

Supplementary information

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Author names: Xiang-yang Xie ^{1#}, Yuan Zeng ^{1#}, Zhi-long Chen ^{1#}, Yu-liang Li ^{1,2}, Wen Lin ³, Hui Liu ^{1*}, Yi-hui Ma ^{4*}, Guo-wei Zhang ^{1*}

Author affiliations: 1 Medical Support Center, General Hospital of Central Theater Command, Wuhan 430070, China; 2 School of Medicine, Wuhan University of Science and Technology, Wuhan 430065, China; 3 Department of Clinical Laboratory, Wuhan Third Hospital (Tongren Hospital of Wuhan University), Wuhan 430060, China; 4 Department of Stomatology, General Hospital of Central Theater Command, Wuhan 430070, China

These authors contributed equally to this work

* Corresponding author(s).

E-mail address of the corresponding authors: pharmacyman@126.com (H.L.), ddsmayihui@163.com (Y.M.) & 1102771944@qq.com (G.Z.);

Table 1: Summary of test sample analysis batches

Analyze the batch number	Analyze batch contents	Number of test samples	Date of detection	Whether the standard curve fit passes	Quality control of whether the sample passes	Report data	Instruments and equipment	remark
001-SES	System suitability evaluation	ON	2024/09/06	ON	ON	be	HR-LC-024HR-MS-024	ON
001	Analysis of plasma test samples of tested animals M001, F002~F003 and M004	120	2024/09/06	be	be	be	HR-LC-024HR-MS-024	ON
002	Analysis of plasma test samples of tested animals M005 and F006	60	2024/09/07	be	be	be	HR-LC-024HR-MS-024	ON
003	Analysis of plasma test samples of M007~M008 and M013~M014 test animals	146	2024/09/07	be	be	be	HR-LC-024HR-MS-024	ON
004	Analysis of plasma test samples of animals M009, F010, M015 and F016	146	2024/09/07	be	be	be	HR-LC-024HR-MS-024	ON
005-SES	System suitability evaluation	ON	2024/09/09	ON	ON	be	HR-LC-024HR-MS-024	ON
005	Analysis of plasma test samples of tested animals No. F011~F012 and F017~F018	146	2024/09/09	be	be	be	HR-LC-024HR-MS-024	ON

Note: ANALYSIS BATCHES ARE SORTED BY INJECTION TIME.

Table 2: System Applicability

Acceptance criteria: RSDs of 15% or less for analyte and internal standard retention times and 15% RSDs for response ratios. It is not used as a criterion for analyzing whether the batch passes or not, and is only used as a reference.

Analyze the batch number	RSD (%)			Testing equipment
	Analyte retention time	Internal standard retention time	Response ratio	
001-SES	0.2	0.3	4.3	HR-LC-024HR-MS-024
005-SES	0.3	0.2	4.3	HR-LC-024HR-MS-024

Table 3: Percent of carryover rate during batch testing

Acceptance Criteria: The interference response of the blank matrix at the analyte retention time after the highest concentration calibration standard should not exceed 20% of the analyte response in the LLOQ sample; The interference response at the retention time of the internal standard should not exceed 5% of the internal standard response in the LLOQ sample.

serial number	Analyze the batch number	Carryover evaluation of analyte carryover response in blank matrix samples	Carryover evaluation of the internal standard residual response in blank matrix samples	Response of LLOQ analytes	LLOQ internal standard response	Residual Rate%		Instruments and equipment
						Analytes	Internal standard	
1	001	0	0	2950	234000	0.0	0.0	HR-LC-024HR-MS-024
2	002	0	0	2490	214000	0.0	0.0	HR-LC-024HR-MS-024
3	003	0	0	2850	218000	0.0	0.0	HR-LC-024HR-MS-024
4	004	0	0	2740	218000	0.0	0.0	HR-LC-024HR-MS-024
5	005	0	0	3150	249000	0.0	0.0	HR-LC-024HR-MS-024

Table 4: Comparison of Weighing Accuracy of Major Stock Fluids

Acceptance criteria: no more than $\pm 5\%$ difference between the two stock solutions, no more than 10% RSD for each parallel sample of the two stock solutions, and at least 5 RMS.

