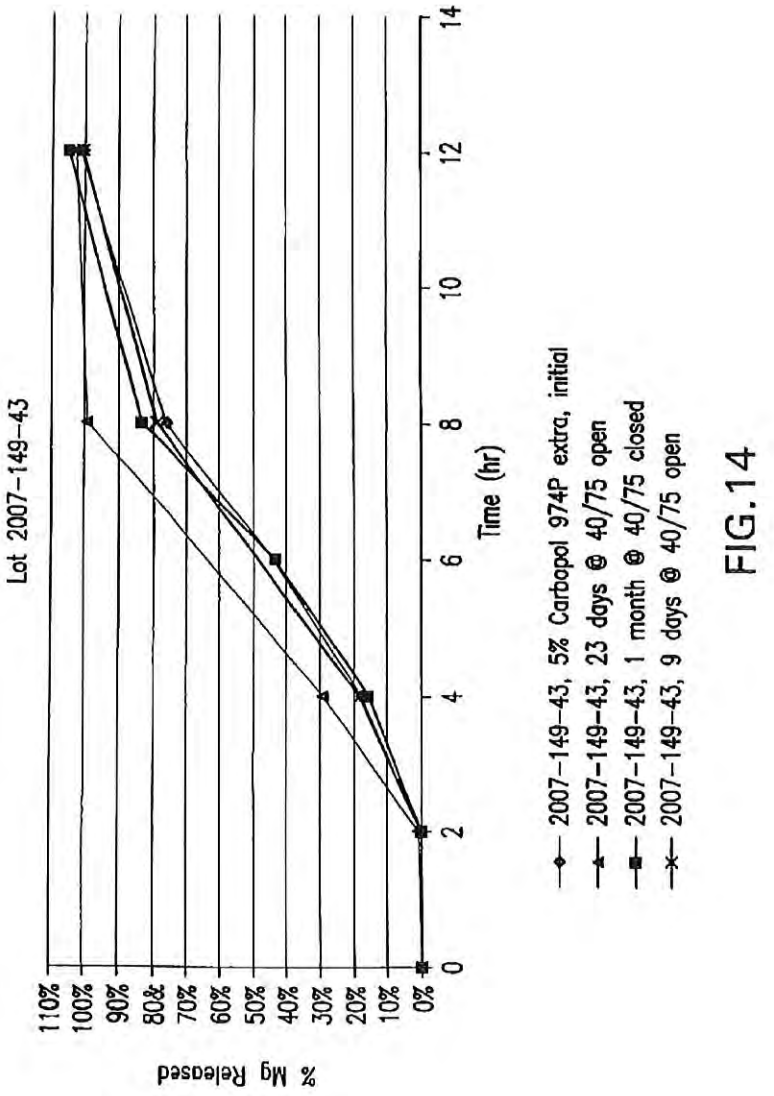

Lot 2007-149-43
% Mg Released
110%
100%
90%
80&
70%
60%
50%
40%
30%
20%
10%
0%
0
2
4
6
8
10
12
14
Time (hr)
2007-149-43, 5% Carbopol 974P extra, initial
2007-149-43, 23 days @ 40/75 open
2007-149-43, 1 month @ 40/75 closed
2007-149-43, 9 days @ 40/75 open

FIG.14

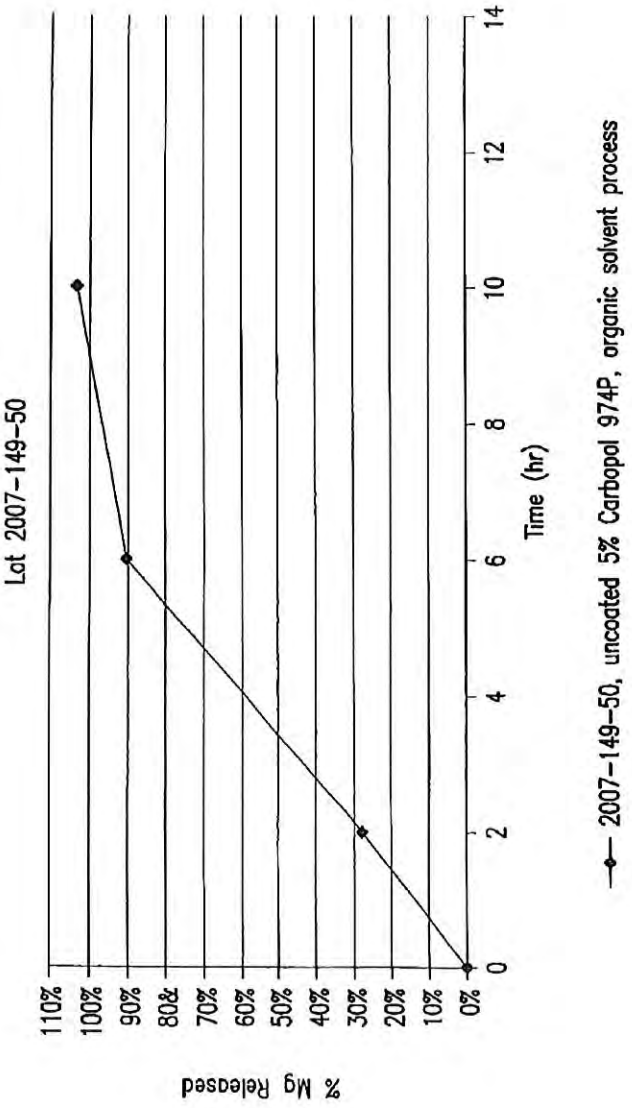

Lot 2007-149-50
% Mg Released
110%
100%
90%
80%
70%
60%
50%
40%
30%
20%
10%
0%
0
2
4
6
8
10
12
14
Time (hr)
2007-149-50, uncoated 5% Carbopol 974P, organic solvent process

