

Ibuprofen:

3.00g Ibuprofen raw drug powder from Acros chemical (part number 258610100, Lot # A0311465) was added to 100.00g Humco Salt-Stable LS Advanced (Humco Holding Group, Texarkana, Texas) 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 Humco Salt-Stable LS 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 Humco Salt-Stable LS Advanced at 90 days.

Attached are 4 chromatographs of Humco Salt-Stable LS Advanced showing 90-Day Standard, and 90-Day Sample of both combination compounds.

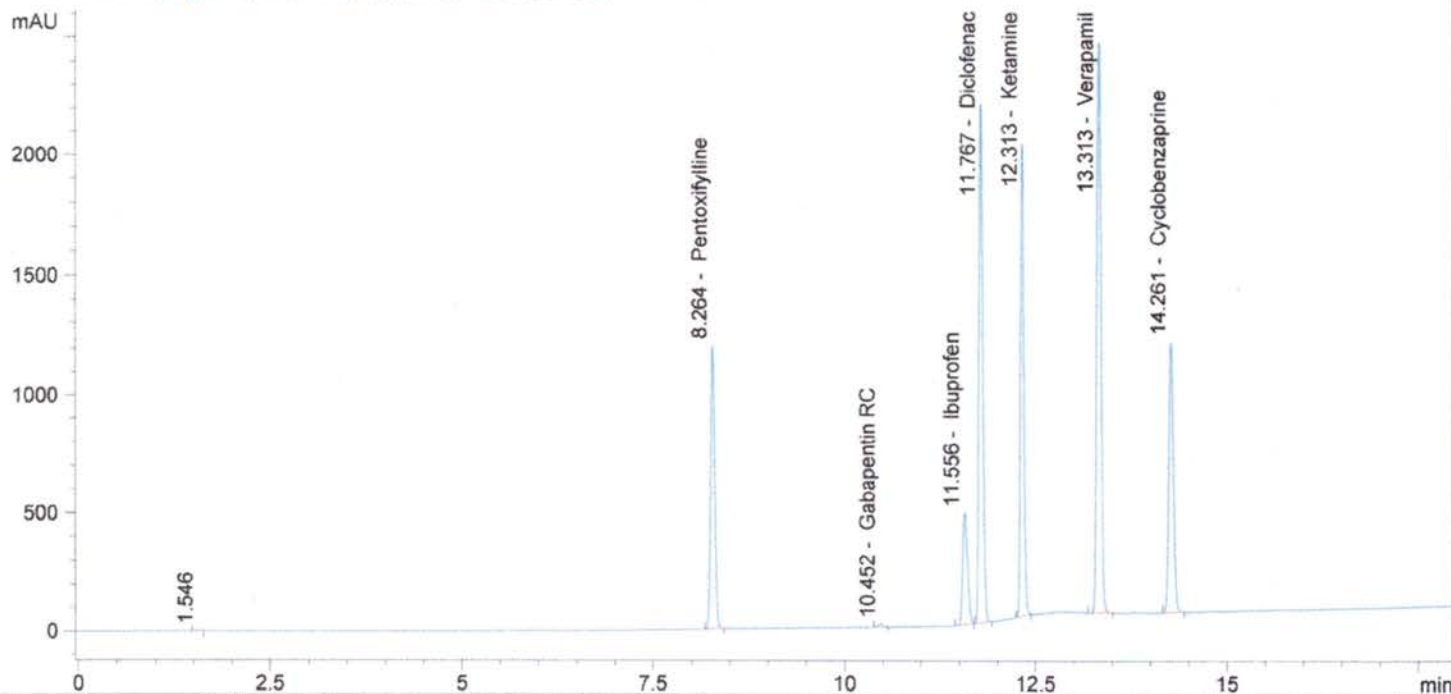
PENT, DICL, KET, VER, CYC, IBU STD IN MEOH  
 XbridgeC18150x4.6x3.5, 1ml/min, 30C Buf5mMNa2B4O7, ACN, MEO  
 H, 80Buf20MEOH HOLD TO2MIN, 58Buf14ACN28MeOH@5.5min to 4  
 3Buf24ACN33MEOH@9min, 46Buf14ACN40MEOH@10MIN, 5 buff  
 47.5ACN/MEOH@16min TILL18 min

