

Drug Metabolism and Distribution

Plasma protein binding as an optimisable parameter for acidic drugs

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Series	Patent	Example number in patent	CXCR2 Hu IL-8 binding pIC ₅₀	plasma PB (% free)	IV PK CL (ml/min/kg)	IV PK Vss (l/kg)
AZD4721	WO 2013008002	Single example	(8.4*)	0.11	2.4	0.19
AZD5069	WO 2006024823	47	9.0 (8.5*)	0.59	4.2	0.32
AZD8309	WO 2001025242	43	9.0	0.29	5.7	0.33
sulfamide	WO 2004011443	2	7.5	2.1	16	0.5
sulfamide	WO 2004011443	27	7.9	1.5	14	1.7
sulfamide	WO 2004011443	31	8.1	3.7	17	0.53
sulfamide	WO 2004011443	36	8.2	1.5	26	1.8
sulfamide	WO 2004011443	37	8.0	1.4	21	0.4
sulfamide	WO 2004011443	39	8.4	1	8	1.4
sulfamide	WO 2004011443	41	8.5	0.57	6.3	0.97
sulfamide	WO 2004011443	106	8.4	3	25	1.1
sulfamide	WO 2004011443	107	8.0	1.8	16	1.5
sulfamide	WO 2004011443	111	8.1	0.62	10	0.63
sulfamide	WO 2004011443	131	8.2	26	34	0.3
sulfamide	WO 2004011443	138	>7.9	1.9	8.5	0.35
thiazolone	WO 2001025242	1	8.0	0.57	5	0.5
thiazolone	WO 2001025242	4	8.7	0.15	3.3	0.3
thiazolone	WO 2001025242	7	8.6	0.75	3	0.27
thiazolone	WO 2001025242	16	8.6	0.48	5.3	0.2
thiazolone	WO 2001025242	20	7.2	0.87	5.7	0.3
thiazolone	WO 2001025242	24	8.3	1.8	17	0.3
thiazolone	WO 2001025242	27	8.3	0.48	18	0.27
thiazolone	WO 2001025242	29	8.0	0.19	5	0.27
thiazolone	WO 2001025242	32	8.8	0.16	10	0.35
thiazolone	WO 2001025242	35	8.4	0.64	5.7	0.2
thiazolone	WO 2001025242	37	8.8	0.22	3	0.27
thiazolone	WO 2001025242	44	8.9	0.082	3.7	0.4
thiazolone	WO 2001025242	45	8.0	0.93	11	0.23
thiazolone	WO 2001025242	47	8.3	0.27	6.7	0.37
thiazolone	WO 2004026880	Single example	8.2	1.5	3.3	0.3

*Updated version of binding assay.