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FIGURE 1 Amount of Oxidized IGF-1

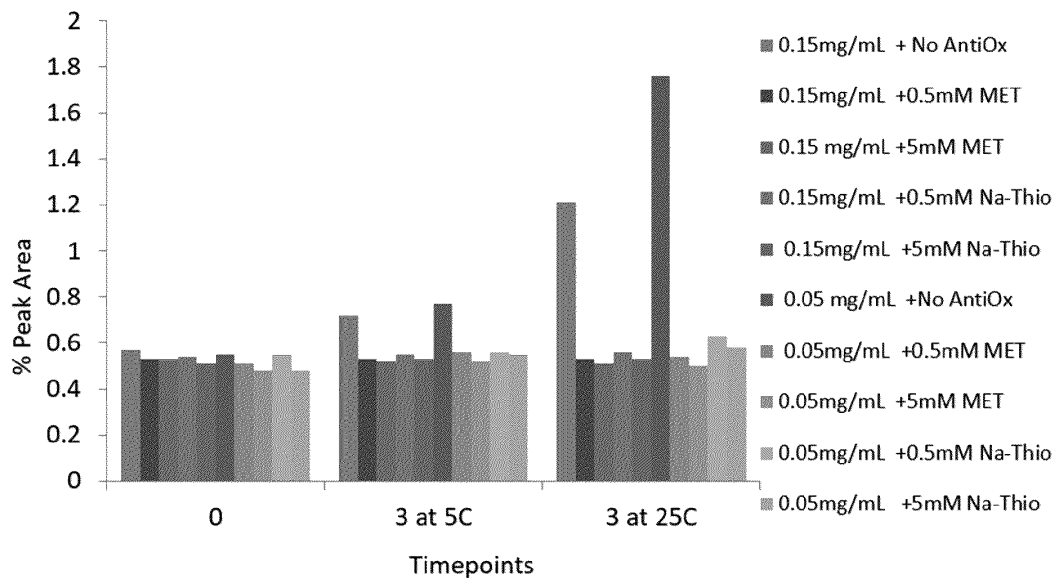


FIGURE 2 Amount of IGFBP-3

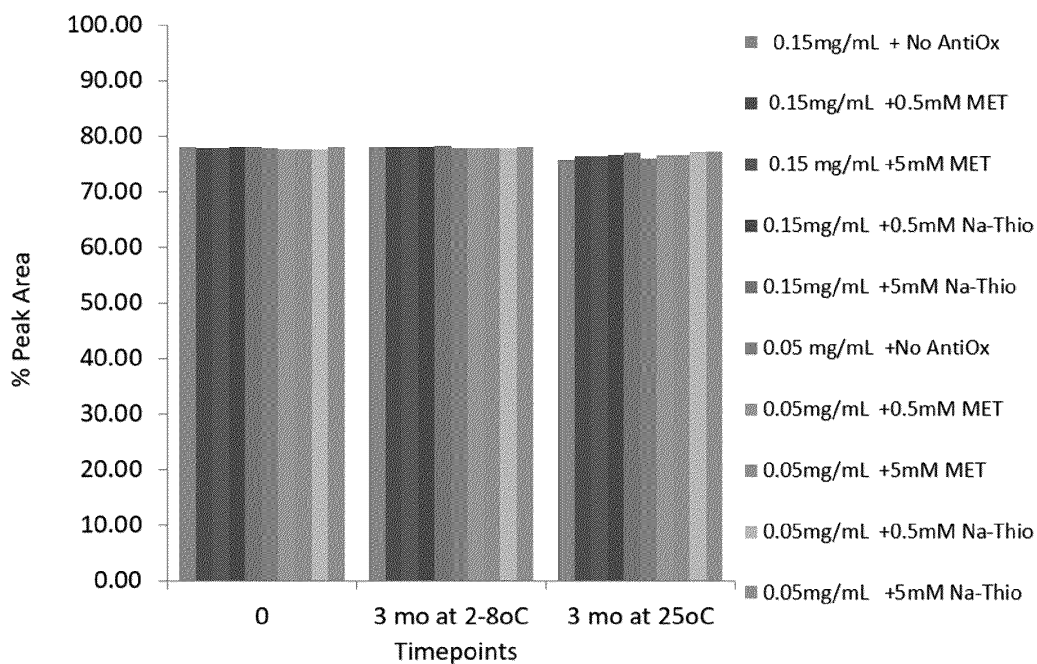


FIGURE 3 Amount of IGF-1

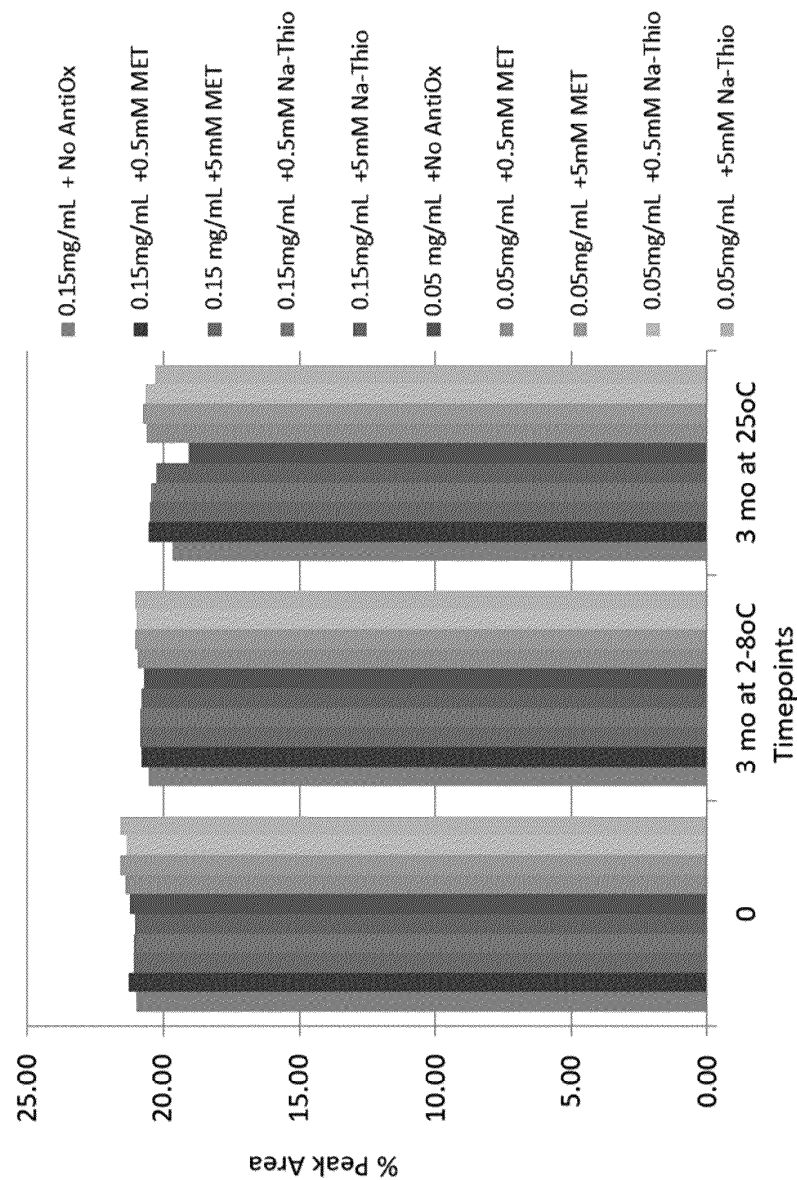


FIGURE 4A ΔOxidized IGF-1

FIGUR E 4B ΔOxidized IGF-1

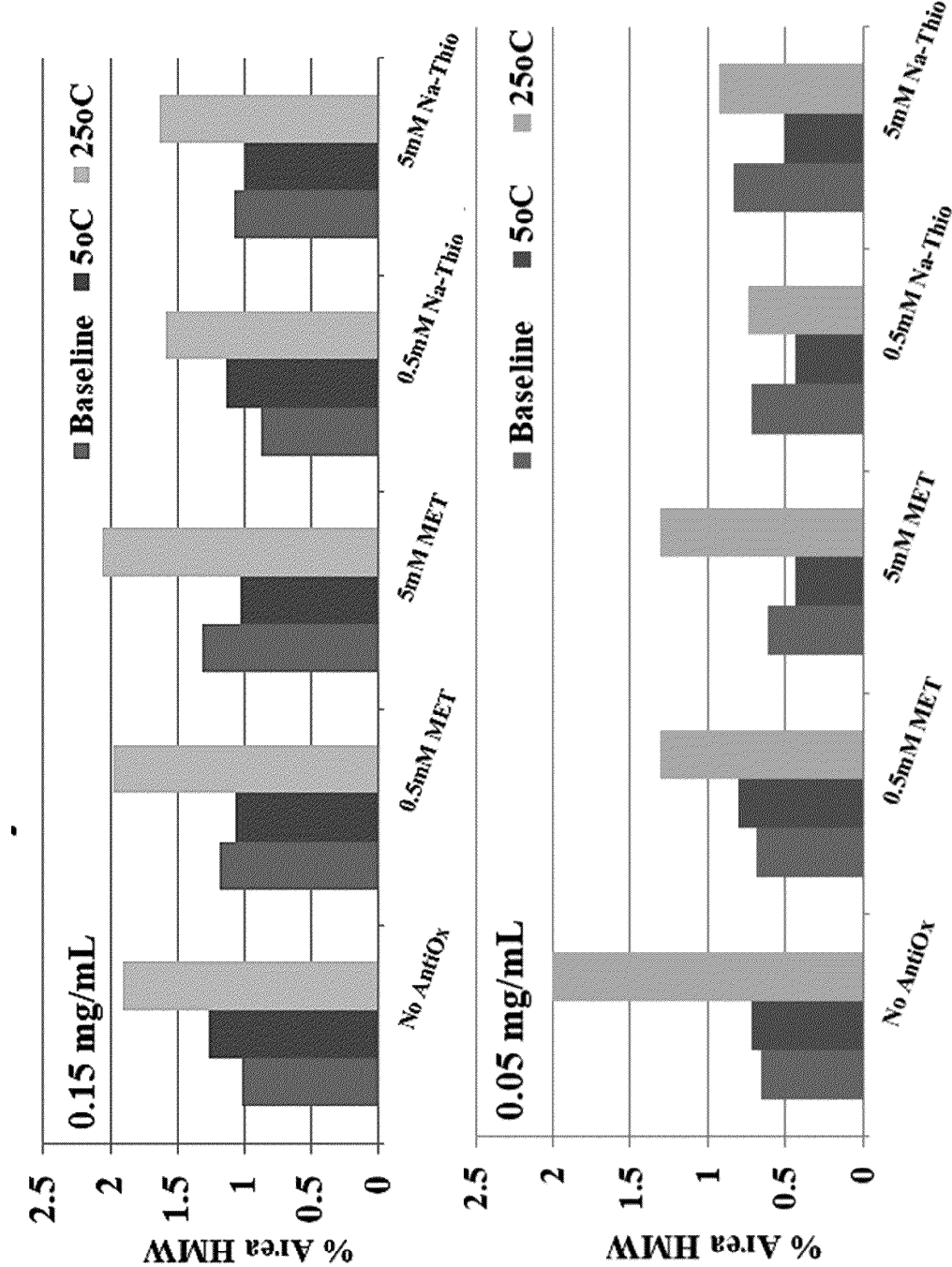


