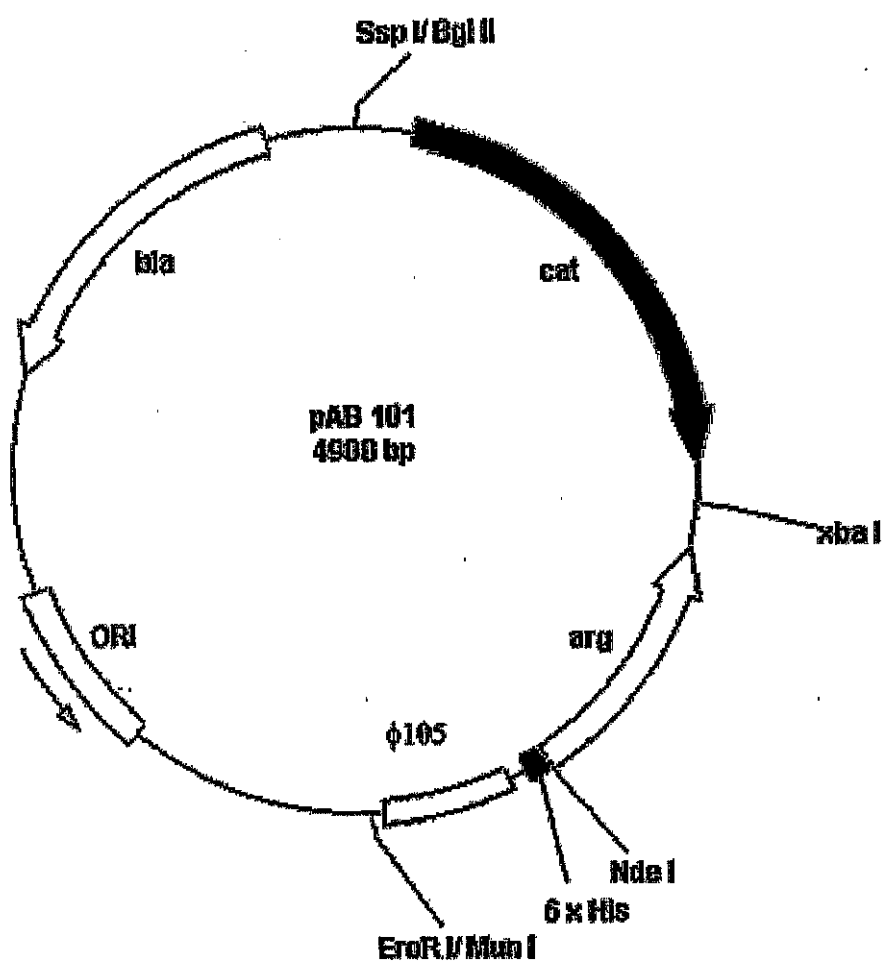


Fig. 1



2/46

Fig. 2A

```

1  gaattgtacg tcaaagagat gaagcagaaa aacgtcgtcg agaagaagct gaacgacaaa
61  aagtgaatat cgagggaagt ccaagaaatg gtgattatga ggggtgtctat ttcacccaaa
121  acggagaata tttattggaa ttaagagtct ctgggactgc tcttgtaa at gtccttgta
181  atttaaagga tattgacata acgaaatggt tgtgtaaaac agggagatta tatcttgata
241  aggttaagaa atttgaaata gttactattc tttcccatga cgtagaaaat caaaagatta
301  taacagaatg ggagtcactc cccagagagg ctttaccoga acaatttgat tcataagaac
361  taattagtag cgctttccaa tggaggcgct tttttatttg ggtagttgca taccactaaa
421  gatgttcagg tgcacatgag cattggagga aaggaacgct ttagggggaa gggaaacctt
481  taaacagtct taatccccct tgattttatg ttctctgtaa actgcgtccg gtaaactctca
541  ggatagacaa tcggcggtta acggccttgag tgcgggggca gtttagaaag aatatgattg
601  gagggtattca tagatgcatc accatcacca tcatatgagc gccagtcca gaacatagg
661  gattattgga gctcctttct caaagggaca gccacgagga ggggtggaag aaggccctac
721  agtattgaga aaggctggct tgcttgagaa acttaaagaa caagagtgtg atgtgaagga
781  ttatggggac ctgccctttg ctgacatccc taatgacagt ccctttcaaa ttgtgaagaa
841  tccaaggtct gtgggaaaag caagcgagca gctggctggc aaggtggcac aagtcaagaa
901  gaacggaaga atcagcctgg tgctggcgcg agaccacagt ttggcaattg gaagcatctc
961  tggccatgcc aggggtccacc ctgatcttgg agtcatctgg gtggatgctc acactgatat
1021 caaactcca ctgacaacca caagtggaaa cttgcatgga caacctgtat ctttcctcct
1081 gaaggaacta aaaggaaaga ttcccgatgt gccaggattc tcctgggtga ctccctgtat
1141 atctgccaag gatatttgtt atattggctt gagagacgtg gacctggggg aacactacat
1201 tttgaaaact ctaggcatta aatacttttc aatgactgaa gtggacagac taggaattgg
1261 caaggtgatg gaagaaacac tcagctatct actaggaaga aagaaaaggc caattcatct
1321 aagttttgat gttgacggac tggacccatc tttcacacca gctactggca caccagtcgt
1381 gggagggtctg acatacagag aaggtctcta catcacagaa gaaatctaca aaacagggtc
1441 actctcagga ttagatataa tggaaagtga cccatccctg gggaagacac cagaagaagt
1501 aactcgaaca gtgaacacag cagttgcaat aaccttggct tgtttcggac ttgctcggga
1561 gggtaatcac aagcctattg actaccttaa cccacctaag taaatgtgga aacatccgat
1621 ataaatctca tagttaatgg cataattaga aagctaata ttttcttaag catagagtta
1681 tccttctaaa gacttggtct ttcagaaaaa tgtttttcca attagtataa actctacaaa
1741 ttcctctctg gtgtaaaatt caagatgtgg aaattctaac ttttttgaaa tttaaaagct
1801 tatattttct aacttggcaa aagacttatc cttagaaaga gaagtgtaca ttgatttcca
1861 attaaaaatt tgctggcatt aaaaataagc acacttacat aagcccccat acatagagtg
1921 ggactcttgg aatcaggaga caaagctacc acatgtggaa aggtactatg tgtccatgtc
1981 attcaaaaaa tgtgattcta ga

```

3/46

Fig. 2B

```

1  atgcatcaccatcaccatcat
   M H H H H H H
22 atgagcgccaagtccagaaccatagggattattggagctcctttc
   M S A K S R T I G I I G A P F
67 tcaaaggacagccacgaggaggggtggaagaaggccctacagta
   S K G Q P R G G V E E G P T V
112 ttgagaaaggctggtctgcttgagaaacttaaagaacaagagtgt
   L R K A G L L E K L K E Q E C
157 gatgtgaaggattatggggacctgccctttgctgacatccctaata
   D V K D Y G D L P F A D I P N
202 gacagtccctttcaaattgtgaagaatccaaggtctgtgggaaaa
   D S P F Q I V K N P R S V G K
247 gcaagcgagcagctggctggcaaggtggcacaagtcaagaagaac
   A S E Q L A G K V A Q V K K N
292 ggaagaatcagcctggtgctgggaggagaccacagtttggcaatt
   G R I S L V L G G D H S L A I
337 ggaagcatctctggccatgccagggtccaccctgatcttggagtc
   G S I S G H A R V H P D L G V
382 atctgggtggatgctcacactgatatacaactccactgacaacc
   I W V D A H T D I N T P L T T
427 acaagtggaaacttgcatggacaacctgtatctttcctcctgaag
   T S G N L H G Q P V S F L L K
472 gaactaaaaggaaagattcccgatgtgccaggattctcctgggtg
   E L K G K I P D V P G F S W V
517 actccctgtatatctgccaaggatattgtgtatattggcttgaga
   T P C I S A K D I V Y I G L R
562 gacgtggaccctgggggaactacatctttgaaaactctaggcatt
   D V D P G E H Y I L K T L G I
607 aaatacttttcaatgactgaagtggacagactaggaattggcaag
   K Y F S M T E V D R L G I G K
652 gtgatggaagaaacactcagctatctactaggaagaaagaaaagg
   V M E E T L S Y L L G R K K R
697 ccaattcatctaagttttgatgttgacggactggacccatctttc
   P I H L S F D V D G L D P S F
742 acaccagctactggcacaccagtcgtgggaggtctgacatacaga
   T P A T G T P V V G G L T Y R
787 gaaggtctctacatcacagaagaaatctacaaaacagggctactc
   E G L Y I T E E I Y K T G L L
832 tcaggattagatataatggaagtgaacccatccctggggaagaca
   S G L D I M E V N P S L G K T
877 ccagaagaagtaactcgaacagtgaaacacagcagttgcaataacc
   P E E V T R T V N T A V A I T
922 ttggcttggtttcggacttgctcgggagggtaatcacaagcctatt
   L A C F G L A R E G N H K P I
967 gactaccttaacccacctaagtaa 990
   D Y L N P P K *

```

WO 2004/000349

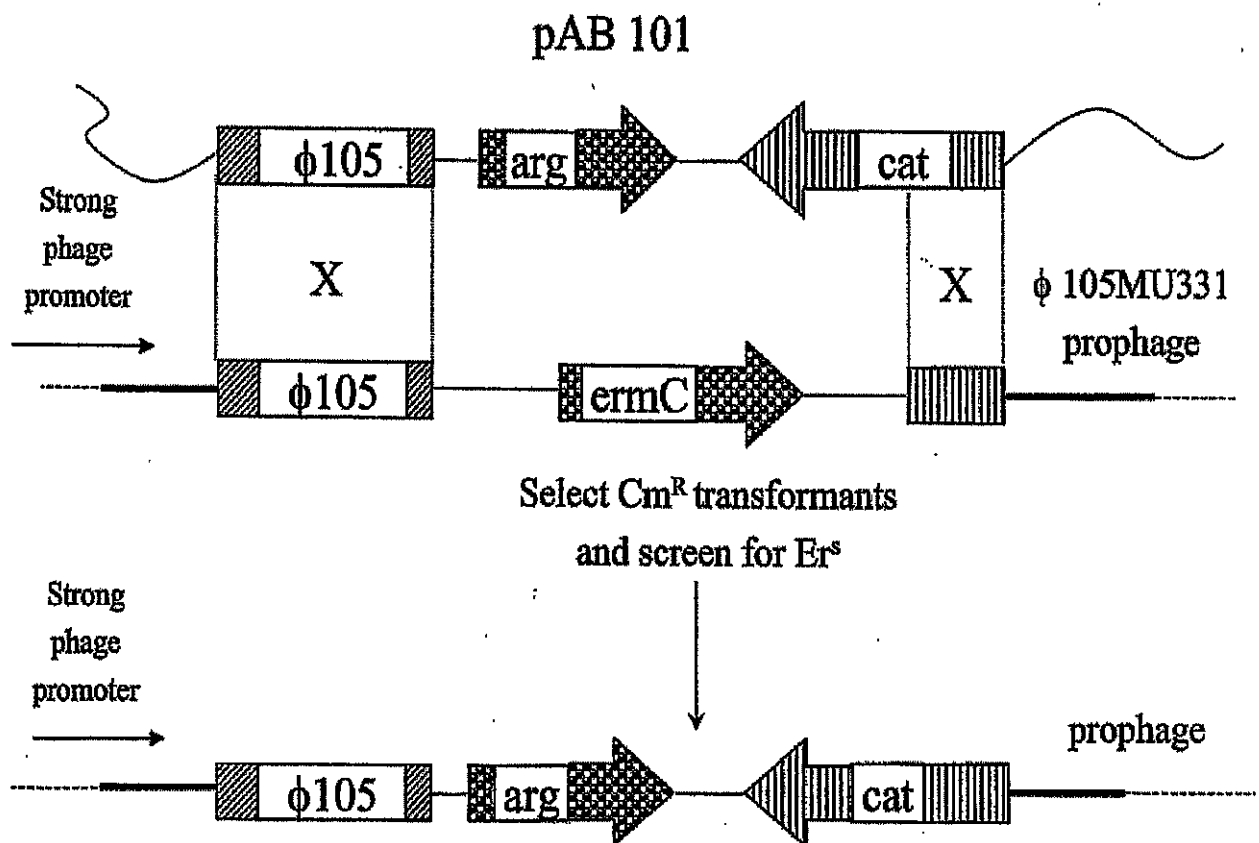
4/46

Fig. 2C

```

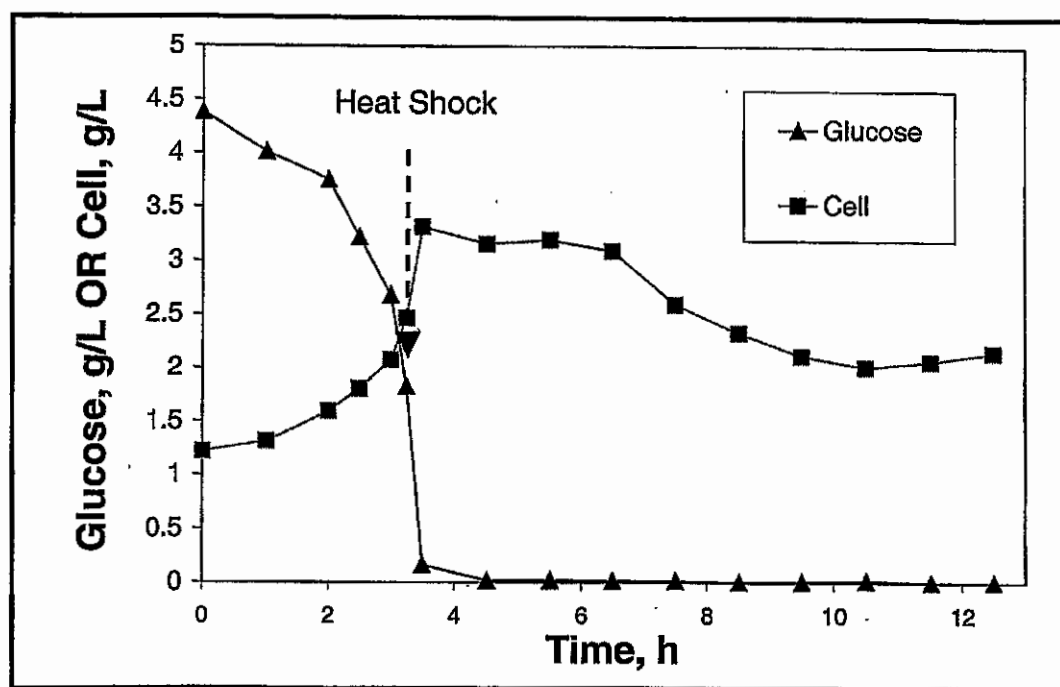
1  atgagcgccaagtccagaacccatagggattattggagctcctttc
   M S A K S R T I G I I G A P F
46  tcaaagggacagccacgaggaggggtggaagaaggccctacagta
   S K G Q P R G G V E E G P T V
91  ttgagaaaggctggtctgcttgagaaacttaagaacaagagtgt
   L R K A G L L E K L K E Q E C
136 gatgtgaaggattatggggacctgccctttgctgacatccctaatt
   D V K D Y G D L P F A D I P N
181 gacagtccctttcaaattgtgaagaatccaaggctctgtgggaaaa
   D S P F Q I V K N P R S V G K
226 gcaagcgagcagctggctggcaagggtggcacaagtcaagaagaac
   A S E Q L A G K V A Q V K K N
271 ggaagaatcagcctggtgctggggcggagaccacagtttggcaatt
   G R I S L V L G G D H S L A I
316 ggaagcatctctggccatgccaggggtccaccctgatcttggagtc
   G S I S G H A R V H P D L G V
361 atctgggtggatgctcacactgatatacaactccactgacaacc
   I W V D A H T D I N T P L T T
406 acaagtggaaacttgcatggacaacctgtatctttcctcctgaag
   T S G N L H G Q P V S F L L K
451 gaactaaaaggaaagattcccgatgtgccaggattctcctgggtg
   E L K G K I P D V P G F S W V
496 actccctgtatatctgccaaggatattgtgtatattggcttgaga
   T P C I S A K D I V Y I G L R
541 gacgtggaccctggggaacactacattttgaaaactctaggcatt
   D V D P G E H Y I L K T L G I
586 aaatacttttcaatgactgaagtggacagactaggaattggcaag
   K Y F S M T E V D R L G I G K
631 gtgatggaagaaacactcagctatctactaggaagaaagaaaagg
   V M E E T L S Y L L G R K K R
676 ccaattcatctaagttttgatgttgacggactggaccatctttc
   P I H L S F D V D G L D P S F
721 acaccagctactggcacaccagtcgtgggaggtctgacatacaga
   T P A T G T P V V G G L T Y R
766 gaaggctctctacatcacagaagaaatctacaaaacagggctactc
   E G L Y I T E E I Y K T G L L
811 tcaggattagatataatggaagtgaacccatccctggggaagaca
   S G L D I M E V N P S L G K T
856 ccagaagaagtaactcgaacagtgaacacagcagttgcaataacc
   P E E V T R T V N T A V A I T
901 ttggcttggtttcggacttgctcgggagggtaatcacaagcctatt
   L A C F G L A R E G N H K P I
946 gactaccttaacccacctaagtaa 969
   D Y L N P P K *

