Mean Niacin Dissolution from Niacin ER 1000mg Tablets Containing Various Levels of METHOCEL® K-15M Premium

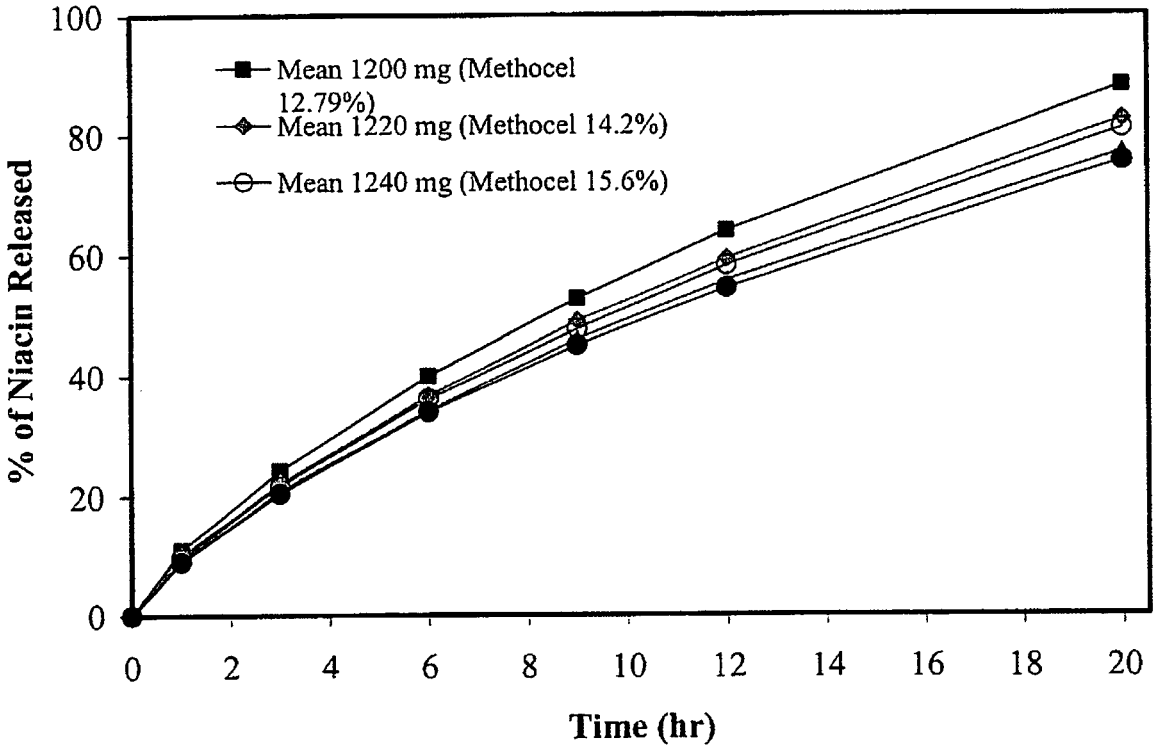


FIGURE 1

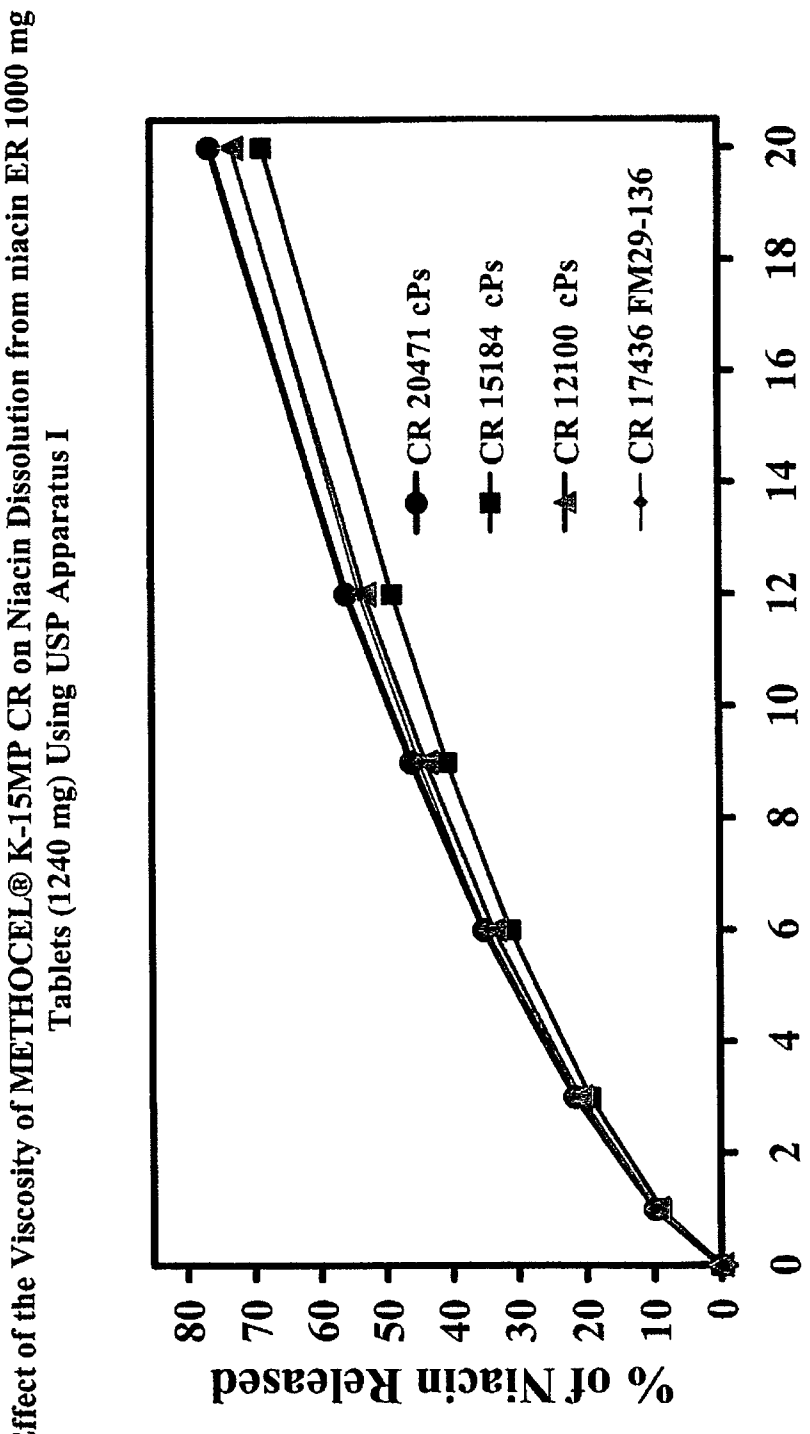

Effect of the Viscosity of METHOCEL® K-15MP CR on Niacin Dissolution from niacin ER 1000 mg Tablets (1240 mg) Using USP Apparatus I
% of Niacin Released
Time (hr)
CR 20471 cPs
CR 15184 cPs
CR 12100 cPs
CR 17436 FM29-136
0
10
20
30
40
50
60
70
80
0
2
4
6
8
10
12
14
16
18
20

FIGURE 2

Niacin Dissolution Profiles from Niacin ER 1000 mg Tablets Produced Using Bulk and 40 Mesh PVP K-90

