



Scientific Study

**B4512, Durabase Advanced Cream
(Ibuprofen Study)**

Not appropriate for regulatory submission.
Please visit www.SpectrumRx.com or
contact Tech Services for the most up-to-
date information contained in this
information package.

Spectrum Pharmacy Products

777 Jersey Avenue
New Brunswick, NJ 08901
Phone 732.214.1300

Ibuprofen:

3.10g Ibuprofen raw drug powder from Acros Chemical (part number 258610100, Lot # A0311465) was added to 100.00g Spectrum Chemical Mfg. Corp. Durabase Advanced and levigated with an electronic mortar and pestle, resulting in a final concentration of 3.0% w/w. This emulsion was then stored at room temperature in the same Unguator container.

Similar steps were used in preparing the following combination compounds:
Compound 1 (5% Diclofenac Na + 3% Ibuprofen + 3% Pentoxifylline + 10% Verapamil HCl)
Compound 2 (2% Baclofen + 1% Bupivacaine HCl + 2% Cyclobenzaprine HCl + 5% Diclofenac Na + 6% Gabapentin + 3% Ibuprofen + 10% Ketamine HCl + 3% Pentoxifylline)

Samples were prepared every 14 days by a 5.00 g accurately weighed sample being transferred to a 50.0 ml volumetric flask. The contents of the flask were diluted to volume with matrix matched mobile phase for HPLC determination.

Results were compared and samples were analyzed each 14 day interval. The limits of acceptance of results were to be < 90% theoretical concentration of initial prepared sample. The results were tabulated for each 14 day interval and examples of chromatography are attached which show standard preparations, initial interval, and latest products.

90-Day Summary:

Compounded at 3.0% w/w in Compound 1 (5% Diclofenac Na + 3% Ibuprofen + 3% Pentoxifylline + 10% Verapamil HCl), stability-indicating HPLC analysis found less than 3% Ibuprofen loss in Spectrum Chemical Mfg. Corp. Durabase Advanced at 90 days.

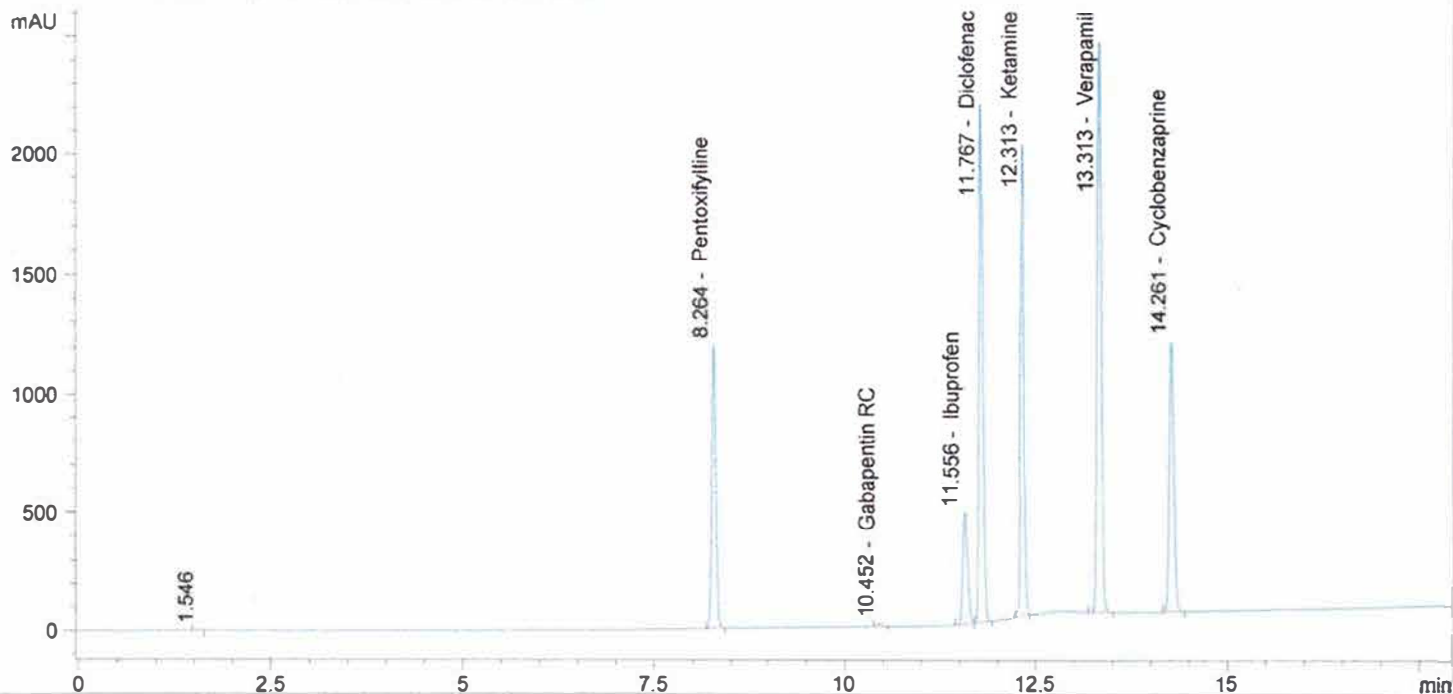
Compounded at 3.0% w/w in Compound 2 (2% Baclofen + 1% Bupivacaine HCl + 2% Cyclobenzaprine HCl + 5% Diclofenac Na + 6% Gabapentin + 3% Ibuprofen + 10% Ketamine HCl + 3% Pentoxifylline), stability-indicating HPLC analysis found negligible Ibuprofen loss in Spectrum Chemical Mfg. Corp. Durabase Advanced at 90 days.