FIGURE 5A ΔAmount IGF-1

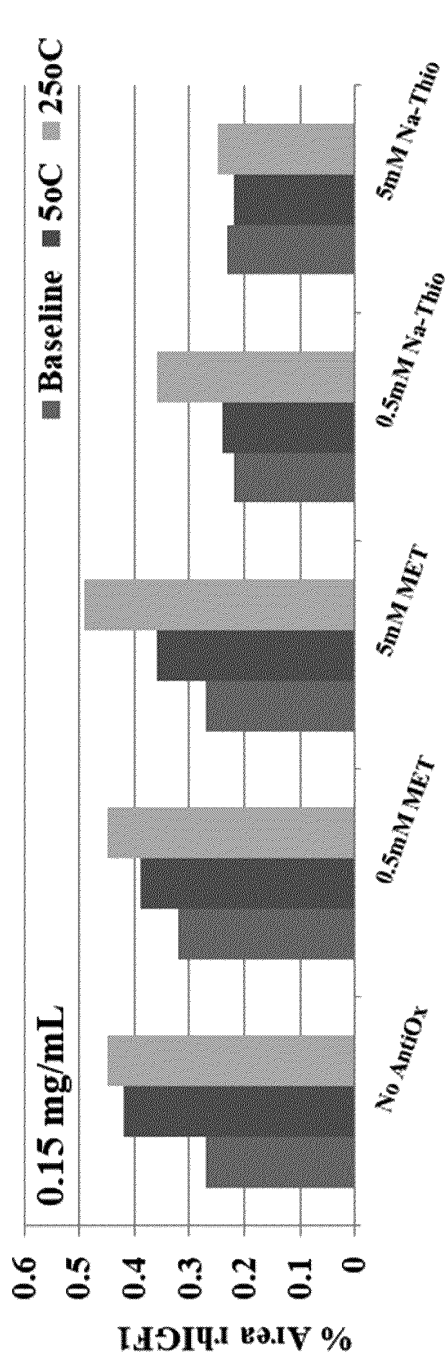
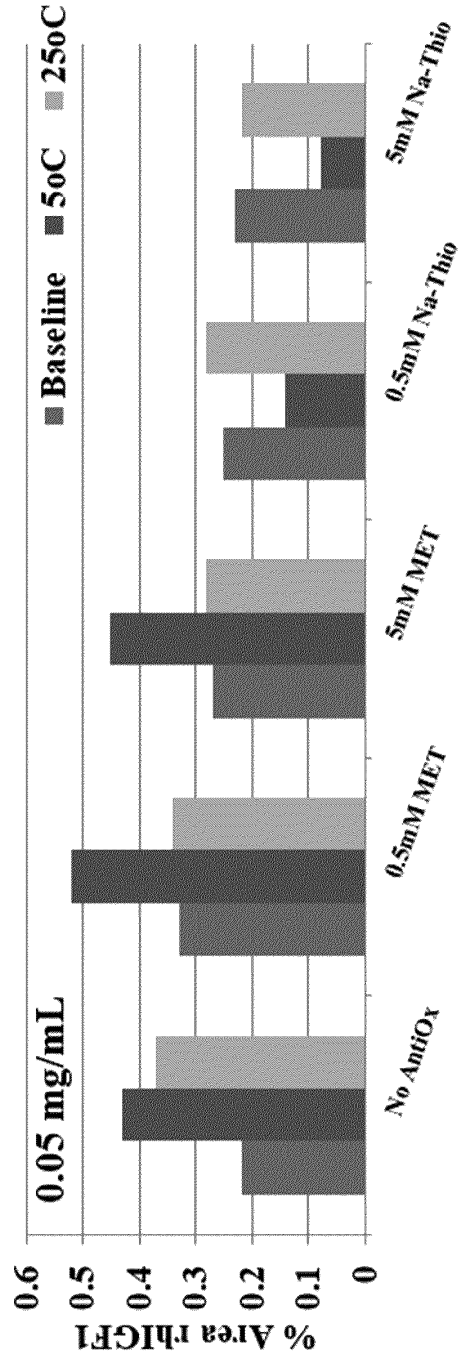


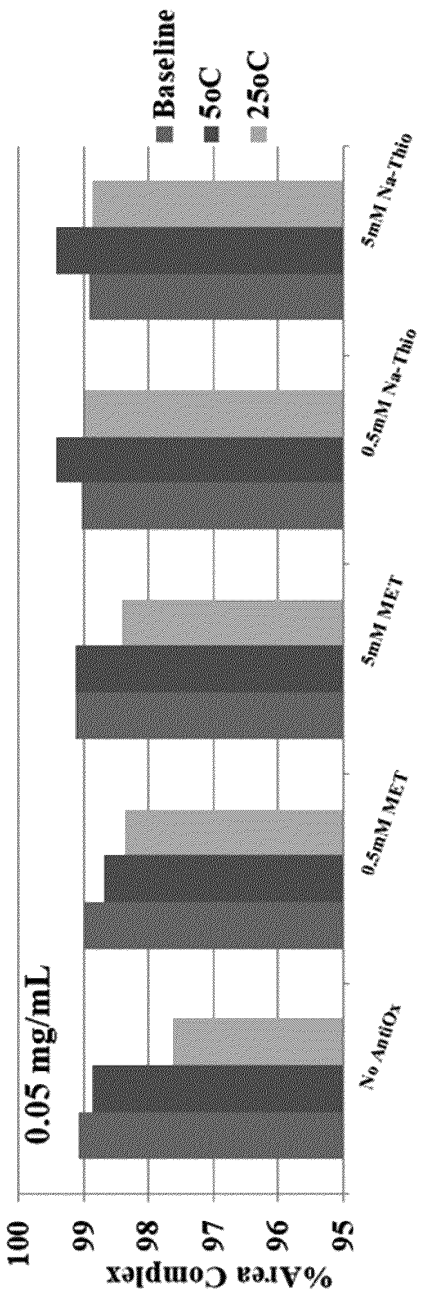
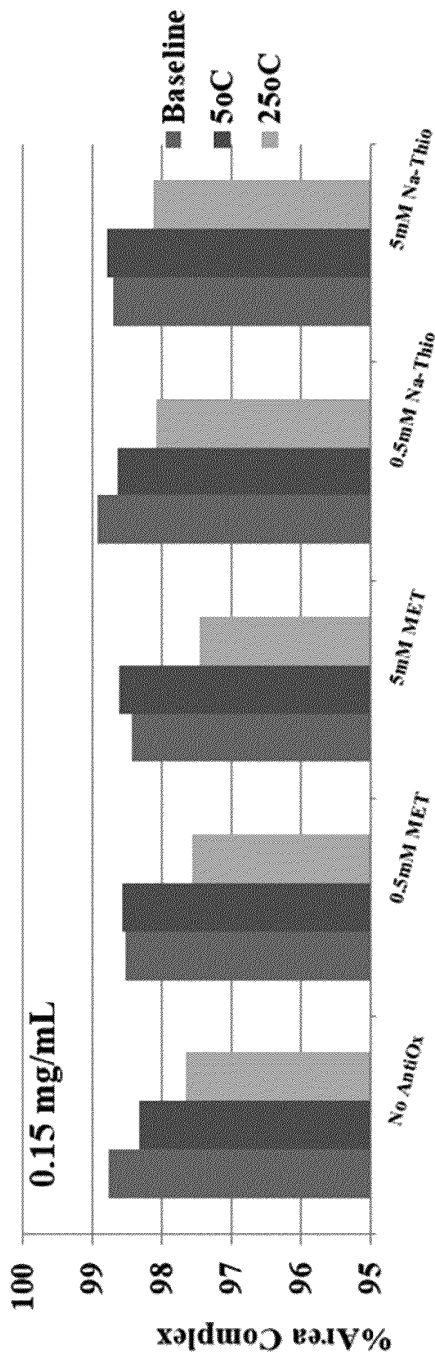
FIGURE 5B ΔAmount IGF-1



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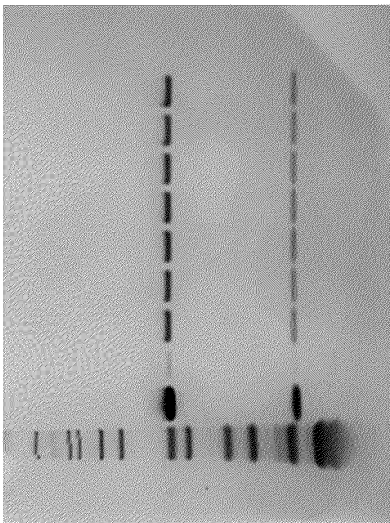
FIGURE 6A Δ Amount IGFBP-3