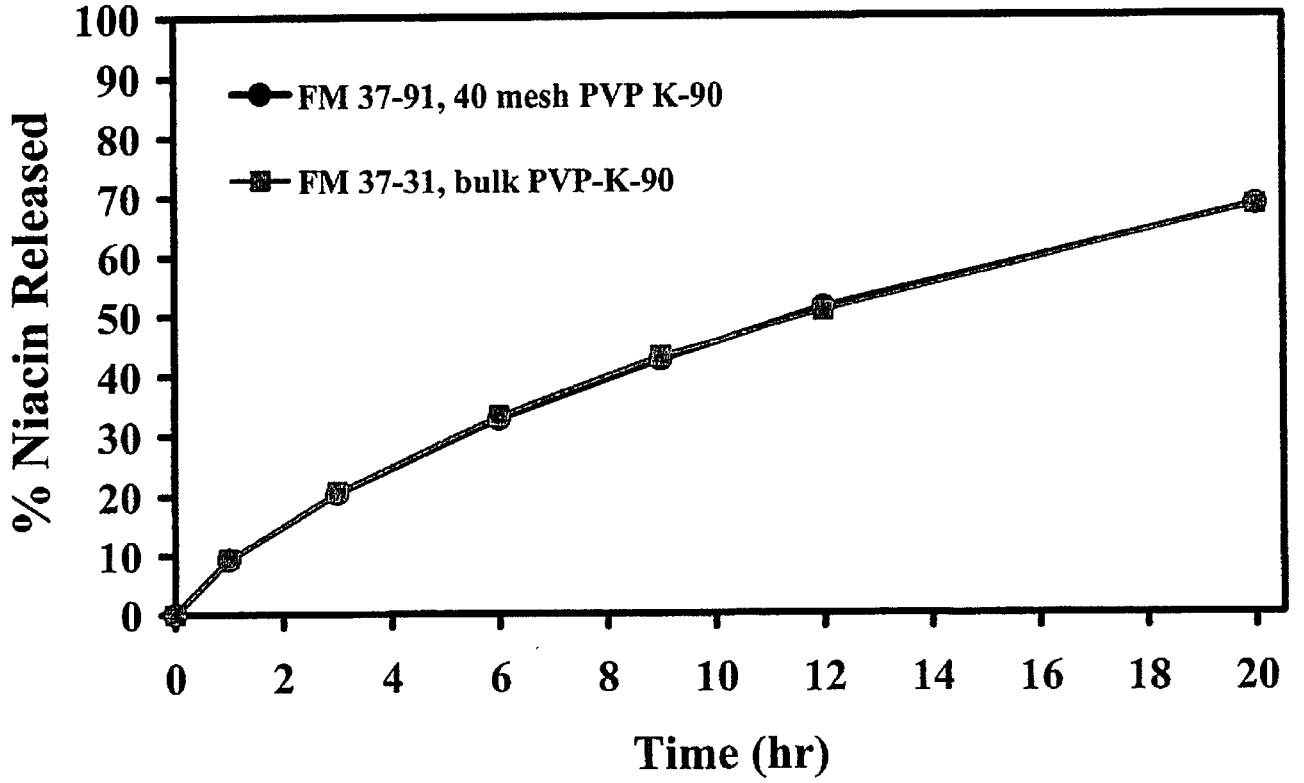


FIGURE 3

Niacin Dissolution from Niacin ER 1000 mg Tablets (1240 mg) with Different Mixing Steps

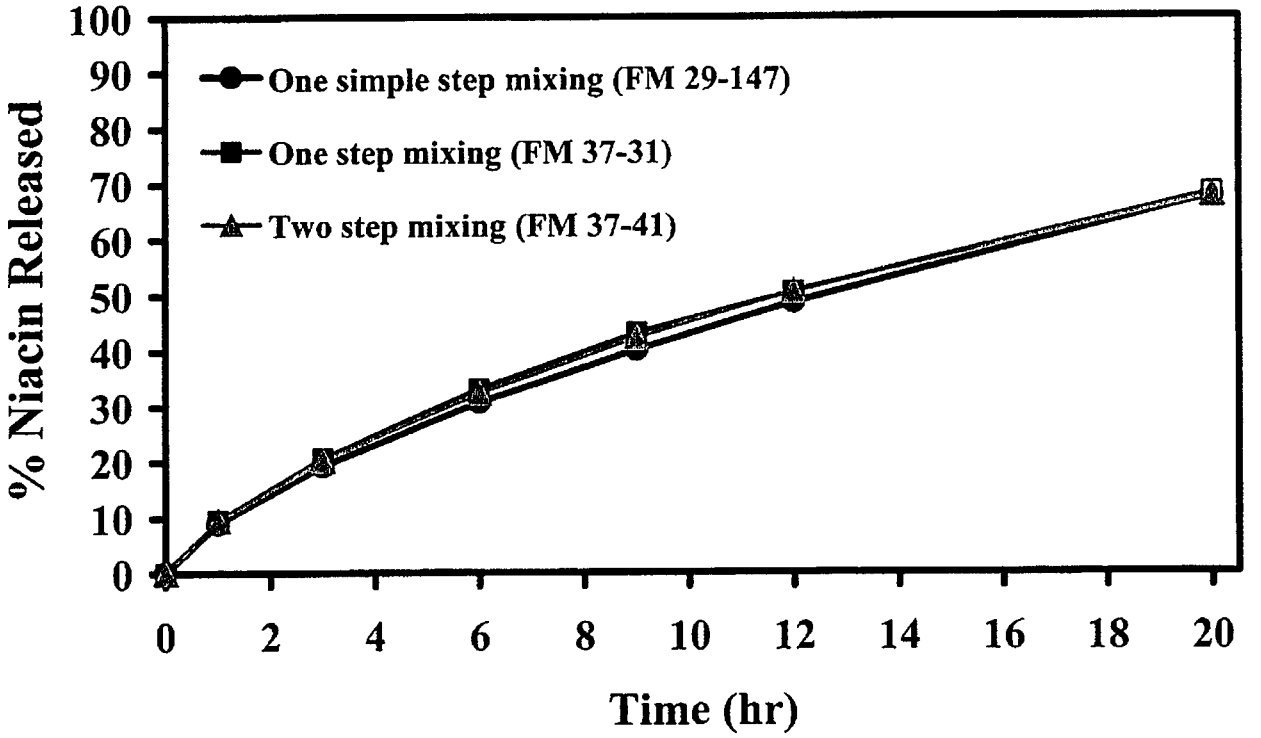


FIGURE 4

FLOW-DIAGRAM OF A DIRECT COMPRESSION MANUFACTURING PROCESS

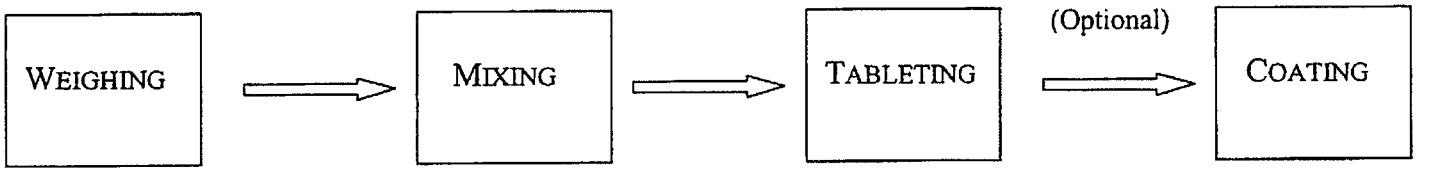
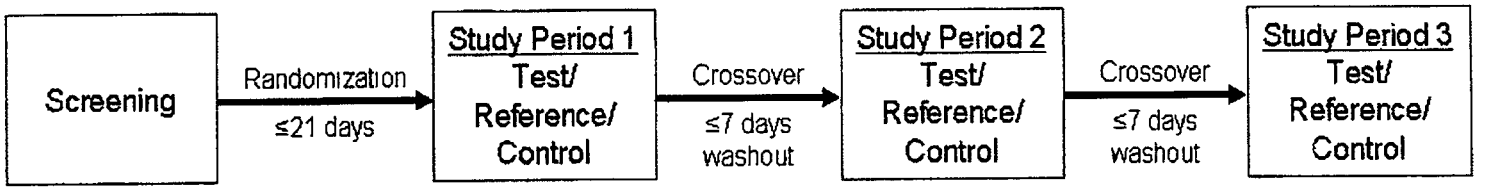


FIGURE 5



Study Treatments

Test	=	2 film-coated 1000 mg *reformulated* niacin ER tablets + 2 uncoated placebo tablets
Reference	=	2 uncoated 1000 mg *commercial* niacin ER tablets + 2 film-coated placebo tablets
Control	=	2 uncoated placebo tablets + 2 film-coated placebo tablets

