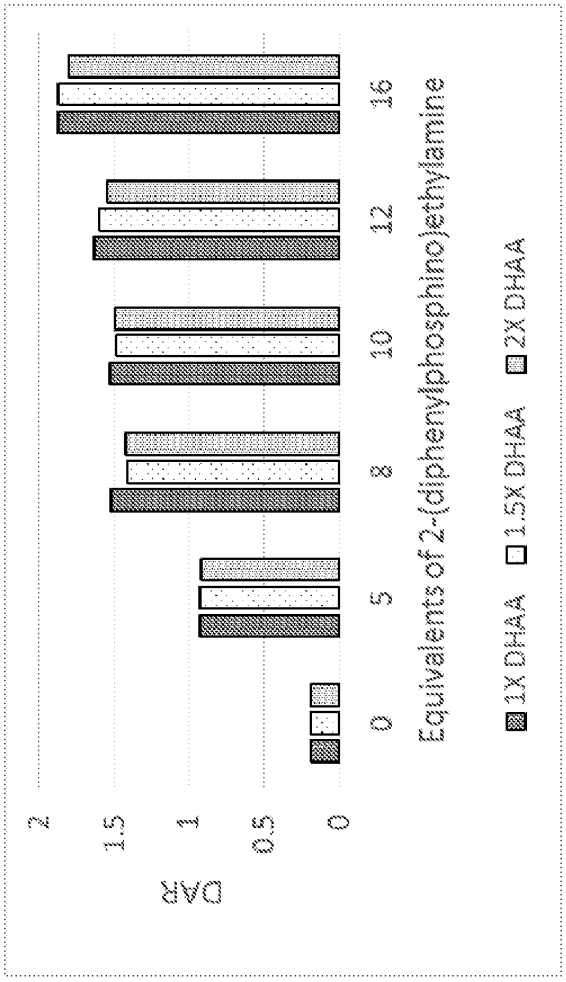

DAR
2
1.5
1
0.5
0
0
5
8
10
12
16
Equivalents of 2-(diphenylphosphino)ethylamine
1X DHAA
1.5X DHAA
2X DHAA

FIG. 1

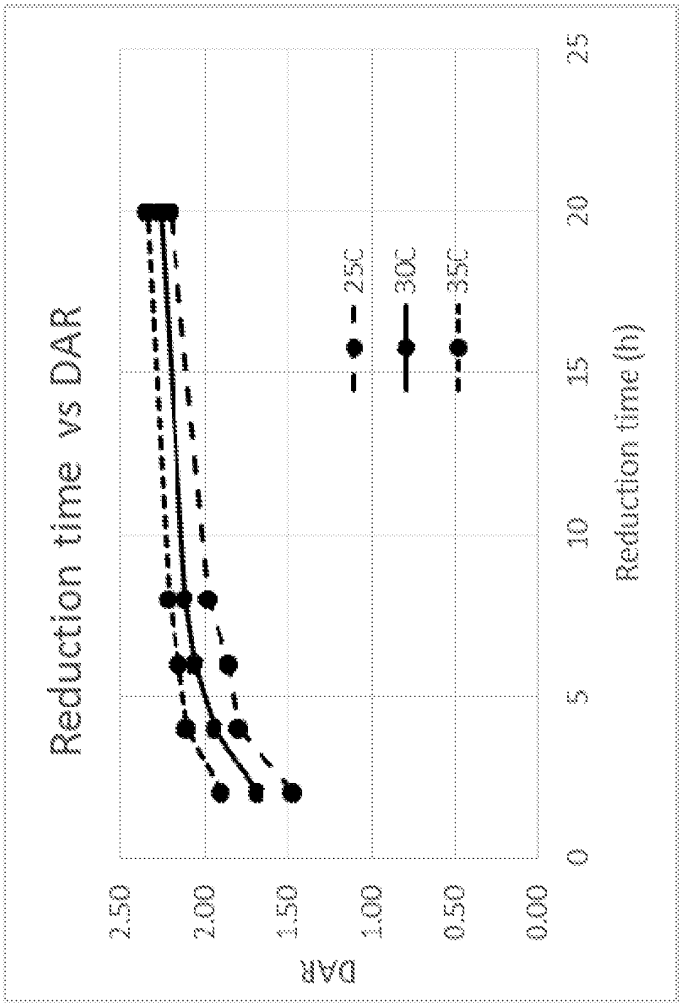

Reduction time vs DAR
DAR
2.50
2.00
1.50
1.00
0.50
0.00
0
5
10
15
20
25
Reduction time (h)
25C
30C
35C