FIG.15

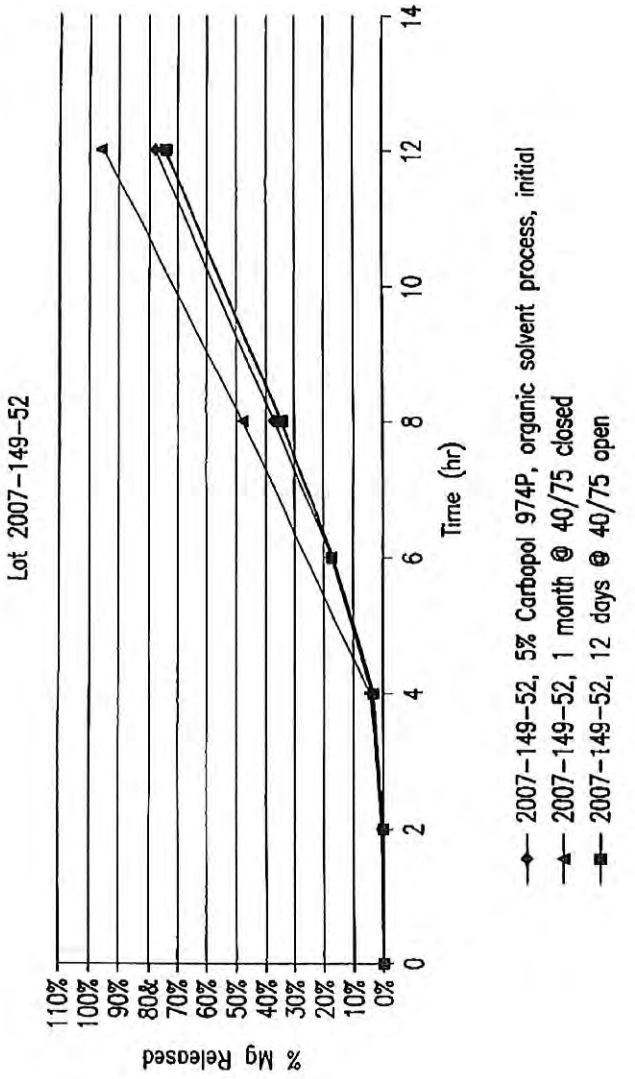

Lot 2007-149-52
% Mg Released
110%
100%
90%
80%
70%
60%
50%
40%
30%
20%
10%
0%
0
2
4
6
8
10
12
14
Time (hr)
2007-149-52, 5% Carbopol 974P, organic solvent process, initial
2007-149-52, 1 month @ 40/75 closed
2007-149-52, 12 days @ 40/75 open

FIG.16

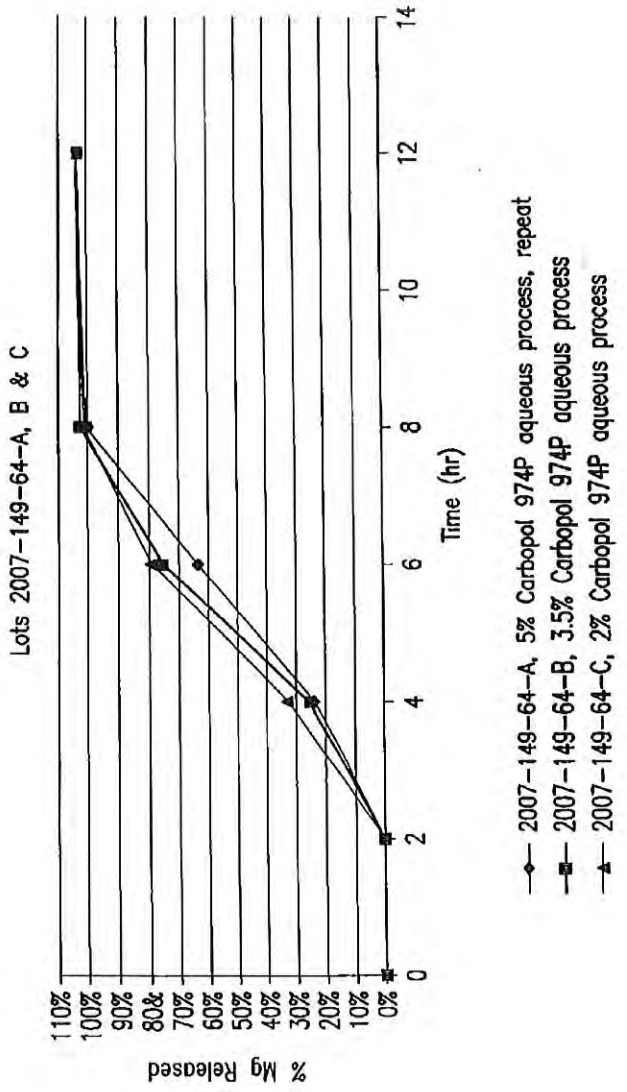

Lots 2007-149-64-A, B & C
% Mg Released
110%
100%
90%
80&
70%
60%
50%
40%
30%
20%
10%
0%
0
2
4
6
8
10
12
14
Time (hr)
2007-149-64-A, 5% Carbopol 974P aqueous process, repeat
2007-149-64-B, 3.5% Carbopol 974P aqueous process
2007-149-64-C, 2% Carbopol 974P aqueous process