FIGURE 6

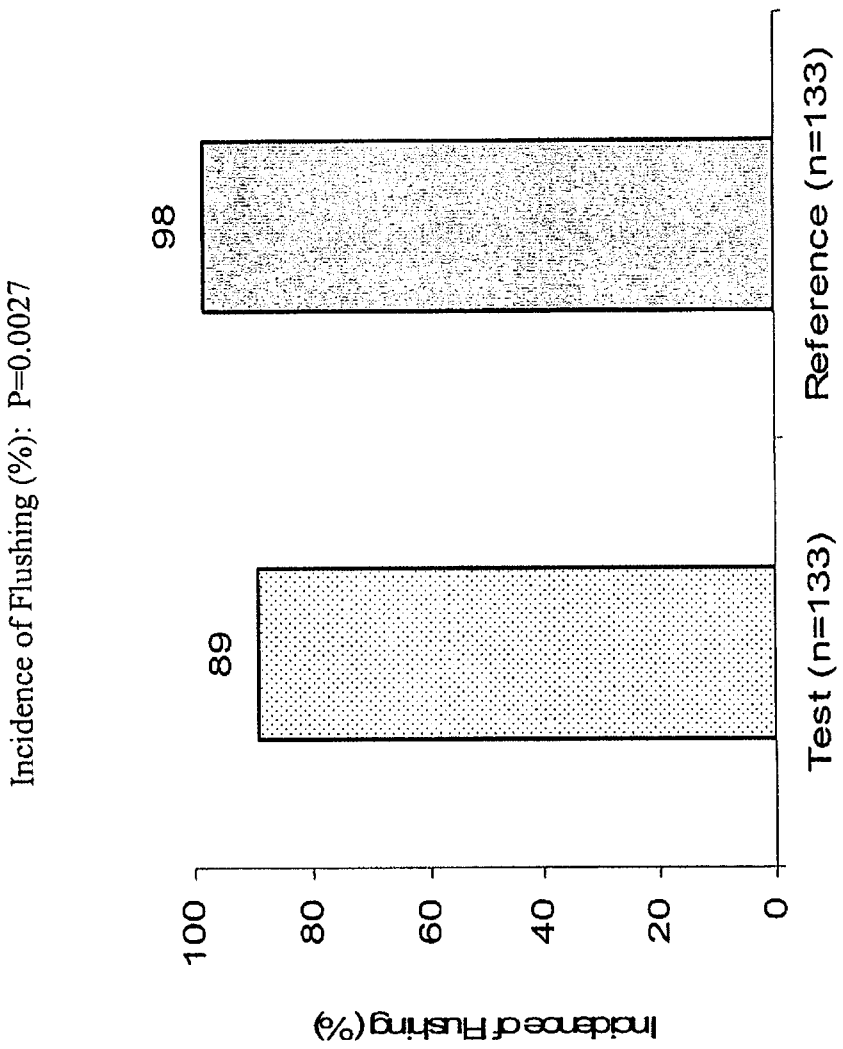

Incidence of Flushing (%): P=0.0027
Incidence of Flushing (%)
100
80
60
40
20
0
89
98
Test (n=133)
Reference (n=133)

FIGURE 7

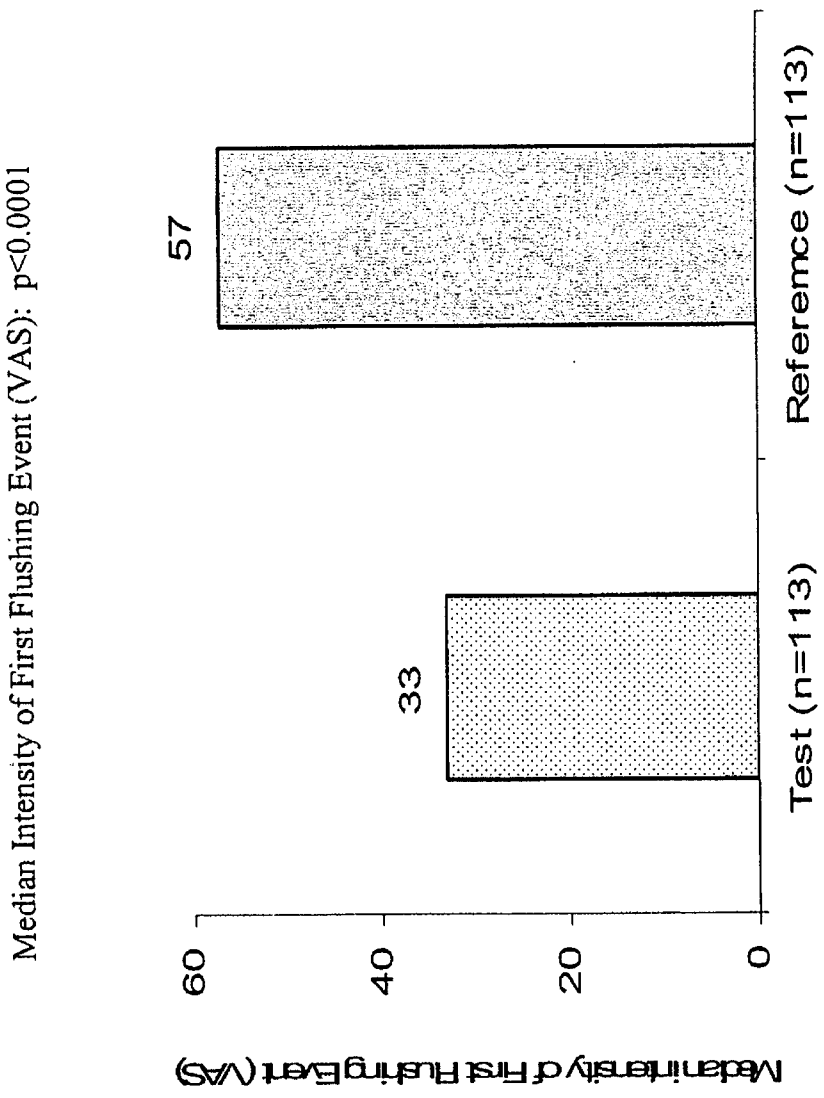

Median Intensity of First Flushing Event (VAS): p<0.0001
Median Intensity of First Flushing Event (VAS)
60
40
20
0
57
33
Test (n=113)
Reference (n=113)

FIGURE 8

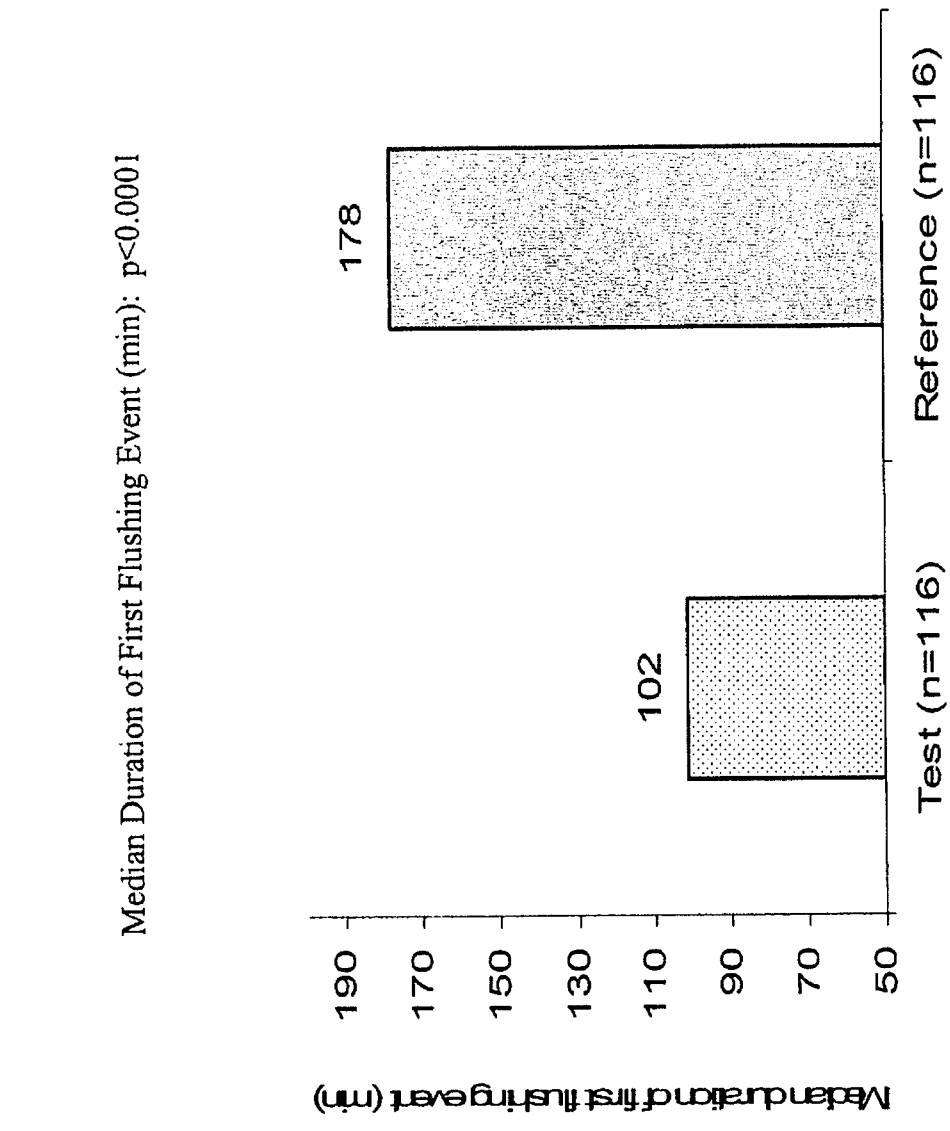

Median Duration of First Flushing Event (min): p<0.0001
Median duration of first flushing event (min)
190
170
150
130
110
90
70
50
178
102
Test (n=116)
Reference (n=116)

FIGURE 9

Characterization of flushing symptoms in the first flushing event in ITT population for Test (formulations of the invention), Reference (*commercial* niacin ER), and Control (placebo).