Attached are 4 chromatographs of Spectrum Chemical Mfg. Corp. Durabase Advanced showing 90-Day Standard, and 90-Day Sample of both combination compounds.

PENT, DICL, KET, VER, CYC, IBU STD IN MEOH
 XbridgeC18150x4.6x3.5, 1ml/min, 30C Buf5mMNa2B4O7, ACN, MEO
 H, 80Buf20MEOH HOLD TO2MIN, 58Buf14ACN28MeOH@5.5min to 4
 3Buf24ACN33MEOH@9min, 46Buf14ACN40MEOH@10MIN, 5 buff
 47.5ACN/MEOH@16min TILL18 min

Injection date and Time 8/27/2013 6:16:06 PM Vial 43 Inj # 2
 Method Inj vol 5ul
 Actual inj vol 5ul

DAD1 B, Sig=210.5 Ref=360,100 (130801\BUD00079.D)



| # | Compound Name | Meas. R | Width | Height | Symmetr | Response Fact | Amount | Area | Area % |
|-------|-----------------|---------|-------|--------|---------|---------------|---------|-------|--------|
| 1.0 | | 1.546 | 0.049 | 3 | 0.652 | 0.00000 | 0.00000 | 10 | 0.03 |
| 2.0 | Gabapentin | 0.000 | 0.000 | 0 | 0.000 | 0.00000 | 0.00000 | 0 | 0.00 |
| 3.0 | Baclofen | 0.000 | 0.000 | 0 | 0.000 | 0.00000 | 0.00000 | 0 | 0.00 |
| 4.0 | Pentoxifylline | 8.264 | 0.057 | 1202 | 0.910 | 4.05347e-5 | 0.17934 | 4424 | 12.70 |
| 5.0 | Clonidine | 0.000 | 0.000 | 0 | 0.000 | 0.00000 | 0.00000 | 0 | 0.00 |
| 6.0 | ketoprofen | 0.000 | 0.000 | 0 | 0.000 | 0.00000 | 0.00000 | 0 | 0.00 |
| 7.0 | Gabapentin RC | 10.452 | 0.064 | 15 | 0.913 | 0.00000 | 0.00000 | 64 | 0.18 |