```



6/46

Fig. 4A



7/46

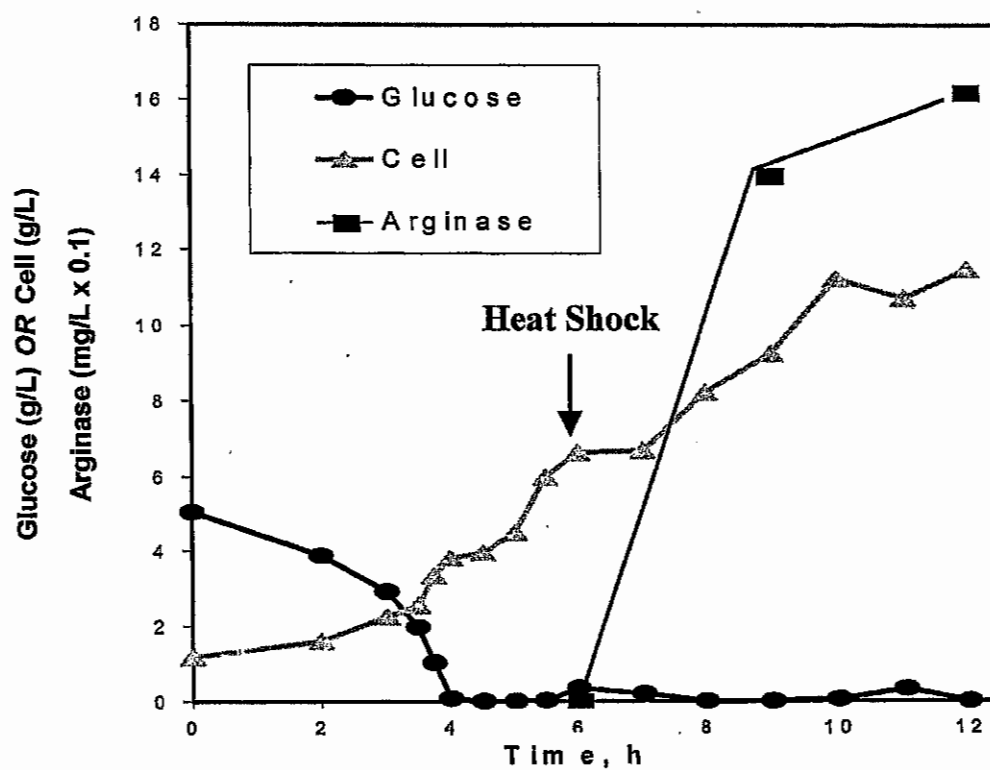
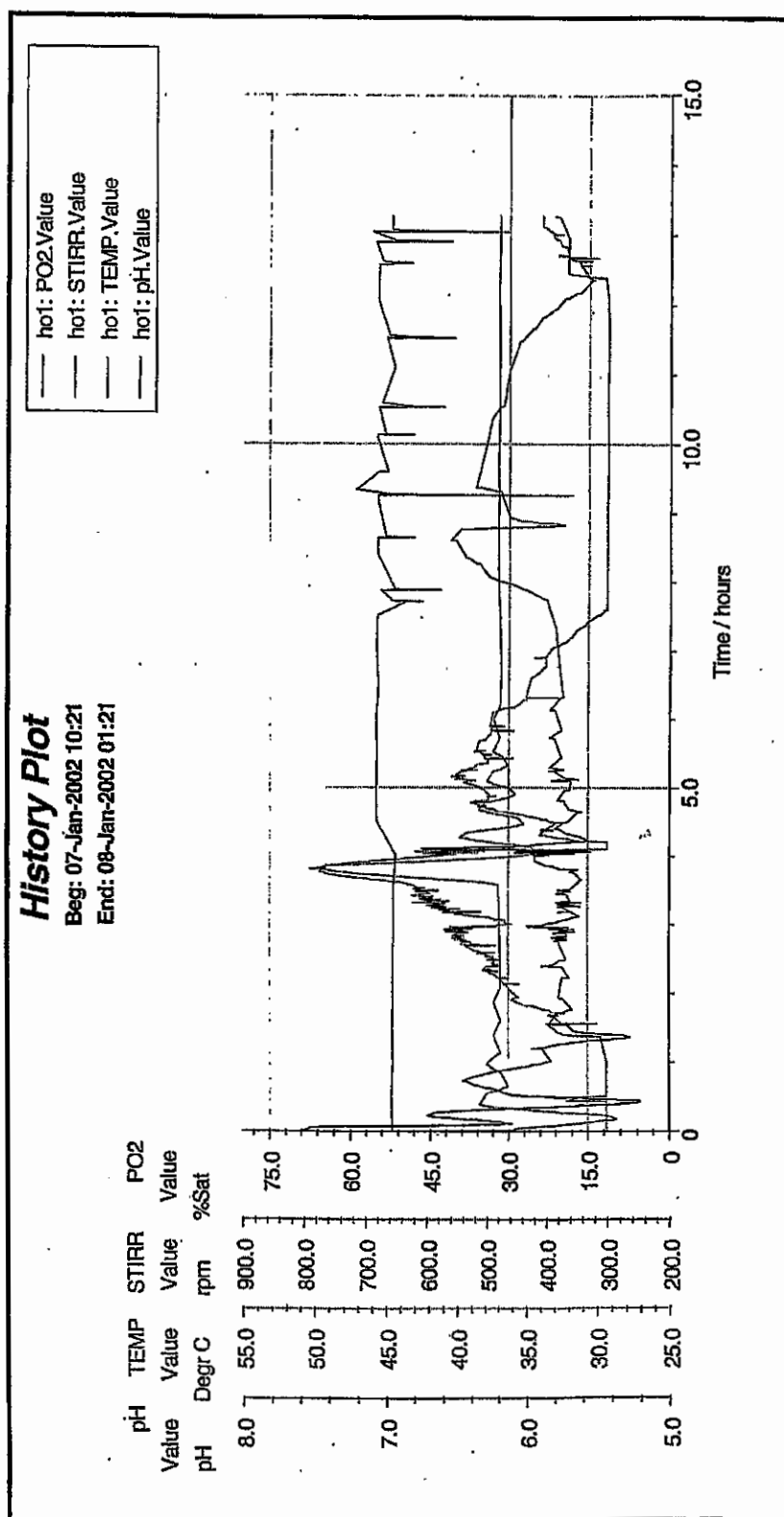


Fig. 4B

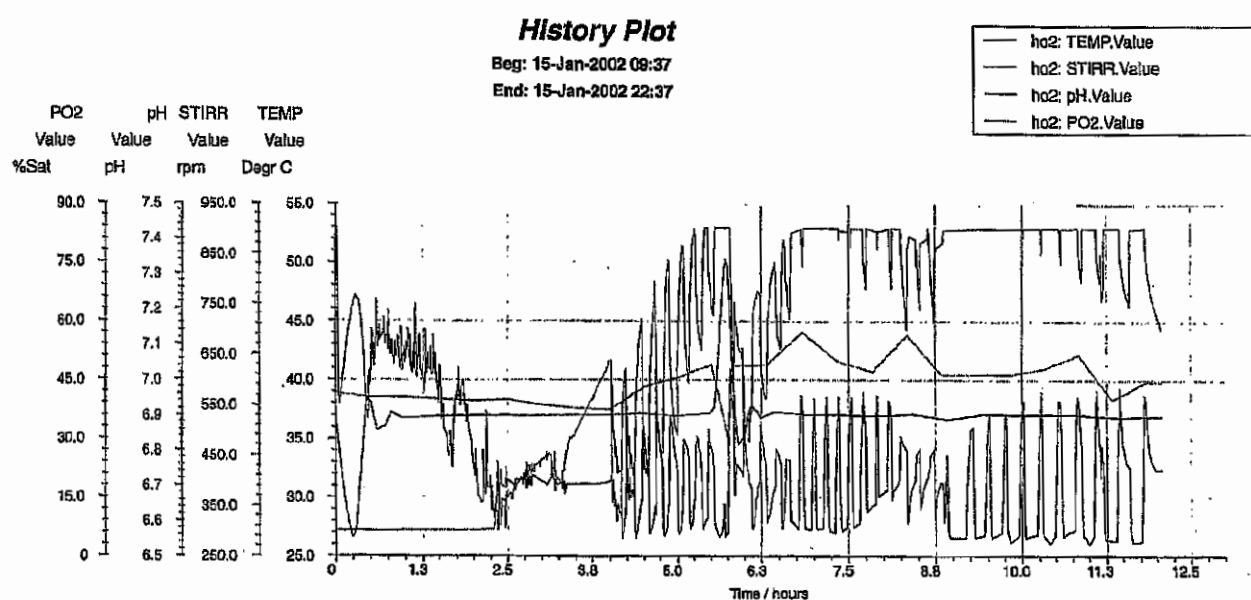
Fig. 5A



WO 2004/000349

9/46

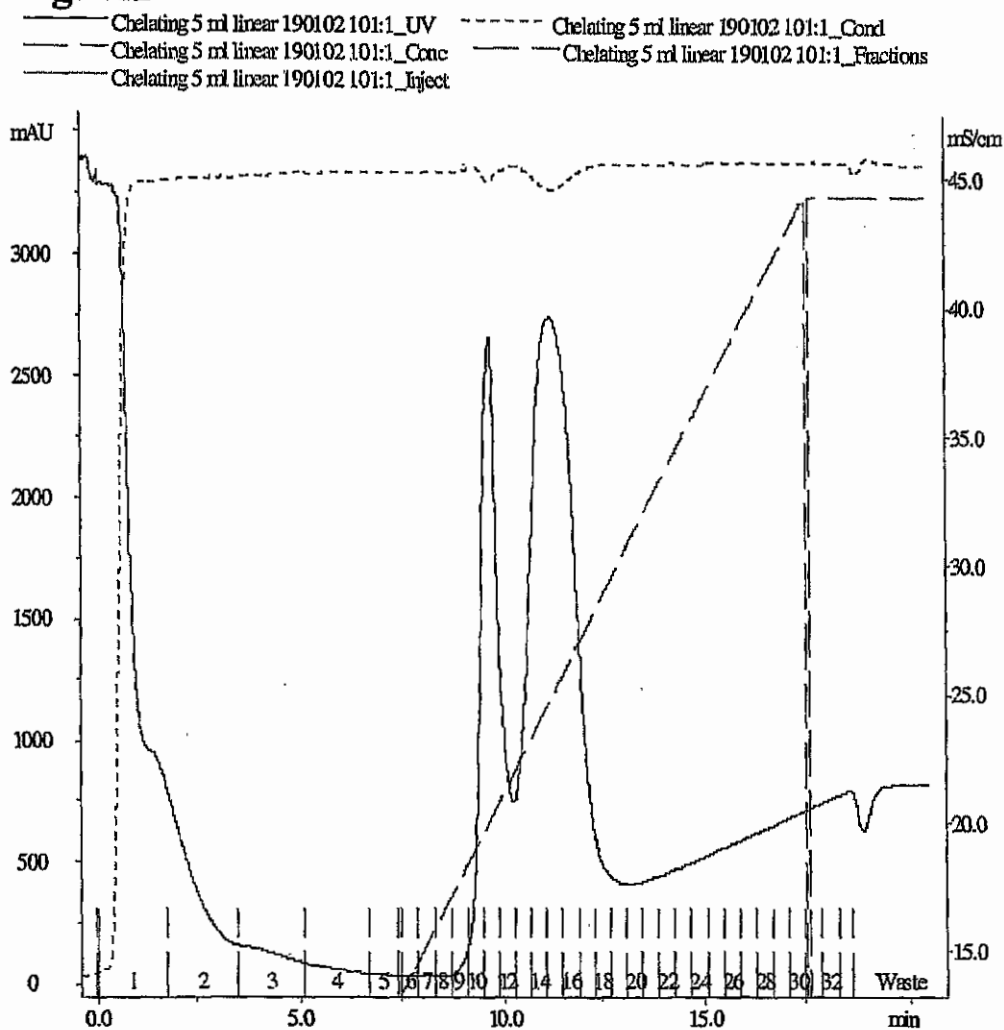
Fig. 5B



WO 2004/000349

10/46

Fig. 6A



Column HiTrap_Chelating_1x5_ml
 Pressure_limit 0.8 {MPa}
 Flow 5.00 {ml/min}
 UV_Averaging_time 2.60
 Start_ConcB 0.00 {%B}
 Equilibrate_with 0.5 {CV}
 Flowthrough_FracSize 8 {ml}
 Empty_loop_with 0 {ml}
 Wash_column_with 7 {CV}
 Start_Frac_at 0 {%B}
 Eluate_FracSize 2 {ml}
 End_Frac_at 100 {%B}
 Target_ConcB_1 100 {%B}
 Length_of_gradient_1 10 {base}
 Target_ConcB_2 0 {%B}
 Length_of_gradient_2 0 {base}
 Target_ConcB_3 0 {%B}
 Length_of_gradient_3 0.00 {base}
 Conc_of_eluent_B 100 {%B}
 Clean_with 4 {CV}
 Reequilibrate_conc 0.00 {%B}
 Reequilibrate_with 0.00 {CV}