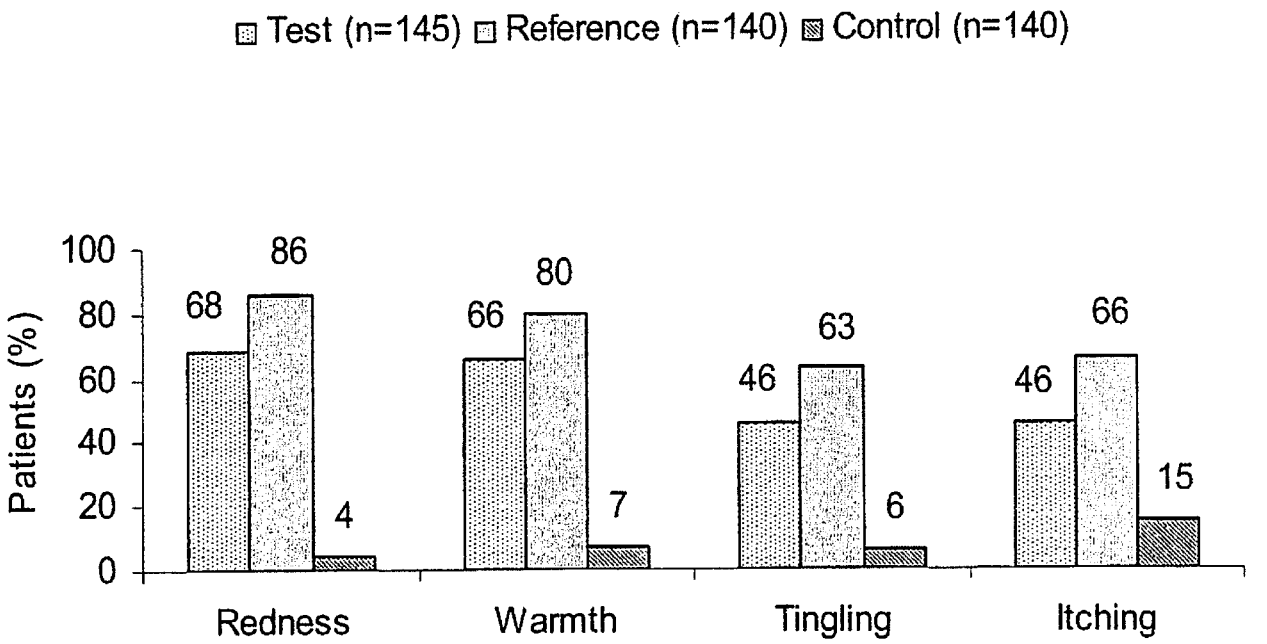
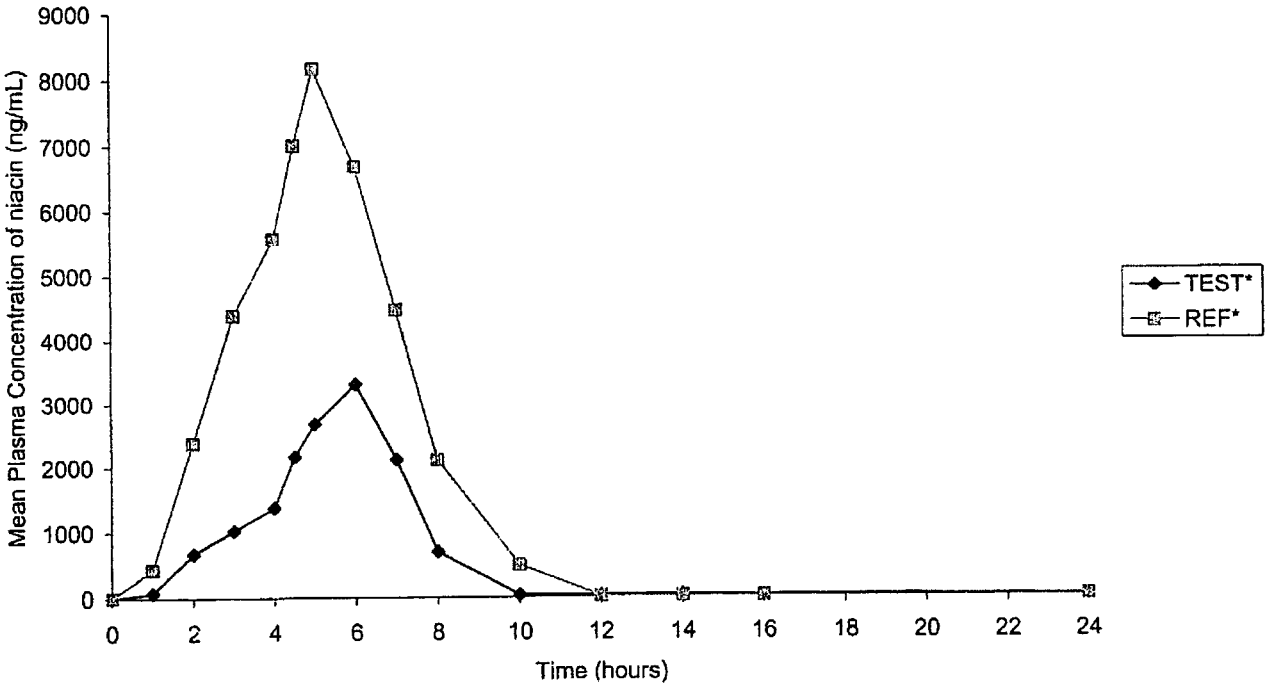


FIGURE 10

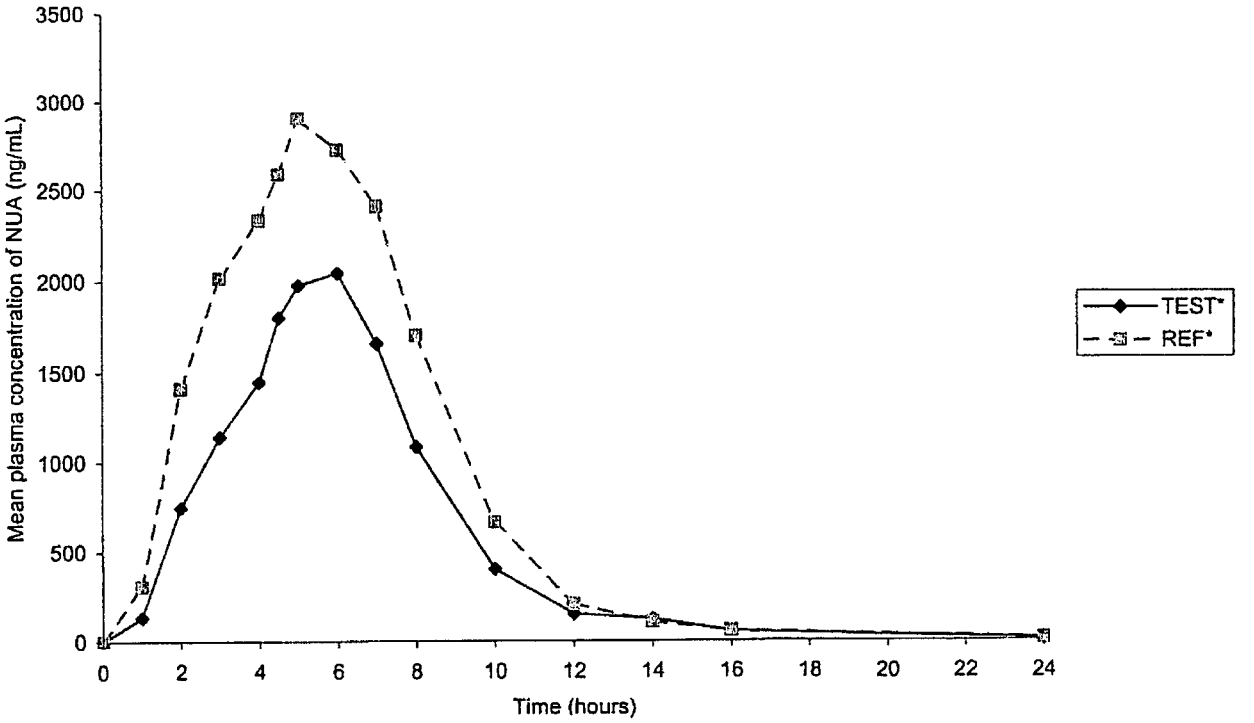
Mean Plasma Concentration of Niacin Against Time after Dosing by Treatment



*TEST: 2 X 1000 mg, reformulated extended-release niacin tablets; REF: 2 X 1000 mg NIASPAN® tablets.