| 8.0 | Flurbiprofen | 0.000 | 0.000 | 0 | 0.000 | 0.00000 | 0.00000 | 0 | 0.00 |
| 9.0 | Ibuprofen | 11.556 | 0.070 | 474 | 0.665 | 8.61798e-5 | 0.18351 | 2129 | 6.11 |
| 10.0 | Diclofenac | 11.767 | 0.057 | 2201 | 0.804 | 3.31767e-5 | 0.25831 | 7786 | 22.34 |
| 11.0 | Ketamine | 12.313 | 0.054 | 2014 | 0.909 | 7.39912e-5 | 0.47976 | 6484 | 18.61 |
| 12.0 | Triclosan | 0.000 | 0.000 | 0 | 0.000 | 0.00000 | 0.00000 | 0 | 0.00 |
| 13.0 | Lidocaine | 0.000 | 0.000 | 0 | 0.000 | 0.00000 | 0.00000 | 0 | 0.00 |
| 14.0 | Verapamil | 13.313 | 0.061 | 2417 | 0.890 | 5.53591e-5 | 0.51370 | 9279 | 26.63 |
| 15.0 | Bupivacaine | 0.000 | 0.000 | 0 | 0.000 | 0.00000 | 0.00000 | 0 | 0.00 |
| 16.0 | Cyclobenzaprine | 14.261 | 0.063 | 1150 | 0.897 | 3.87244e-5 | 0.18093 | 4672 | 13.41 |
| 17.0 | Amitriptyline | 0.000 | 0.000 | 0 | 0.000 | 0.00000 | 0.00000 | 0 | 0.00 |
| total | | | | | | | 1.79556 | 34849 | 100.00 |

03192013@143 265.1MG/50ML MEOH
 XbridgeC18150x4.6x3.5,1ml/min,30C Buf5mMNa2B4O7,ACN,MEO
 H, 80Buf20MEOH HOLD TO2MIN,58Buf14ACN28MeOH@5.5min to 4
 3Buf24ACN33MEOH@9min,46Buf14ACN40MEOH@10MIN,5 buff
 47.5ACN/MEOH@16min TILL18 min

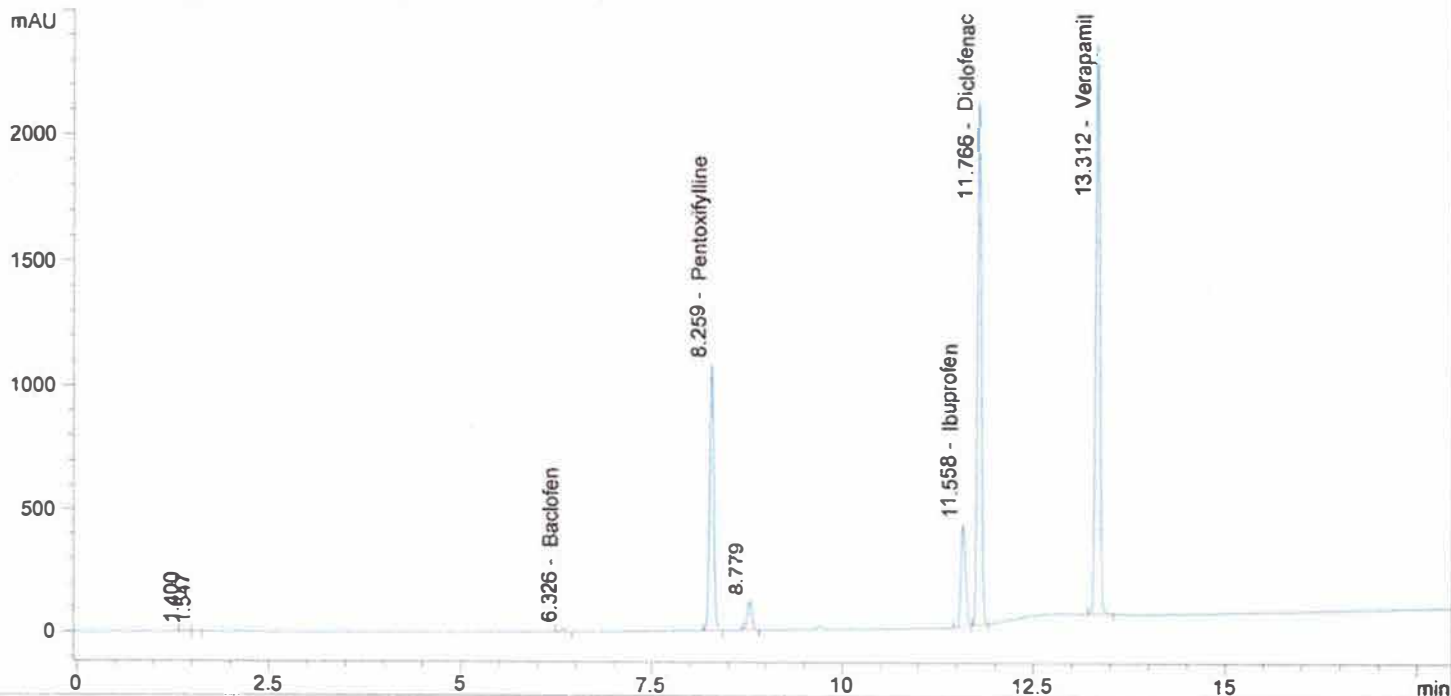
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Injection date and Time 8/27/2013 7:25:53 PM