FIG.17

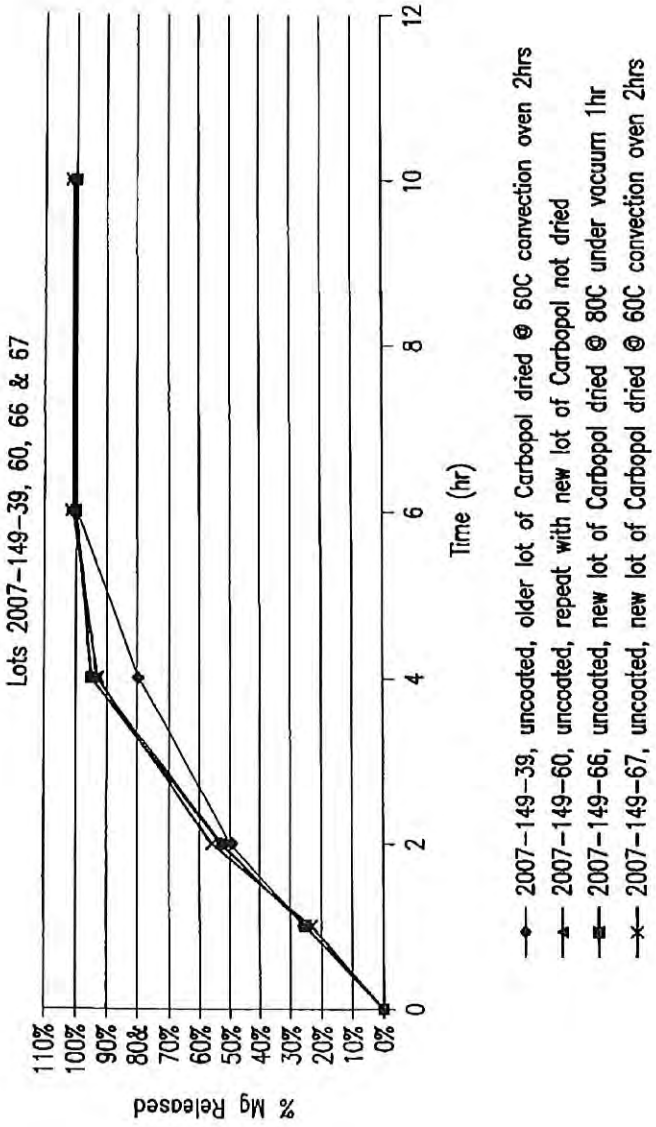

Lots 2007-149-39, 60, 66 & 67
% Mg Released
110%
100%
90%
80%
70%
60%
50%
40%
30%
20%
10%
0%
0
2
4
6
8
10
12
Time (hr)
2007-149-39, uncoated, older lot of Carbopol dried @ 60C convection oven 2hrs
2007-149-60, uncoated, repeat with new lot of Carbopol not dried
2007-149-66, uncoated, new lot of Carbopol dried @ 80C under vacuum 1hr
2007-149-67, uncoated, new lot of Carbopol dried @ 60C convection oven 2hrs

FIG.18

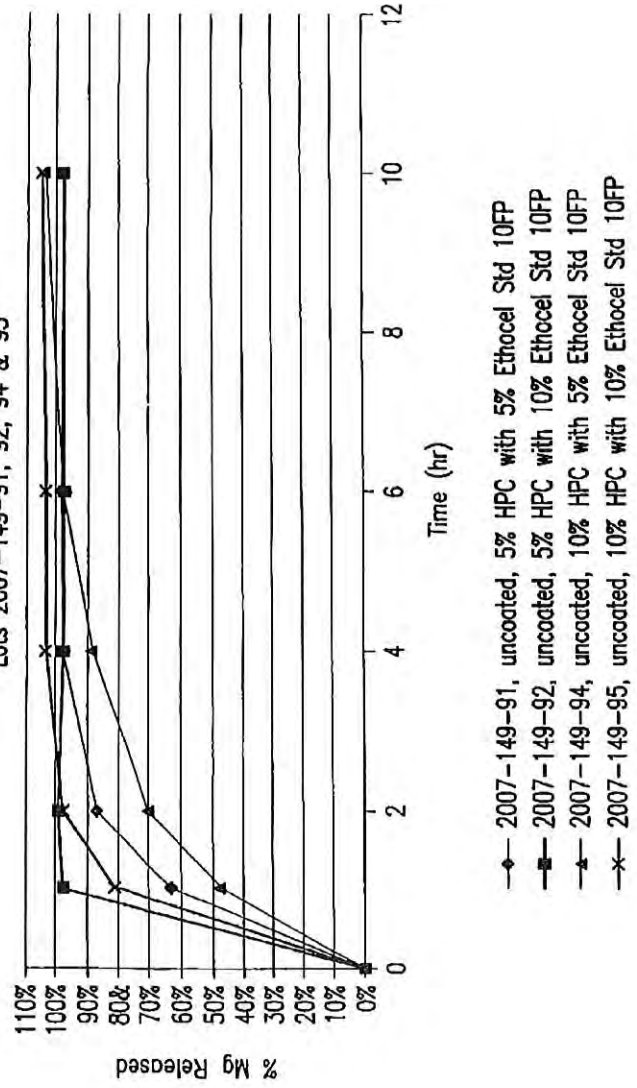

Lots 2007-149-91, 92, 94 & 95
% Mg Released
110%
100%
90%
80%
70%
60%
50%
40%
30%
20%
10%
0%
0
2
4
6
8
10
12
Time (hr)
2007-149-91, uncoated, 5% HPC with 5% Ethocel Std 10FP
2007-149-92, uncoated, 5% HPC with 10% Ethocel Std 10FP
2007-149-94, uncoated, 10% HPC with 5% Ethocel Std 10FP
2007-149-95, uncoated, 10% HPC with 10% Ethocel Std 10FP

FIG.19

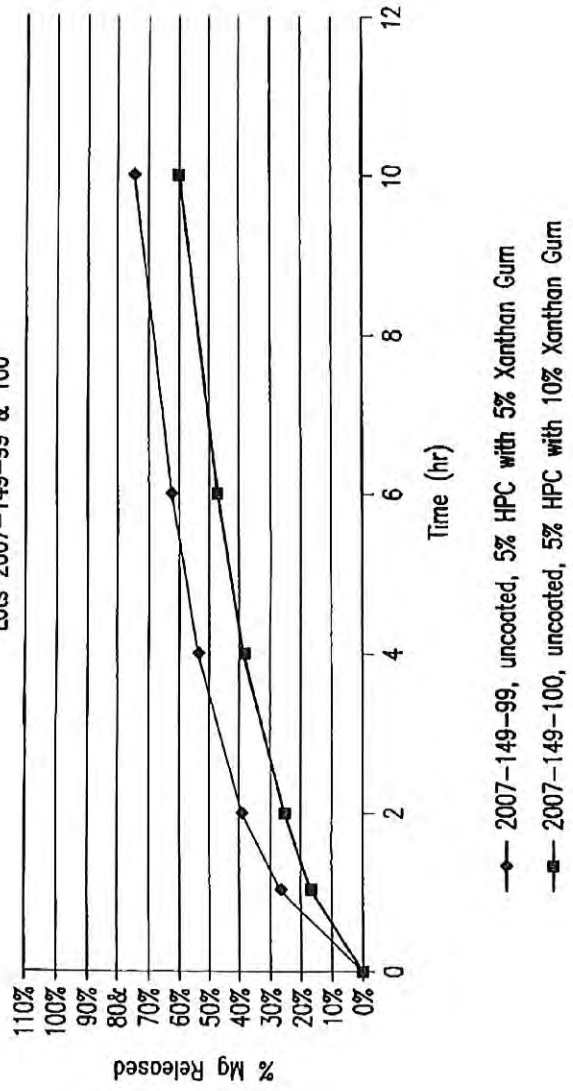

Lots 2007-149-99 & 100
% Mg Released
110%
100%
90%
80&
70%
60%
50%
40%
30%
20%
10%
0%
0
2
4
6
8
10
12
Time (hr)
2007-149-99, uncoated, 5% HPC with 5% Xanthan Gum
2007-149-100, uncoated, 5% HPC with 10% Xanthan Gum