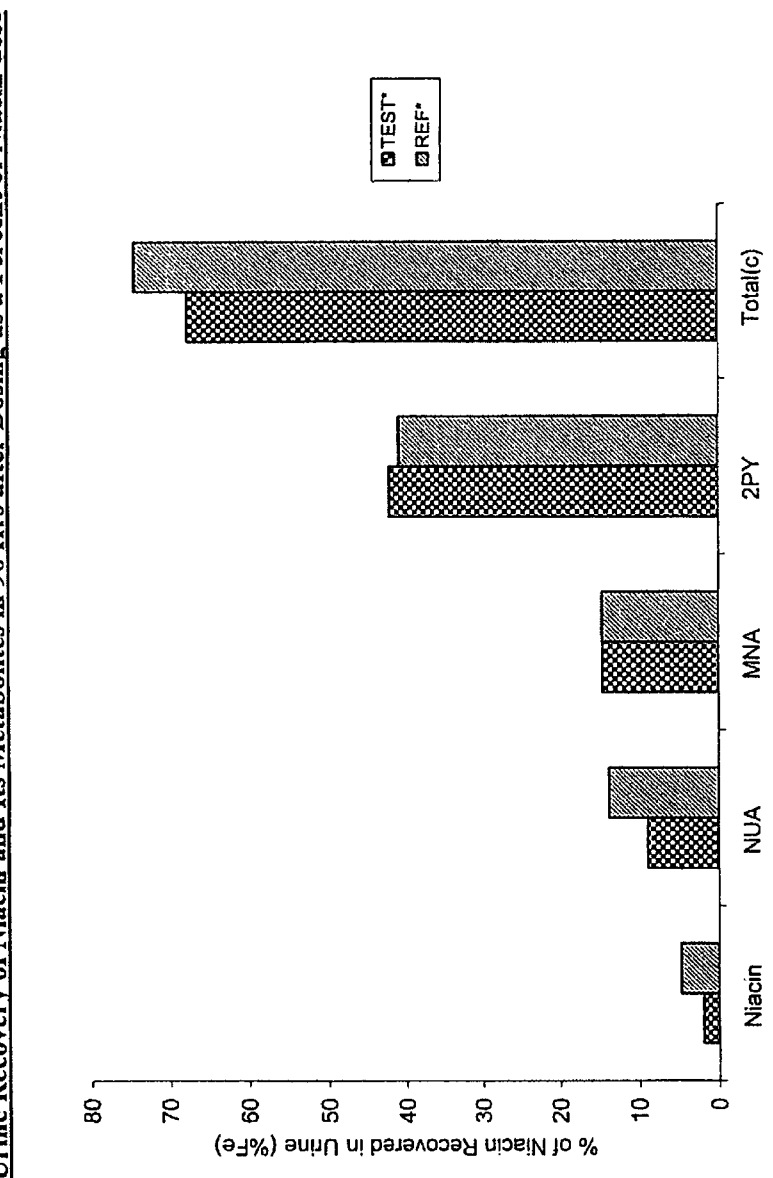
FIGURE 11

Mean Plasma Concentration of NUA Against Time after Dosing by Treatment



*TEST: 2 X 1000 mg, reformulated extended-release niacin tablets; REF: 2 X 1000 mg NIASPAN® tablets.

FIGURE 12



TEST: 2 X 1000 mg, reformulated extended-release niacin tablets; REF: 2 X 1000 mg NIASPAN® tablets.

FIGURE 13

Mean Plasma Niacin Profiles (Linear and Semi-log)

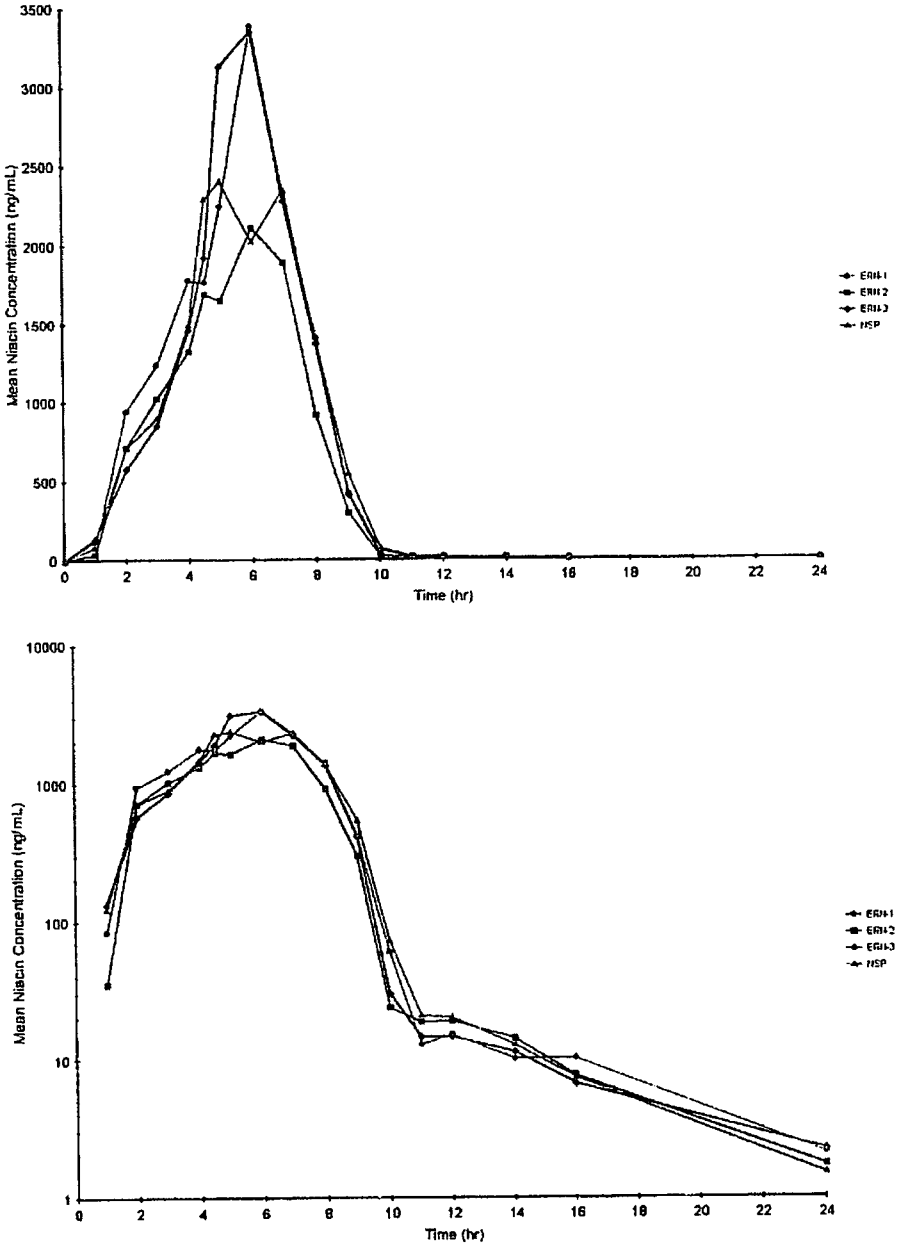


FIGURE 14

Mean Plasma NUA Profiles (Linear and Semi-log)