Vial 55 Inj # 1

Method Inj vol 5ul
 Actual inj vol 5ul

DAD1 B, Sig=210.5 Ref=360,100 (130801\BUD00082.D)



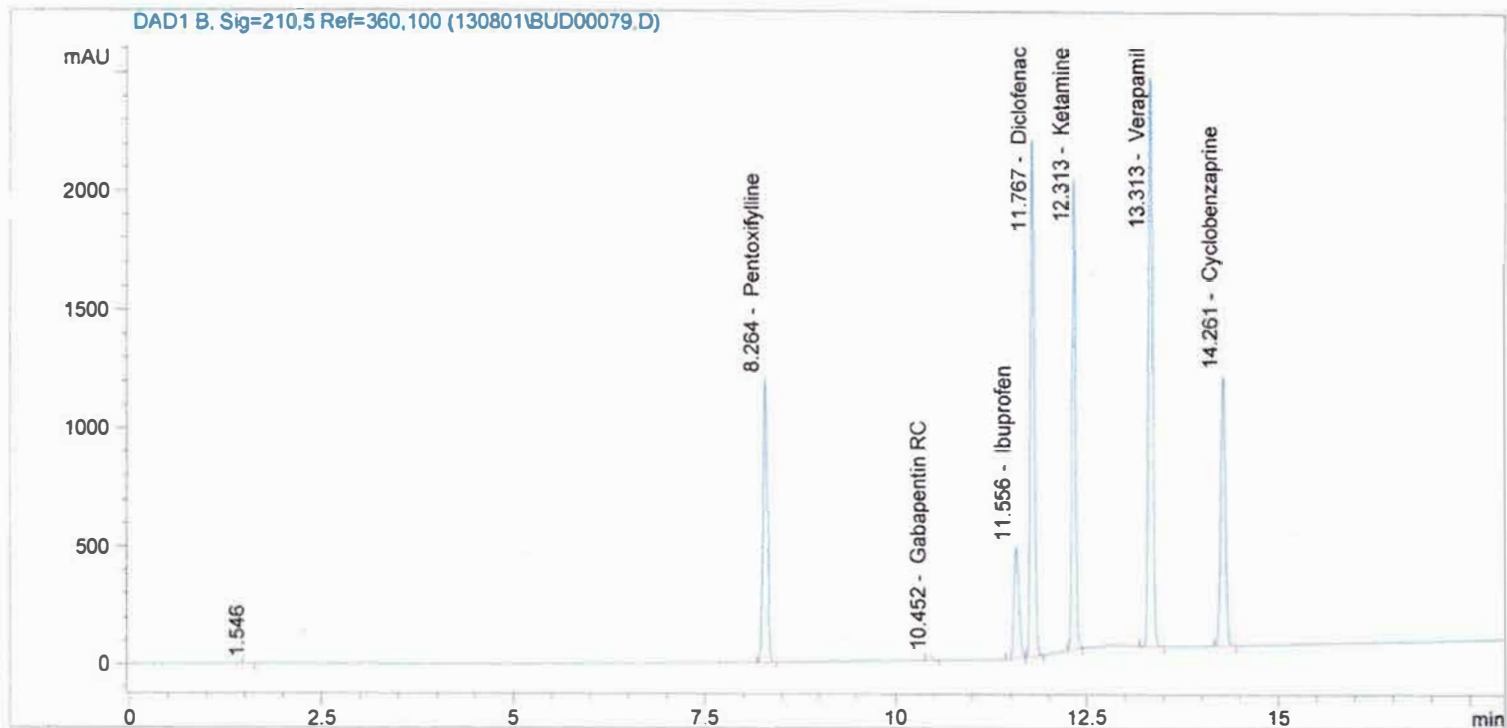
| # | Compound Name | Meas. R | Width | Height | Symmetr | Response Fact | Amount | Area | Area % |
|-------|-----------------|---------|-------|--------|---------|---------------|----------|-------|--------|
| 1.0 | | 1.400 | 0.055 | 7 | 1.042 | 0.00000 | 0.00000 | 25 | 0.11 |
| 2.0 | | 1.547 | 0.054 | 3 | 0.566 | 0.00000 | 0.00000 | 13 | 0.06 |
| 3.0 | Gabapentin | 0.000 | 0.000 | 0 | 0.000 | 0.00000 | 0.00000 | 0 | 0.00 |
| 4.0 | Baclofen | 6.326 | 0.071 | 13 | 0.916 | 0.00000 | 0.00000 | 59 | 0.26 |
| 5.0 | Pentoxifylline | 8.259 | 0.057 | 1084 | 0.915 | 4.05347e-5 | 3.06163 | 4006 | 17.71 |
| 6.0 | | 8.779 | 0.065 | 121 | 0.904 | 0.00000 | 0.00000 | 513 | 2.27 |
| 7.0 | Clonidine | 0.000 | 0.000 | 0 | 0.000 | 0.00000 | 0.00000 | 0 | 0.00 |
| 8.0 | ketoprofen | 0.000 | 0.000 | 0 | 0.000 | 0.00000 | 0.00000 | 0 | 0.00 |