11/46

Fig. 6B

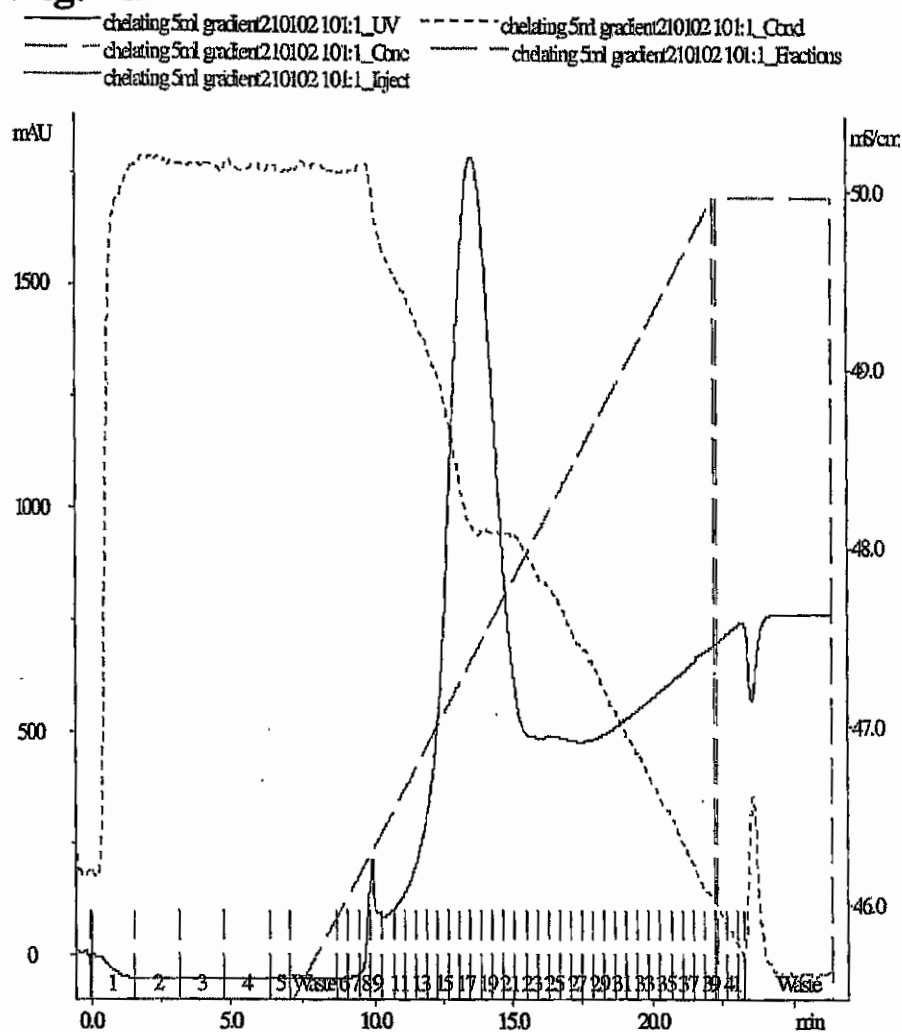
M 11 12 13 14 15 16 17 18 M 19 20 21 23 25 27 29 31



WO 2004/000349

12/46

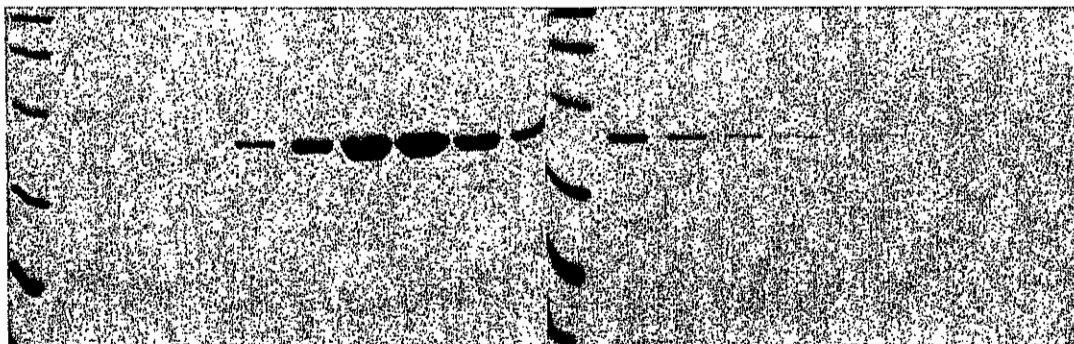
Fig. 7A



Column HiTrap_Chelating_1x5_ml
 Pressure_limit 0.8 {MPa}
 Flow 5.00 {ml/min}
 UV_Averaging_time 2.60
 Start_ConcB 0.00 {%B}
 Equilibrate_with 0.5 {CV}
 Flowthrough_FracSize 8 {ml}
 Empty_loop_with 0 {ml}
 Wash_column_with 7 {CV}
 Start_Frac_at 10 {%B}
 Eluate_FracSize 2 {ml}
 End_Frac_at 100 {%B}
 Target_ConcB_1 100 {%B}
 Length_of_gradient_1 15 {base}
 Target_ConcB_2 0 {%B}
 Length_of_gradient_2 0.00 {base}
 Target_ConcB_3 0 {%B}
 Length_of_gradient_3 0.00 {base}
 Conc_of_eluent_B 100 {%B}
 Clean_with 4.00 {CV}
 Reequilibrate_conc 0.00 {%B}
 Reequilibrate_with 0.00 {CV}

Fig. 7B

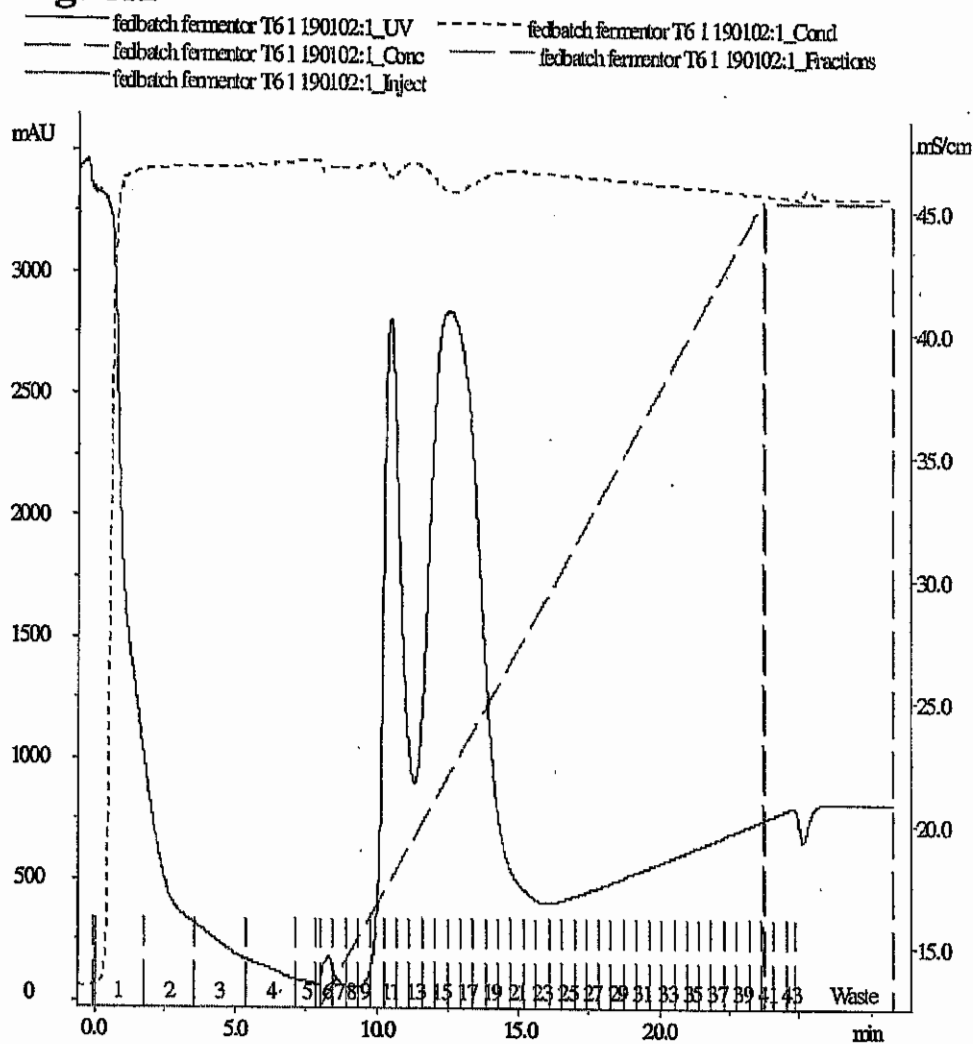
M 9 10 11 13 15 17 19 21 23 M 25 27 29 31 33 35 37 39



WO 2004/000349

14/46

Fig. 8A

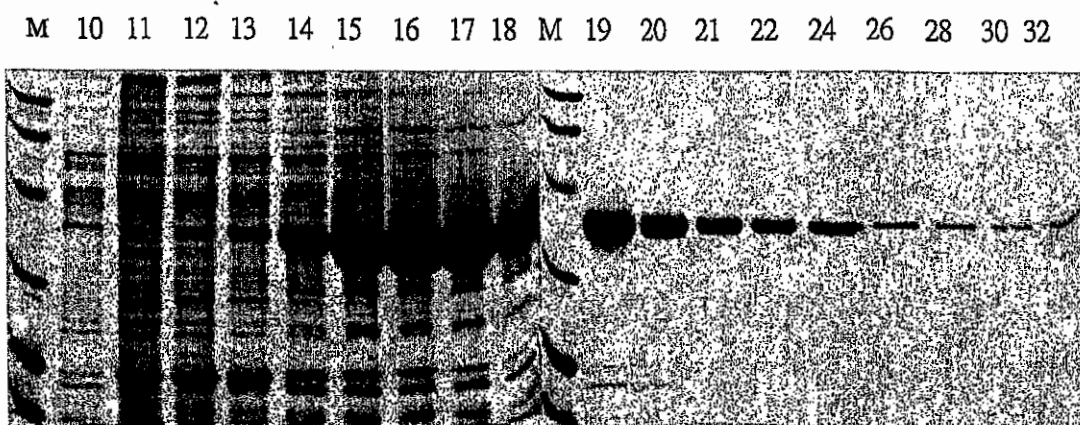


Column HiTrap_Chelating_1x5_ml
 Pressure_limit 0.8 {MPa}
 Flow 5.00 {ml/min}
 UV_Averaging_time 2.60
 Start_ConcB 0.00 {%B}
 Equilibrate_with 0.5 {CV}
 Flowthrough_FracSize 8 {ml}
 Empty_loop_with 0 {ml}
 Wash_column_with 7 {CV}
 Start_Frac_at 0 {%B}
 Eluate_FracSize 2 {ml}
 End_Frac_at 100 {%B}
 Target_ConcB_1 100 {%B}
 Length_of_gradient_1 14 {base}
 Target_ConcB_2 0 {%B}
 Length_of_gradient_2 0.00 {base}
 Target_ConcB_3 0 {%B}
 Length_of_gradient_3 0.00 {base}
 Conc_of_eluent_B 100 {%B}
 Clean_with 4.00 {CV}
 Reequilibrate_conc 0.00 {%B}
 Reequilibrate_with 0.00 {CV}

WO 2004/000349

15/46

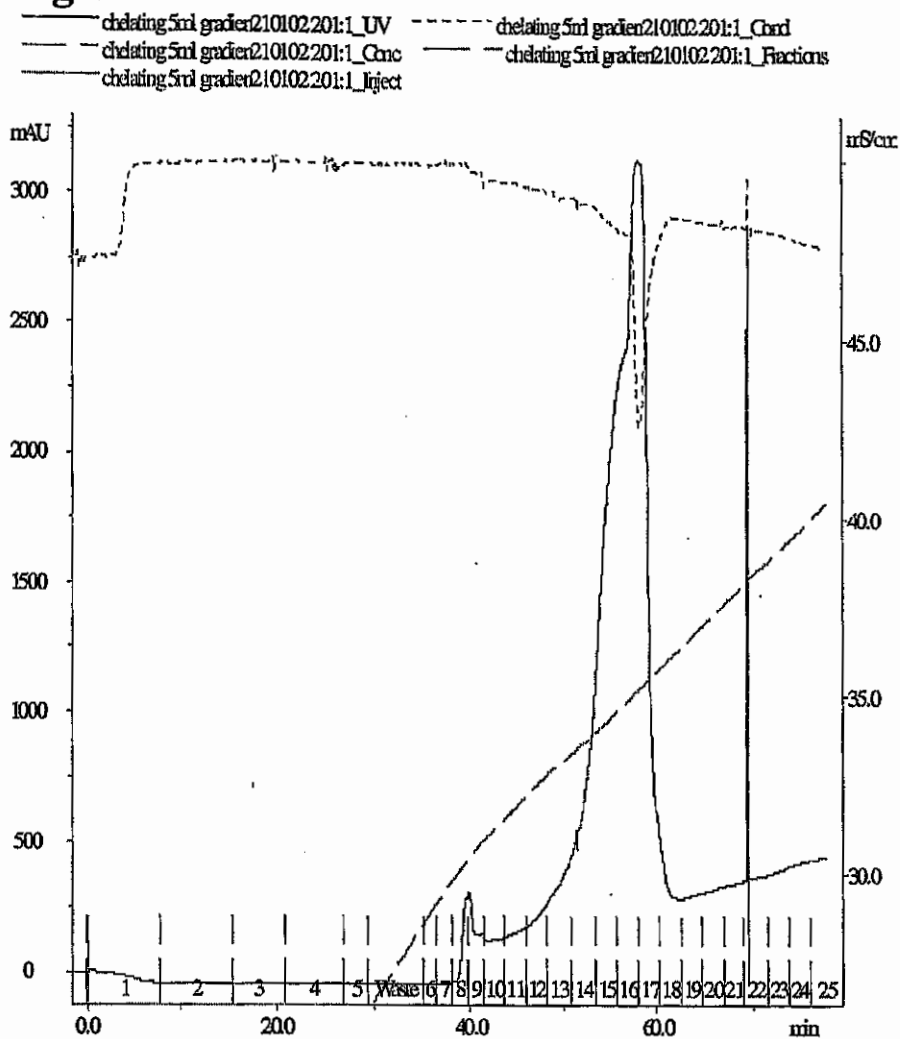
Fig. 8B



WO 2004/000349

16/46

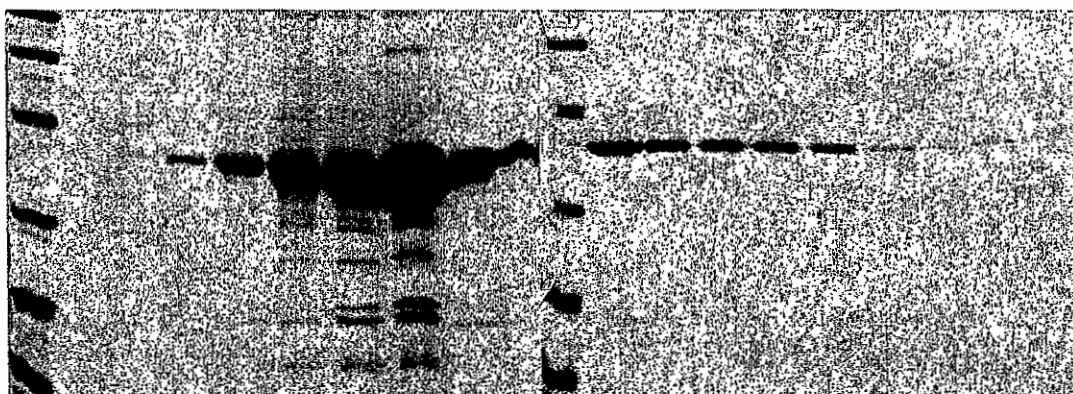
Fig. 9A



Column HiTrap_Chelating_1x5_ml
 Pressure_limit 0.8 {MPa}
 Flow 5.00 {ml/min}
 UV_Averaging_time 2.60
 Start_ConcB 0.00 {%B}
 Equilibrate_with 0.2 {CV}
 Flowthrough_FracSize 8 {ml}
 Empty_loop_with 0 {ml}
 Wash_column_with 7 {CV}
 Start_Frac_at 10 {%B}
 Eluate_FracSize 2 {ml}
 End_Frac_at 100 {%B}
 Target_ConcB_1 100 {%B}
 Length_of_gradient_1 15 {base}
 Target_ConcB_2 0 {%B}
 Length_of_gradient_2 0.00 {base}
 Target_ConcB_3 0 {%B}
 Length_of_gradient_3 0.00 {base}
 Conc_of_eluent_B 100 {%B}
 Clean_with 4.00 {CV}
 Reequilibrate_conc 0.00 {%B}
 Reequilibrate_with 0.00 {CV}