FIGURE 6B Δ Amount IGFBP-3



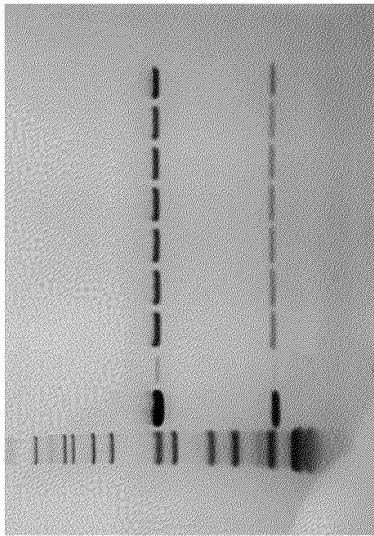
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FIGURE 7A



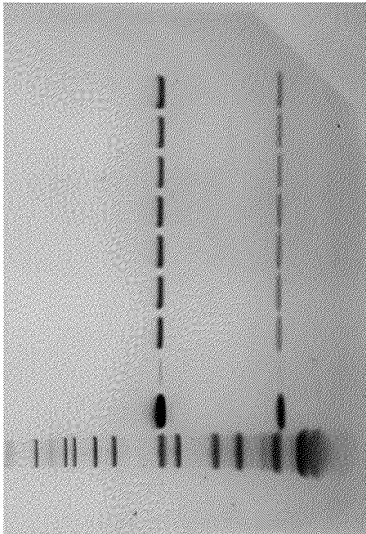
Lanes	Load (µg)
1	Blank
2	Mark 12 Standard
3	Complex Reference Standard (DS)
4	1% Intensity Marker
5	150 µg/mL Control 5°C Sarstedt tube
6	150 µg/mL No Antioxidant
7	150 µg/mL +0.5mM L-Met
8	150 µg/mL +5mM L-Met
9	150 µg/mL +0.5mM Na-Thio
10	150 µg/mL 5mM Na-Thio
11	150µg/mL Control -65°C Sarstedt tube
12	Blank

FIGURE 7B



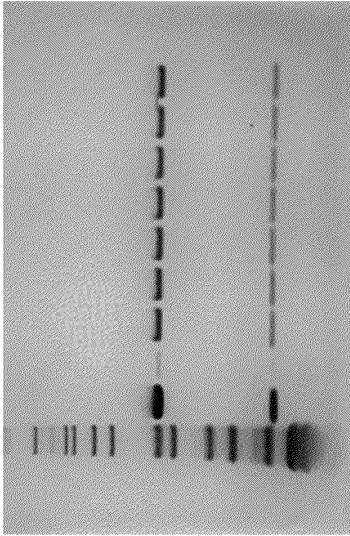
Lanes	Load (µg)
1	Blank
2	Mark 12 Standard
3	Complex Reference Standard (DS)
4	1% Intensity Marker
5	50 µg/mL Control 5°C Sarstedt tube
6	50 µg/mL No Antioxidant
7	50 µg/mL +0.5mM L-Met
8	50 µg/mL +5mM L-Met
9	50 µg/mL +0.5mM Na-Thio
10	50 µg/mL 5mM Na-Thio
11	50µg/mL Control -65°C Sarstedt tube
12	Blank

FIGURE 7C



Lanes	Blank	Load (µg)
1	Blank	
2	Mark 12 Standard	
3	Complex Reference Standard (DS)	6.0
4	1% Intensity Marker	0.06
5	150 µg/mL Control 5°C Sarstedt tube	0.65
6	150 µg/mL No Antioxidant	0.65
7	150 µg/mL +0.5mM L-Met	0.65
8	150 µg/mL +5mM L-Met	0.65
9	150 µg/mL +0.5mM Na-Thio	0.65
10	150 µg/mL 5mM Na-Thio	0.65
11	150µg/mL Control -65°C Sarstedt tube	0.65
12	Blank	

FIGURE 7D



Lanes	Blank	Load (µg)
1	Blank	
2	Mark 12 Standard	
3	Complex Reference Standard (DS)	6.0
4	1% Intensity Marker	0.06
5	50 µg/mL Control 5°C Sarstedt tube	0.65
6	50 µg/mL No Antioxidant	0.65
7	50 µg/mL +0.5mM L-Met	0.65
8	50 µg/mL +5mM L-Met	0.65
9	50 µg/mL +0.5mM Na-Thio	0.65
10	50 µg/mL 5mM Na-Thio	0.65
11	50µg/mL Control -65°C Sarstedt tube	0.65
12	Blank	

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FIGURE 8A Lyophilization

a. Temperature Profile

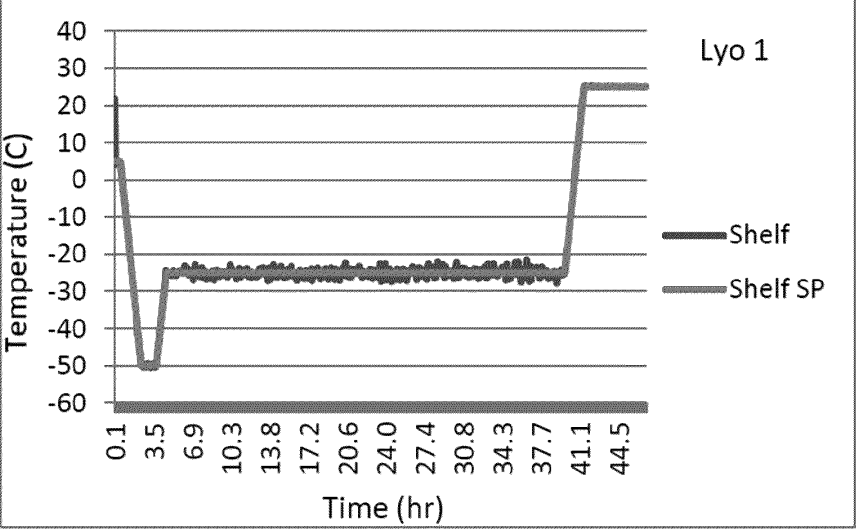
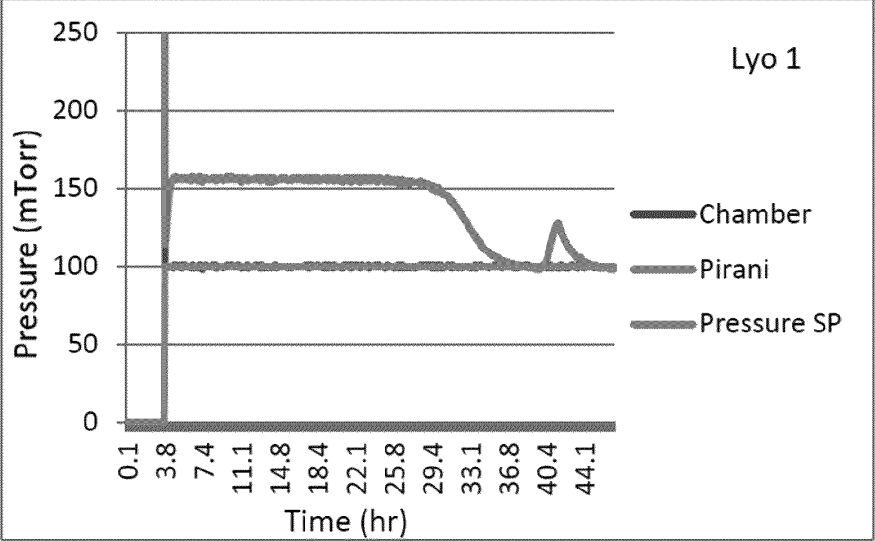


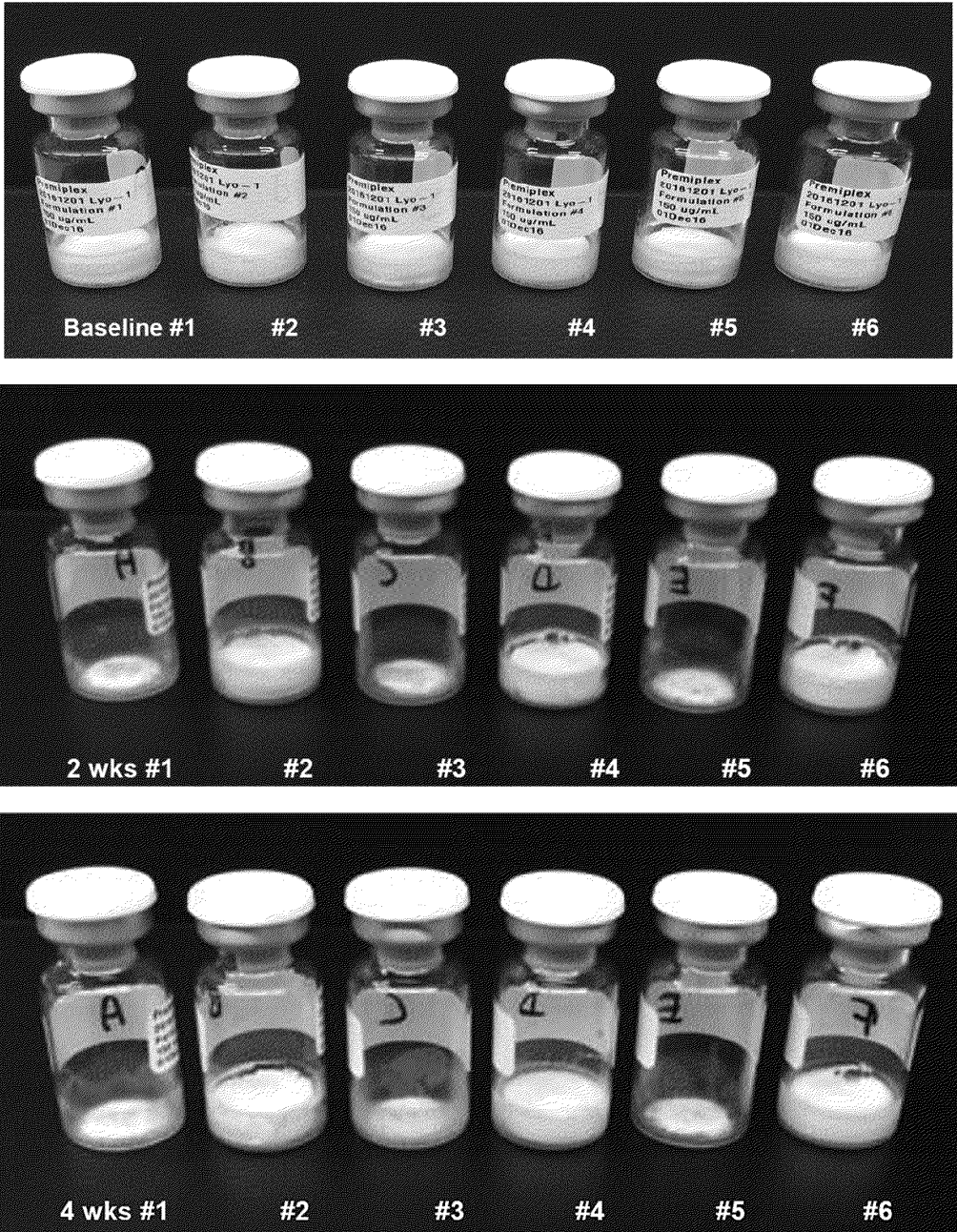
FIGURE 8B Lyophilization

b. Pressure Profile



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FIGURE 9 (A baseline; B 2 weeks at 60°C; C 4 weeks at 60°C)