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

Vial 43 Inj # 2

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 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

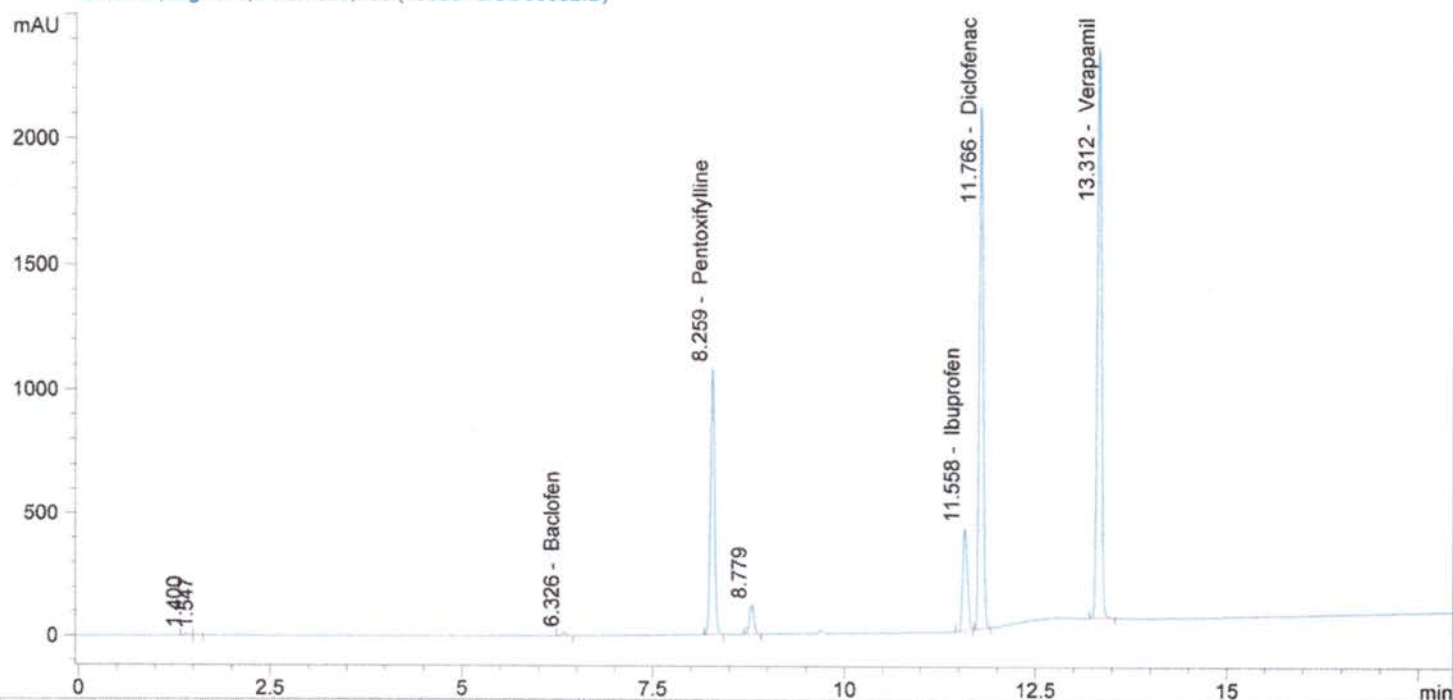
HUMCO 03192013@143 265.1MG/50ML MEOH  
 XbridgeC18150x4.6x3.5,1ml/min,30C Buf5mMNa2B4O7,ACN,MEO  
 H, 80Buf20MEOH HOLD TO2MIN,58Buf14ACN28MeOH@5.5min to 4  
 3Buf24ACN33MEOH@9min,46Buf14ACN40MEOH@10MIN,5 buff  
 47.5ACN/MEOH@16min TILL18 min