FIG. 2

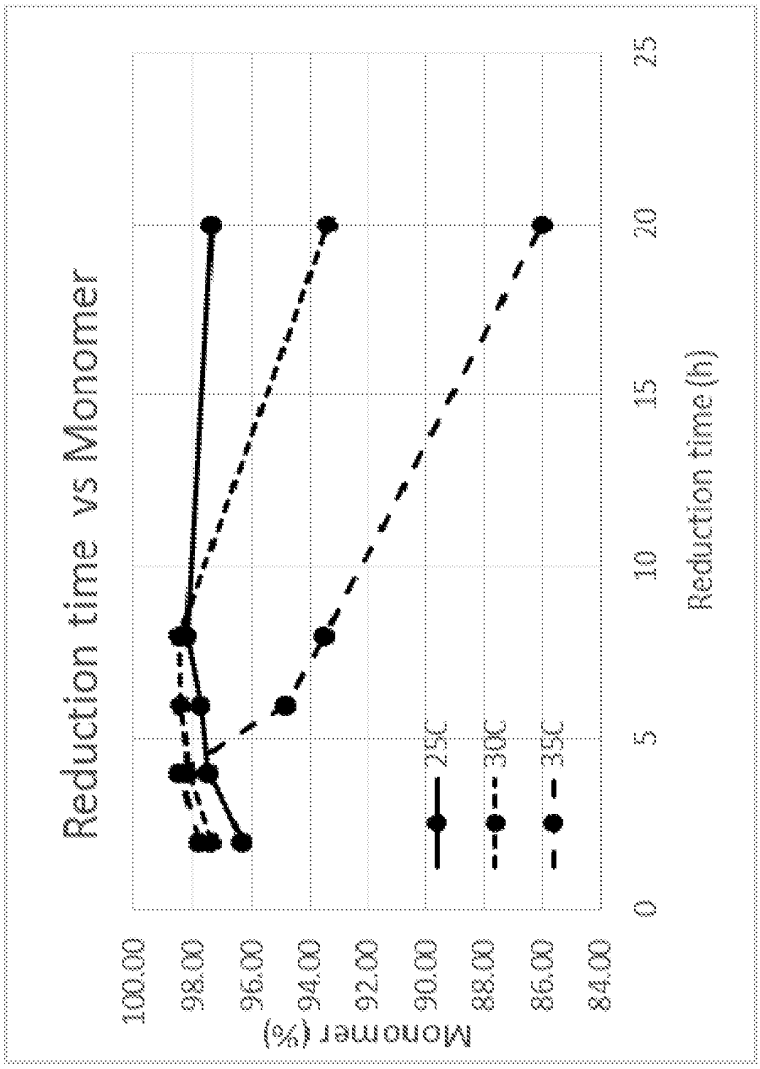

Reduction time vs Monomer
Monomer (%)
100.00
98.00
96.00
94.00
92.00
90.00
88.00
86.00
84.00
0
5
10
15
20
25
Reduction time (h)
25C
30C
35C