Fig. 9B

M 8 10 12 14 15 16 17 18 19 M 20 22 24 E1 E2 E3 E4 E5 E6



18/46

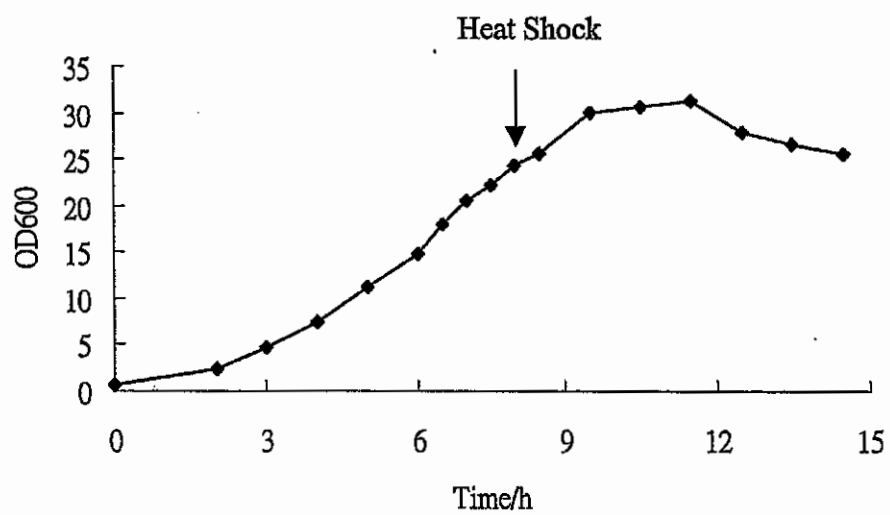
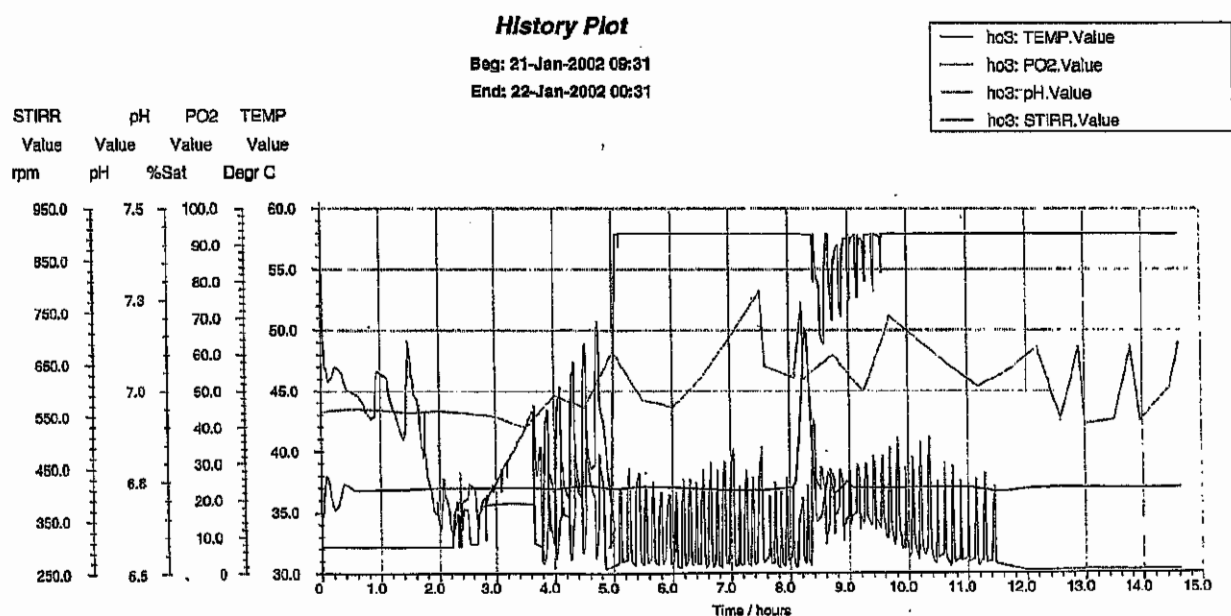
Fig. 10

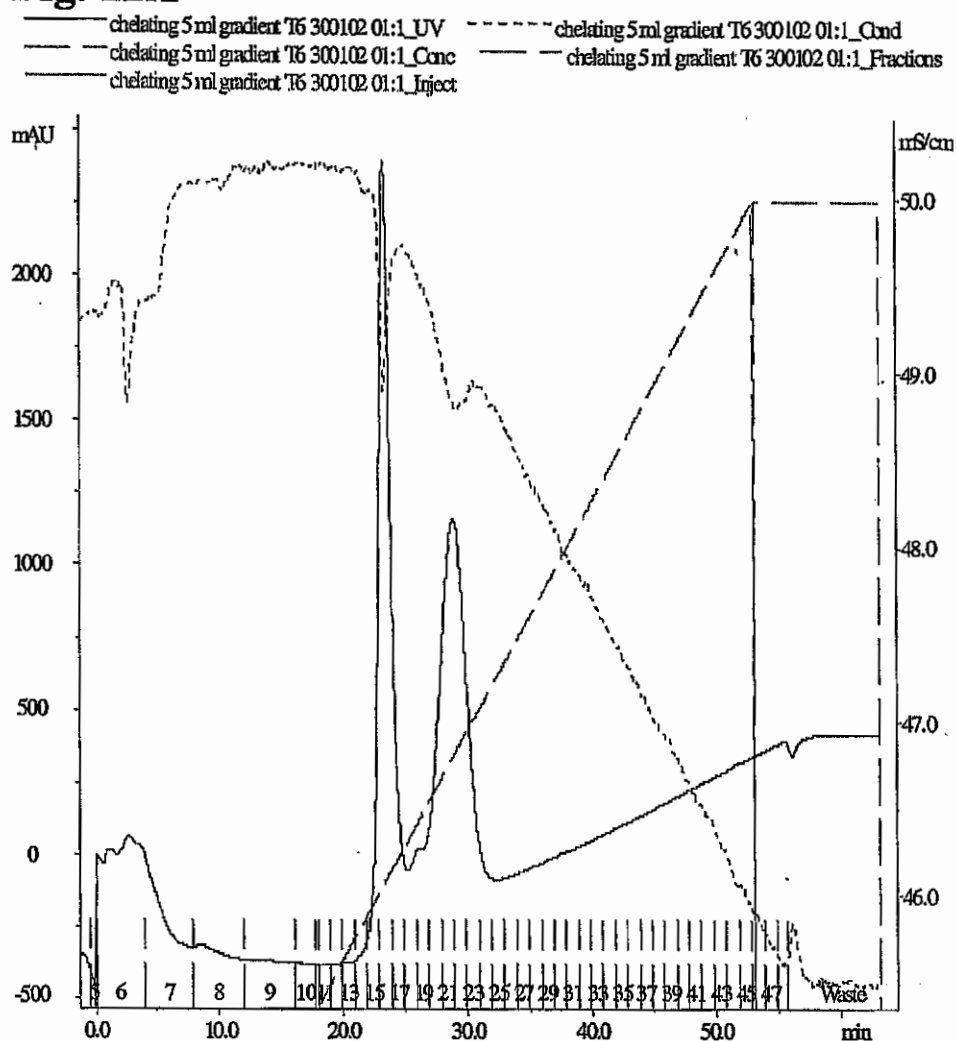
Fig. 11



WO 2004/000349

20/46

Fig. 12A



Column HiTrap_Cheating_1x5_ml
 Pressure_limit 0.5 {MPa}
 Flow 2 {ml/min}
 UV_Averaging_time 2.60
 Start_ConcB 0.00 {%B}
 Equilibrate_with 2 {CV}
 Flowthrough_FracSize 8 {ml}
 Empty_loop_with 0 {ml}
 Wash_column_with 7 {CV}
 Start_Frac_at 0 {%B}
 Eluate_FracSize 2 {ml}
 End_Frac_at 100 {%B}
 Target_ConcB_1 100 {%B}
 Length_of_gradient_1 14 {base}
 Target_ConcB_2 0 {%B}
 Length_of_gradient_2 0.00 {base}
 Target_ConcB_3 0 {%B}
 Length_of_gradient_3 0.00 {base}
 Conc_of_eluent_B 100 {%B}
 Clean_with 4.00 {CV}
 Reequilibrate_conc 0.00 {%B}
 Reequilibrate_with 0.00 {CV}

Fig. 12B

M crude 16 19 20 21 22 23 25 27 M 29 31 33 35 37 39 41 43 45

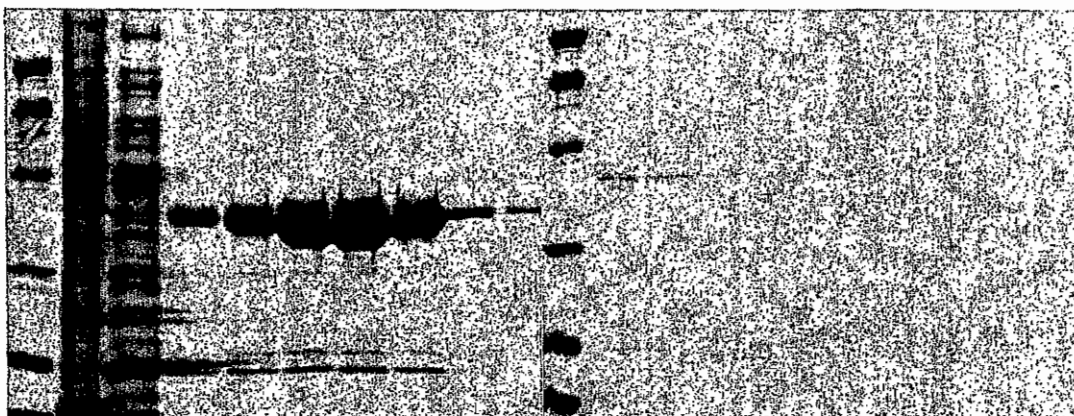
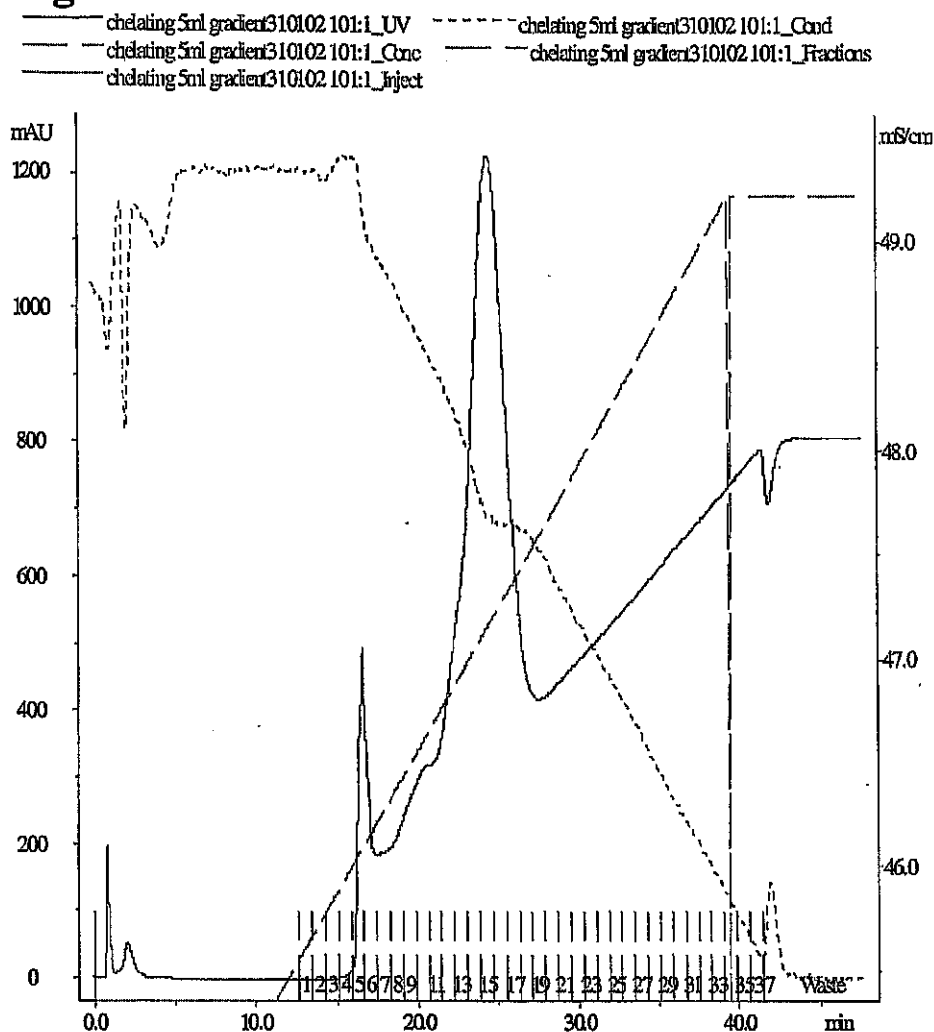


Fig. 13A



Column HITrap_Chelating_1x5_ml
 Pressure_limit 0.8 {MPa}
 Flow 2.5 {ml/min}
 UV_Averaging_time 2.60
 Start_ConcB 0.00 {%B}
 Equilibrate_with 0 {CV}
 Flowthrough_FracSize 0 {ml}
 Empty_loop_with 0 {ml}
 Wash_column_with 5.5 {CV}
 Start_Frac_at 5 {%B}
 Eluate_FracSize 2 {ml}
 End_Frac_at 100 {%B}
 Target_ConcB_1 100 {%B}
 Length_of_gradient_1 14 {base}
 Target_ConcB_2 0 {%B}
 Length_of_gradient_2 0.00 {base}
 Target_ConcB_3 0 {%B}
 Length_of_gradient_3 0.00 {base}
 Conc_of_eluent_B 100 {%B}
 Clean_with 4.00 {CV}
 Reequilibrate_conc 0.00 {%B}
 Reequilibrate_with 0.00 {CV}