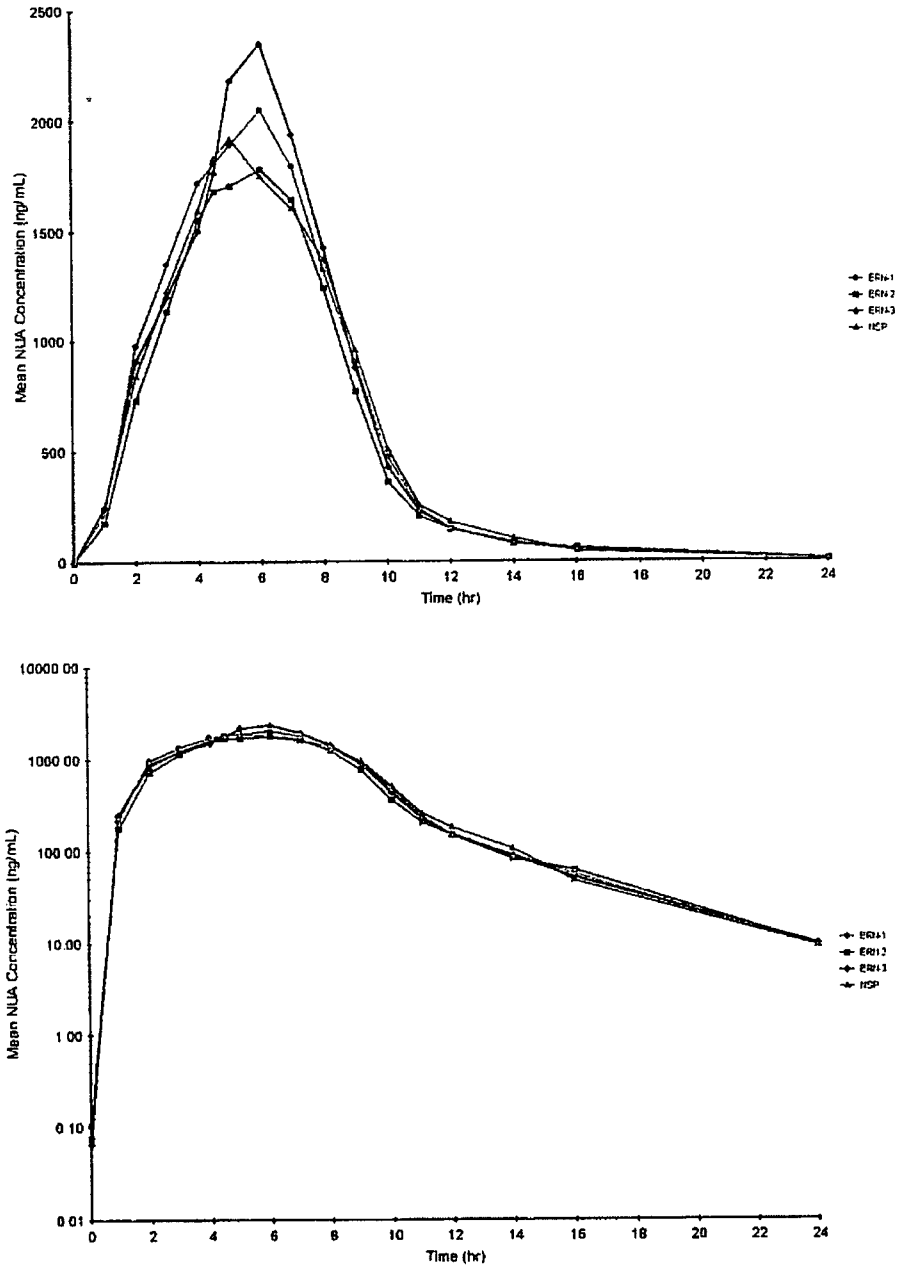


FIGURE 15

Mean Urinary Recovery as Percent of Niacin Dose

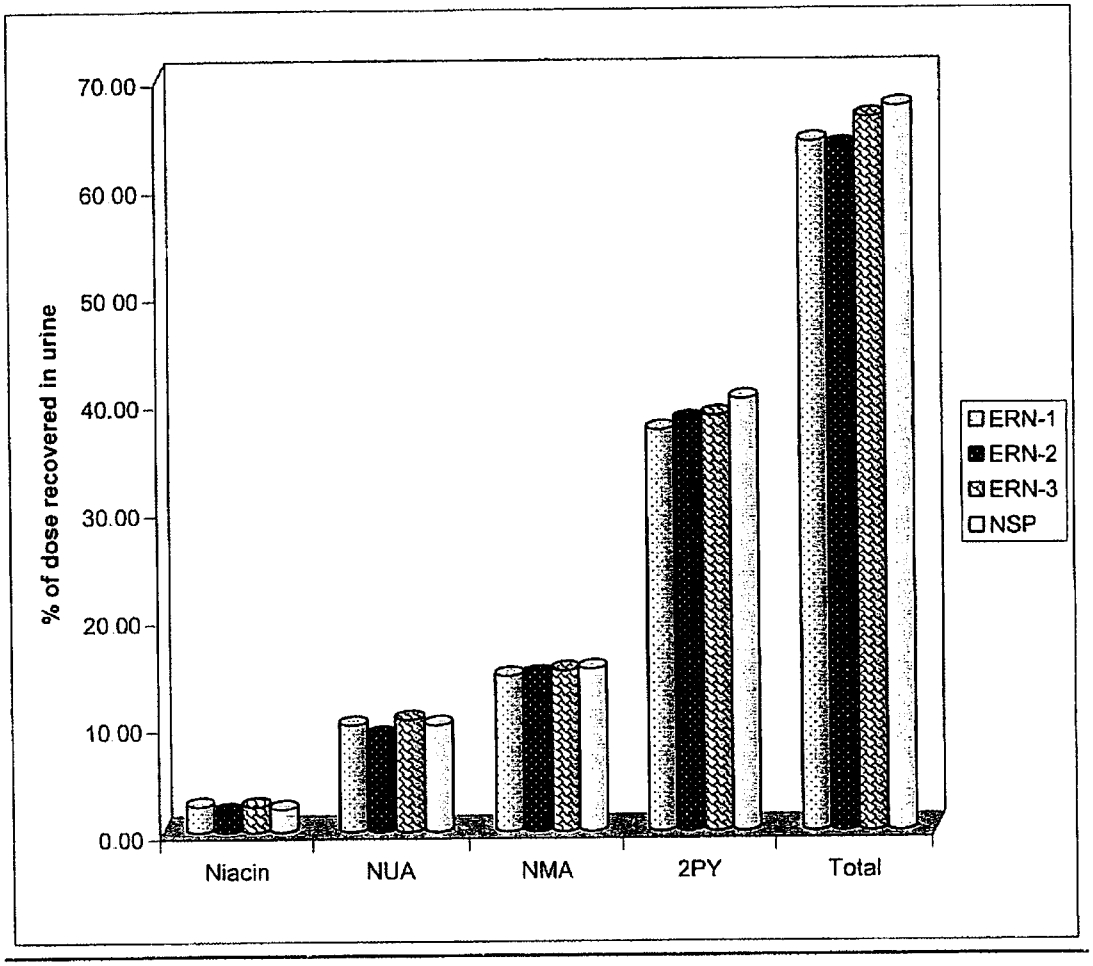
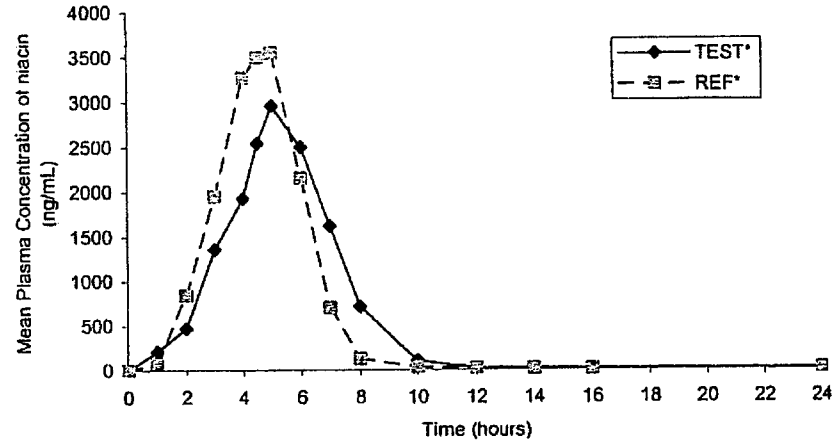
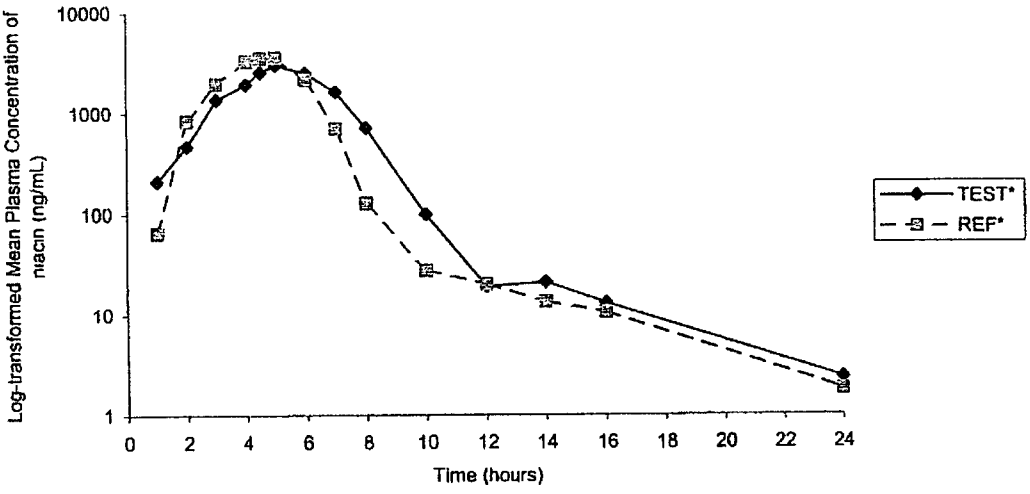