FIG. 3

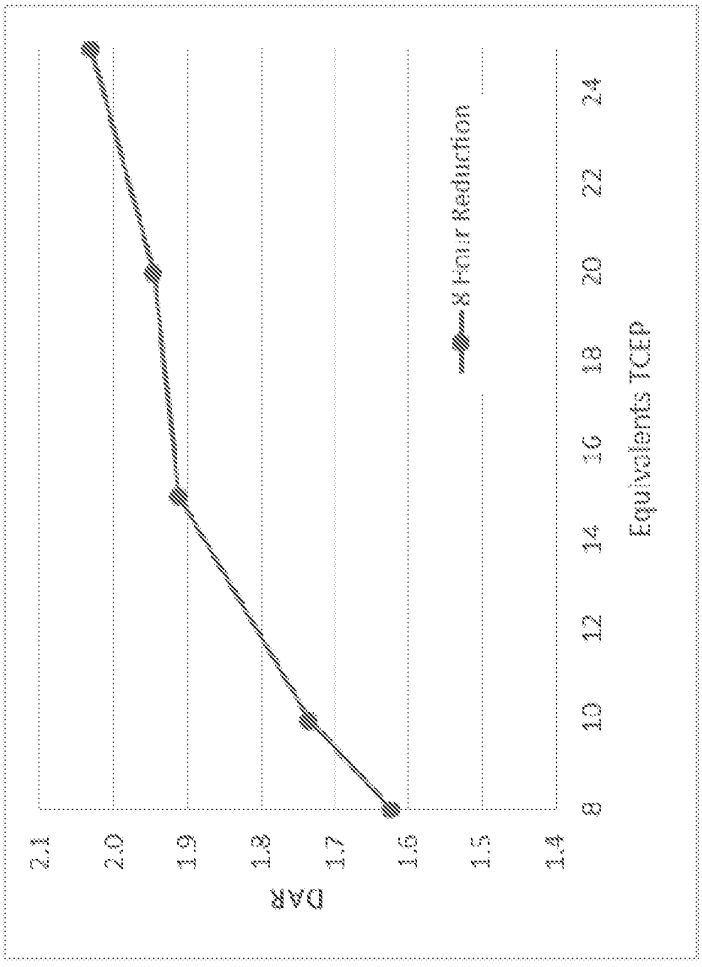

DAR
2.1
2.0
1.9
1.8
1.7
1.6
1.5
1.4
8
10
12
14
16
18
20
22
24
Equivalents TCEP
8 Hour Reduction