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FIGURE 10A SE-UPLC for Lyophilization Run 1

a. Protein Complex rhIGF-1/rhIGFBP-3

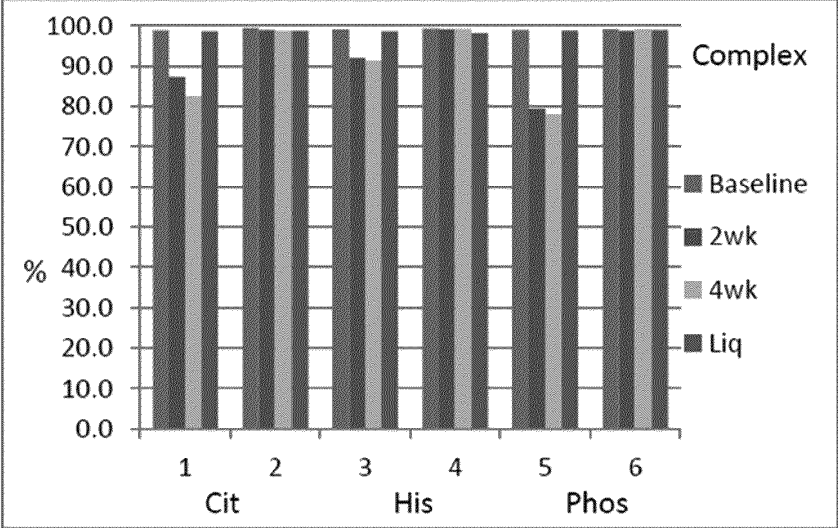
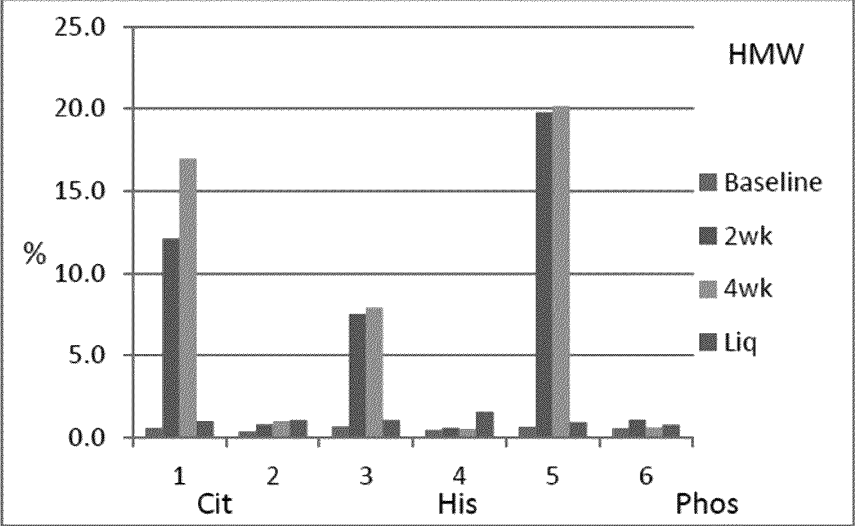


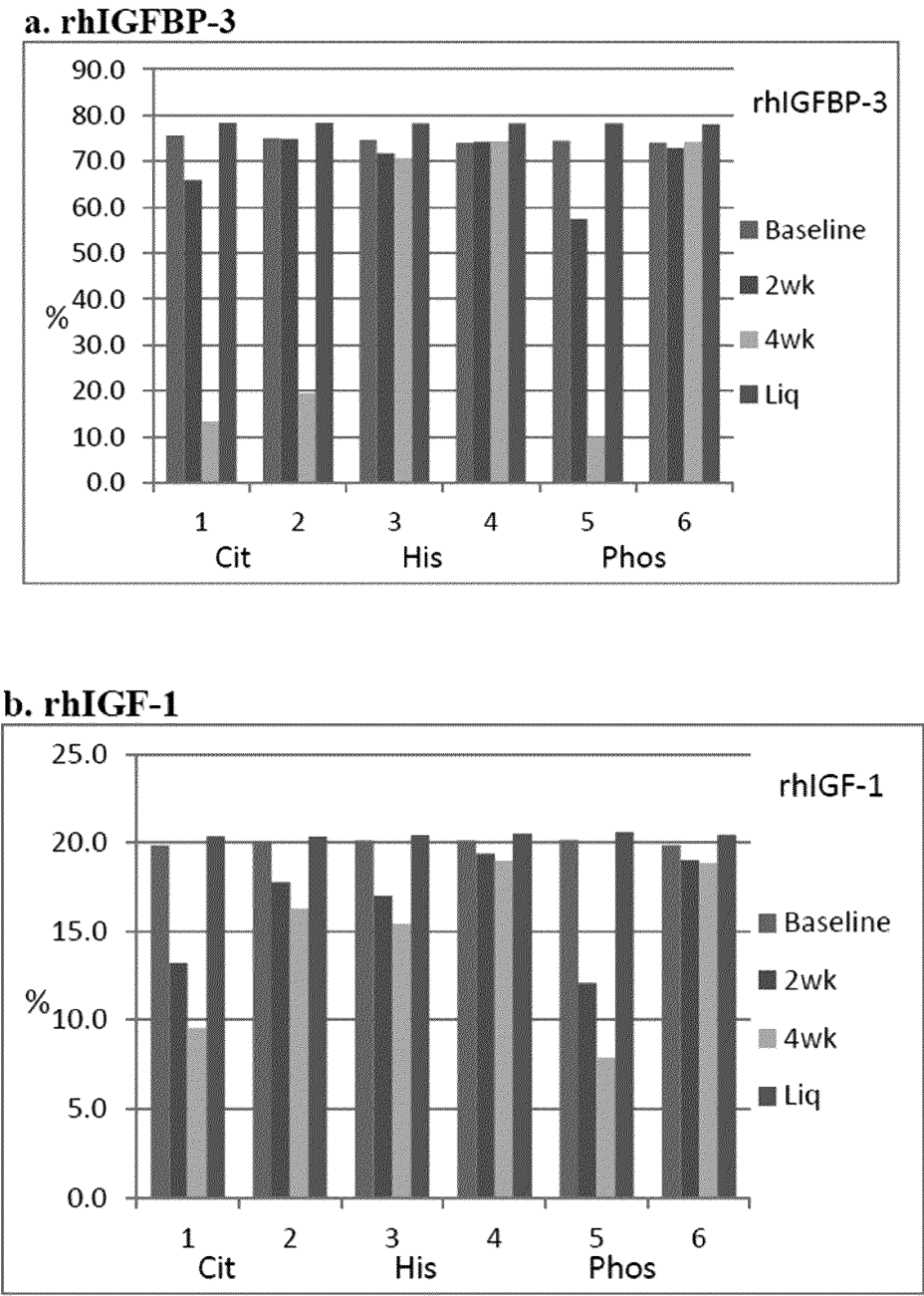
FIGURE 10B

b. High Molecular Weight Species



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FIGURE 11



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FIGURE 11 cont.

c. Oxidized rhIGF-1

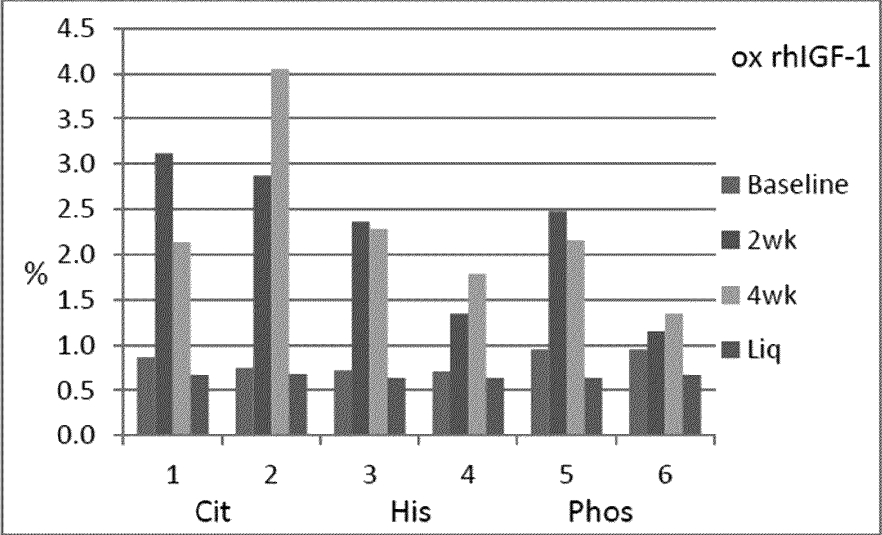
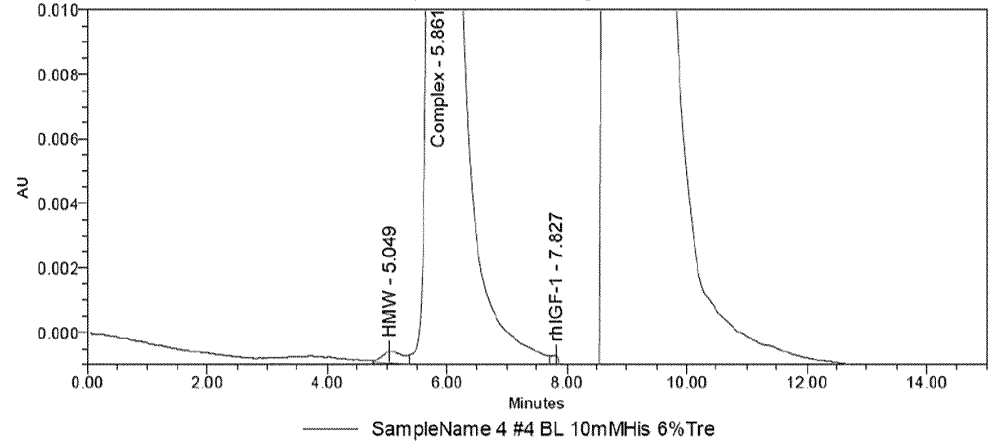


