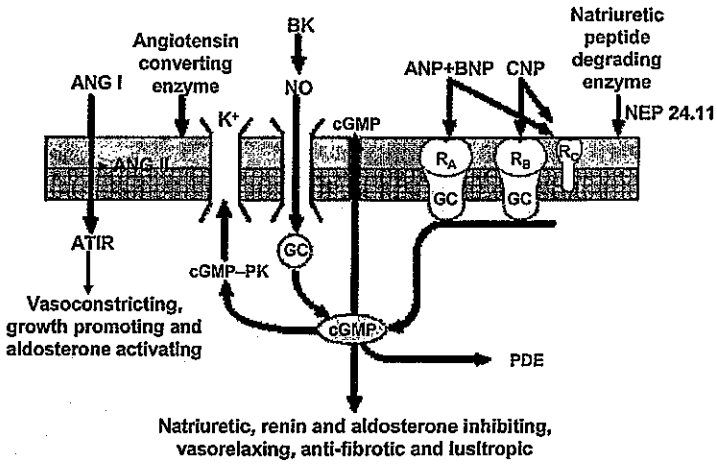

BK
Angiotensin converting enzyme
Natriuretic peptide degrading enzyme
ANG I
NO
ANP+BNP
CNP
NEP 24.11
K+
cGMP
ANG II
R_A
R_B
R_C
GC
GC
ATIR
GC
cGMP-PK
Vasoconstricting, growth promoting and aldosterone activating
cGMP
PDE
Natriuretic, renin and aldosterone inhibiting, vasorelaxing, anti-fibrotic and lusitropic

Figure 1

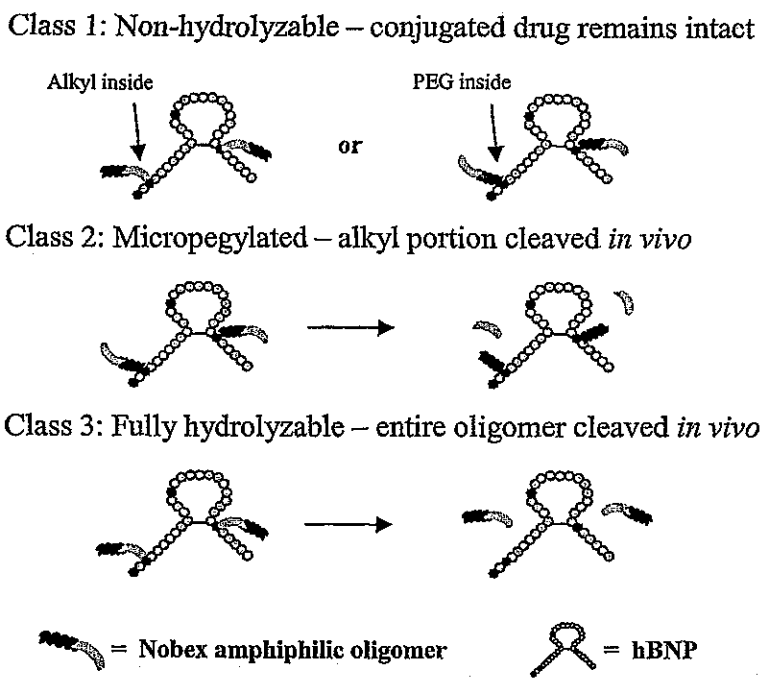

Class 1: Non-hydrolyzable – conjugated drug remains intact
Alkyl inside
PEG inside
or
Class 2: Micropegylated – alkyl portion cleaved *in vivo*
Class 3: Fully hydrolyzable – entire oligomer cleaved *in vivo*
= Nobex amphiphilic oligomer
= hBNP

Figure 2

Figure 3:

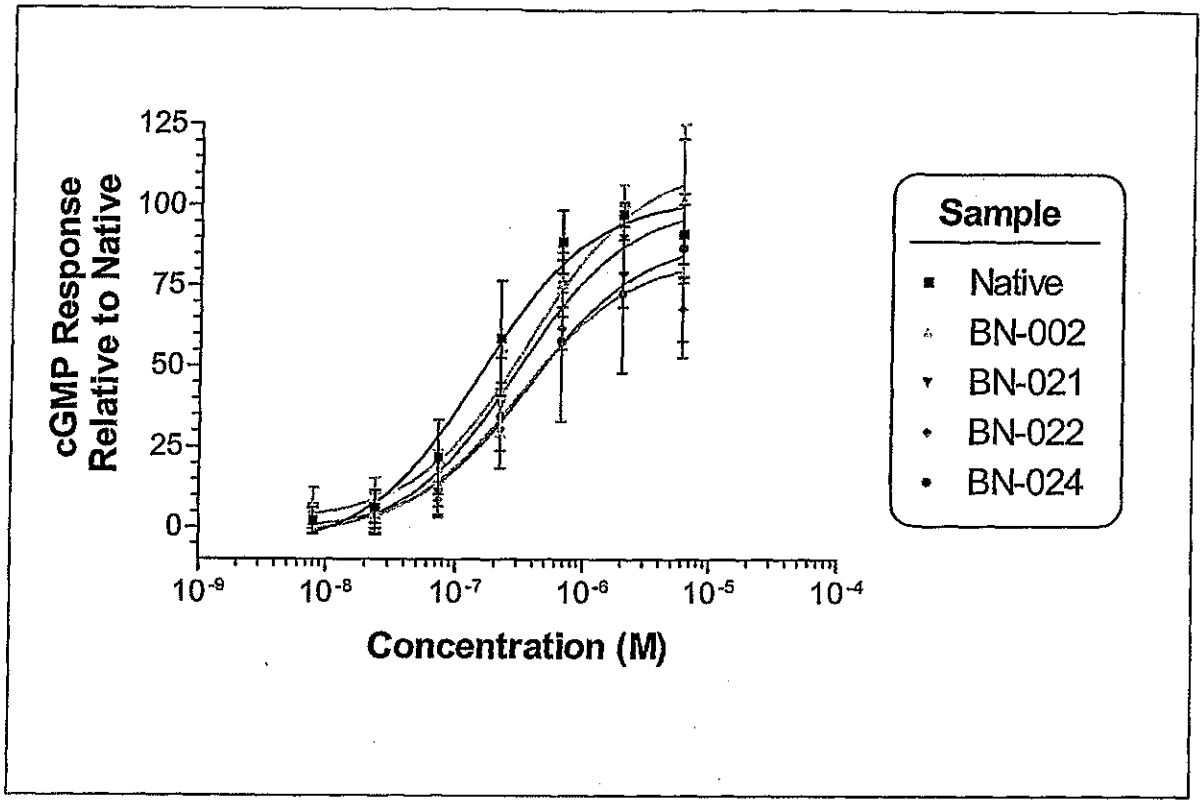

cGMP Response Relative to Native
125
100
75
50
25
0
10^{-9}
10^{-8}
10^{-7}
10^{-6}
10^{-5}
10^{-4}
Concentration (M)
Sample
Native
BN-002
BN-021
BN-022
BN-024

Figure 4:

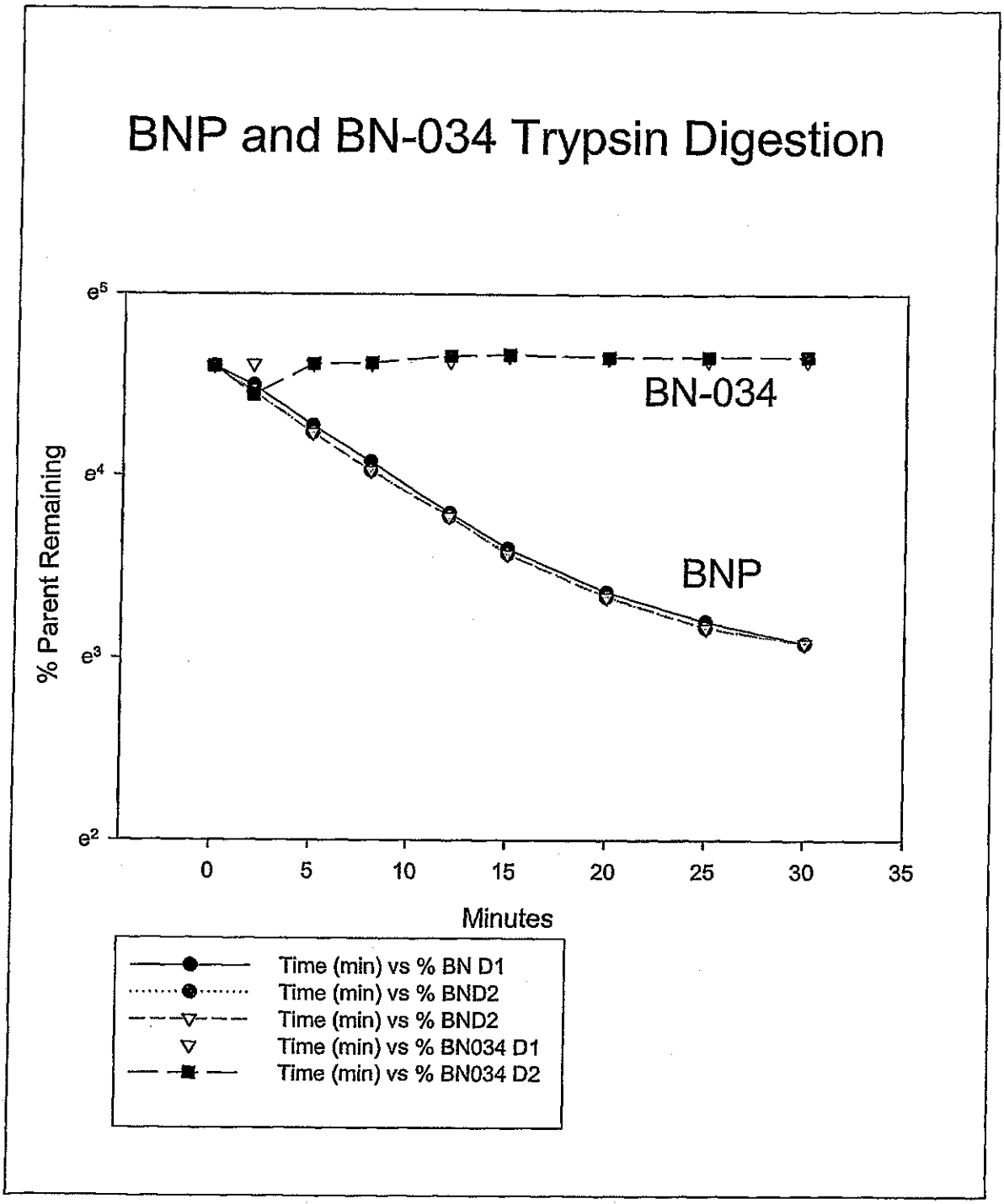
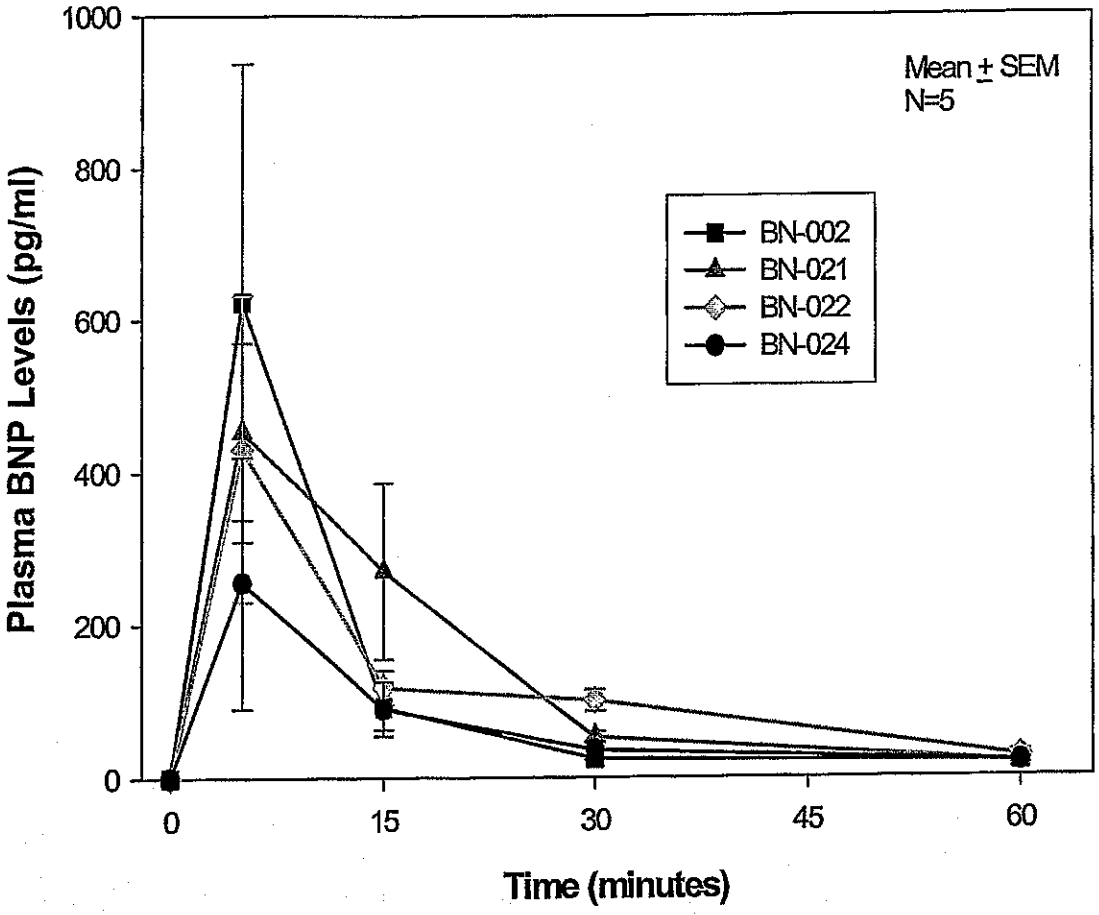