FIGURE 16

Mean Plasma Concentration (upper Figure) and Log-transformed Mean Plasma Concentration (lower Figure) of Niacin against Time after Dosing by Treatment

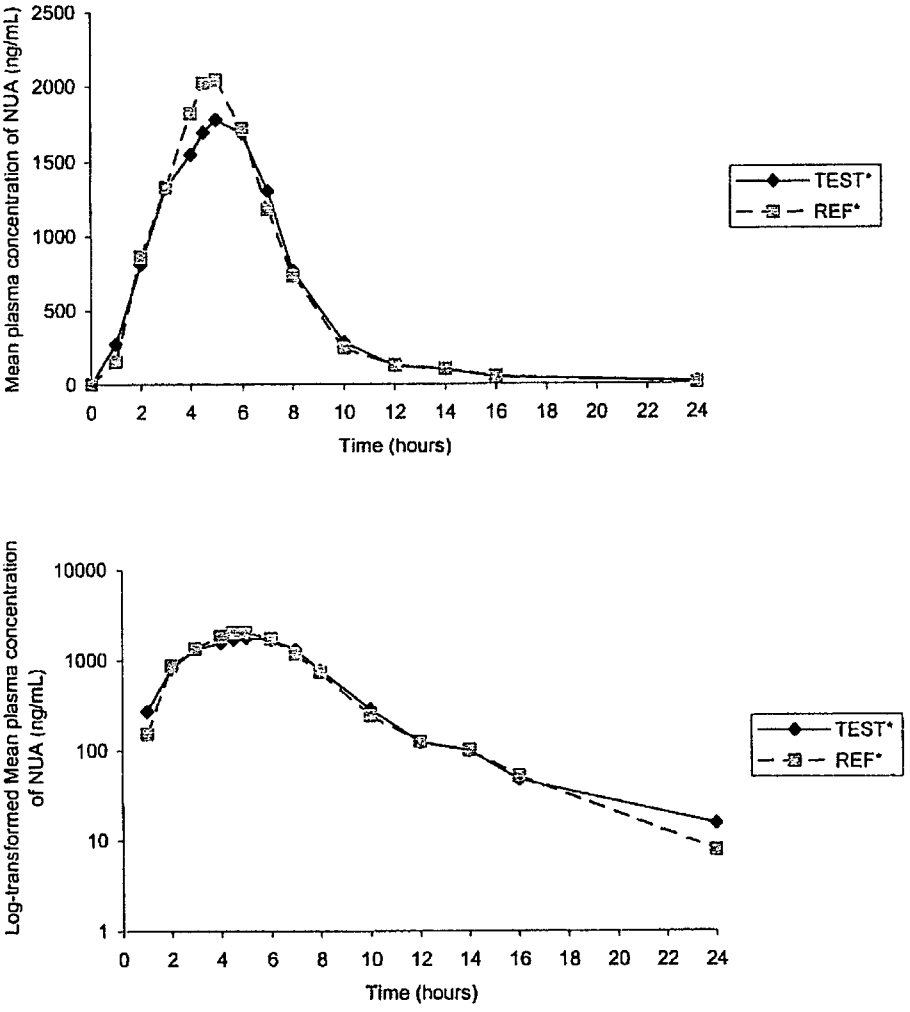




*TEST: 2 X 1000 mg coated, reformulated extended-release niacin tablets; REF: 2 X 1000 mg uncoated, reformulated extended-release niacin tablets.

FIGURE 17

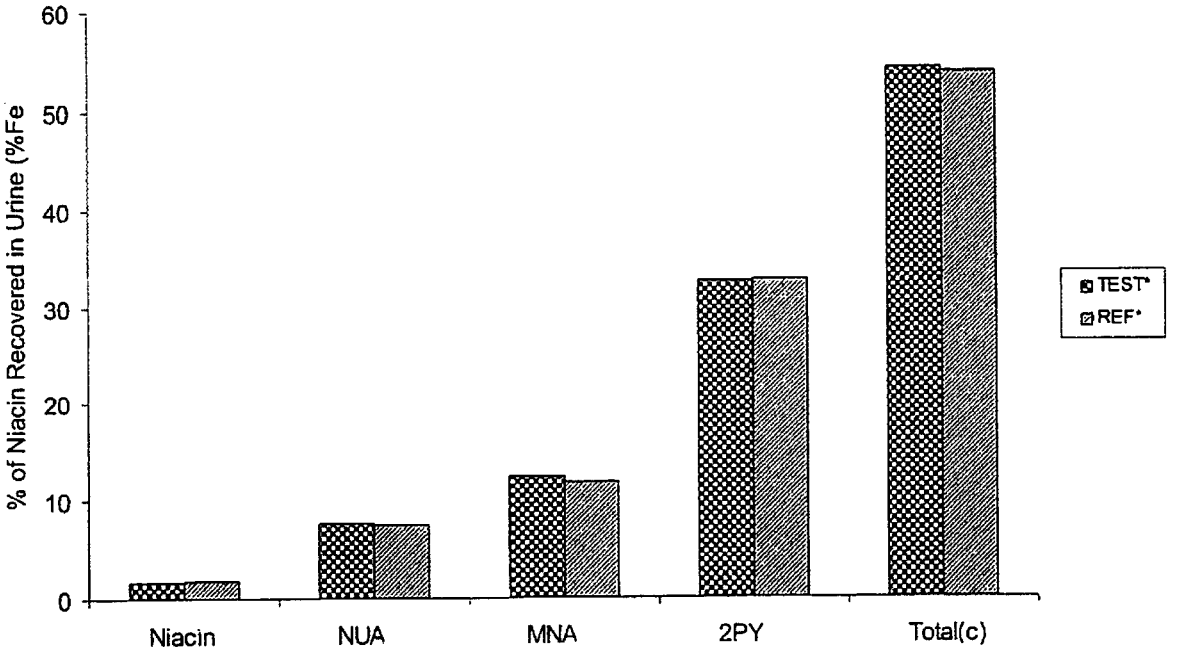
Mean Plasma Concentration (upper Figure) and Log-transformed Mean Plasma Concentration (lower Figure) of NUA against Time after Dosing by Treatment



* TEST: 2 X 1000 mg coated, reformulated extended-release niacin tablets; REF: 2 X 1000 mg uncoated, reformulated extended-release niacin tablets.

FIGURE 18

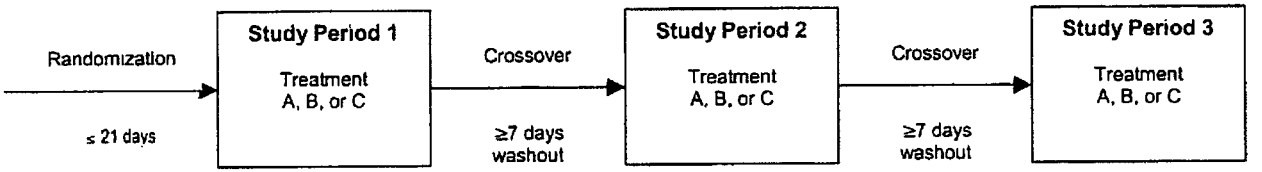
Mean Urine Recovery of Niacin and Its Metabolites in 96 Hrs after Dosing as a Percent of Niacin Dose



*TEST: 2 X 1000 mg coated, reformulated extended-release niacin tablets; REF: 2 X 1000 mg uncoated, reformulated extended-release niacin tablets.