FIGURE 12A

a. Formulation #4 at Baseline (Lyophilization Run 1)



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FIGURE 12B

b. Formulation #3 at 4 Weeks, 60°C (Lyophilization Run 1)

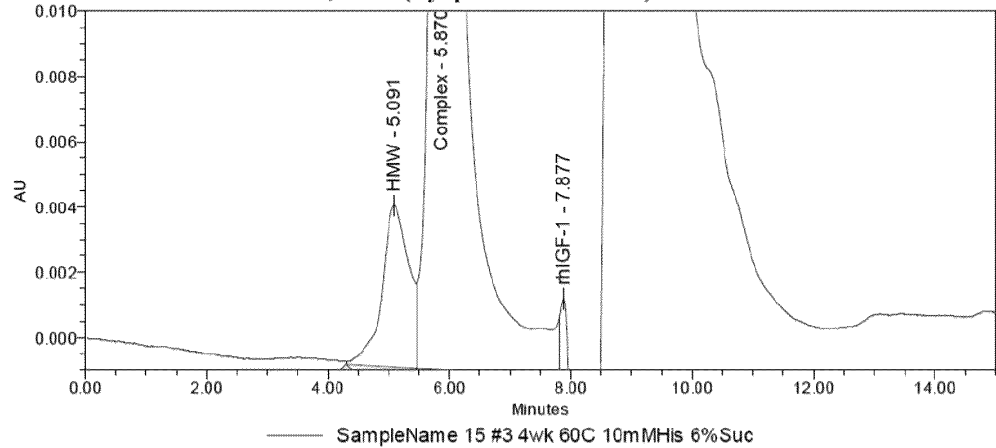
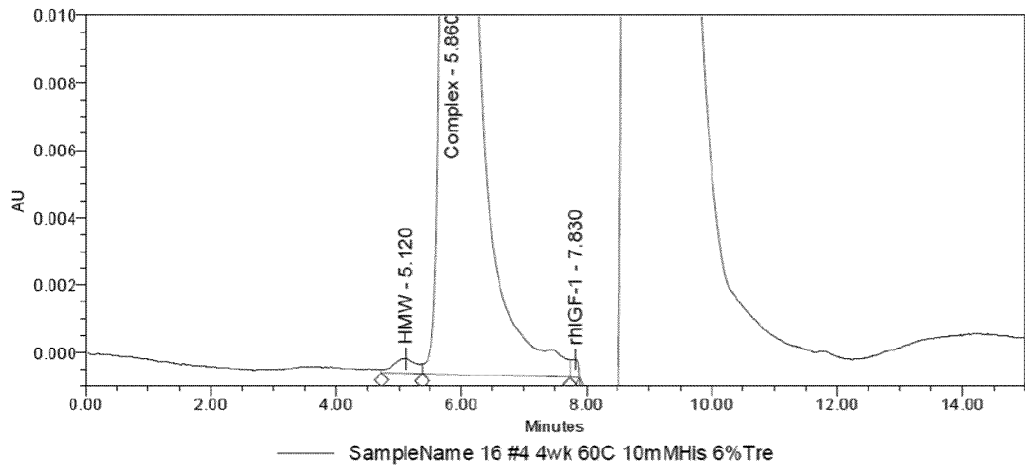


FIGURE 12C

c. Formulation #4 at 4 Weeks, 60°C (Lyophilization Run 1)



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FIGURE 13A

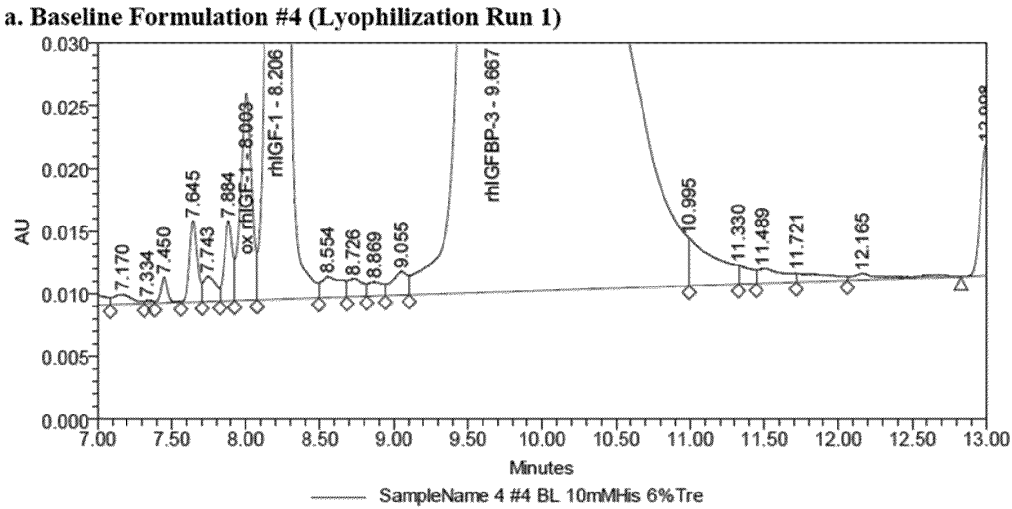


FIGURE 13B

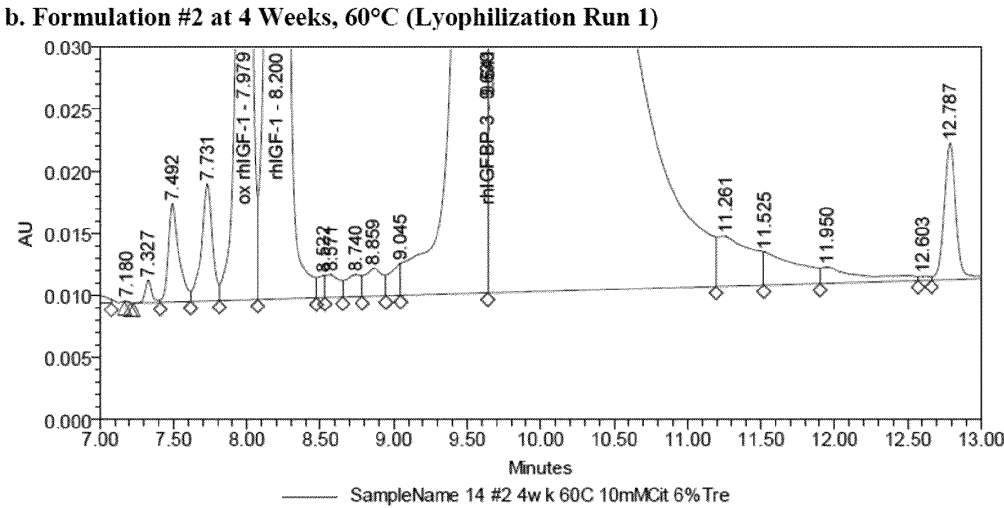


FIGURE 13C

c. Formulation #3 at 4 Weeks, 60°C (Lyophilization Run 1)

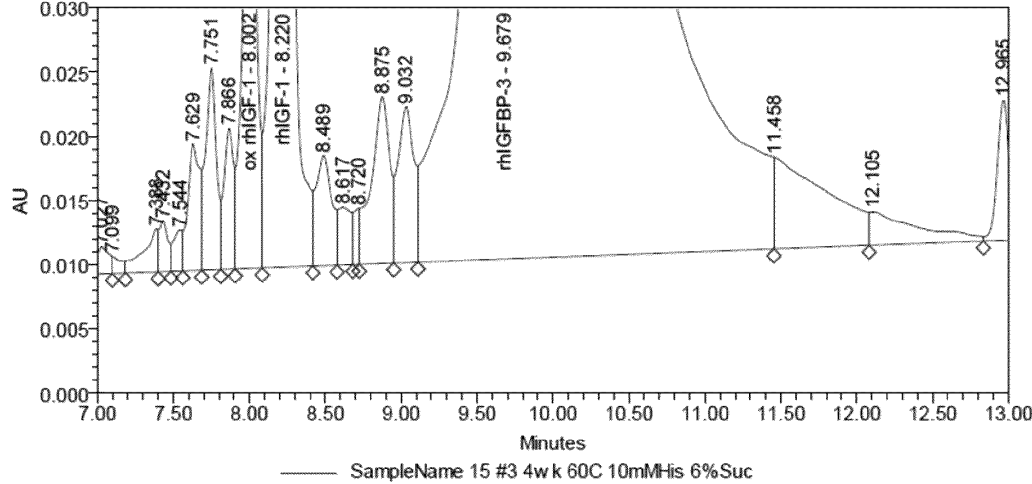


FIGURE 13D

d. Formulation #4 at 4 Weeks, 60°C (Lyophilization Run 1)