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

Vial 55 Inj # 1

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 Method Inj vol 5ul  
 Actual inj vol 5ul

DAD1 B, Sig=210,5 Ref=360,100 (130801\BUD00082.D)

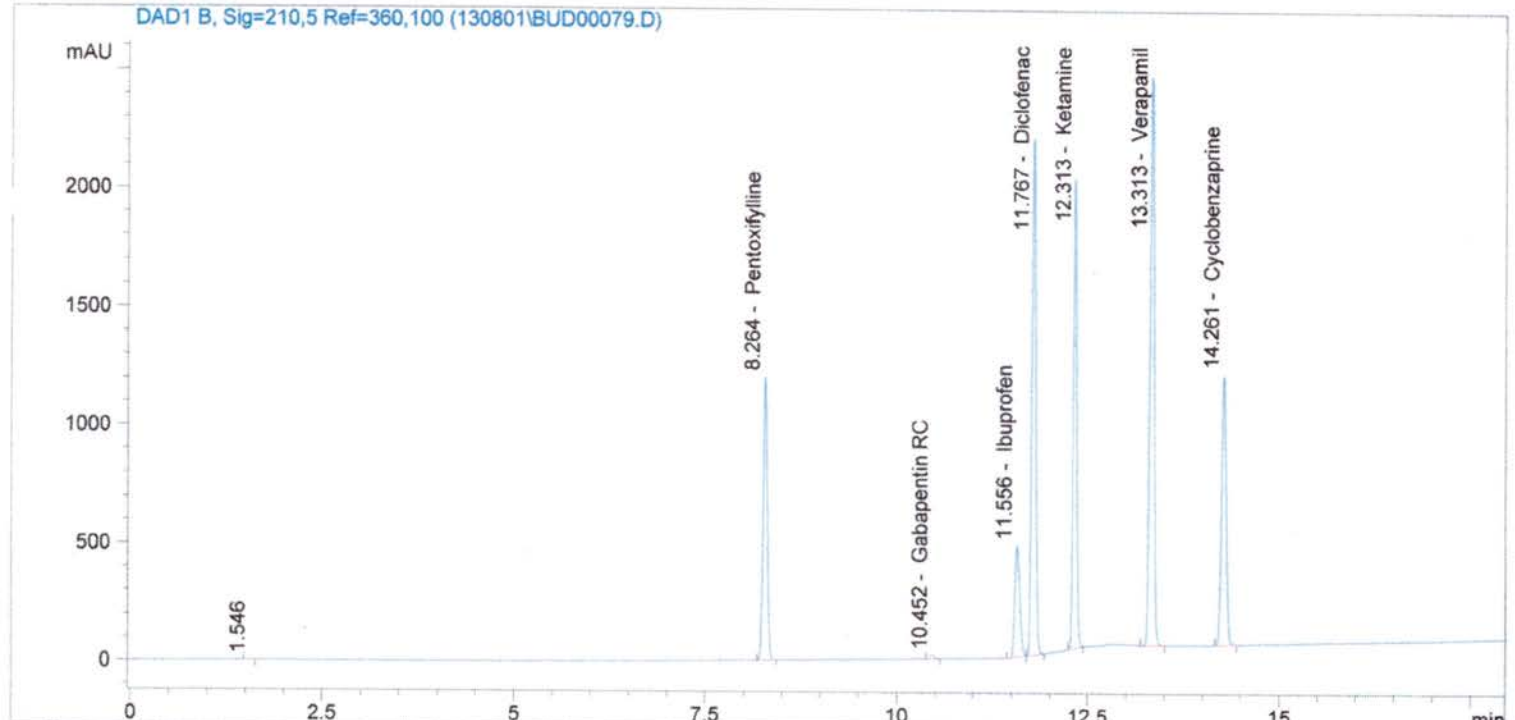


#	Compound Name	Meas. R	Width	Height	Symmetr	Response Fact	Amount	Area	Area %
1.0		1.400	0.055	7	1.042	0.00000	0.00000	25	0.11
2.0		1.547	0.054	3	0.566	0.00000	0.00000	13	0.06
3.0	Gabapentin	0.000	0.000	0	0.000	0.00000	0.00000	0	0.00
4.0	Baclofen	6.326	0.071	13	0.916	0.00000	0.00000	59	0.26
5.0	Pentoxifylline	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 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