Fig. 13B

M 7 9 11 12 13 14 15 16 17 M 18 20 22 24 26 28 30 32 34

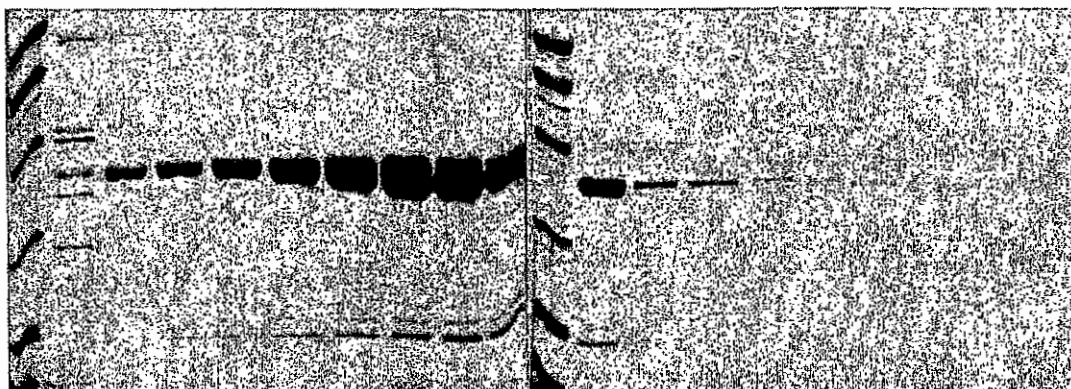
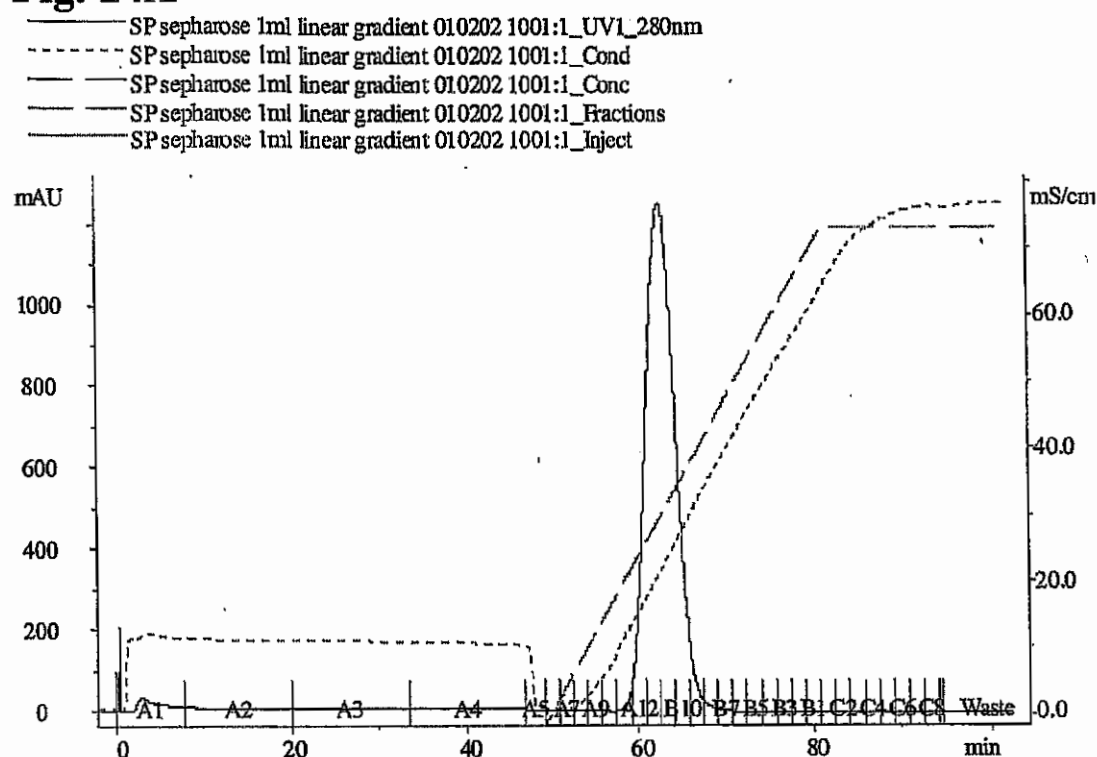


Fig. 14A

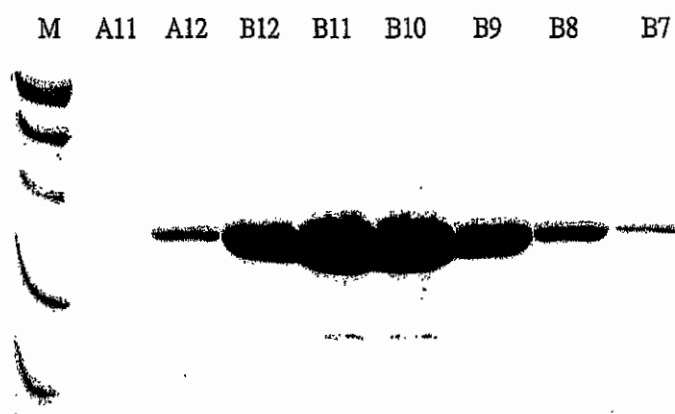


Column HiTrap_SP_FF_1_ml
 Flow_Rate 1.00 {ml/min}
 Column_PressureLimit 0.40 {MPa}
 Wavelength_1 280 {nm}
 Wavelength_2 OFF {nm}
 Wavelength_3 OFF {nm}
 Averaging_Time_UV 5.12 {sec}
 Pump_A_Inlet A1
 Pump_B_Inlet B1
 Wash_Inlet_A1_ OFF
 Wash_Inlet_A2_ OFF
 Wash_Inlet_B1_ OFF
 Wash_Inlet_B2_ OFF
 Start_ConcB 0 {%B}
 Compensation_Volume 8 {ml}
 Equilibrate_with 0 {CV}
 Flowthrough_TubeType 18mm
 Flowthrough_FracSize 8 {ml}
 Flowthrough_StartAt FirstTube
 Empty_loop_with 31.500 {ml}
 Wash_column_with 2 {CV}
 _Start_Frac_at 0 {%B}
 _End_Frac_at 100 {%B}
 TubeType_EluatFrac 18mm
 Eluate_Frac_Size 1 {ml}
 EluateFrac_StartAt NextTube
 Target_ConcB 100 {%B}
 Length_of_Gradient 20.00 {base}
 Gradient_Delay 8 {ml}
 Clean_with 5.00 {CV}

WO 2004/000349

25/46

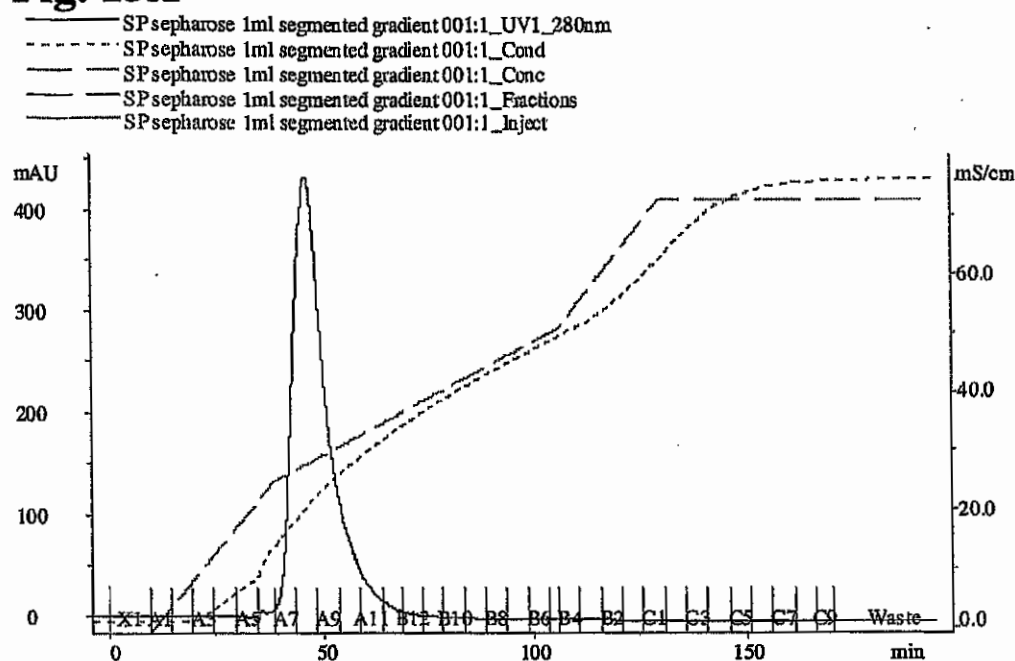
Fig. 14B



WO 2004/000349

26/46

Fig. 15A

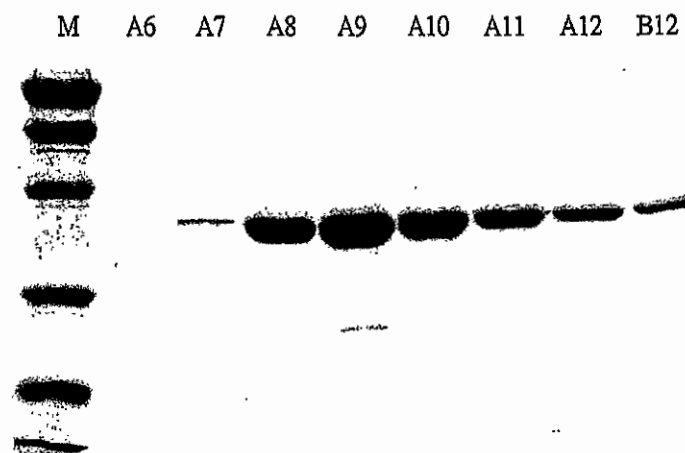


Column HiTrap_SP_FF_1_ml
 Flow_Rate 0.40 {ml/min}
 Column_PressureLimit 0.50 {MPa}
 Wavelength_1 280 {nm}
 Wavelength_2 OFF {nm}
 Wavelength_3 OFF {nm}
 Averaging_Time_UV 5.12 {sec}
 Pump_A_Inlet A1
 Pump_B_Inlet B1
 Wash_Inlet_A1_ OFF
 Wash_Inlet_A2_ OFF
 Wash_Inlet_B1_ OFF
 Wash_Inlet_B2_ OFF
 Start_ConcB 0 {%B}
 Compensation_Volume 8 {ml}
 Equilibrate_with 0 {CV}
 Flowthrough_TubeType 30mm
 Flowthrough_FracSize 40 {ml}
 Flowthrough_StartAt TubeNumber[X.1]
 Empty_loop_with 0.000 {ml}
 Wash_column_with 2 {CV}
 1_Tube_Type 18mm
 1_Fraction_Size 1 {ml}
 1_Start_at FirstTube
 Target_ConcB_1 35 {%B}
 Length_of_Gradient_1 6.00 {base}
 2_Tube_Type 18mm
 2_Fraction_Size 1 {ml}
 2_Start_at NextTube
 Target_ConcB_2 70 {%B}
 Length_of_Gradient_2 14.00 {base}
 3_Tube_Type 18mm
 3_Fraction_Size 1 {ml}
 3_Start_at NextTube
 Target_ConcB_3 100 {%B}
 Length_of_Gradient_3 5.00 {base}
 Gradient_Delay 8 {ml}
 Clean_with 5.00 {CV}

WO 2004/000349

27/46

Fig. 15B



28/46

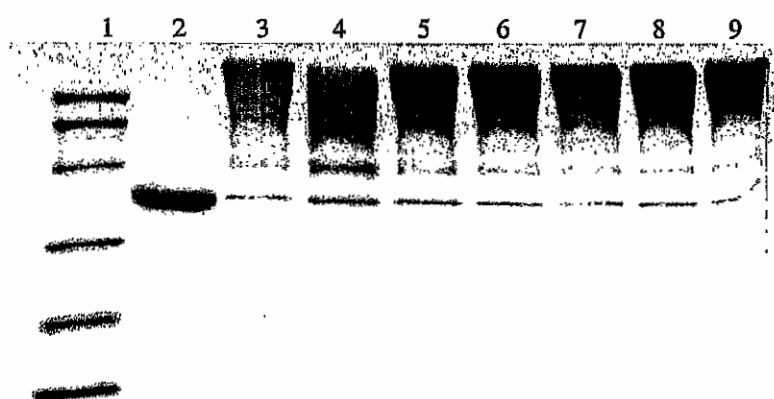
Fig. 16A

Fig. 16B

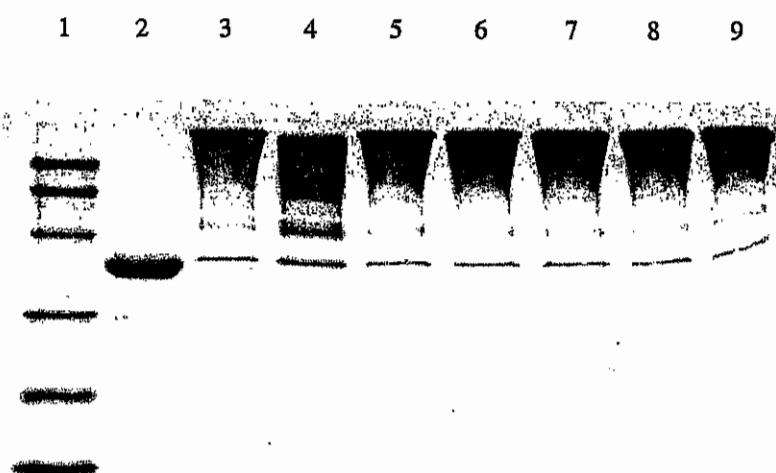
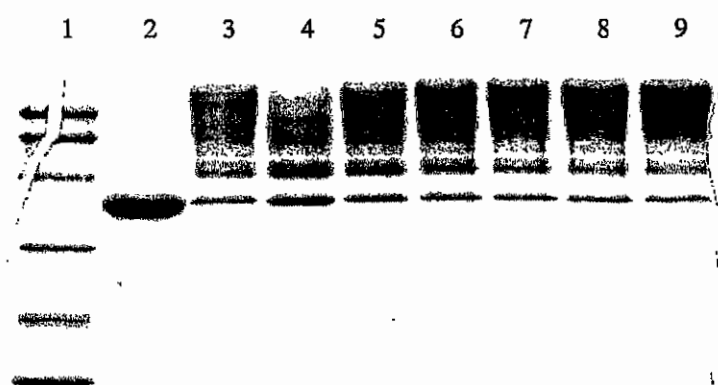