Analyze the batch number	001*	
Date of detection	2024/08/19	
Solution code	S01-1 (for the preparation of CAL)	S01-2 (for QC)
The date of the weighing	2024/08/19	2024/08/19
Weighing Weight(mg)	12.4521	12.7246
Dissolution volume (mL)	1.686	1.723
Response ratio	0.327	0.341
	0.322	0.325
	0.332	0.315
	0.324	0.322
	0.306	0.320
	0.337	0.323
average value	0.325	0.324
SD	0.0107	0.00885
RSD (%)	3.3	2.7
n	6	6
Variance (%)	0.1	

Note: *This stock weighing accuracy comparison data is derived from Lot 001 of Item HR-202407D196.

Table 5: Summary of standard curves for analysis batches**Acceptance criteria:** The R2 value of the standard curve fitting should not be less than 0.9801.

Date of detection	Analyze the batch number	slope	intercept	R2	Labeled concentration of LLOQ (ng/mL)	ULOQ 标示浓度 (ng/mL)
2024/09/06	001	0.00130	-0.0000384	0.9990	10.0	10000
2024/09/07	002	0.00118	-0.0000195	0.9994	10.0	10000
2024/09/07	003	0.00128	0.000113	0.9988	10.0	10000
2024/09/07	004	0.00126	0.000550	0.9968	10.0	10000
2024/09/09	005	0.00124	0.000291	0.9990	10.0	10000
average value		0.00125	0.000179	0.999	ON	
SD		0.0000460	0.000246	0.00103		
RSD (%)		3.7	137.0	0.1		
n		5	5	5		

Table 6: Summary table of the back-calculated concentration (ng/mL) and accuracy deviation (%) of the calibration standard in the analysis batch

Acceptance criteria: at least 75% for each standard curve and no more than $\pm 15\%$ for the accuracy of at least 6 calibration standards (no more than $\pm 20\%$ for the lower limit of quantification).

Date of detection	Analyze the batch number	CAL-1 (10.0 ng/mL)		CAL-2 (20.0 ng/mL)		CAL-3 (100 ng/mL)		CAL-4 (400 ng/mL)		CAL-5 (2000 ng/mL)		CAL-6 (5000 ng/mL)		CAL-7 (9000 ng/mL)		CAL-8 (10000 ng/mL)	
		Backcalculated concentration (ng/mL)	Accuracy deviation (%)	Backcalculated concentration (ng/mL)	Accuracy deviation (%)	Backcalculated concentration (ng/mL)	Accuracy deviation (%)	Backcalculated concentration (ng/mL)	Accuracy deviation (%)	Backcalculated concentration (ng/mL)	Accuracy deviation (%)	Backcalculated concentration (ng/mL)	Accuracy deviation (%)	Backcalculated concentration (ng/mL)	Accuracy deviation (%)	Backcalculated concentration (ng/mL)	Accuracy deviation (%)
2024/09/06	001	9.78	-2.2	20.8	4.0	102	2.0	394	-1.5	2050	2.5	5000	0.0	9010	0.1	9470	-5.3
2024/09/07	002	9.88	-1.2	20.5	2.5	99.4	-0.6	402	0.5	1930	-3.5	5160	3.2	8990	-0.1	9920	-0.8
2024/09/07	003	10.1	1.0	19.4	-3.0	103	3.0	412	3.0	1990	-0.5	5070	1.4	9050	0.6	9430	-5.7
2024/09/07	004	9.51	-4.9	21.9	9.5	102	2.0	399	-0.3	1900	-5.0	5170	3.4	9080	0.9	9460	-5.4
2024/09/09	005	10.0	0.0	19.9	-0.5	104	4.0	393	-1.8	2000	0.0	5180	3.6	9010	0.1	9500	-5.0
average value		9.85	ON	20.5	ON	102	ON	400	ON	1974	ON	5116	ON	9028	ON	9556	ON
SD		0.227		0.951		1.71		7.65		59.4		78.3		36.3		205	
RSD (%)		2.3		4.6		1.7		1.9		3.0		1.5		0.4		2.1	
Average accuracy deviation (%)		-1.5		2.5		2.1		0.0		-1.3		2.3		0.3		-4.4	
n		5		5		5		5		5		5		5		5	