FIG.20

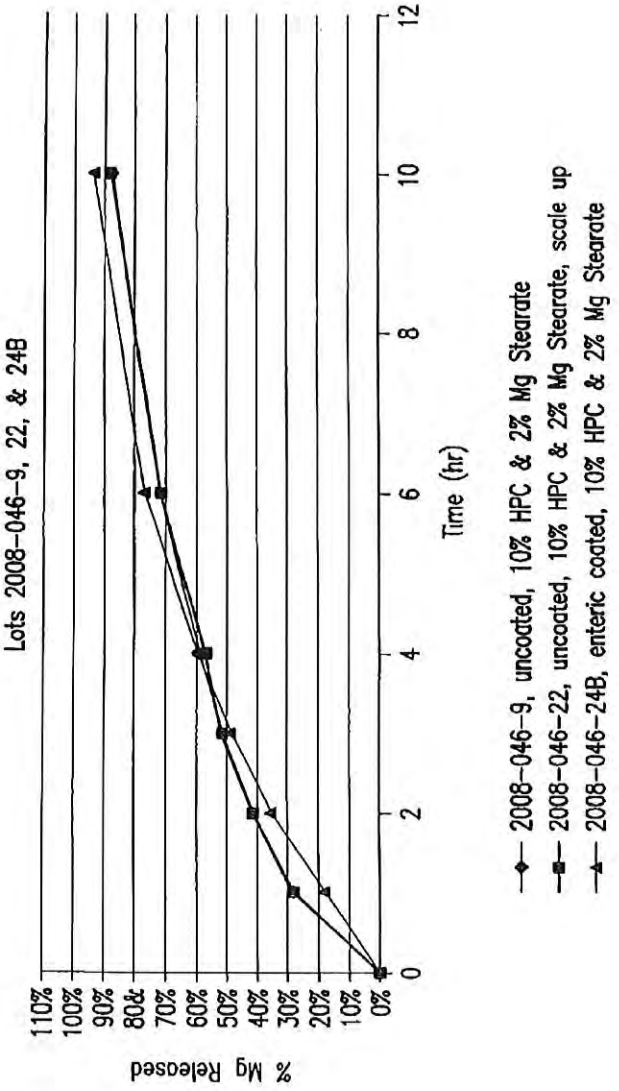

Lots 2008-046-9, 22, & 24B
% Mg Released
110%
100%
90%
80%
70%
60%
50%
40%
30%
20%
10%
0%
0
2
4
6
8
10
12
Time (hr)
2008-046-9, uncoated, 10% HPC & 2% Mg Stearate
2008-046-22, uncoated, 10% HPC & 2% Mg Stearate, scale up
2008-046-24B, enteric coated, 10% HPC & 2% Mg Stearate

FIG.21

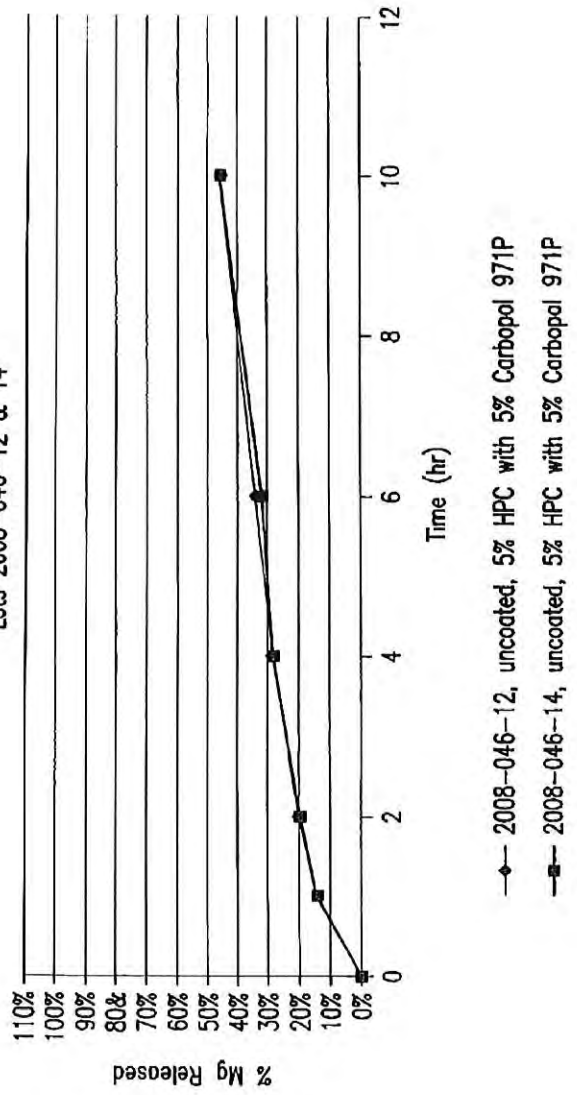

Lots 2008-046-12 & 14
% Mg Released
110%
100%
90%
80%
70%
60%
50%
40%
30%
20%
10%
0%
0
2
4
6
8
10
12
Time (hr)
2008-046-12, uncoated, 5% HPC with 5% Carbopol 971P
2008-046-14, uncoated, 5% HPC with 5% Carbopol 971P