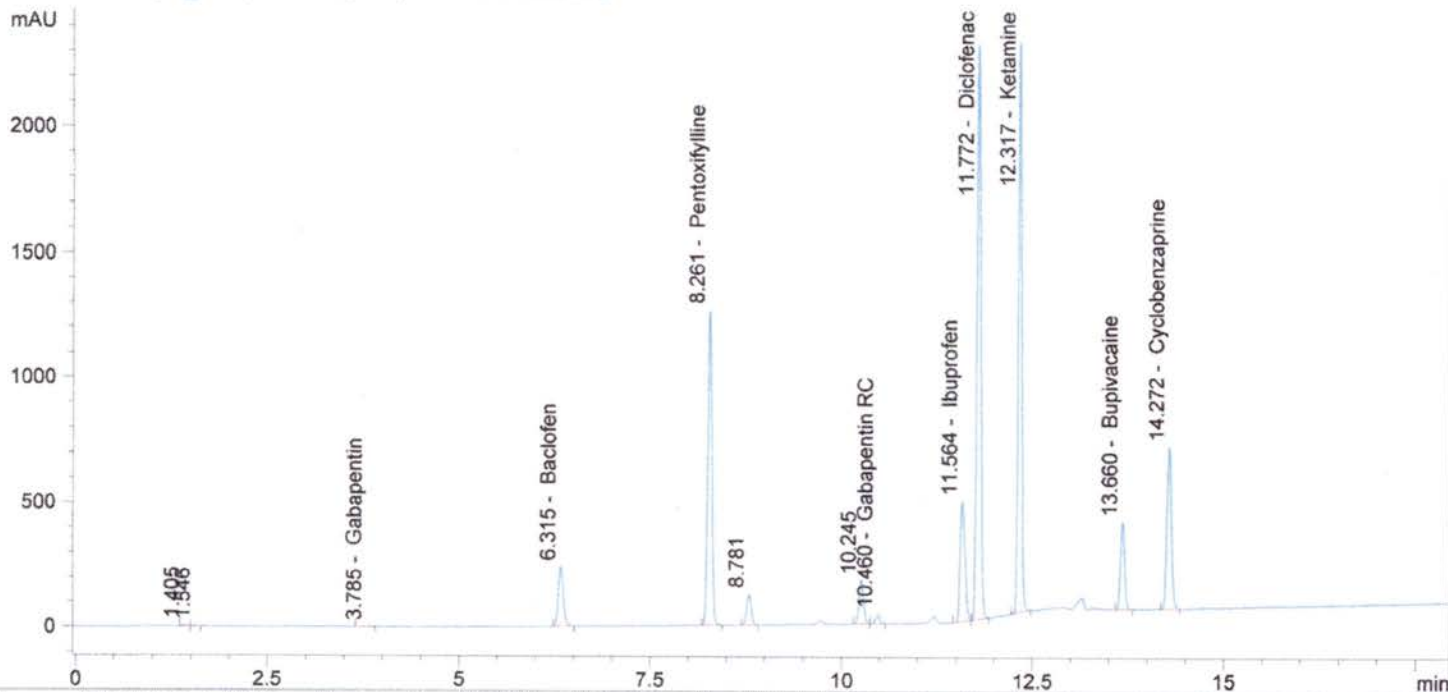
HUMCO 03192013@135 302.6MG/50ML MEOH  
 XbridgeC18150x4.6x3.5,1ml/min,30C Buf5mMNa2B4O7,ACN,MEO  
 H, 80Buf20MEOH HOLD TO2MIN,58Buf14ACN28MeOH@5.5min to 4  
 3Buf24ACN33MEOH@9min,46Buf14ACN40MEOH@10MIN,5 buff  
 47.5ACN/MEOH@16min TILL18 min

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