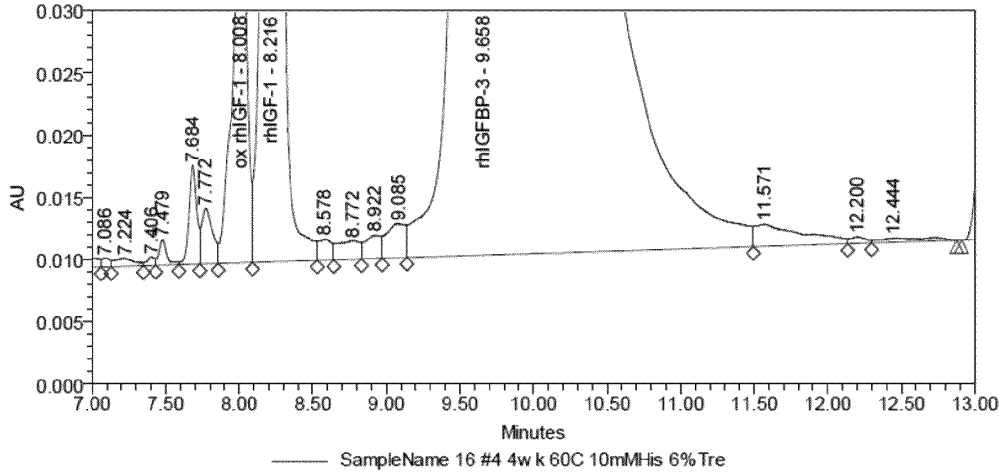
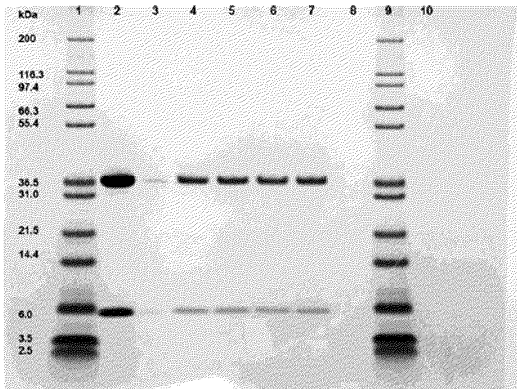


FIG. 13D

FIGURE 14A

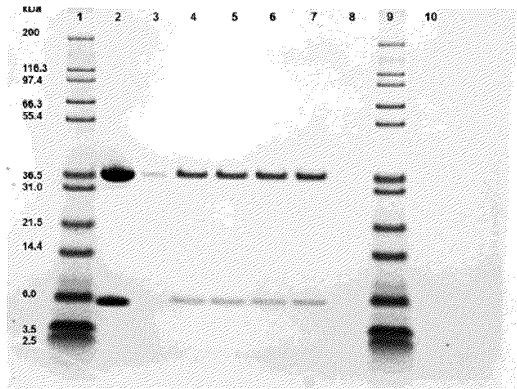
a. Baseline (Lyophilization Run 2)



- 1 – MW standard
- 2 – Complex Reference Standard) Lot PR20151115178-Eng)
- 3 – 1% Intensity Marker (Lot PR20151115178-Eng)
- 4 – Formulation #1 Baseline
- 5 – Formulation #2 Baseline
- 6 – Formulation #3 Baseline
- 7 – Formulation #4 Baseline
- 8 – Formulation #5 Baseline
- 9 – MW standard

FIGURE 14B

b. 4 Weeks, 40°C (Lyophilization Run 2)



- 1 – MW standard
- 2 – Complex Reference Standard) Lot PR20151115178-Eng)
- 3 – 1% Intensity Marker (Lot PR20151115178-Eng)
- 4 – Formulation #1 4wks, 40°C
- 5 – Formulation #2 4wks, 40°C
- 6 – Formulation #3 4wks, 40°C
- 7 – Formulation #4 4wks, 40°C
- 8 – Formulation #5 4wks, 40°C
- 9 – MW standard

FIGURE 15A

a. Temperature Profile

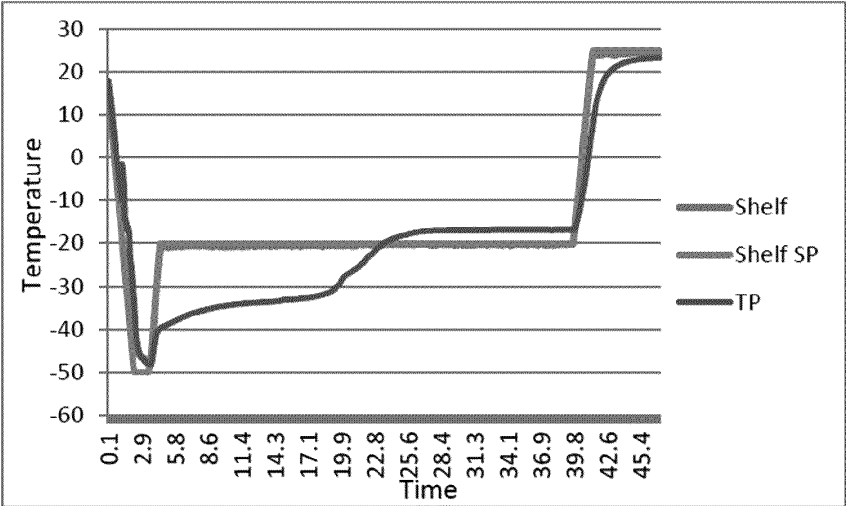
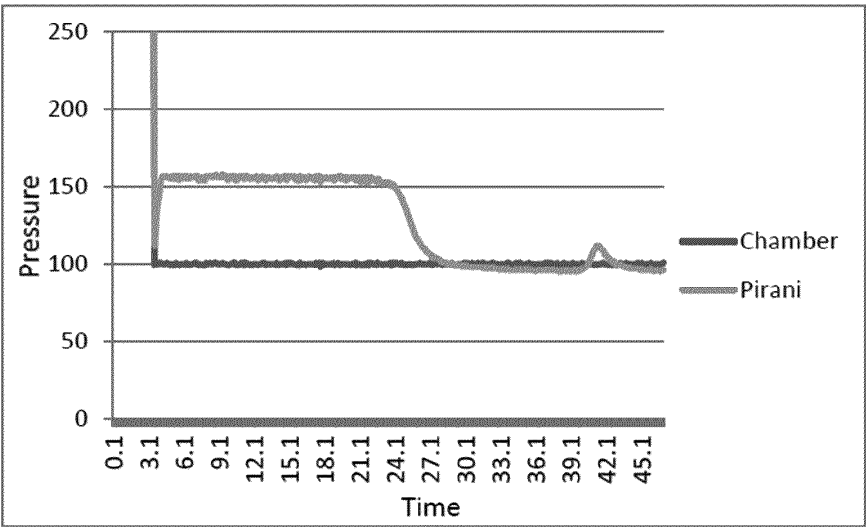


FIGURE 15B

b. Pressure Profile



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FIGURE 16A SE-UPLC for Lyophilization Run 2

a. Protein Complex rhIGF-1/rhIGFBP-3

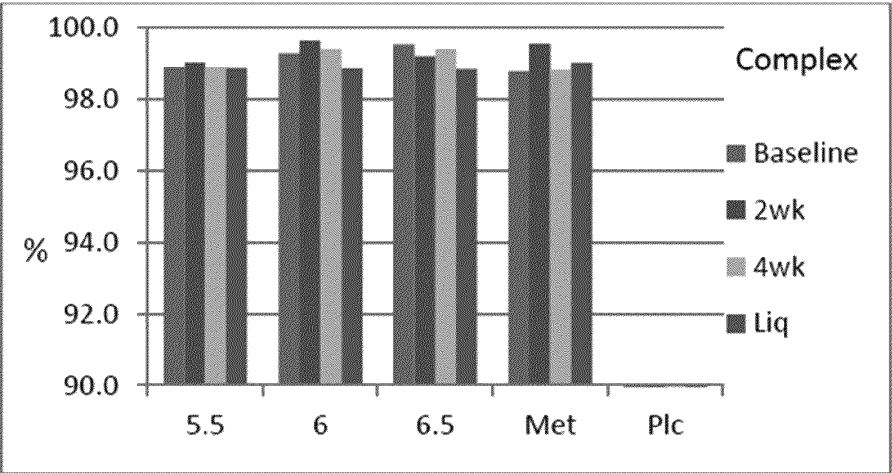
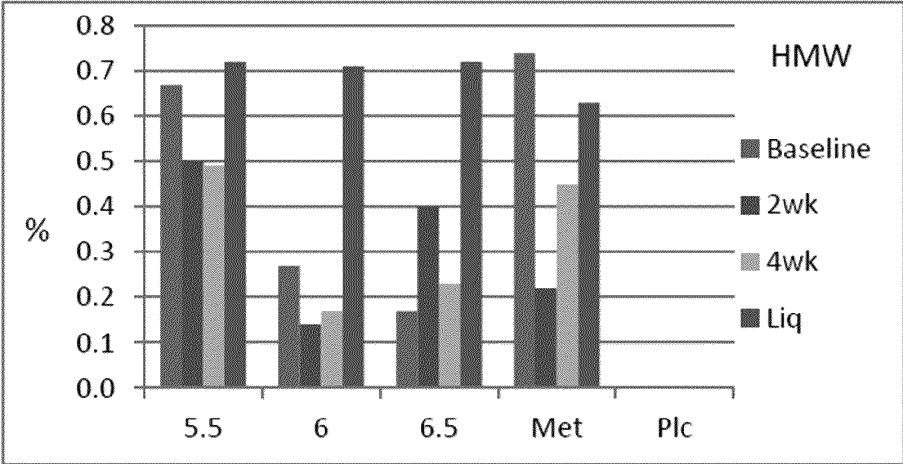