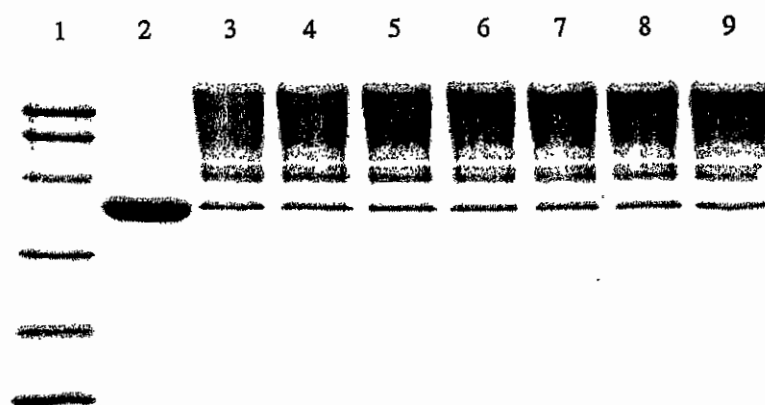
Fig. 17A



WO 2004/000349

31/46

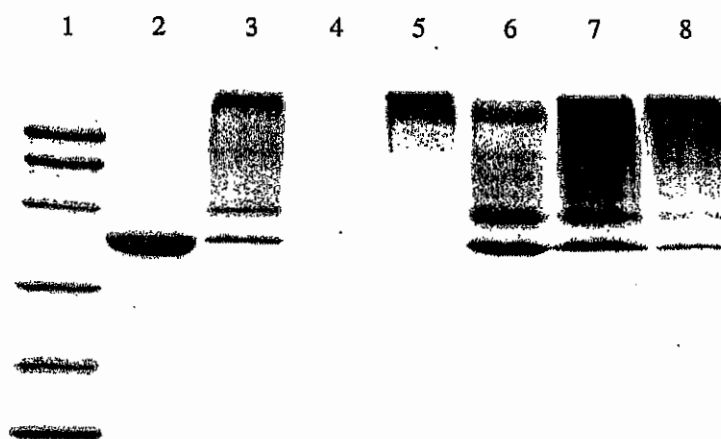
Fig. 17B



WO 2004/000349

32/46

Fig. 18A



WO 2004/000349

33/46

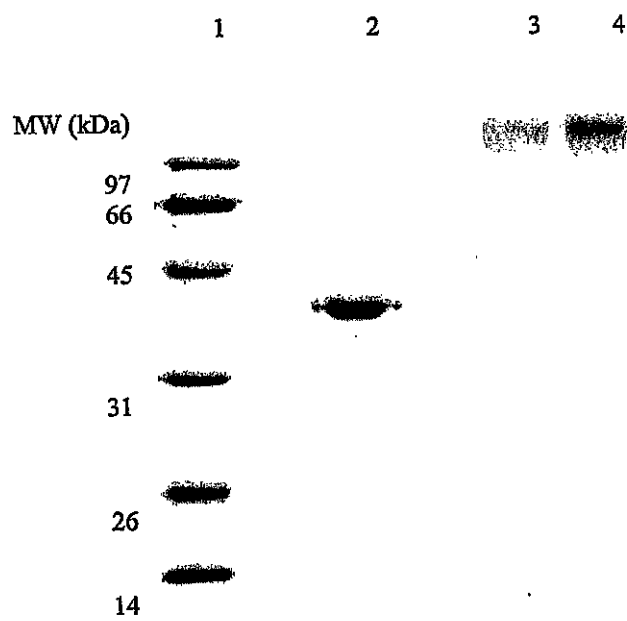
Fig. 18B

Fig. 19A

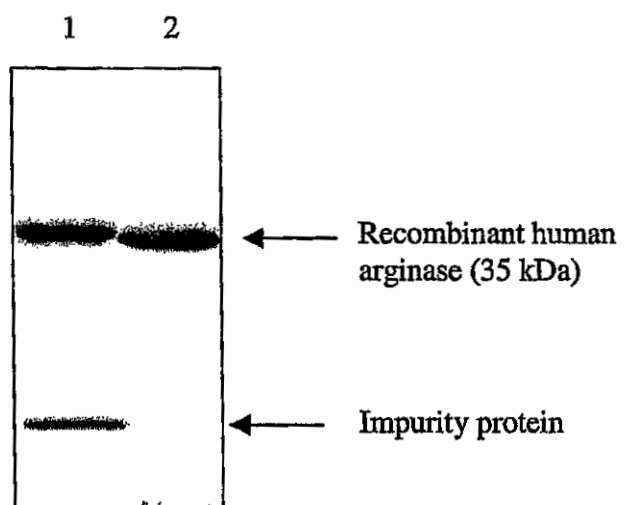
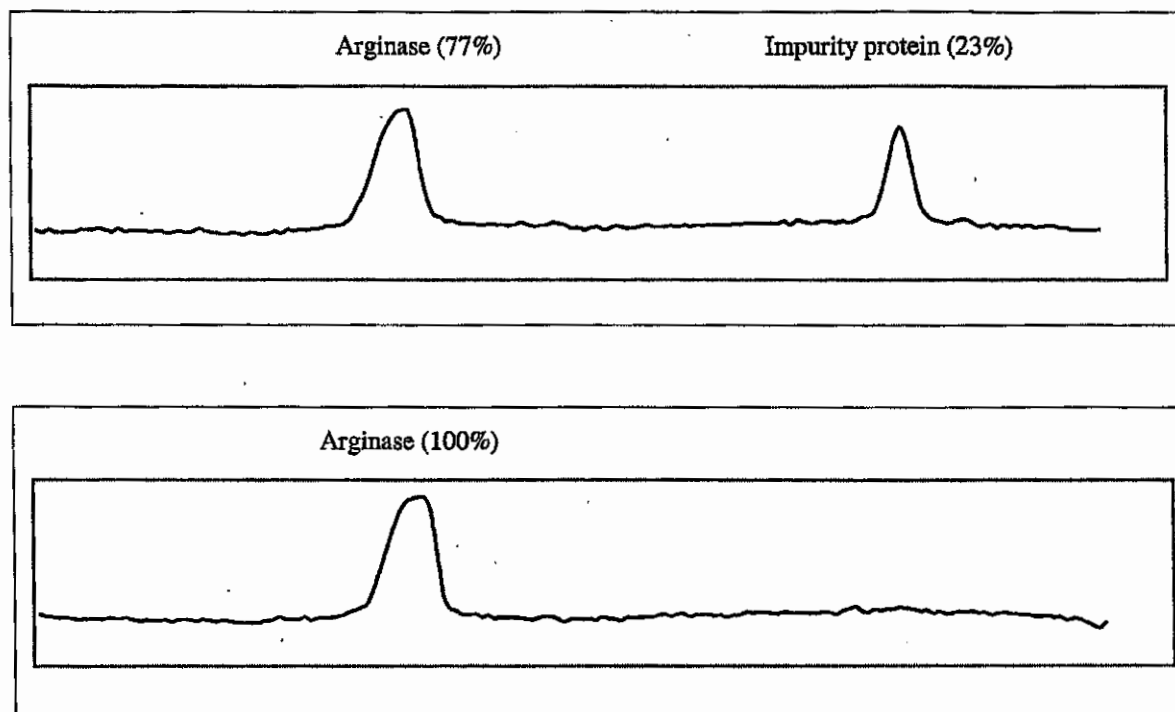
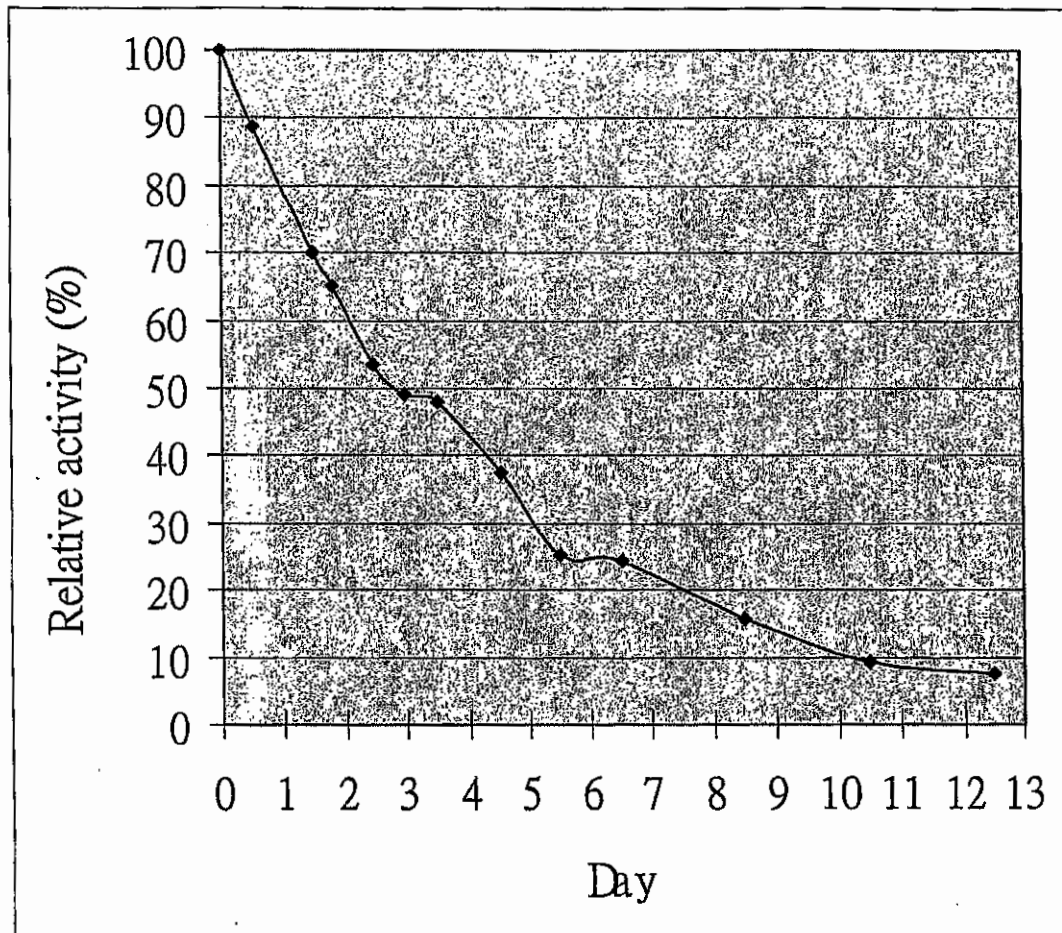


Fig. 19B

36/46

Fig. 20



37/46

Fig. 21

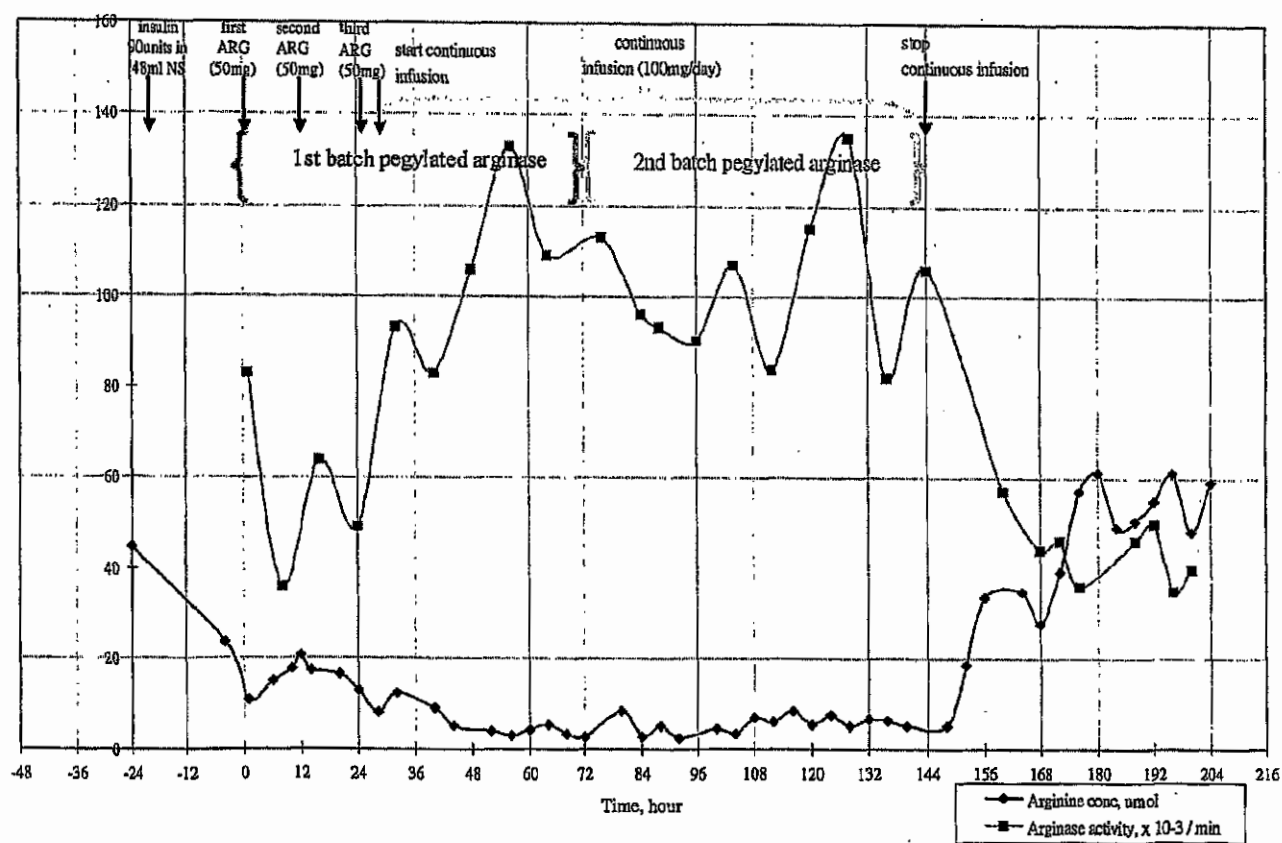
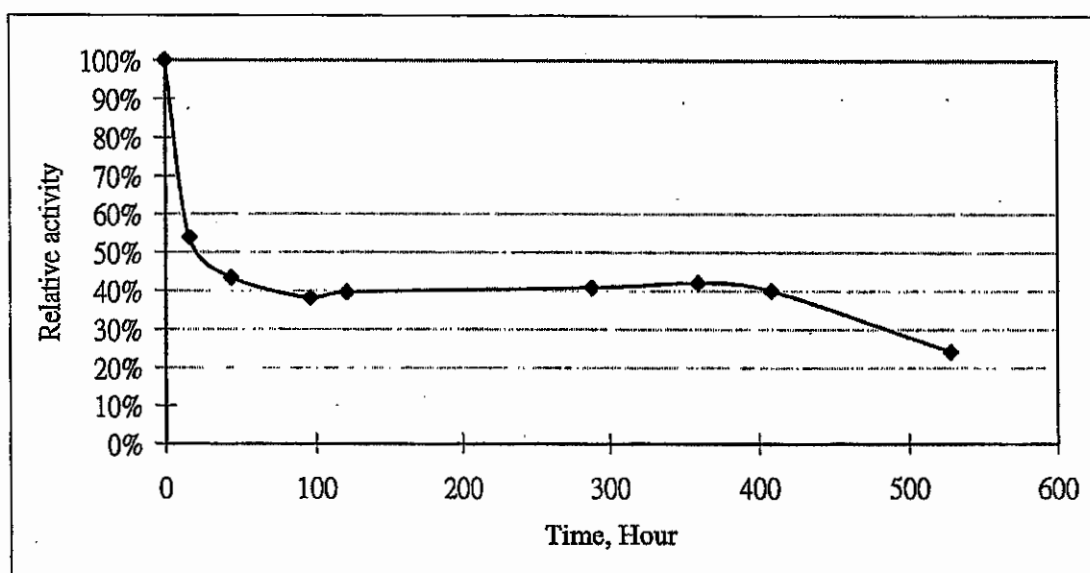