FIGURE 19

Example 6 Study Design



		Pretreatment	Treatment
A = ASA Pretreatment	=	2 x aspirin 325 mg tablets	2 x reformulated niacin ER 1000 mg tablets + 2 x placebo tablets
B = Concomitant ASA	=	2 x placebo tablets	2 x reformulated niacin ER 1000 mg tablets + 2 x aspirin 325 mg tablets
C = R-Niacin ER Alone	=	2 x placebo tablets	2 x reformulated niacin ER 1000 mg tablets + 2 x placebo tablets

FIGURE 20

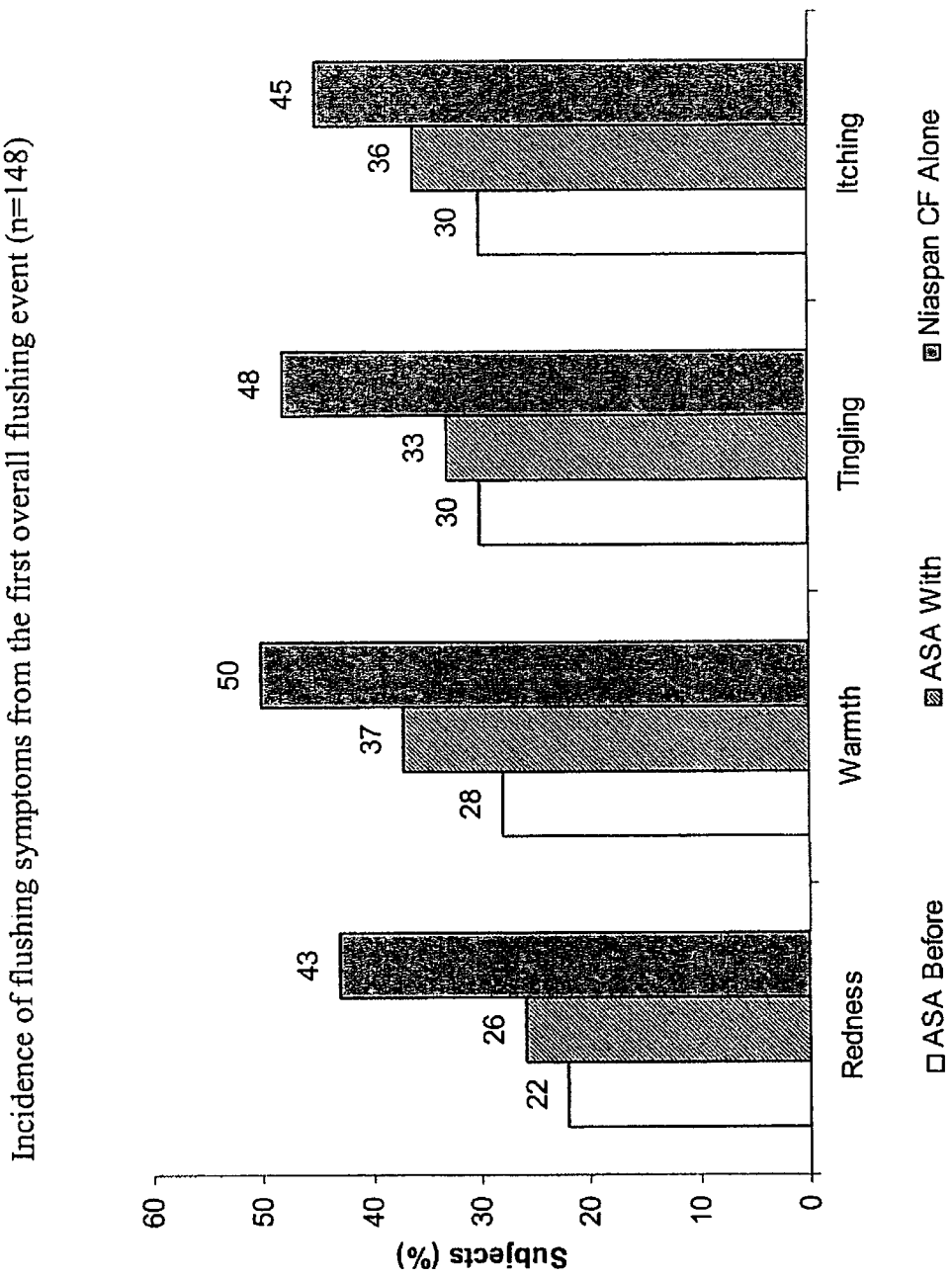

Incidence of flushing symptoms from the first overall flushing event (n=148)
Subjects (%)
60
50
40
30
20
10
0
22
26
43
28
37
50
30
33
48
30
36
45
Redness
Warmth
Tingling
Itching
ASA Before
ASA With
Niaspan CF Alone

FIGURE 21

Incidence of flushing events in two flush provocation studies
(rNER = Reformulated Niacin ER –Example 3)

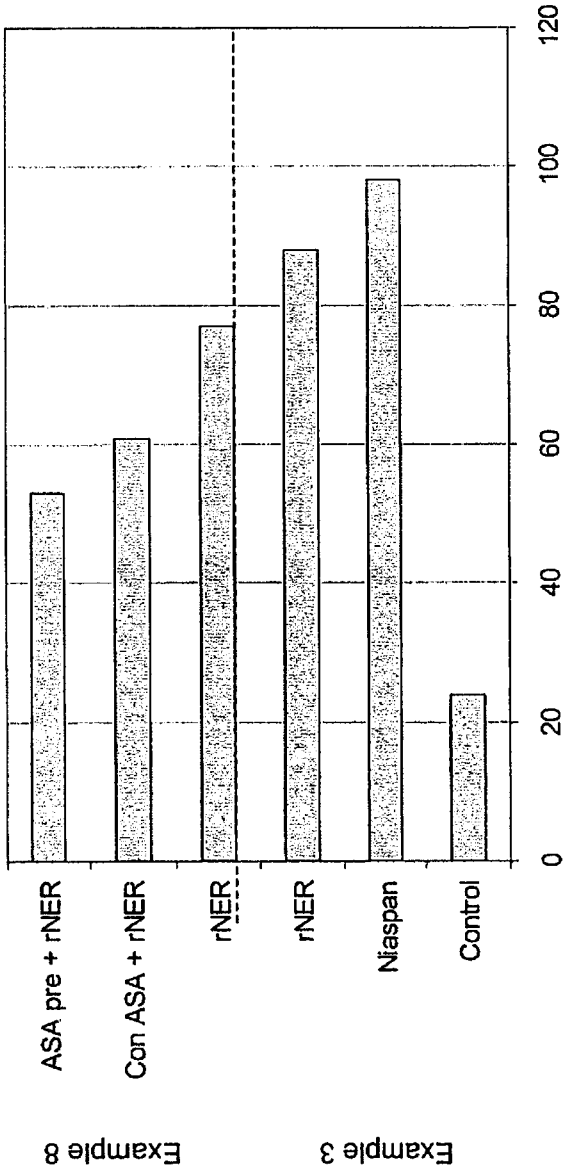


FIGURE 22

Intensity of flushing events in two flush provocation studies
(rNER = Reformulated Niacin ER: Example 3)

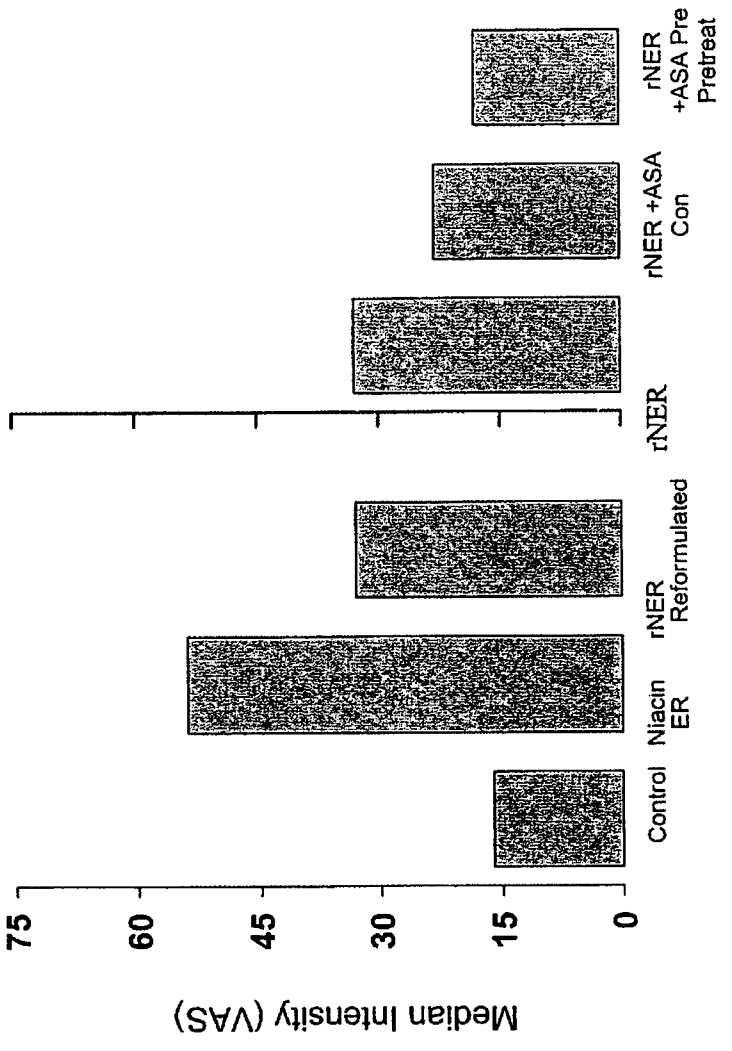


FIGURE 23