BNP and BN-034 Trypsin Digestion
% Parent Remaining
e5
e4
e3
e2
BN-034
BNP
0
5
10
15
20
25
30
35
Minutes
Time (min) vs % BN D1
Time (min) vs % BND2
Time (min) vs % BND2
Time (min) vs % BN034 D1
Time (min) vs % BN034 D2

Figure 5:

Figure 5: Plasma levels of hBNP conjugates at various times after oral dosing.



NOBEX Corporation

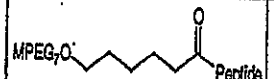
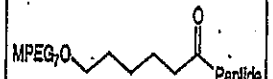
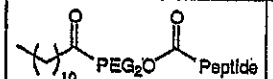
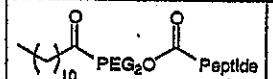
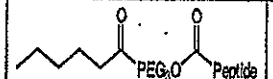
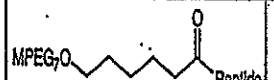
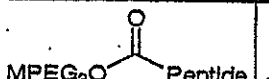
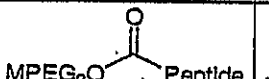
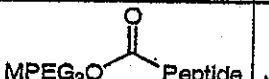
NOBEX Number	Oligomer Structure	#of Oligomers	Average EC50	Standard Deviation	Average Emax	Standard Deviation	Hydrolyzable	n=
Native BNP Lot UCB 050703	N/A	N/A	2.35E-07	1.1E-07	100.0	0.0	N/A	44
BN-002		Mono-1	4.44E-07	3.0E-08	101.0	6.8	No	2
BN-002 Scaled Up		Mono-1	3.48E-07	2.29E-07	112.6	30.3	No	3
BN-003		Tri	>1.00E-05	N/A	<20.0	N/A	No	4
BN-004		Tetra	>1.00E-05	N/A	<20.0	N/A	No	2
BN-007		Tri	>1.00E-05	N/A	<20.0	N/A	Micropegylated	2
BN-008		Tetra	>1.00E-05	N/A	<20.0	N/A	Micropegylated	2
BN-010		Tetra	>1.00E-05	N/A	<20.0	N/A	Micropegylated	3
BN-011		Mono-2	1.11E-06	3.3E-07	71.2	21.2	No	2
BN-012		Di	1.71E-06	2.5E-07	60.8	19.2	No	2
BN-013		Tetra MPEG 3 of BN-010	>1.00E-05	N/A	<20.0	N/A	MPEG 3	3
BN-014		Tri MPEG 2 of BN-007	>1.00E-05	N/A	26.5	7.4	MPEG 2	2
BN-015		Tetra MPEG 2 of BN-008	>1.00E-05	N/A	<20.0	N/A	MPEG 2	2