FIGURE 16B

b. High Molecular Weight Species



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FIGURE 17A RU-UPLC for Lyophilization Run 2

a. rhIGFBP-3

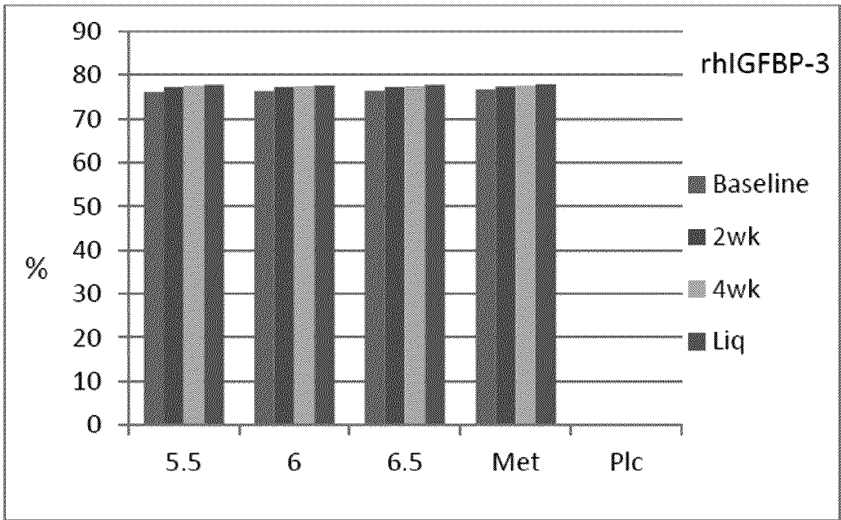


FIGURE 17B

b. rhIGF-1

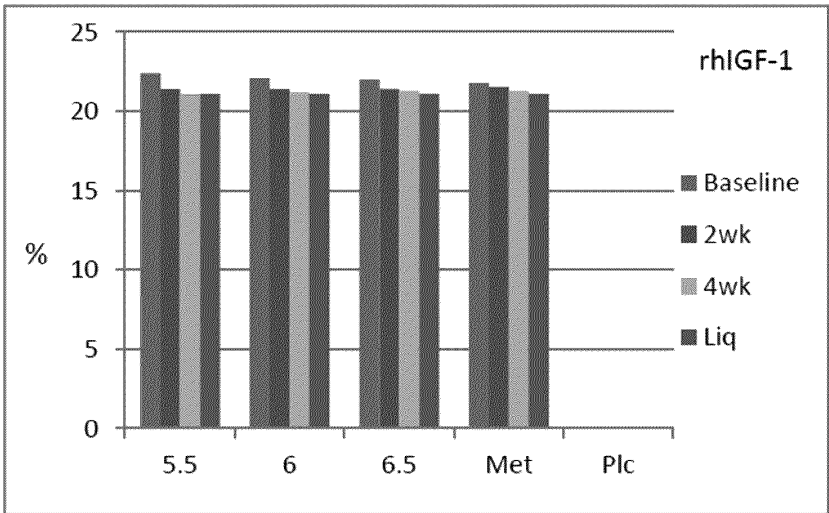


FIGURE 17C

c. Oxidized rhIGF-1

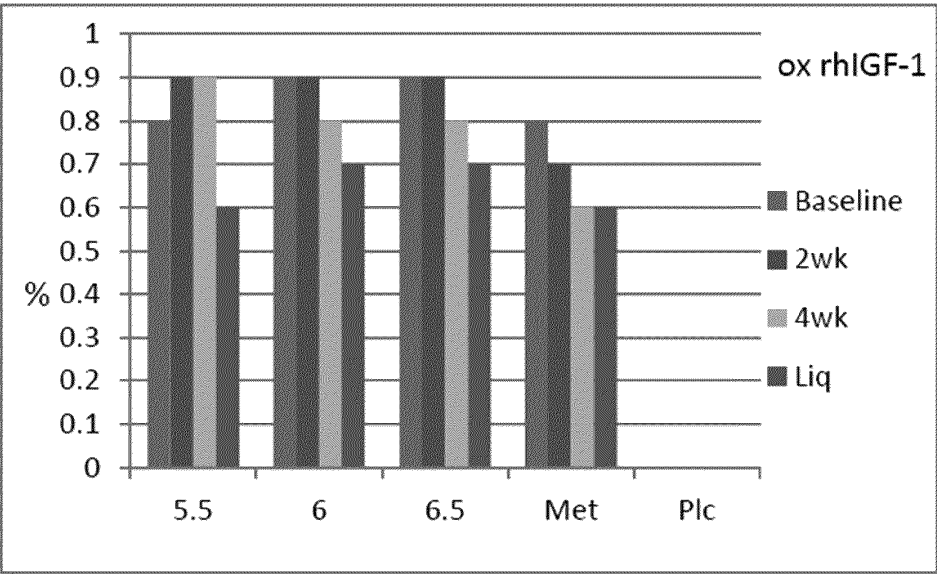


FIGURE 18A

a. Formulation #2 at Baseline (Lyophilization Run 2)

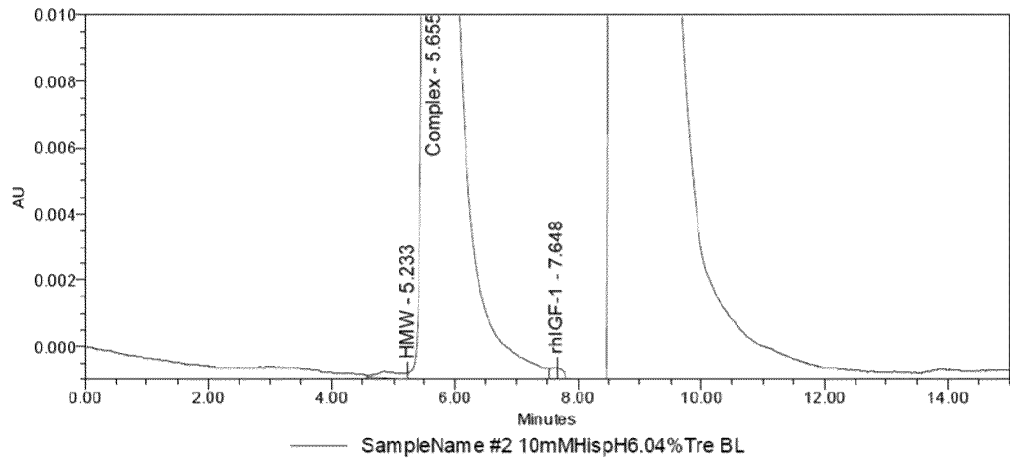


FIGURE 18B

b. Formulation #1 at 4 Weeks, 40°C (Lyophilization Run 2)

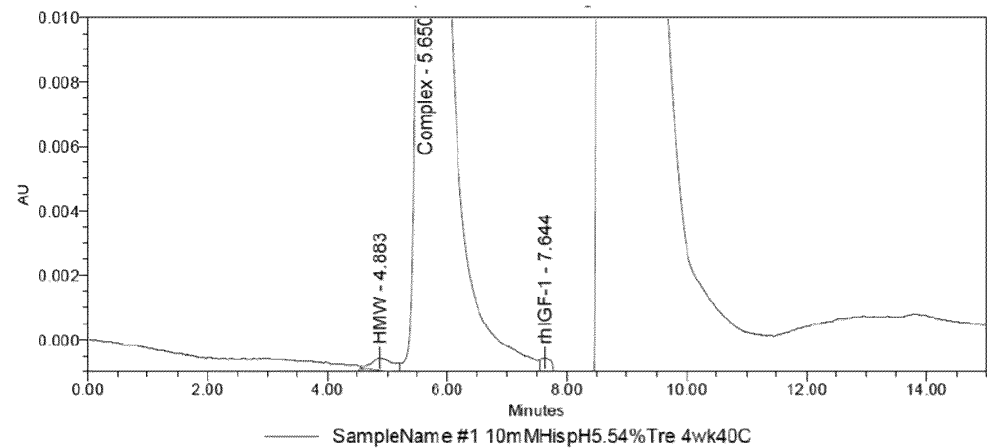
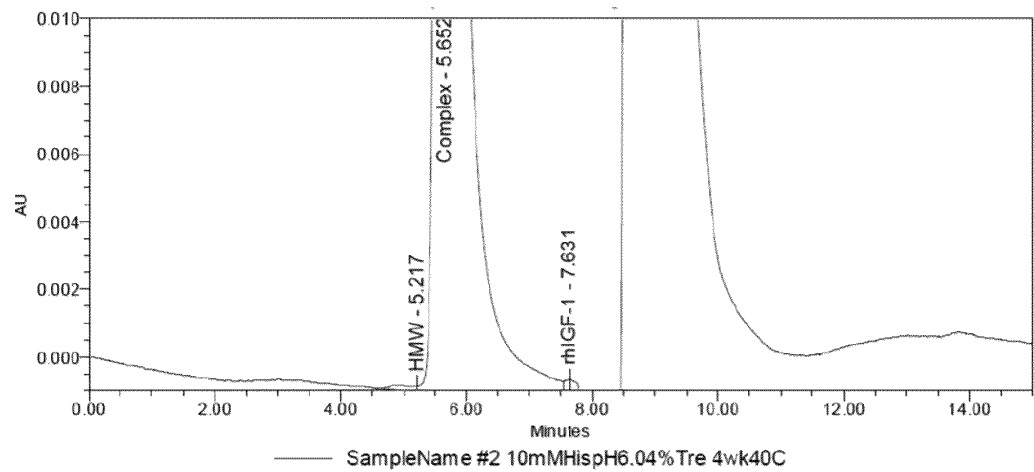


FIGURE 18C

c. Formulation #2 at 4 Weeks, 40°C (Lyophilization Run 2)



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FIGURE 18D

d. Formulation #3 at 4 Weeks, 40°C (Lyophilization Run 2)