Table 7: Summary table of measured concentrations and accuracy deviations (%) of QC samples in the analysis batch

Acceptance Criteria: At least 2/3 of the QC samples (except DQC) in each analytical lot with at least 50% accuracy deviation of QC samples at each concentration level and no more than $\pm 15\%$. At least 50% of DQCs have an accuracy deviation of no more than $\pm 15\%$, and DQCs are not used as a criterion for the passage of an analytical batch, but are only used to evaluate the acceptability of the diluted sample.

Analyze the batch number	The date of the analysis	Quality control samples accounted for % of the batch of samples	LQC		MQC		HQC		DQC	
			30.0 ng/mL		3000 ng/mL		7500 ng/mL		40000 ng/mL	
			Determination concentration (ng/mL)	Accuracy Deviation %	Determination concentration (ng/mL)	Accuracy Deviation %	Determination concentration (ng/mL)	Accuracy Deviation %	Determination concentration (ng/mL)	Accuracy Deviation %
001	2024/09/06	10.0	30.0	0.0	3010	0.3	7400	-1.3	34500	-13.8
			31.6	5.3	3130	4.3	7200	-4.0	34600	-13.5
			29.5	-1.7	2970	-1.0	7620	1.6	33500*	-16.3
			30.3	1.0	3000	0.0	7770	3.6	35700	-10.8
002	2024/09/07	10.0	29.6	-1.3	3070	2.3	7840	4.5	36000	-10.0
			30.1	0.3	3010	0.3	7550	0.7	39100	-2.3
			ON	ON	ON	ON	ON	ON	35500	-11.3
			ON	ON	ON	ON	ON	ON	37900	-5.3
003	2024/09/07	8.2	30.7	2.3	2980	-0.7	7600	1.3	ON	ON
			30.2	0.7	2960	-1.3	8020	6.9	ON	ON
			30.1	0.3	3040	1.3	7750	3.3	ON	ON
			29.6	-1.3	3060	2.0	7710	2.8	ON	ON
004	2024/09/07	8.2	30.9	3.0	3050	1.7	7220	-3.7	ON	ON
			30.9	3.0	2950	-1.7	7470	-0.4	ON	ON
			29.4	-2.0	3170	5.7	7720	2.9	ON	ON
			32.0	6.7	3040	1.3	7700	2.7	ON	ON
005	2024/09/09	8.2	30.8	2.7	3150	5.0	7850	4.7	ON	ON
			31.0	3.3	3140	4.7	8000	6.7	ON	ON
			31.7	5.7	3220	7.3	8170	8.9	ON	ON
			34.5	15.0	3180	6.0	7880	5.1	ON	ON
average value		ON	30.7	ON	3063	ON	7693	ON	35850	ON
SD			1.22		83.2		261		1845	
RSD(%)			4.0		2.7		3.4		5.1	
Average Accuracy (%)			102.4		102.1		102.6		89.6	
Average accuracy deviation (%)			2.4		2.1		2.6		-10.4	
n			18		18		18		8	

Note: *Exceeding the acceptable criteria, the relevant results are included in the statistics.