| 9.0 | Gabapentin RC | 0.000 | 0.000 | 0 | 0.000 | 0.00000 | 0.00000 | 0 | 0.00 |
| 10.0 | Flurbiprofen | 0.000 | 0.000 | 0 | 0.000 | 0.00000 | 0.00000 | 0 | 0.00 |
| 11.0 | Ibuprofen | 11.558 | 0.068 | 418 | 0.695 | 8.61798e-5 | 2.93374 | 1806 | 7.98 |
| 12.0 | Diclofenac | 11.766 | 0.058 | 2119 | 0.831 | 3.31767e-5 | 4.64431 | 7425 | 32.82 |
| 13.0 | Ketamine | 0.000 | 0.000 | 0 | 0.000 | 0.00000 | 0.00000 | 0 | 0.00 |
| 14.0 | Triclosan | 0.000 | 0.000 | 0 | 0.000 | 0.00000 | 0.00000 | 0 | 0.00 |
| 15.0 | Lidocaine | 0.000 | 0.000 | 0 | 0.000 | 0.00000 | 0.00000 | 0 | 0.00 |
| 16.0 | Verapamil | 13.312 | 0.061 | 2296 | 0.889 | 5.53591e-5 | 9.15748 | 8774 | 38.79 |
| 17.0 | Bupivacaine | 0.000 | 0.000 | 0 | 0.000 | 0.00000 | 0.00000 | 0 | 0.00 |
| 18.0 | Cyclobenzaprine | 0.000 | 0.000 | 0 | 0.000 | 0.00000 | 0.00000 | 0 | 0.00 |
| 19.0 | Amitriptyline | 0.000 | 0.000 | 0 | 0.000 | 0.00000 | 0.00000 | 0 | 0.00 |
| total | | | | | | | 19.79716 | 22620 | 100.00 |