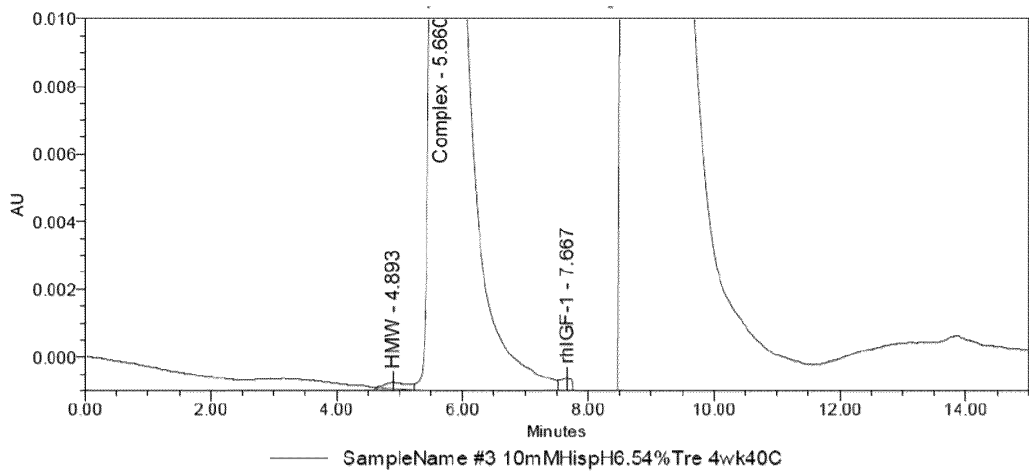
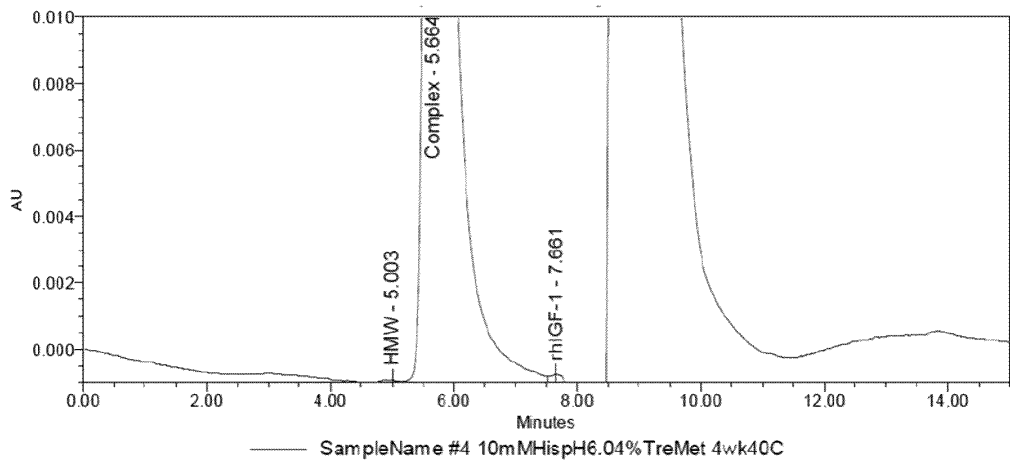


FIGURE 18E

e. Formulation #4 at 4 Weeks, 40°C (Lyophilization Run 2)



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FIGURE 18F

f. Formulation #4 at 48 hrs, Liquid Storage at Room Temperature (Lyophilization Run 2)

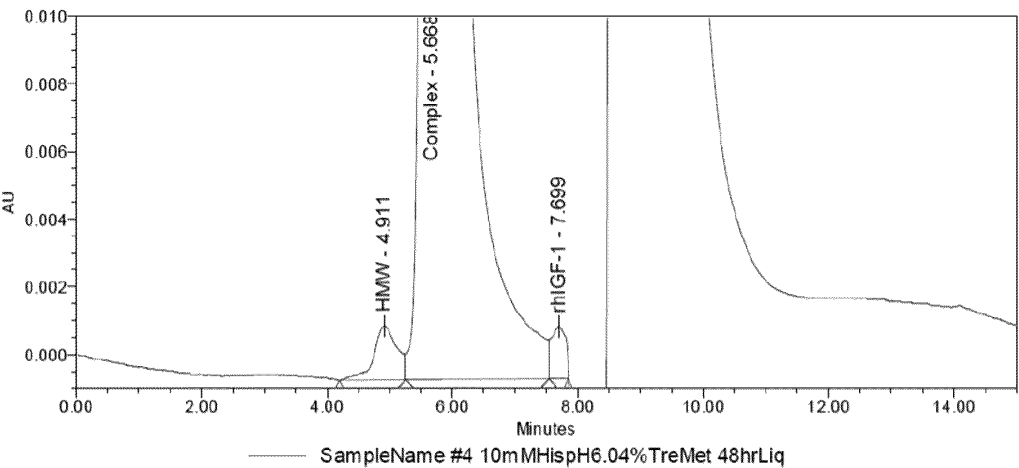


FIGURE 19A RU-UPLC Profiles of Selected Formulation

a. Formulation #4 at Baseline (Lyophilization Run 2)

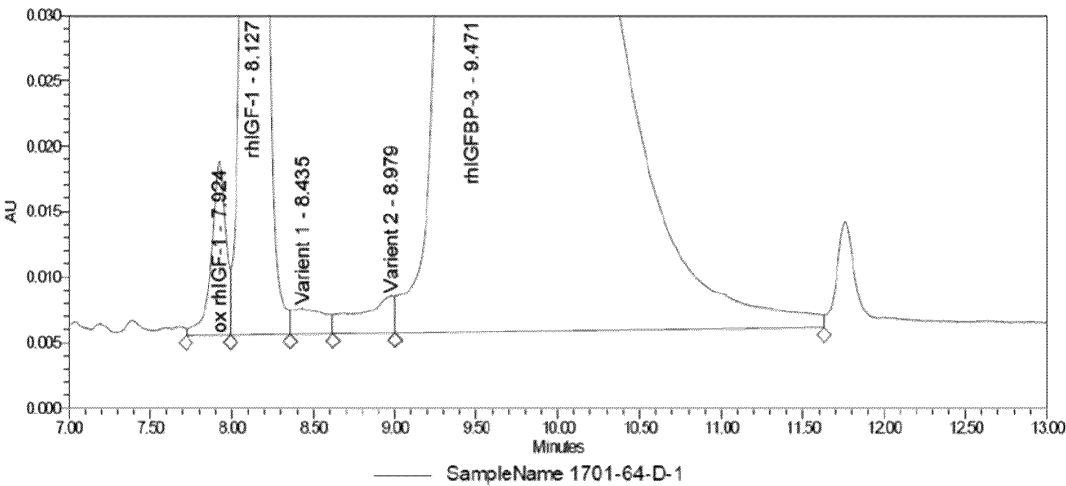


FIGURE 19B

b. Formulation #4 at 4 Weeks, 40°C (Lyophilization Run 2)

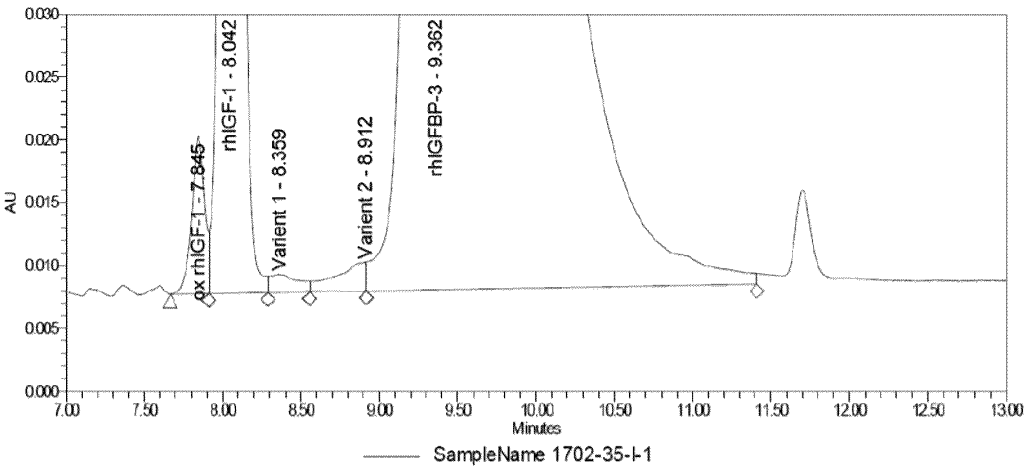


FIGURE 19C

c. Formulation #4 at 48 hrs, Liquid Storage at Room Temperature (Lyophilization Run 2)

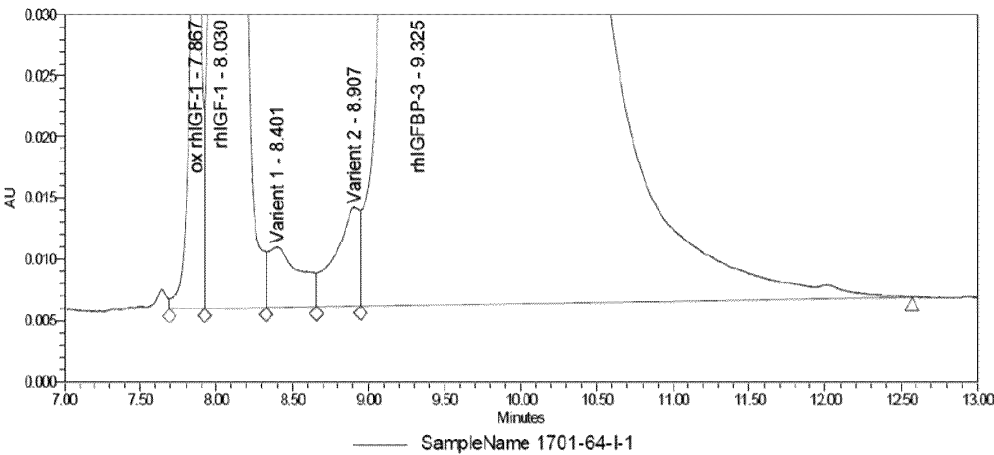


FIGURE 20A

a. Baseline (Lyophilization Run 2)

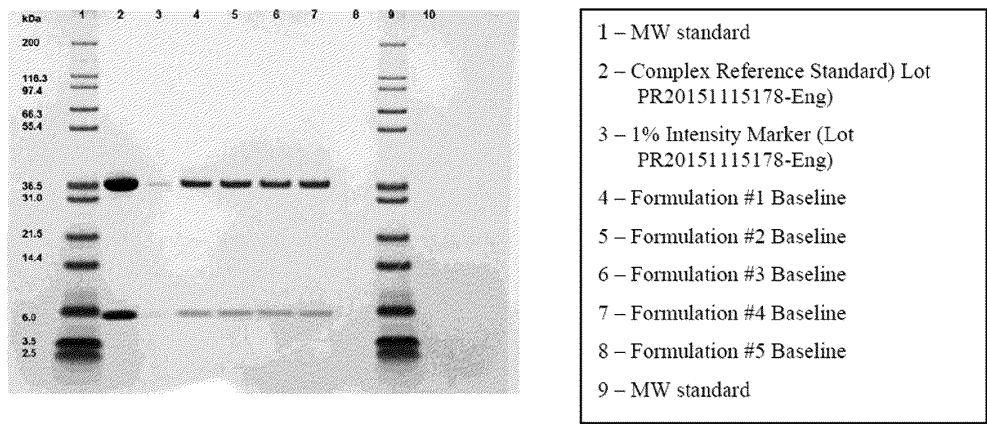


FIGURE 20B

b. 4 Weeks, 40°C (Lyophilization Run 2)