FIG. 6A

NOBEX Corporation

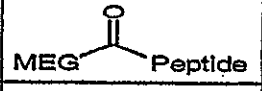
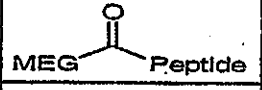
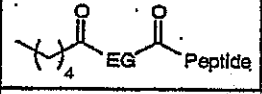
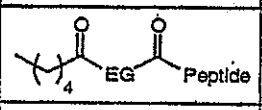
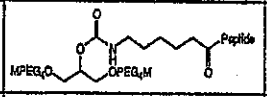
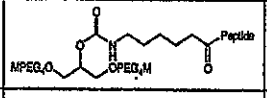
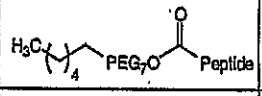
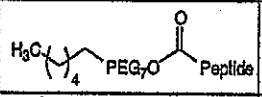
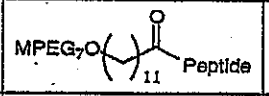
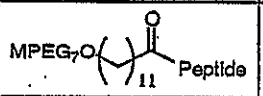
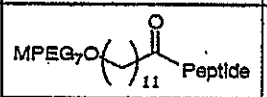
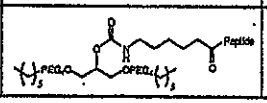
NOBEX Number	Oligomer Structure	#of Oligomers	Average EC50	Standard Deviation	Average Emax	Standard Deviation	Hydrolyzable	n=
BN-016		Tetra	>1.00E-05	N/A	24.6	6.5	MEG	2
BN-017		Penta	>1.00E-05	N/A	<20.0	N/A	MEG	1
BN-018		Tetra	>1.00E-05	N/A	<20.0	N/A	No	2
BN-019		Penta	>1.00E-05	N/A	<20.0	N/A	No	1
BN-021		Mono-1	3.69E-07	2.2E-07	91.8	1.9	No	2
BN-021 Scaled Up		Mono-1	3.45E-07	1.2E-07	90.1	0.0	No	3
BN-022		Mono-1	2.81E-07	8.1E-08	75.7	9.2	No	2
BN-022 Scaled Up		Mono-1	4.18E-07	7.03E-08	81.2	12.8	No	3
BN-024		Mono-1	3.21E-07	1.8E-07	106.2	42.7	No	2
BN-024 Scaled Up		Mono-1	3.14E-07	2.26E-07	57.8	12.2	No	3
BN-025		DI-1	>1.00E-05	N/A	43.6	3.0	No	2
BN-028		Mono-1	>1.00E-05	N/A	28.3	2.4	No	2