PENT, DICL, KET, VER, CYC, IBU STD IN MEOH
 XbridgeC18150x4.6x3.5,1ml/min,30C Buf5mMNa2B4O7,ACN,MEO
 H, 80Buf20MEOH HOLD TO2MIN,58Buf14ACN28MeOH@5.5min to 4
 3Buf24ACN33MEOH@9min,46Buf14ACN40MEOH@10MIN,5 buff
 47.5ACN/MEOH@16min TILL18 min

Injection date and Time 8/27/2013 6:16:06 PM

Vial 43 Inj # 2

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 Method Inj vol 5ul
 Actual inj vol 5ul



| # | Compound Name | Meas. R | Width | Height | Symmetr | Response Fact | Amount | Area | Area % |
|-------|-----------------|---------|-------|--------|---------|---------------|---------|-------|--------|
| 1.0 | | 1.546 | 0.049 | 3 | 0.652 | 0.00000 | 0.00000 | 10 | 0.03 |
| 2.0 | Gabapentin | 0.000 | 0.000 | 0 | 0.000 | 0.00000 | 0.00000 | 0 | 0.00 |
| 3.0 | Baclofen | 0.000 | 0.000 | 0 | 0.000 | 0.00000 | 0.00000 | 0 | 0.00 |
| 4.0 | Pentoxifylline | 8.264 | 0.057 | 1202 | 0.910 | 4.05347e-5 | 0.17934 | 4424 | 12.70 |
| 5.0 | Clonidine | 0.000 | 0.000 | 0 | 0.000 | 0.00000 | 0.00000 | 0 | 0.00 |
| 6.0 | ketoprofen | 0.000 | 0.000 | 0 | 0.000 | 0.00000 | 0.00000 | 0 | 0.00 |
| 7.0 | Gabapentin RC | 10.452 | 0.064 | 15 | 0.913 | 0.00000 | 0.00000 | 64 | 0.18 |
| 8.0 | Flurbiprofen | 0.000 | 0.000 | 0 | 0.000 | 0.00000 | 0.00000 | 0 | 0.00 |
| 9.0 | Ibuprofen | 11.556 | 0.070 | 474 | 0.665 | 8.61798e-5 | 0.18351 | 2129 | 6.11 |
| 10.0 | Diclofenac | 11.767 | 0.057 | 2201 | 0.804 | 3.31767e-5 | 0.25831 | 7786 | 22.34 |
| 11.0 | Ketamine | 12.313 | 0.054 | 2014 | 0.909 | 7.39912e-5 | 0.47976 | 6484 | 18.61 |
| 12.0 | Triclosan | 0.000 | 0.000 | 0 | 0.000 | 0.00000 | 0.00000 | 0 | 0.00 |
| 13.0 | Lidocaine | 0.000 | 0.000 | 0 | 0.000 | 0.00000 | 0.00000 | 0 | 0.00 |
| 14.0 | Verapamil | 13.313 | 0.061 | 2417 | 0.890 | 5.53591e-5 | 0.51370 | 9279 | 26.63 |
| 15.0 | Bupivacaine | 0.000 | 0.000 | 0 | 0.000 | 0.00000 | 0.00000 | 0 | 0.00 |
| 16.0 | Cyclobenzaprine | 14.261 | 0.063 | 1150 | 0.897 | 3.87244e-5 | 0.18093 | 4672 | 13.41 |
| 17.0 | Amitriptyline | 0.000 | 0.000 | 0 | 0.000 | 0.00000 | 0.00000 | 0 | 0.00 |
| total | | | | | | | 1.79556 | 34849 | 100.00 |