FIG. 4

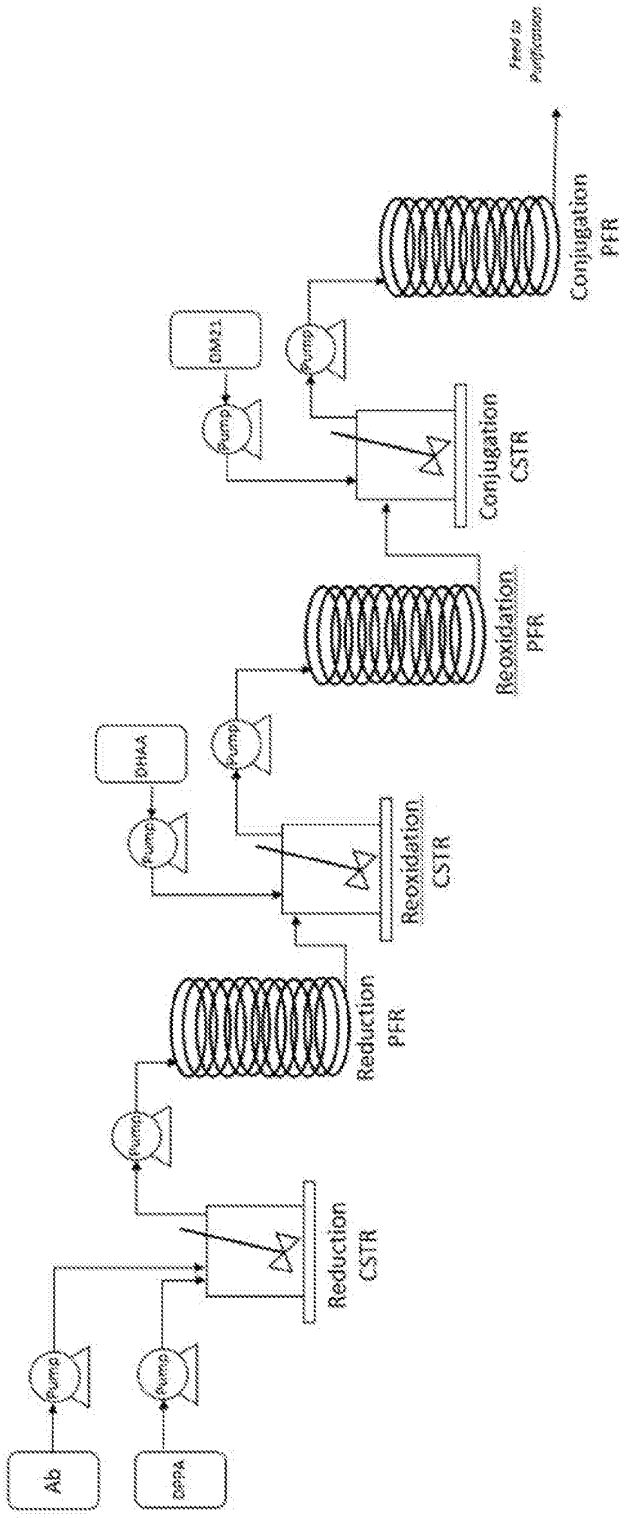

Ab
EDTA
Reduction CSTR
Reduction PFR
DHAA
Reoxidation CSTR
Reoxidation PFR
DM21
Conjugation CSTR
Conjugation PFR
Feed to Purification

FIG. 5

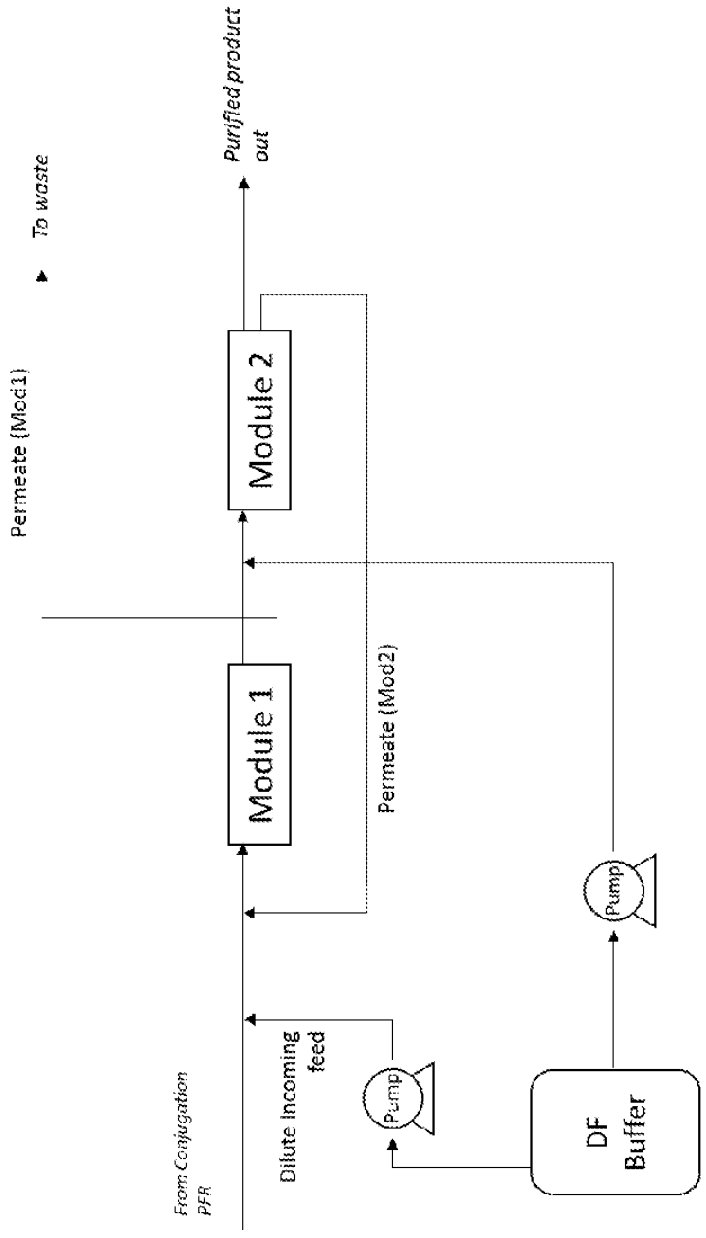

From Conjugation PFR
Dilute Incoming feed
Pump
Module 1
Permeate (Mod2)
Module 2
Permeate (Mod1)
To waste
Purified product out
Pump
DF Buffer