Table 8: Summary table of blood concentration data for single administration (ketorolac tromethamine TITs) (ng/mL).

ketorolac tromethamine TITs single oral dose - 35 mg										
Time (h)	P1			P2			Total			
	Animal No.			Animal No.			n	Mean	SD	RSD %
	Male	Female		Male		Female				
	M001	F002	F003	M004	M005	F006				
0	BLQ	BLQ	BLQ	BLQ	BLQ	BLQ	0	ON	ON	ON
0.167	BLQ	13.6	24.8	824	1280	302	5	489	551	112.7
0.5	215	261	889	1080	1100	1080	6	771	420	54.5
1	1710	397	1070	1010	1280	967	6	1072	429	40.0
2	2180	663	2030	988	1980	1520	6	1560	619	39.7
3	2660	3070	2710	2060	2080	2260	6	2473	404	16.4
4	2800	3640	3020	2620	2370	2380	6	2805	479	17.1
5	2940	3860	3110	2870	2390	2250	6	2903	575	19.8
6	1380	3400	3200	1690	1510	2000	6	2197	882	40.1
8	786	1300	1710	577	783	1030	6	1031	415	40.3
10	709	1560	2030	555	451	1150	6	1076	624	58.0
14	233	1260	1520	704	592	1370	6	947	510	53.9
24	109	339	248	820	402	728	6	441	278	63.0
36	25.8	71.8	204	165	118	86.8	6	112	64.8	57.9
48	BLQ	33.6	290	145	80.3	57.3	5	121	103	85.0

Table-9: Summary table of blood concentration data for a single dose (ketorolac tromethamine tablets) (ng/mL).

ketorolac tromethamine tablets Single oral dose - 35 mg										
Time (h)	P2			P1			Total			
	Animal No.			Animal No.			n	Mean	SD	RSD %
	Male	Female		Male		Female				
	M001	F002	F003	M004	M005	F006				
0	BLQ	BLQ	BLQ	BLQ	BLQ	BLQ	0	ON	ON	ON
0.0833	BLQ	11.7	108	123	95.1	236	5	115	80.3	70.0
0.167	89.3	127	1240	740	560	1660	6	736	621	84.4
0.333	5340	637	5980	2230	4370	5450	6	4001	2117	52.9
0.5	10700	1180	8160	3520	5920	8330	6	6302	3494	55.4
1	8500	2230	8950	6600	7080	7000	6	6727	2388	35.5
2	6790	8240	7620	6460	6100	5010	6	6703	1140	17.0
4	5560	5630	6390	6400	4740	3960	6	5447	954	17.5
6	2890	3920	4290	3750	2610	2630	6	3348	727	21.7
8	501	1530	3440	792	852	1410	6	1421	1063	74.8
10	313	1400	2640	653	655	1000	6	1110	835	75.2
14	429	1270	1860	538	383	371	6	809	618	76.4
24	243	663	1230	321	136	139	6	455	426	93.6
36	16.3	69.3	746	99.7	194	24.8	6	192	279	145.6
48	19.3	45.5	707	50.8	144	20.4	6	165	270	163.9

Table 10: Summary of blood concentration data for repeated dosing (ketorolac tromethamine-D1) (ng/mL).

ketorolac tromethamine TITs oral - 35 mg - D1										
Time (h)	Male			Female			Total			
	Animal No.			Animal No.			n	Mean	SD	RSD %
	M007	M008	M009	F010	F011	F012				
0	BLQ	BLQ	BLQ	BLQ	BLQ	BLQ	0	ON	ON	ON
0.167	107	241	689	291	BLQ	362	5	338	217	64.3
0.5	602	855	1280	1300	355	1160	6	925	389	42.0
1	1160	1130	1320	2160	1250	1750	6	1462	409	28.0
2	2600	1900	2620	2860	3110	2830	6	2653	413	15.6
3	2400	2760	3640	3550	4470	3650	6	3412	734	21.5
4	2150	2790	4060	4290	4990	4320	6	3767	1071	28.4
5	1770	2710	3480	3540	4230	4320	6	3342	967	28.9
6	1460	2520	2670	2490	3810	3420	6	2728	820	30.0
8	1280	2640	1940	1650	3030	2330	6	2145	648	30.2
10	1090	2180	1250	1430	2350	1620	6	1653	509	30.8
14	642	1370	501	910	1390	937	6	958	365	38.1
24	223	330	201	403	587	186	6	322	155	48.1

Table 11: Summary table of blood concentration data for repeated dosing (ketorolac tromethamine TITs-D5,6) (ng/mL).