FIG.22

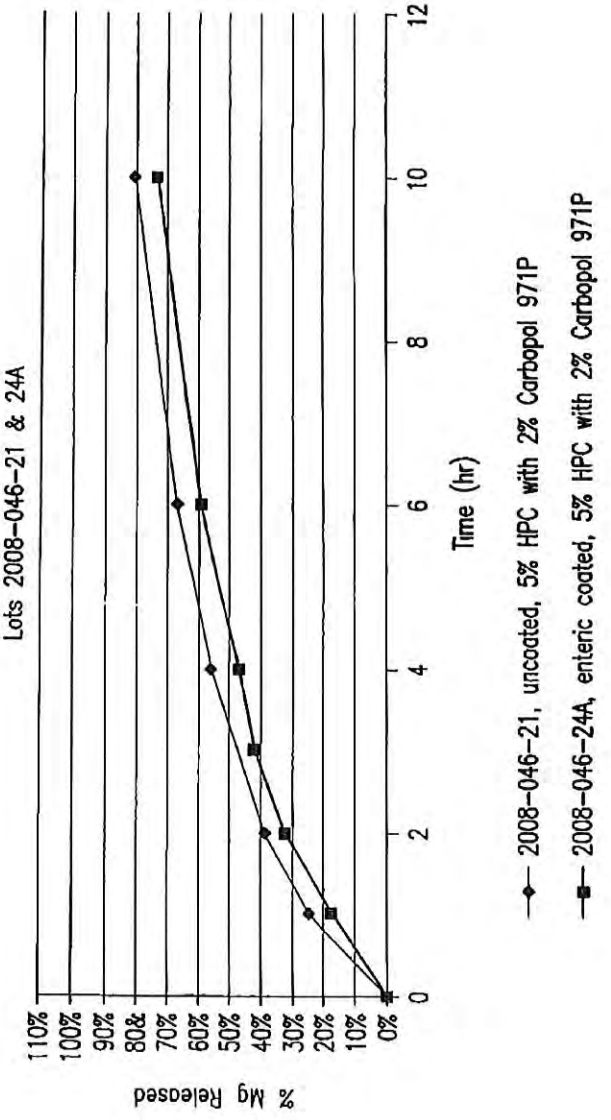

Lots 2008-046-21 & 24A
% Mg Released
110%
100%
90%
80%
70%
60%
50%
40%
30%
20%
10%
0%
0
2
4
6
8
10
12
Time (hr)
2008-046-21, uncoated, 5% HPC with 2% Carbopol 971P
2008-046-24A, enteric coated, 5% HPC with 2% Carbopol 971P

FIG.23

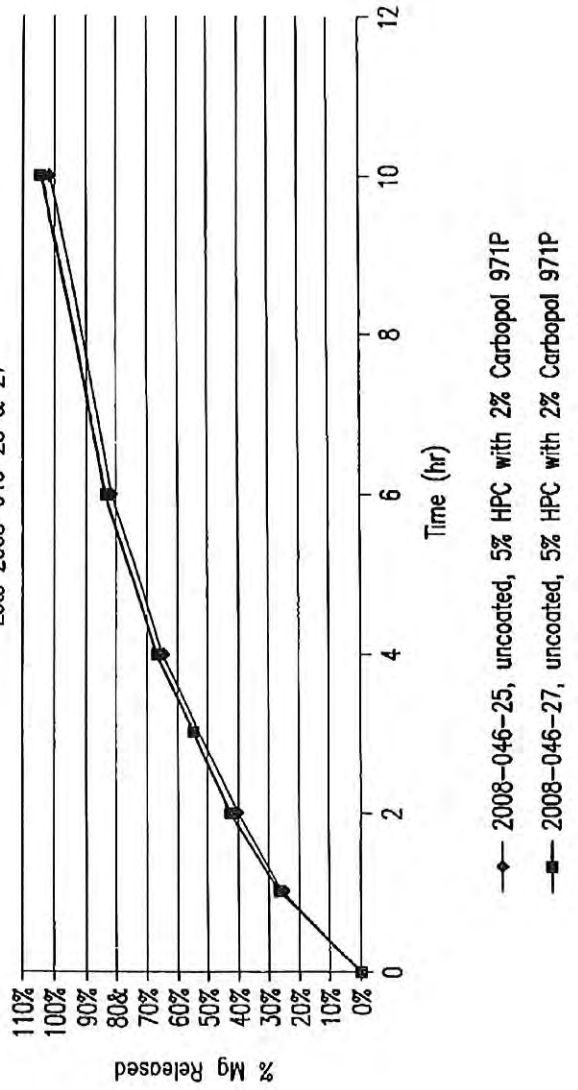

Lots 2008-046-25 & 27
% Mg Released
110%
100%
90%
80&
70%
60%
50%
40%
30%
20%
10%
0%
0
2
4
6
8
10
12
Time (hr)
2008-046-25, uncoated, 5% HPC with 2% Carbopol 971P
2008-046-27, uncoated, 5% HPC with 2% Carbopol 971P

FIG.24

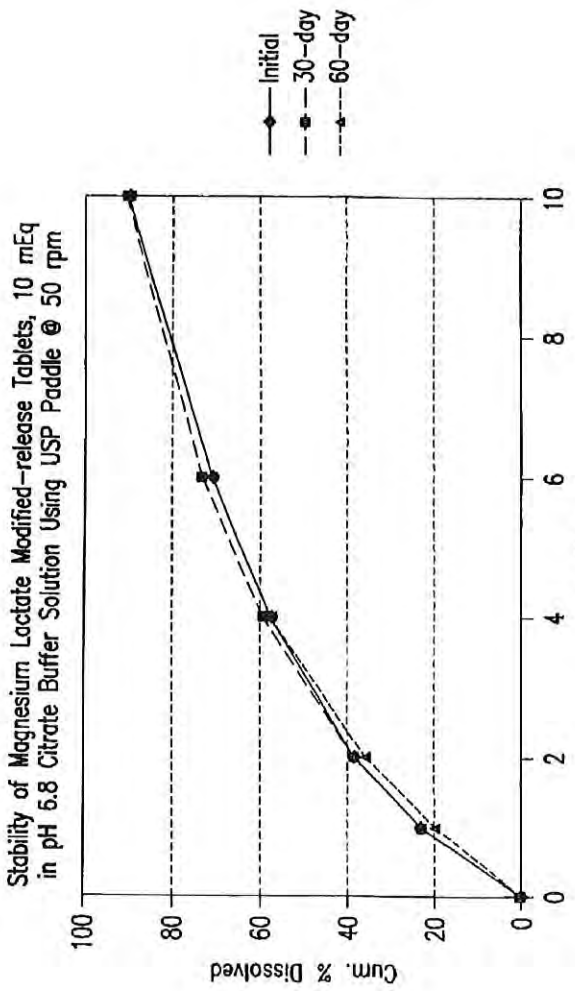

Stability of Magnesium Lactate Modified-release Tablets, 10 mEq
in pH 6.8 Citrate Buffer Solution Using USP Paddle @ 50 rpm
Initial
30-day
60-day
Cum. % Dissolved
100
80
60
40
20
0
0
2
4
6
8
10
Time (Hours)