FIG. 6

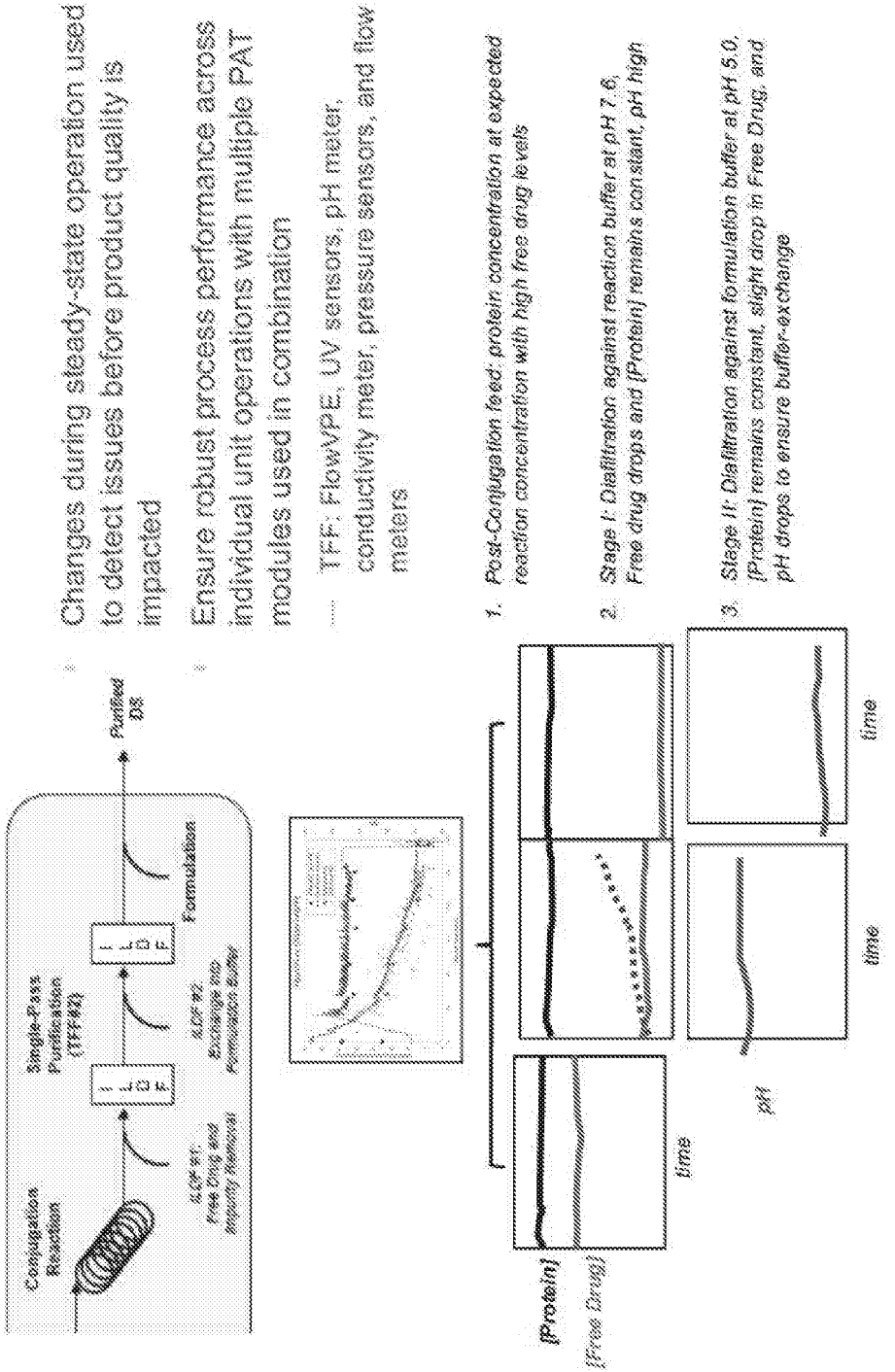

Conjugation Reaction
Single-Pass Purification (TFF#2)
TFF #1: Free Drug and Impurity Removal
TFF #2: Exchange into Formulation Buffer
Formulation
Purified ADC
Changes during steady-state operation used to detect issues before product quality is impacted
Ensure robust process performance across individual unit operations with multiple PAT modules used in combination
TFF: FlowVPE, UV sensors, pH meter, conductivity meter, pressure sensors, and flow meters
1. Post-Conjugation feed: protein concentration at expected reaction concentration with high free drug levels
2. Stage I: Diafiltration against reaction buffer at pH 7.6, Free drug drops and [Protein] remains constant, pH high
3. Stage II: Diafiltration against formulation buffer at pH 5.0, [Protein] remains constant, slight drop in Free Drug, and pH drops to ensure buffer-exchange
[Protein]
[Free Drug]
time
pH
time
time