Ketolac tromethamine biphasic controlled-release tablets Oral - 35 mg - D5,6										
Time (h)	Male			Female			Total			
	Animal No.			Animal No.			n	Mean	SD	RSD %
	M007	M008	M009	F010	F011	F012				
5-1	253	338	2670	551	175	290	6	713	967	135.7
6-1	311	129	2520	214	153	101	6	571	958	167.6

Table 12: Summary table of blood concentration data for repeated dosing (ketorolac tromethamine TITs-D7) (ng/mL).

ketorolac tromethamine TITs oral - 35 mg - D7										
Time (h)	Male			Female			Total			
	Animal No.			Animal No.			n	Mean	SD	RSD %
	M007	M008	M009	F010	F011	F012				
0	455	528	1820	167	214	167	6	559	637	114.0
0.167	1150	2140	2370	274	217	146	6	1050	1005	95.8
0.5	1620	2050	2900	1400	1370	555	6	1649	783	47.5
1	2120	2130	3660	2220	1560	1360	6	2175	807	37.1
2	2970	2400	4600	3130	1690	2130	6	2820	1021	36.2
3	2970	2610	4810	2480	1410	2260	6	2757	1133	41.1
4	2700	2530	4670	2310	1250	2510	6	2662	1113	41.8
5	3240	1710	3770	1760	1100	2700	6	2380	1024	43.0
6	3100	1450	3890	1710	1080	2630	6	2310	1080	46.8
8	2720	853	3720	1670	840	2000	6	1967	1117	56.8
10	2390	648	3640	1160	550	1400	6	1631	1185	72.6
14	1570	499	2880	2390	366	904	6	1435	1031	71.9
24	682	121	2250	914	154	212	6	722	815	112.8
36	534	19.2	1420	284	30.1	20.6	6	385	547	142.2
48	402	25.4	1160	242	13.1	15.1	6	310	445	143.8

Table 13: Summary table of blood drug concentration data for repeated dosing (ketorolac tromethamine tablets-D1 first time) (ng/mL).

Ketorlac tromethamine tablets orally - 15 mg - D1 for the first time										
Time (h)	Male			Female			Total			
	Animal No.			Animal No.			n	Mean	SD	RSD %
	M013	M014	M015	F016	F017	F018				
0	BLQ	BLQ	BLQ	BLQ	BLQ	BLQ	0	ON	ON	ON
0.0833	23.8	114	43.8	98.5	623	1720	6	437	667	152.6
0.167	725	1280	669	1540	1930	3710	6	1642	1121	68.3
0.333	2210	1790	1470	5550	2140	3770	6	2822	1554	55.1
0.5	2370	1800	1890	5090	1880	3350	6	2730	1294	47.4
1	1970	2050	1780	4280	1510	2600	6	2365	1005	42.5
2	1120	2090	1650	3150	1580	1930	6	1920	689	35.9
4	574	1820	1170	2220	918	1530	6	1372	605	44.1
5	430	1180	801	1880	581	1050	6	987	519	52.6

Table 14: Summary table of blood concentration data for repeated dosing (ketorolac tromethamine tablets-D6 second and third times) (ng/mL).

ketorolac tromethamine tablets orally - 10 mg - D6 second and third times										
Time (Day)	Male			Female			Total			
	Animal No.			Animal No.			n	Mean	SD	RSD %
	M013	M014	M015	F016	F017	F018				
6-2	538	1300	900	2940	966	1580	6	1371	847	61.8
6-3	663	1160	1030	2950	1090	2240	6	1522	878	57.7

Table 15: Summary table of blood concentration data for repeated dosing (ketorolac tromethamine tablets-D7) (ng/mL).