Fig. 22

39/46

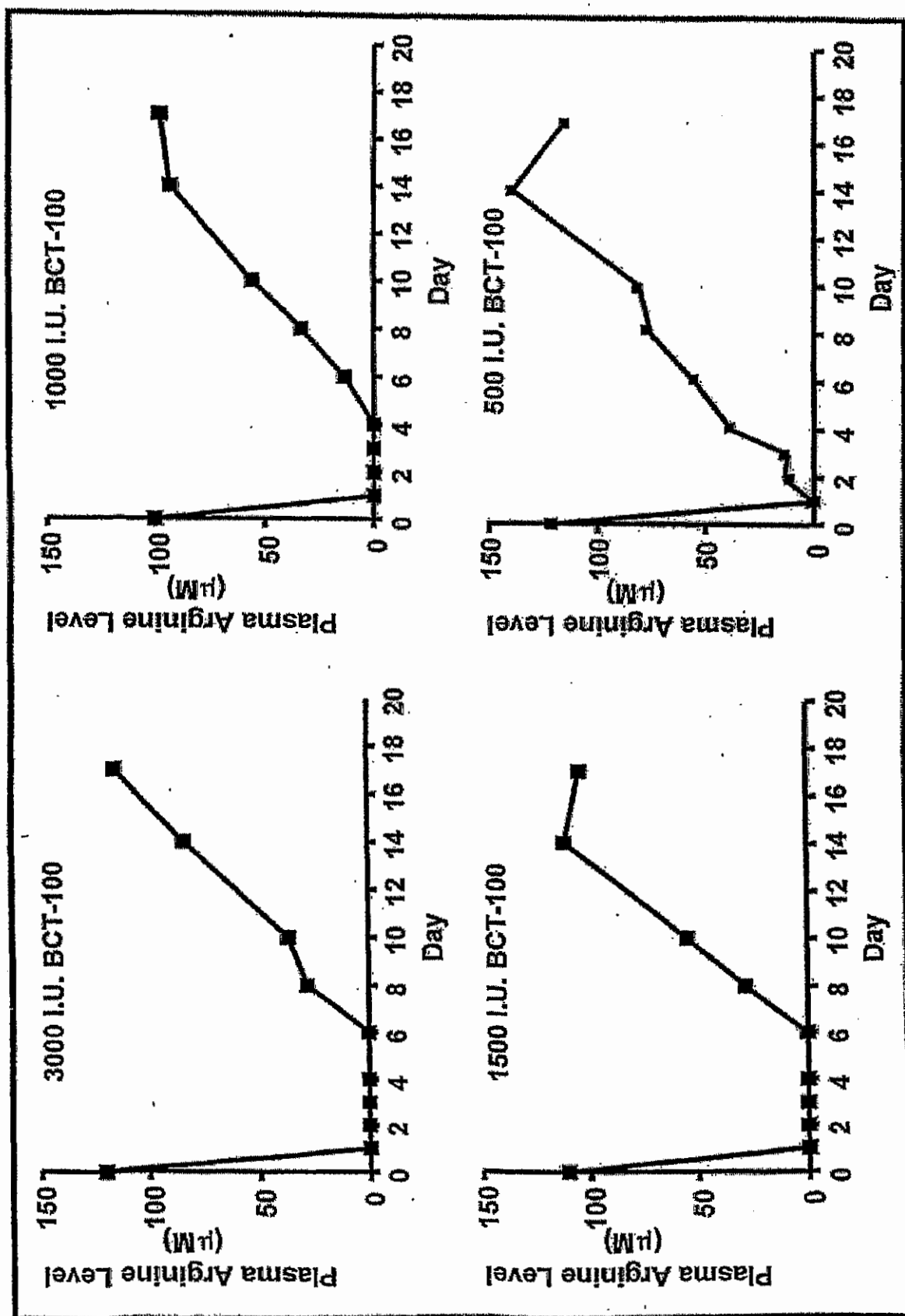


Fig. 23

40/46

Drug effect on Hep3B

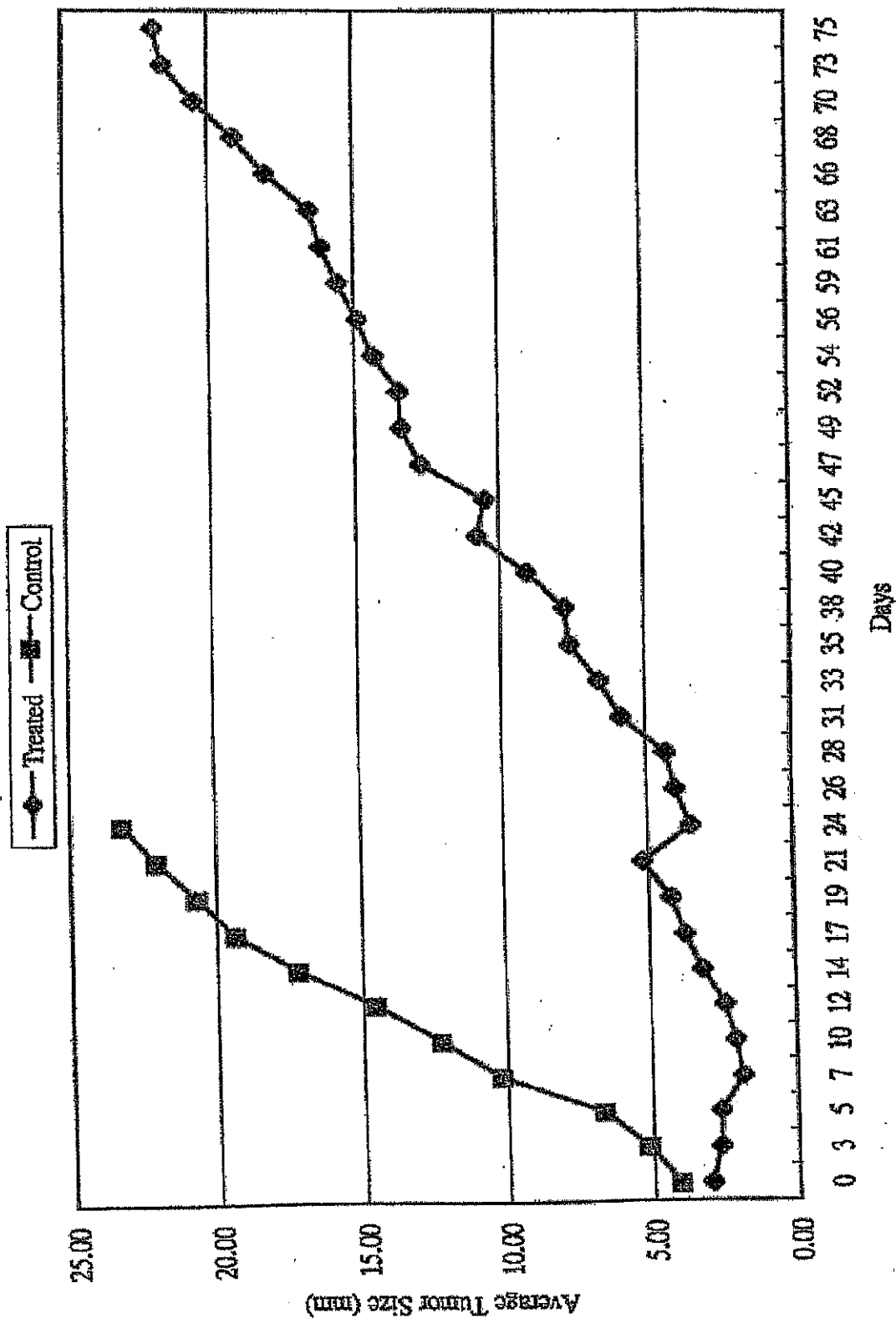


Fig.24

Drug effect on PLC/PRF/5 -Size changes

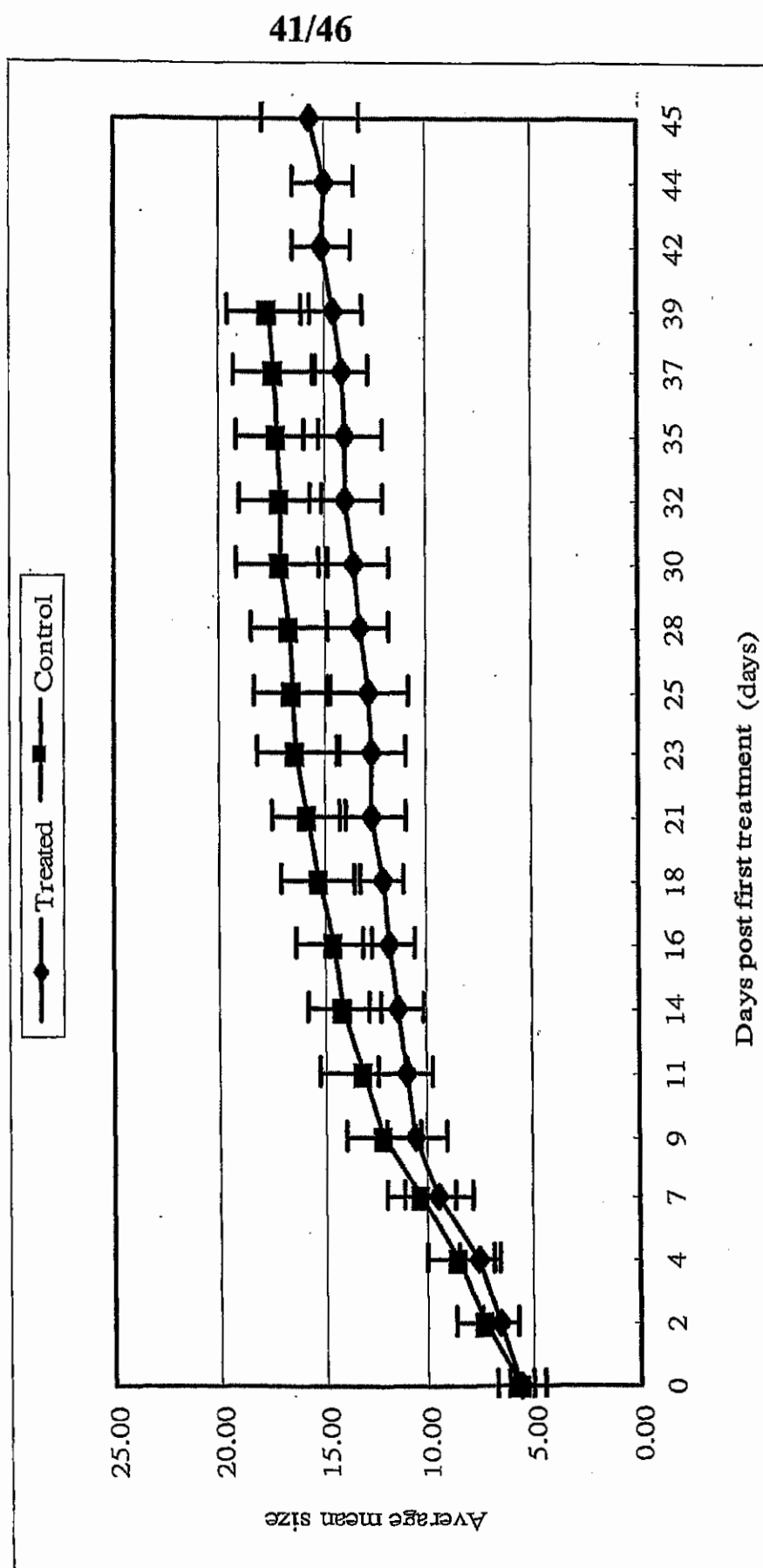


Fig. 25A

42/46

Drug effect on PLC/PRF/5 – Weight changes

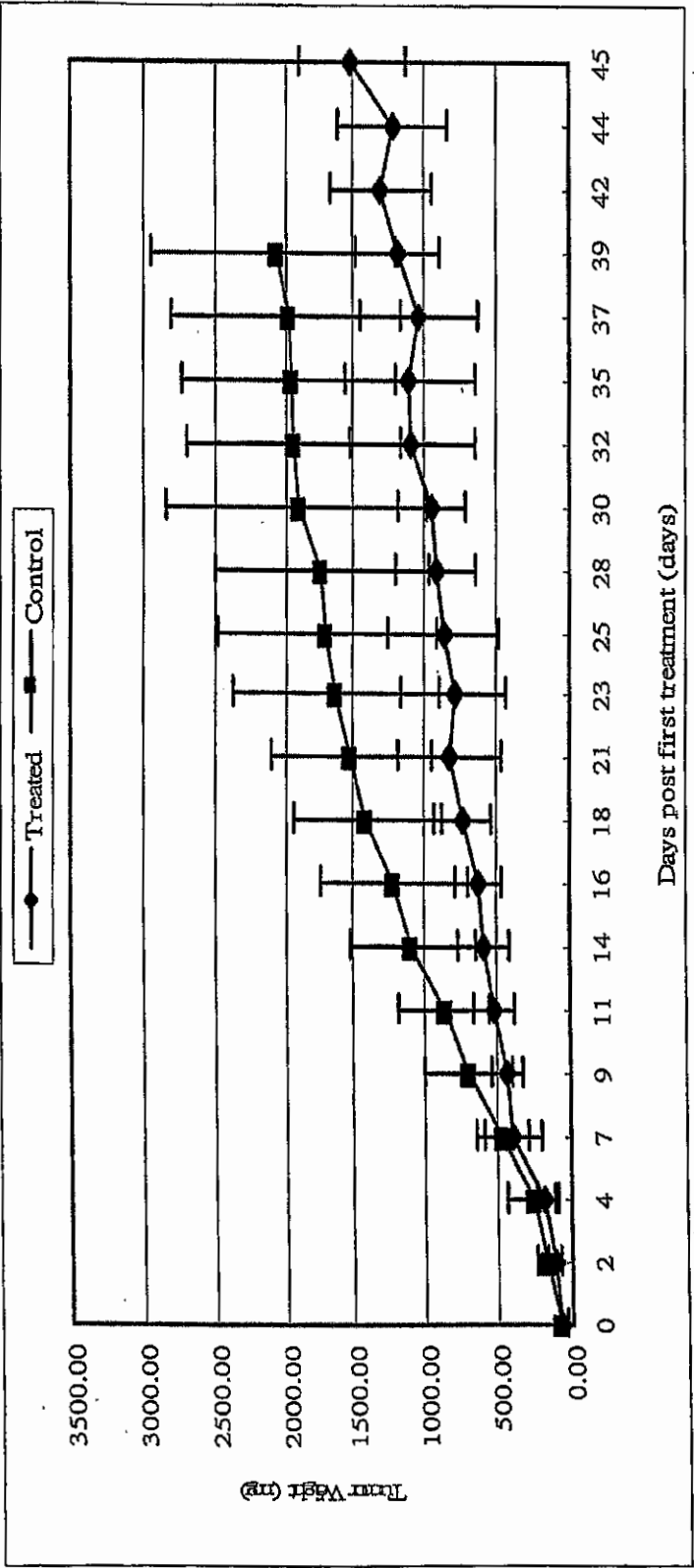


Fig. 25B

Drug effect on Huh-7 - Weight changes