FIG.25

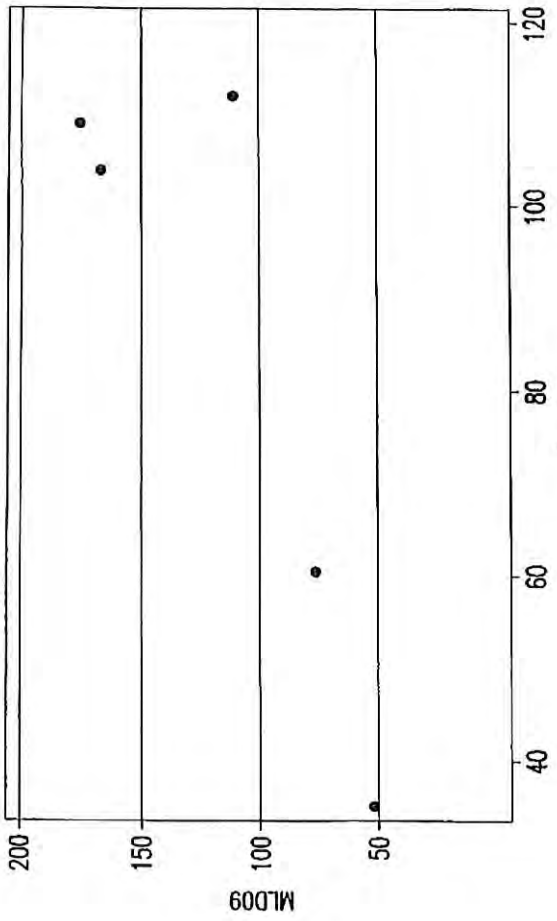
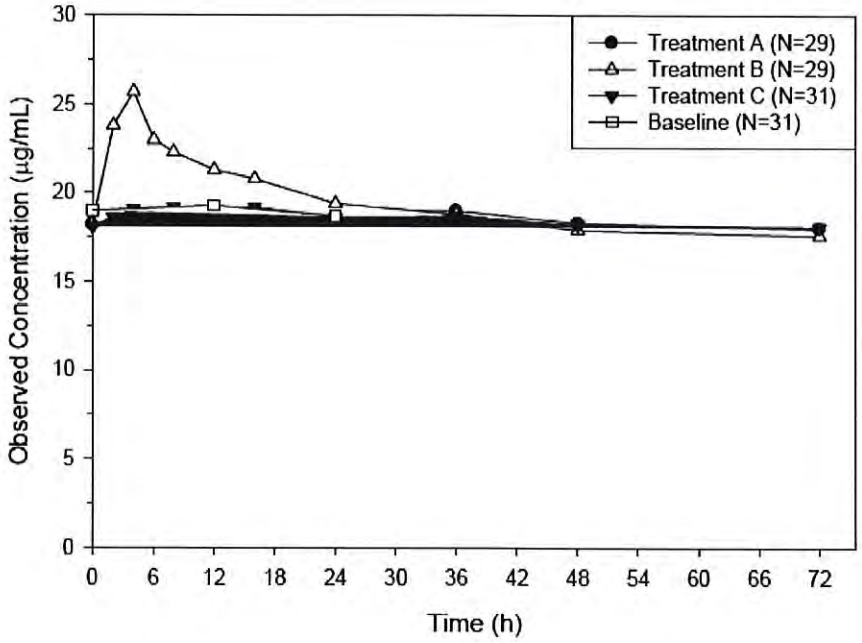