FIG. 6B

NOBEX Corporation

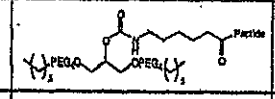
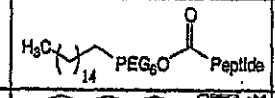
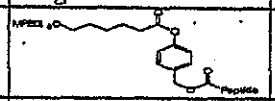
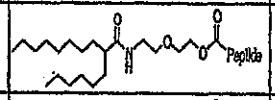
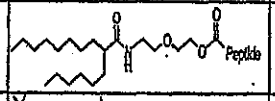
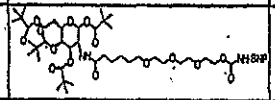
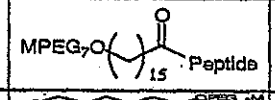
NOBEX Number	Oligomer Structure	#of Oligomers	Average EC50	Standard Deviation	Average Emax	Standard Deviation	Hydrolyzable	n=
BN-029		Mono-2	>1.00E-05	N/A	34.0	13.3	No	2
BN-030		Mono-2	1.26E-07	4.7E-08	53.6	5.6	No	2
BN-033		Mono-1/Mono-2 mixture	1.38E-07	#DIV/0!	81.1	#DIV/0!	Yes	1
BN-034		Di-mixture	2.75E-07	3.3E-07	23.9	8.4	Yes	2
BN-038		Di-mixture	2.24E-06	2.1E-06	62.3	31.0	Yes	2
BN-041		Mono-1	3.58E-07	1.8E-07	30.5	6.9	No	2
BN-042		Mono-4	1.46E-07	9.5E-08	37.9	12.2	No	3
BN-046		Mono-1/Mono-2 Mixture	2.45E-07	1.2E-07	60.5	23.6	No	3
BN-047		Mon0-1/Mono-2 Mixture	8.15E-07	5.5E-07	40.2	6.6	No	4
BN-048		Mono-1	6.31E-07	6.6E-09	98.3	9.3	Yes	2
BN-049		Mono-2	1.25E-06	1.5E-08	75.2	11.7	Yes	2
BN-050		Mono-1	1.71E-07	5.2E-08	94.4	22.9	No	3

FIG. 6C

NOBEX Corporation

NOBEX Number	Oligomer Structure	#of Oligomers	Average EC50	Standard Deviation	Average Emax	Standard Deviation	Hydrolyzable	n=
BN-050 (scale-up)		Mono-1	4.33E-07	1.5E-07	104.6	23.2	No	2
BN-051		Mono-1	5.55E-07	2.4E-07	106.2	16.6	No	3
BN-052		Mono-1/ Mono-2 Mixture	2.12E-07	1.0E-08	60.1	7.4	No	2
BN-053		Mono-1	2.65E-07	7.39E-08	99.0	8.6	No	3