ketorolac tromethamine tablets orally - 35 mg - D7										
Time (h)	Male			Female			Total			
	Animal No.			Animal No.			n	Mea n	SD	RSD %
	M013	M014	M015	F016	F017	F018				
0	233	228	444	1460	317	1030	6	619	510	82.4
0.0833	236	2050	1260	1520	1010	1040	6	1186	603	50.8
0.167	491	2660	1790	1510	2130	1260	6	1640	746	45.5
0.333	2020	2600	2320	1710	2450	3470	6	2428	602	24.8
0.5	2990	2430	2440	2110	2650	4430	6	2842	830	29.2
1	2510	2160	2210	5920	2280	4570	6	3275	1589	48.5
2	1540	2000	1770	4850	1260	3910	6	2555	1465	57.3
4	1100	1760	1400	3590	1150	2890	6	1982	1026	51.8
5	1010	1780	1280	2810	1070	2420	6	1728	749	43.3
5.0833	1070	1840	1220	3150	1080	2530	6	1815	865	47.7
5.167	1480	2470	1270	3740	1780	3040	6	2297	965	42.0
5.333	2830	2840	1200	5610	2880	3660	6	3170	1441	45.5
5.5	3100	2700	1710	5710	2700	4340	6	3377	1424	42.2
6	2420	2240	2230	5760	2180	3840	6	3112	1444	46.4
7	1150	1320	1400	4840	1010	2930	6	2108	1509	71.6
9	651	448	708	3900	691	2000	6	1400	1346	96.2
10	607	332	530	4180	645	1720	6	1336	1477	110.6
10.0833	680	336	523	3910	679	1900	6	1338	1376	102.8
10.167	723	359	486	4060	1110	2900	6	1606	1519	94.5
10.333	1100	786	642	3830	2070	3960	6	2065	1503	72.8
10.5	1820	1060	829	4200	2320	4030	6	2377	1449	61.0
11	2800	2030	1360	4510	2510	4070	6	2880	1204	41.8
12	2440	1880	1740	4950	2190	3890	6	2848	1286	45.1
14	1730	2290	846	6180	1570	2170	6	2464	1891	76.7
16	1230	1950	566	4800	1310	1560	6	1903	1490	78.3
18	1050	1800	462	5040	1110	1170	6	1772	1656	93.5
20	1250	1660	349	3790	1000	743	6	1465	1223	83.4
24	239	171	110	4160	170	257	6	851	1622	190.5
34	74.1	30.6	BLQ	1800	74.4	32.8	5	402	782	194.2
46	47.1	24.7	23.3	893	32.8	70.5	6	182	349	191.8
58	23.1	BLQ	14.2	259	17.4	40.2	5	70.8	106	149.3
82	BLQ	BLQ	BLQ	118	BLQ	39.8	2	78.9	ON	ON

Table 16: Results of pharmacokinetic parameters for single administration (ketorolac tromethamine TITs).

Test article	route of administration	Dosage administered (mg)	cycle	Animal number	R2	LZ (1/h)	t1/2 (h)	Tmax* (h)	Cmax (ng/mL)	AUC0-t (h*µg/mL)	AUC0-∞ (h*µg/mL)	AUC_%Extrap (%)	CEO/F (S)	CL/F (L/hr)	MRT0-t (h)	MRT0-∞ (h)
ketorolac tromethamine TITs (T)	Single oral dose	35	P1	M001	0.9846	0.101	6.88	5.00	2940	20.7	21.0	1.2	16.6	1.67	6.91	7.38
				F002	0.9842	0.108	6.45	5.00	3860	37.6	37.9	0.8	8.58	0.922	10.5	10.9
				F003	0.7178	0.0576	12.0	6.00	3200	43.9	48.9	10.3	12.4	0.715	12.4	17.8
			P2	M004	0.8068	0.0563	12.3	5.00	2870	32.1	34.7	7.4	17.9	1.01	14.8	18.5
				M005	0.9546	0.0635	10.9	5.00	2390	26.2	27.5	4.6	20.1	1.27	11.9	14.2
				F006	0.9298	0.0859	8.07	4.00	2380	37.2	37.8	1.8	10.8	0.925	12.9	13.8
			total	N	6	6	6	6	6	6	6	6	6	6	6	6
				Mean	0.896	0.0786	9.44	5.00 (4.00, 6.00)	2940	33.0	34.6	4.35	14.4	1.09	11.6	13.8
				SD	0.109	0.0226	2.63		554	8.44	9.64	3.84	4.48	0.338	2.67	4.20
				CV%	12.2	28.7	27.8		18.8	25.6	27.8	88.1	31.2	31.1	23.1	30.5