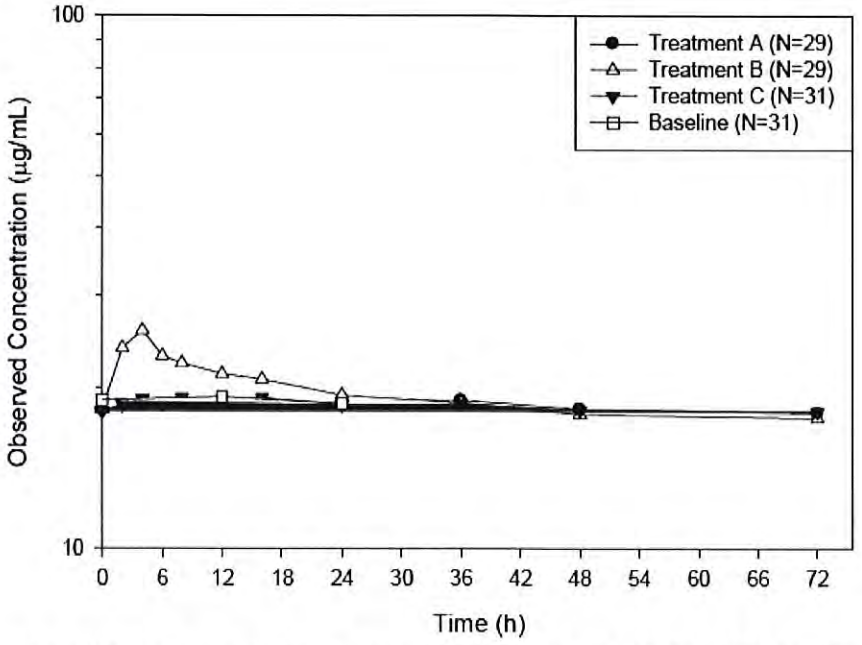

FIG.26

# FIGURE 27-1

**Linear Scale**




**Semilog Scale**



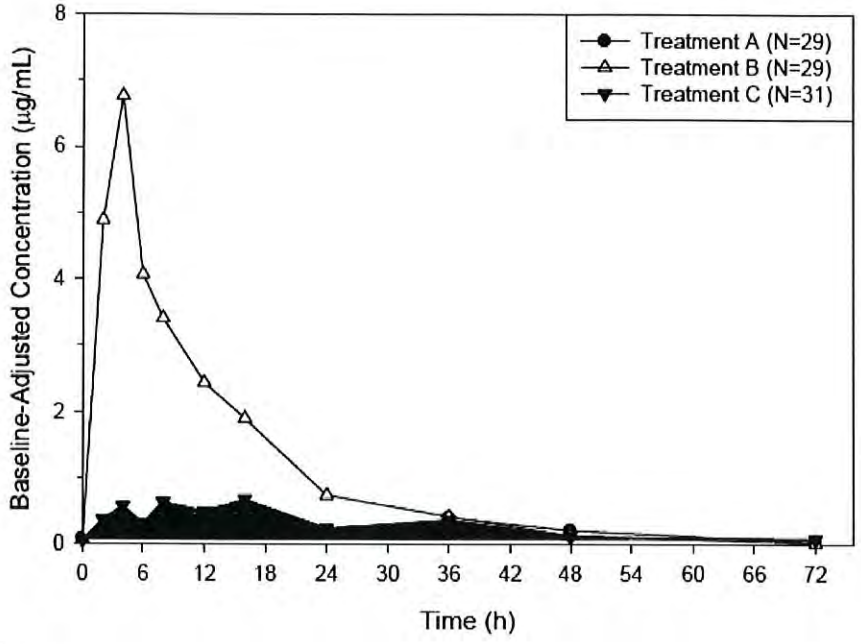

Treatment A: Single oral dose of 20 mEq MLD administered as 2 x 10 mEq MLD ER caplets in the fasted state.

Treatment B: Single IV infusion of 20 mEq magnesium sulfate administered over 4 hours in the fasted state.

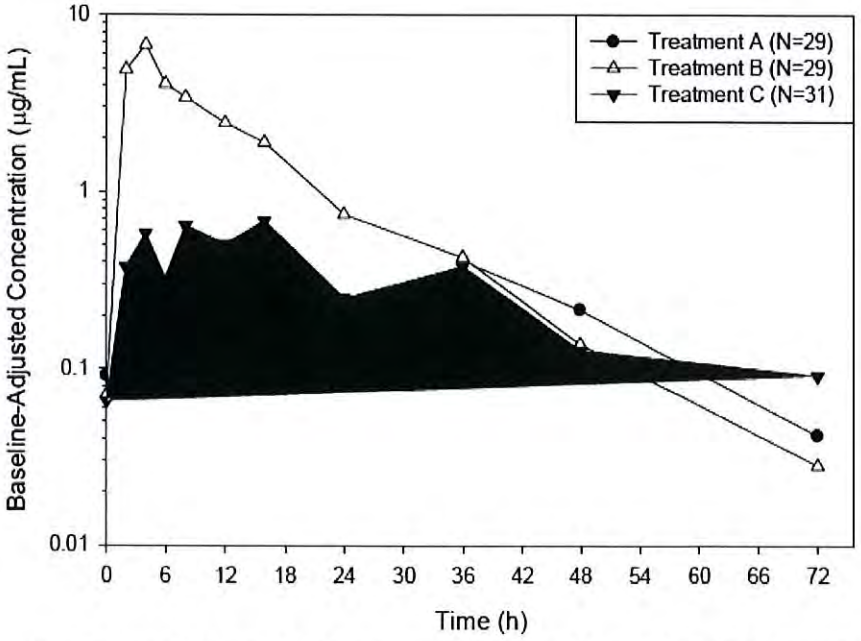
Treatment C: Single oral dose of 20 mEq MLD administered as 2 x 10 mEq MLD ER caplets in the fed state.