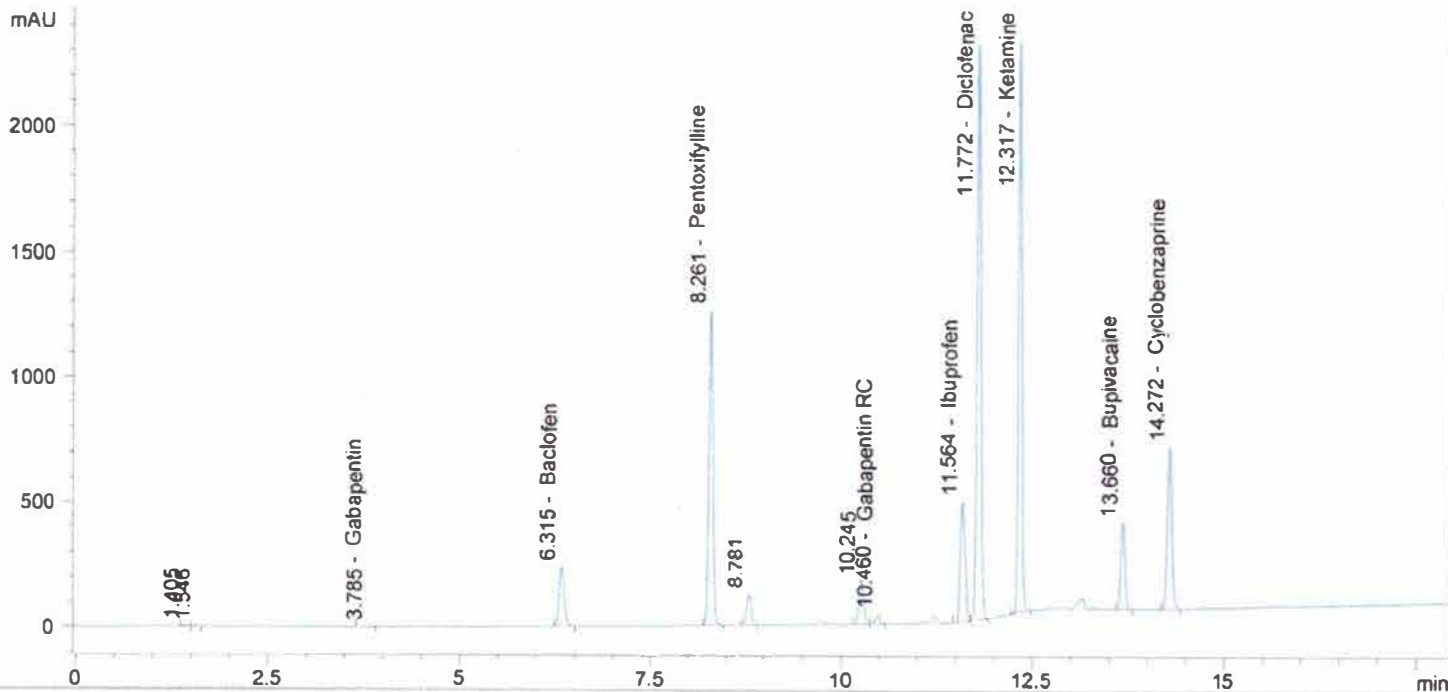
03192013@135 302.6MG/50ML MEOH
 XbridgeC18150x4.6x3.5,1ml/min,30C Buf5mMNa2B4O7,ACN,MEO
 H, 80Buf20MEOH HOLD TO2MIN,58Buf14ACN28MeOH@5.5min to 4
 3Buf24ACN33MEOH@9min,46Buf14ACN40MEOH@10MIN,5 buff
 47.5ACN/MEOH@16min TILL18 min