Note: *T_{max} is expressed as the median (min, max).

Table 17: Results of pharmacokinetic parameters for a single administration (ketorolac tromethamine tablets).

Test article	route of administration	Dosage administered (mg)	cycle	Animal number	R2	LZ (1/h)	t1/2 (h)	Tmax* (h)	Cmax (ng/mL)	AUC0-t (h*µg/mL)	AUC0-∞ (h*µg/mL)	AUC_%Extrap (%)	CEO/F (S)	CL/F (L/hr)	MRT0-t (h)	MRT0-∞ (h)
Ketorlac tromethamine tablets (R)	take orally	35	P2	M001	0.8567	0.133	5.21	0.500	10700	45.9	46.0	0.3	5.72	0.761	5.33	5.48
				F002	0.9468	0.107	6.47	2.00	8240	58.2	58.6	0.7	5.58	0.597	9.07	9.42
				F003	0.9173	0.0349	19.9	1.00	8950	97.9	118	17.2	8.49	0.296	13.3	24.2
			P1	M004	0.9899	0.0697	9.95	1.00	6600	48.9	49.7	1.5	10.1	0.705	7.13	7.94
				M005	0.6960	0.0771	8.99	1.00	7080	43.0	44.8	4.2	10.1	0.780	7.59	9.81
				F006	0.9450	0.131	5.27	0.500	8330	40.2	40.4	0.4	6.60	0.867	5.65	5.85
			total	N	6	6	6	6	6	6	6	6	6	6	6	6
				Mean	0.892	0.0922	9.30	1.00	8317	55.7	59.6	4.04	7.77	0.668	8.01	10.4
				SD	0.106	0.0386	5.54	(0.500, 2.00)	1454	21.6	29.3	6.59	2.10	0.203	2.92	6.95
				CV%	11.8	41.9	59.6		17.5	38.8	49.2	163.2	27.0	30.4	36.5	66.6

Note: *T_{max} is expressed as the median (min, max).

Table 18: Results of pharmacokinetic parameters for multiple administrations (ketorolac tromethamine TITs-D1).

Constituencies	route of administration	Dosage administered (mg)	gender	Animal number	R2	LZ (1/h)	t1/2 (h)	Tmax* (h)	Cmax (ng/mL)	AUC0-t (h*µg/mL)	AUC0-∞ (h*µg/mL)	AUC_%Extrap (%)	CEO/F (S)	CL/F (L/hr)	MRT0-t (h)	MRT0-∞ (h)
ketorolac tromethamine TITs (T)	take orally	35	male	M007	0.9978	0.111	6.26	2.00	2600	23.7	25.7	7.8	12.3	1.36	7.88	9.85
				M008	0.9982	0.136	5.09	4.00	2790	38.3	40.7	6.0	6.31	0.860	8.94	10.3
				M009	0.9588	0.151	4.58	4.00	4060	31.6	33.0	4.0	7.01	1.06	6.85	7.81
			female	F010	0.9958	0.0890	7.79	4.00	4290	36.2	40.7	11.1	9.66	0.860	7.80	10.9
				F011	0.9913	0.105	6.58	4.00	4990	49.4	54.9	10.1	6.05	0.637	8.54	11.1
				F012	0.9991	0.157	4.42	4.00	4320	39.1	40.3	2.9	5.54	0.868	7.35	8.03
			total	N	6	6	6	6	6	6	6	6	6	6	6	6
				Mean	0.990	0.125	5.79	4.00 (2.00, 4.00)	3842	36.4	39.2	7.00	7.81	0.941	7.90	9.65
				SD	0.0156	0.0273	1.32		943	8.53	9.74	3.29	2.63	0.246	0.760	1.41
				CV%	1.6	21.8	22.8		24.5	23.4	24.8	46.9	33.7	26.1	9.6	14.6

Note: *T_{max} is expressed as the median (min, max).