# FIGURE 27-2

**Linear Scale**



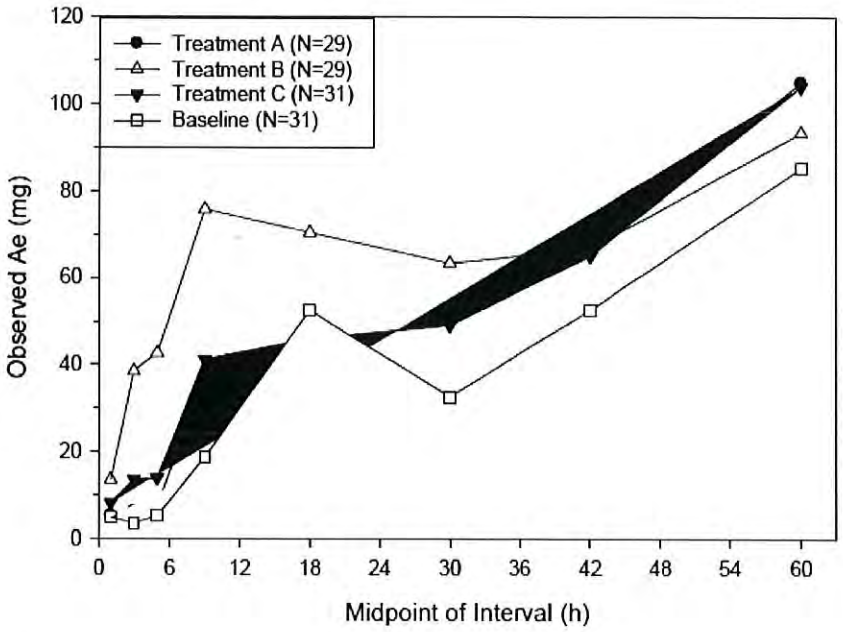

**Semilog Scale**



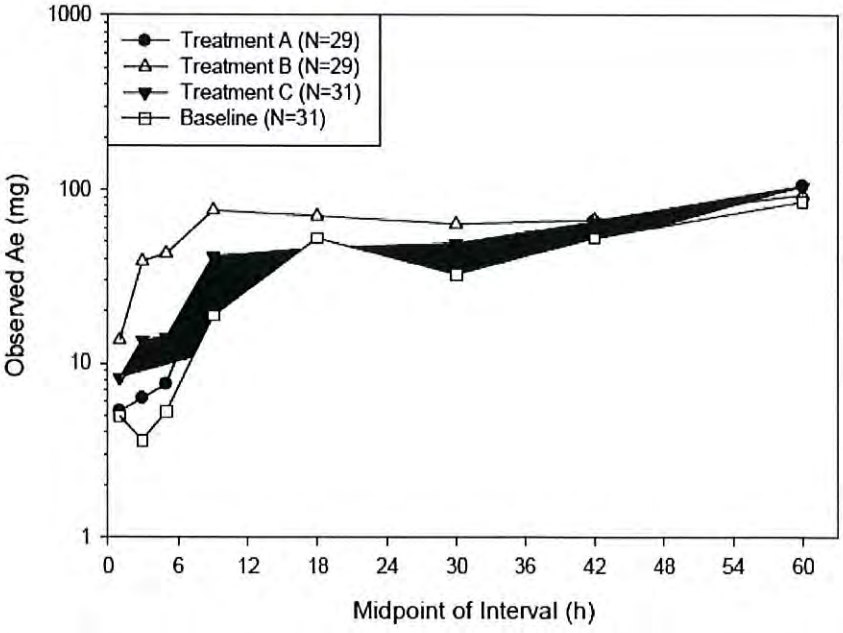

Treatment A: Single oral dose of 20 mEq MLD administered as 2 x 10 mEq MLD ER caplets in the fasted state.
Treatment B: Single IV infusion of 20 mEq magnesium sulfate administered over 4 hours in the fasted state.
Treatment C: Single oral dose of 20 mEq MLD administered as 2 x 10 mEq MLD ER caplets in the fed state.

# FIGURE 27-3

**Linear Scale**



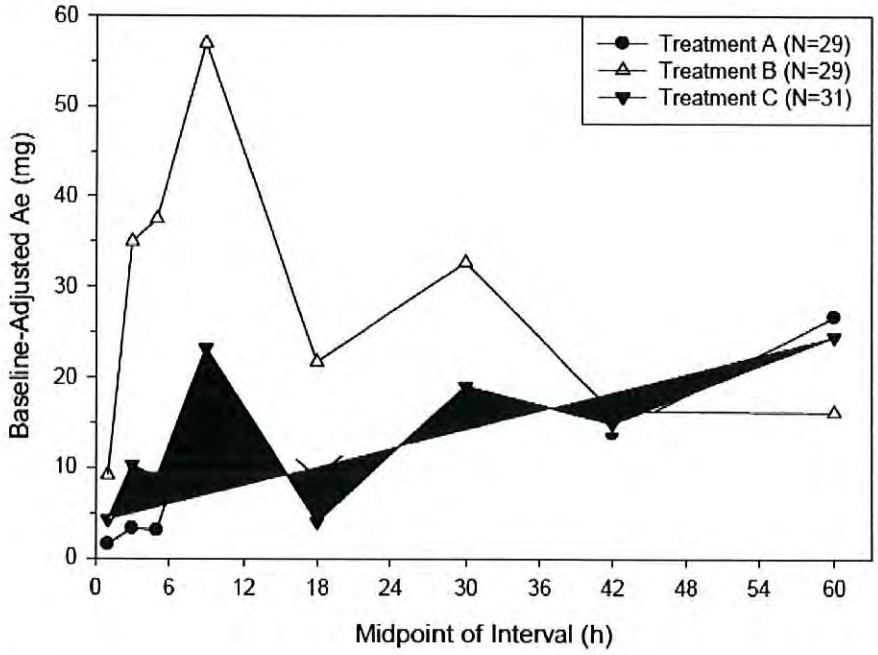

**Semilog Scale**



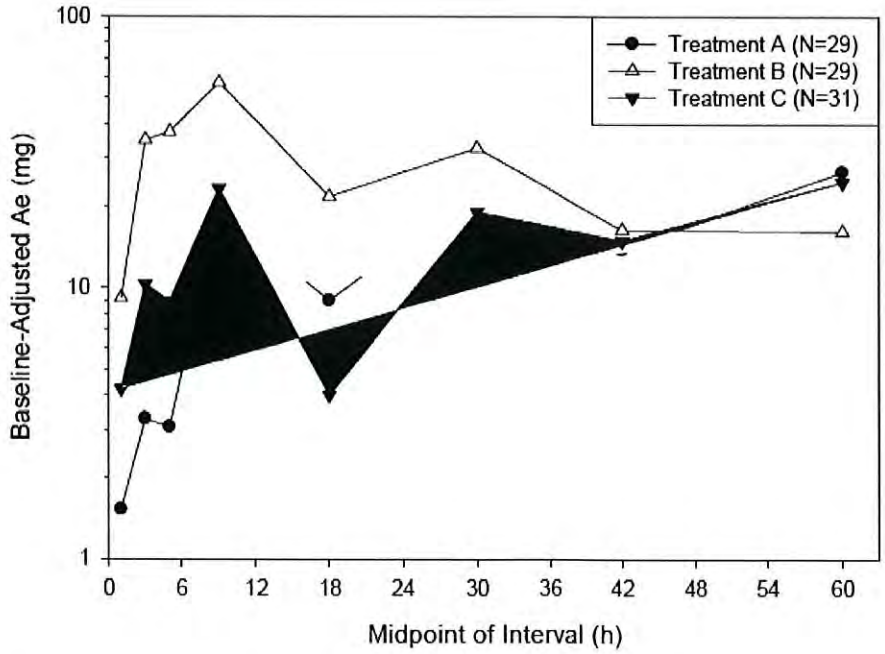

Treatment A: Single oral dose of 20 mEq MLD administered as 2 x 10 mEq MLD ER caplets in the fasted state.
Treatment B: Single IV infusion of 20 mEq magnesium sulfate administered over 4 hours in the fasted state.
Treatment C: Single oral dose of 20 mEq MLD administered as 2 x 10 mEq MLD ER caplets in the fed state.

# FIGURE 27-4

**Linear Scale**




**Semilog Scale**




Treatment A: Single oral dose of 20 mEq MLD administered as 2 x 10 mEq MLD ER caplets in the fasted state.
Treatment B: Single IV infusion of 20 mEq magnesium sulfate administered over 4 hours in the fasted state.
Treatment C: Single oral dose of 20 mEq MLD administered as 2 x 10 mEq MLD ER caplets in the fed state.