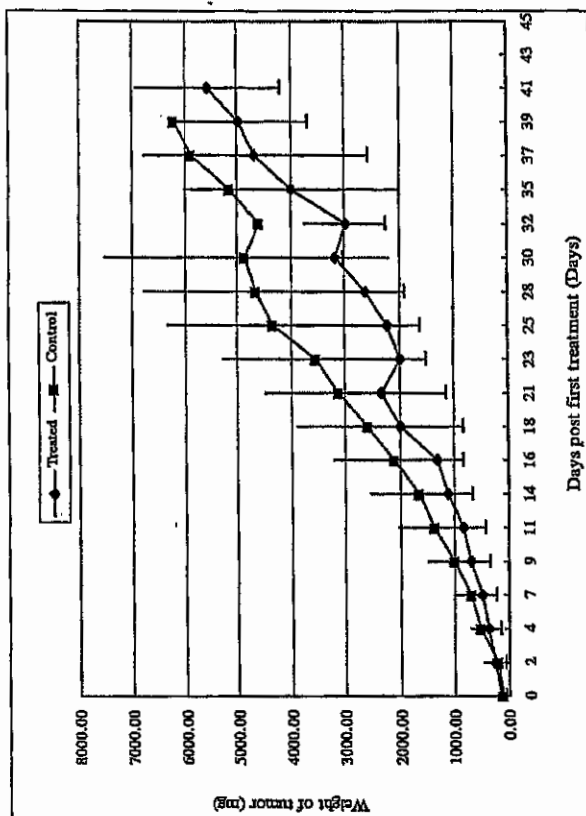


Fig. 26B

Drug effect on Huh-7 - Size changes

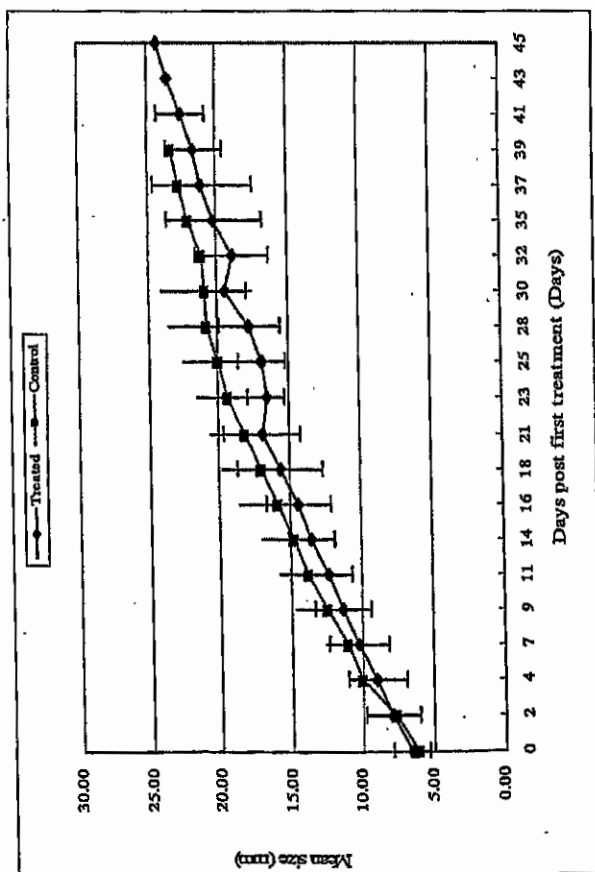
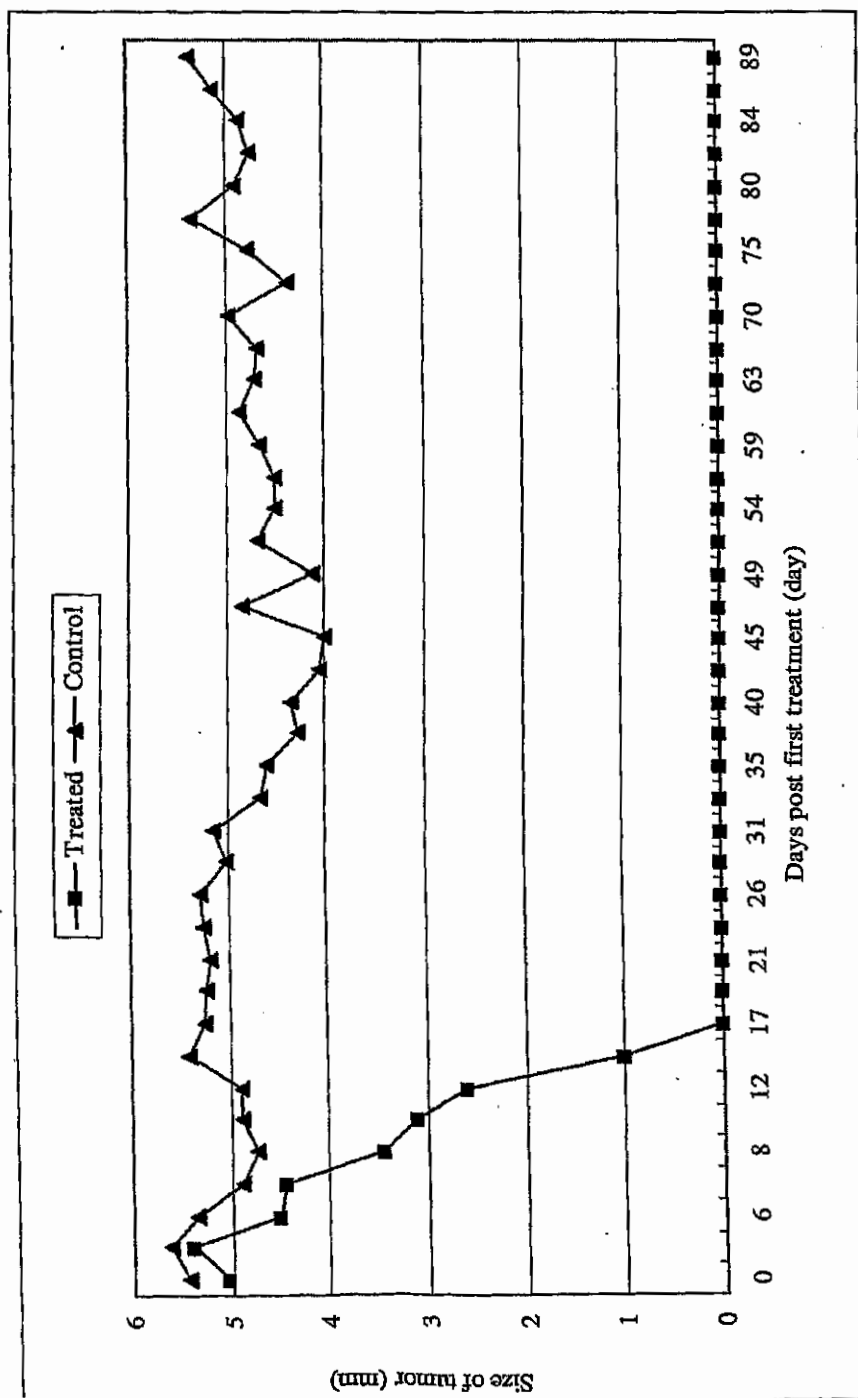


Fig. 26A

44/46

Drug effect on MCF-7 – Size changes

**Fig.27**

45/46

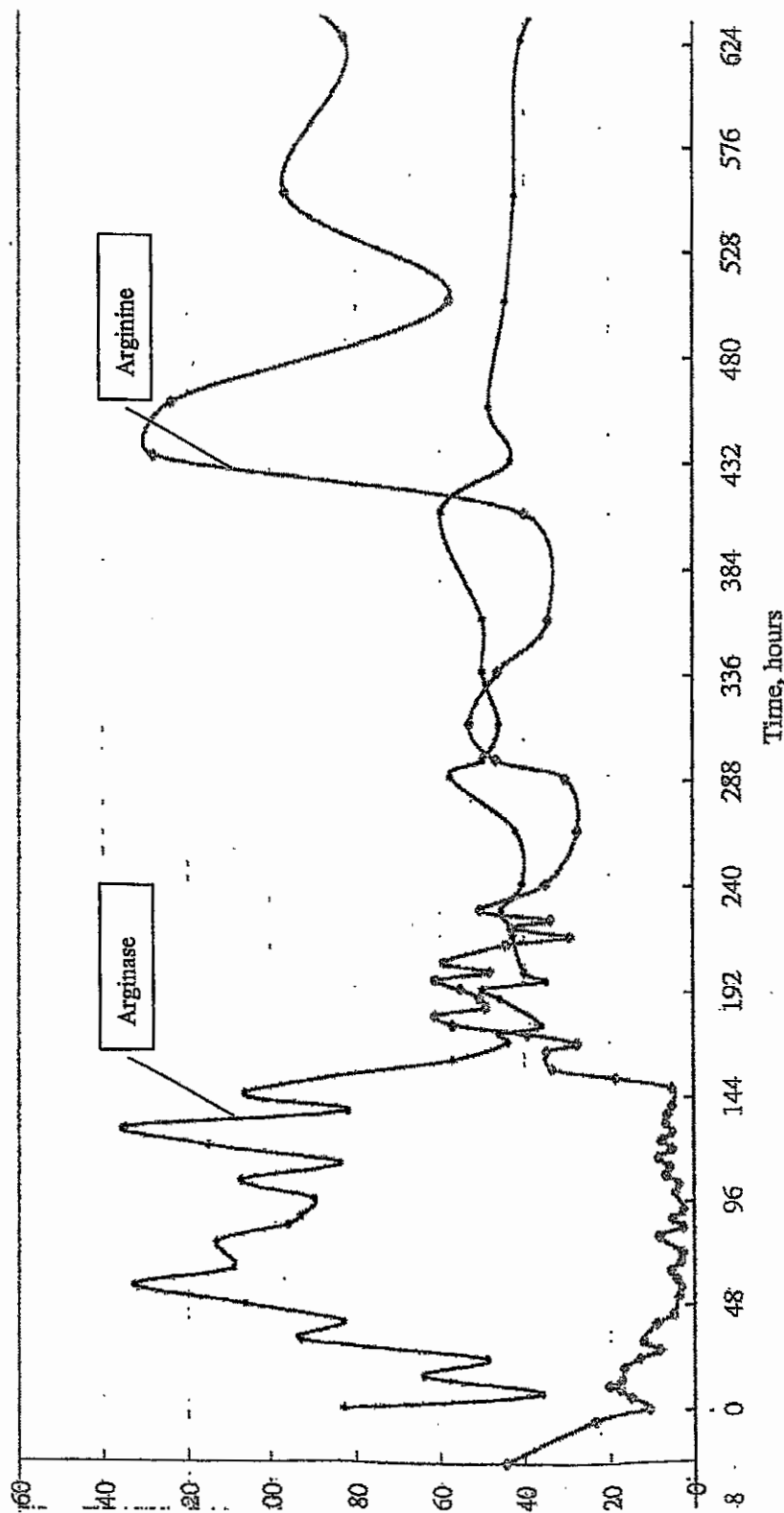


Fig. 28

46/46

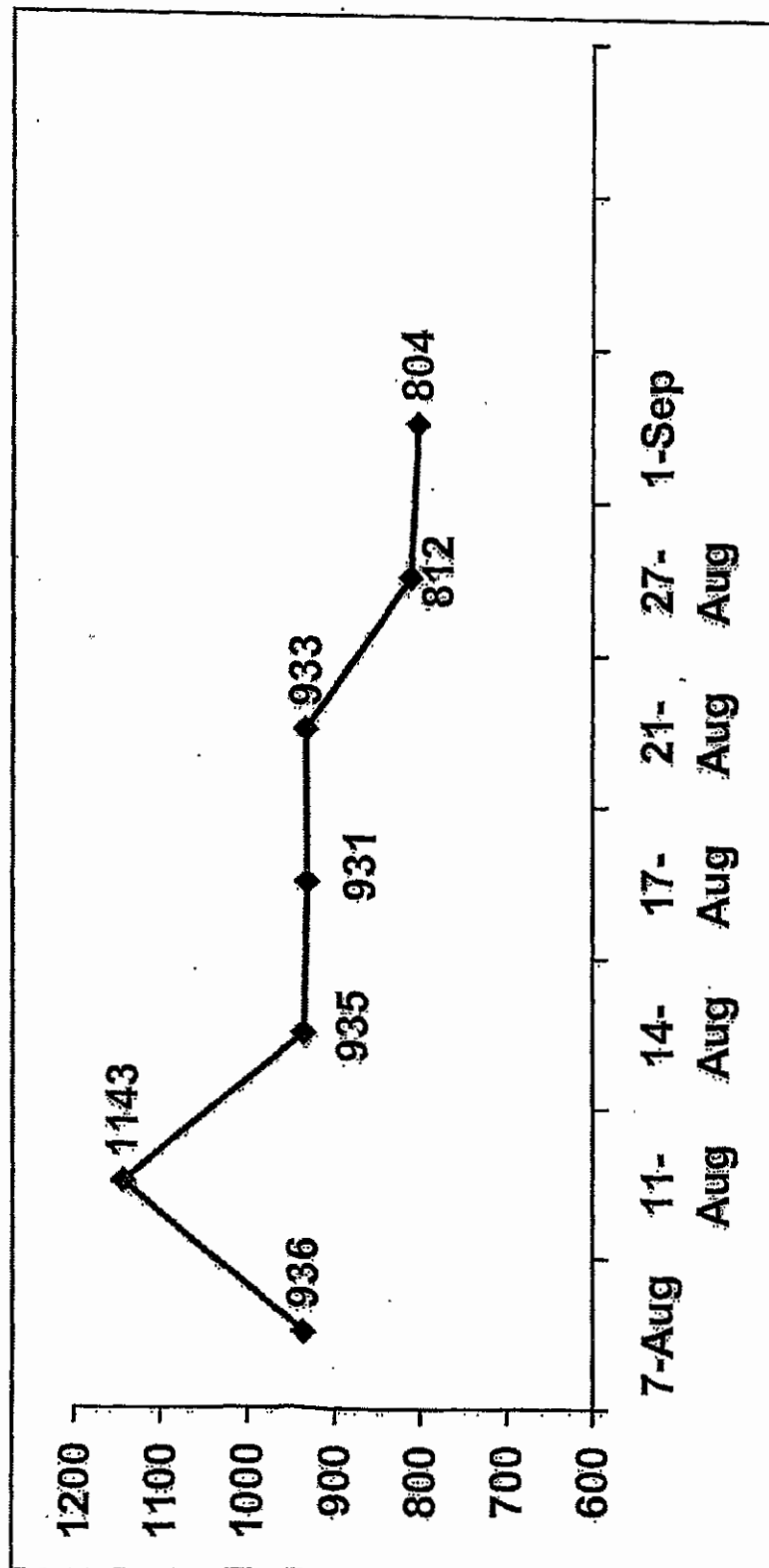


Fig. 29