FIG. 7

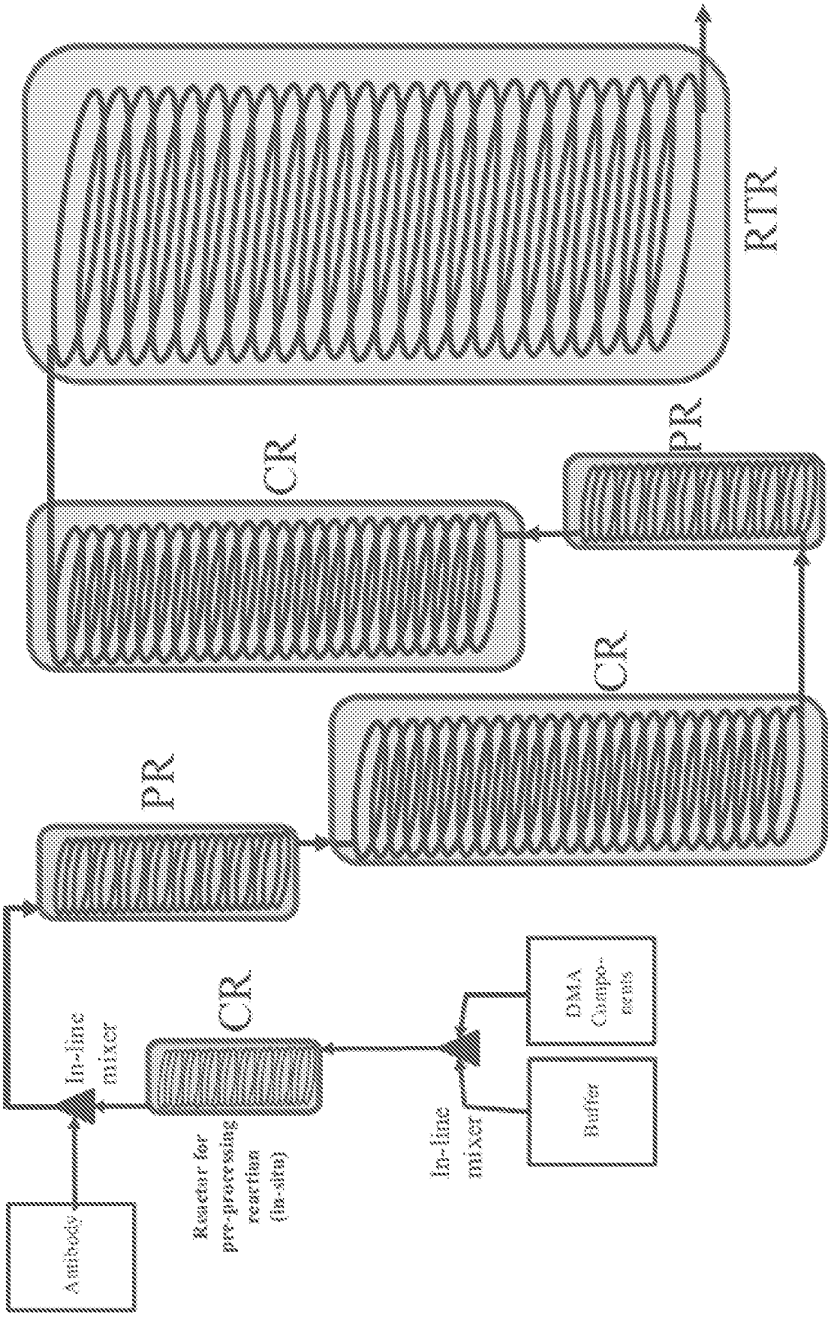

RTR
CR
PR
CR
PR
CR
In-line mixer
Reactor for pre-processing reaction (in-situ)
In-line mixer
DMA Compo-nents
Buffer
Antibody

FIG. 8