Injection date and Time 8/27/2013 6:39:17 PM

Vial 54 Inj # 1

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 Method Inj vol 5ul
 Actual inj vol 5ul

DAD1 B, Sig=210.5 Ref=360.100 (130801\BUD00080.D)



| # | Compound Name | Meas. R | Width | Height | Symmetr | Response Fact | Amount | Area | Area % |
|-------|-----------------|---------|-------|--------|---------|---------------|----------|-------|--------|
| 1.0 | | 1.405 | 0.054 | 7 | 0.836 | 0.00000 | 0.00000 | 23 | 0.08 |
| 2.0 | | 1.546 | 0.054 | 3 | 0.594 | 0.00000 | 0.00000 | 12 | 0.04 |
| 3.0 | Gabapentin | 3.785 | 0.115 | 1 | 1.065 | 0.00000 | 0.00000 | 6 | 0.02 |
| 4.0 | Baclofen | 6.315 | 0.076 | 242 | 0.759 | 0.00000 | 0.00000 | 1155 | 3.98 |
| 5.0 | Pentoxifylline | 8.261 | 0.059 | 1263 | 0.905 | 4.05347e-5 | 3.11033 | 4644 | 15.99 |
| 6.0 | | 8.781 | 0.065 | 124 | 0.911 | 0.00000 | 0.00000 | 528 | 1.82 |
| 7.0 | Clonidine | 0.000 | 0.000 | 0 | 0.000 | 0.00000 | 0.00000 | 0 | 0.00 |
| 8.0 | ketoprofen | 0.000 | 0.000 | 0 | 0.000 | 0.00000 | 0.00000 | 0 | 0.00 |
| 9.0 | | 10.245 | 0.068 | 175 | 0.891 | 0.00000 | 0.00000 | 753 | 2.59 |
| 10.0 | Gabapentin RC | 10.460 | 0.065 | 40 | 0.930 | 0.00000 | 0.00000 | 166 | 0.57 |
| 11.0 | Flurbiprofen | 0.000 | 0.000 | 0 | 0.000 | 0.00000 | 0.00000 | 0 | 0.00 |
| 12.0 | Ibuprofen | 11.564 | 0.070 | 482 | 0.670 | 8.61798e-5 | 3.04826 | 2141 | 7.37 |
| 13.0 | Diclofenac | 11.772 | 0.055 | 2298 | 0.808 | 3.31767e-5 | 4.46159 | 8139 | 28.03 |
| 14.0 | Ketamine | 12.317 | 0.055 | 2295 | 0.910 | 7.39912e-5 | 9.21583 | 7538 | 25.96 |
| 15.0 | Triclosan | 0.000 | 0.000 | 0 | 0.000 | 0.00000 | 0.00000 | 0 | 0.00 |
| 16.0 | Lidocaine | 0.000 | 0.000 | 0 | 0.000 | 0.00000 | 0.00000 | 0 | 0.00 |
| 17.0 | Verapamil | 0.000 | 0.000 | 0 | 0.000 | 0.00000 | 0.00000 | 0 | 0.00 |
| 18.0 | Bupivacaine | 13.660 | 0.057 | 349 | 0.930 | 0.00000 | 0.00000 | 1298 | 4.47 |
| 19.0 | Cyclobenzaprine | 14.272 | 0.063 | 649 | 0.901 | 3.87244e-5 | 1.68494 | 2633 | 9.07 |
| 20.0 | Amitriptyline | 0.000 | 0.000 | 0 | 0.000 | 0.00000 | 0.00000 | 0 | 0.00 |
| total | | | | | | | 21.52094 | 29035 | 100.00 |