FIG. 6D

Chromatograph showing preparative run for BN-54

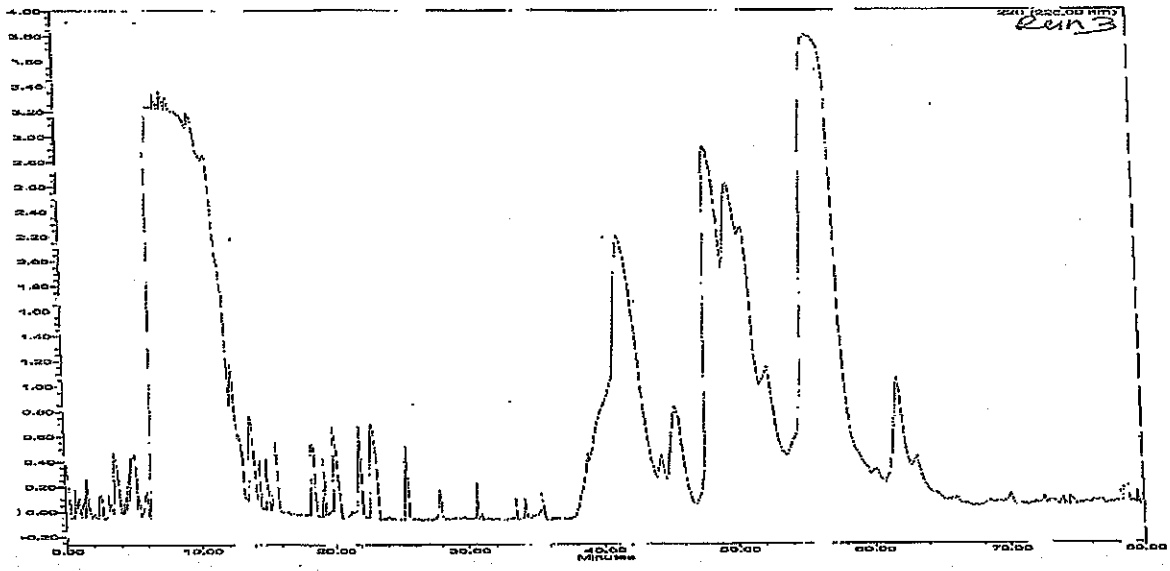


Figure 7

Chromatogram of BNP Standard

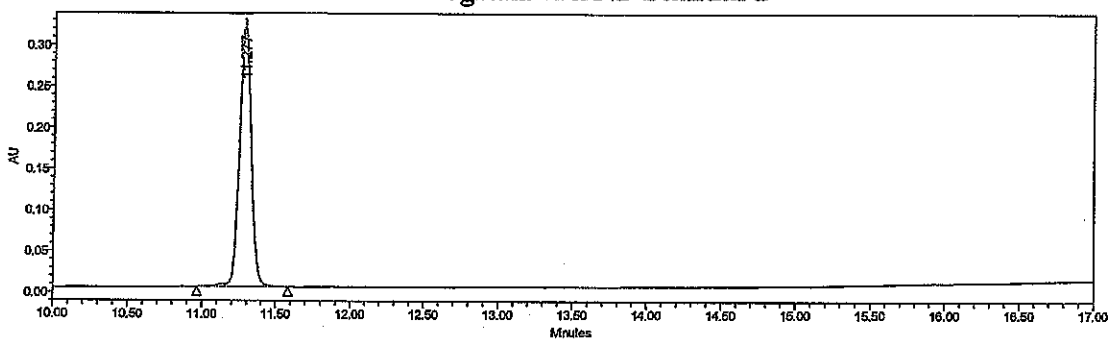


Figure 8

Chromatogram of Nobex-BN054
Protein Content 74.8%

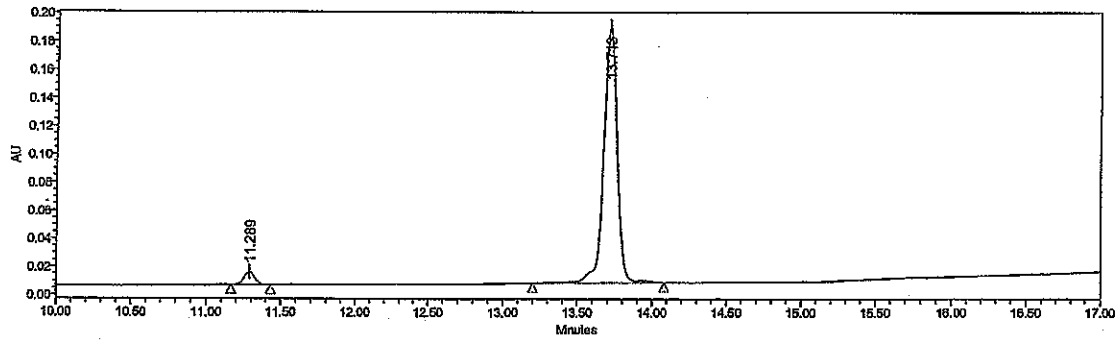


Figure 9

Chromatogram of Nobex-BN054
Protein Content 73.4%

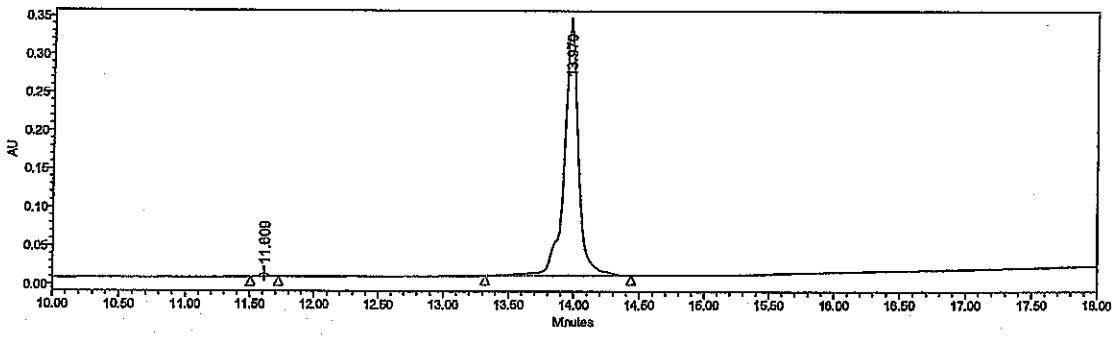


Figure 10