Table 19: Results of pharmacokinetic parameters for multiple administration (ketorolac tromethamine TITs-D7).

Constituents	Administration Way	Administration dosage (mg)	gender	Animal number	R2	LZ (1/h)	t1/2 (h)	Tmax,ss* (h)	Cmax,ss (ng/mL)	Cmin,ss (ng/mL)	Cavg,ss (ng/mL)	AUC0-t (h*µg/mL)	AUC0-24 (h*µg/mL)	AUC0-t (h*µg/mL)	AUC0-∞ (h*µg/mL)	AUC _{%Extrap} (%)	CE0/F (S)	CLss/F (L/hr)	MRT0-∞ (h)	DF (%)	R [#]
ketorolac tromethamine TITs (T)	take orally	35	male	M007	0.9982	0.0220	31.5	5.00	3240	455	1922	59.0	46.1	46.1	77.3	23.6	34.4	0.759	25.4	144.9	1.95
				M008	0.9319	0.112	6.19	3.00	2610	121	925	23.3	22.2	22.2	23.5	1.0	14.1	1.58	7.88	269.00	0.580
				M009	0.9856	0.0300	23.1	3.00	4810	1820	3256	116	78.2	78.2	154	25.1	15.0	0.448	33.9	91.8	2.47
			female	F010	0.9193	0.0700	9.91	2.00	3130	167	1779	53.0	42.7	42.7	56.5	6.1	11.7	0.820	18.4	166.6	1.18
				F011	0.9932	0.107	6.47	2.00	1690	154	648	16.9	15.5	15.5	17.0	0.7	21.0	2.25	9.60	237.1	0.314
				F012	0.9686	0.133	5.20	5.00	2700	146	1268	32.0	30.4	30.4	32.2	0.4	8.62	1.15	9.49	201.4	0.777
			total	N	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6
				Mean	0.966	0.0791	13.7	3.00	3030	477	1633	50.0	39.2	39.2	60.1	9.48	17.5	1.17	17.4	185	1.21
				SD	0.0332	0.0460	11.0	(2.00, 5.00)	1030	669	932	36.1	22.4	22.4	51.3	11.7	9.27	0.656	10.5	64.3	0.840
				CV%	3.4	58.2	79.8		34.0	140.3	57.1	72.3	57.1	57.1	85.3	123.7	53.1	56.2	60.2	34.7	69.3

Note: *T_{max,ss} is expressed as the median (min, max).

[#]R=AUC0-24 (G3 组 D7)/AUC0-t (G3 组 D1)。

Table 20: Results of pharmacokinetic parameters for multiple dosing (ketorolac tromethamine tablets-D1 first).

Constituencies	route of administration	Dosage administered (mg)	gender	Animal number	R2	LZ (1/h)	t1/2 (h)	Tmax* (h)	Cmax (ng/mL)	AUC0-t (h*µg/mL)	AUC0-∞ (h*µg/mL)	AUC_%Extrap (%)	CEO/F (S)	CL/F (L/hr)	MRT0-t (h)	MRT0-∞ (h)
Ketorlac tromethamine tablets (R)	take orally	15	male	M013	0.9988	0.321	2.16	0.500	2370	5.48	6.82	19.6	6.84	2.20	1.80	3.04
				M014	ON	ON	ON	2.00	2090	9.06	ON	ON	ON	ON	2.44	ON
				M015	0.9396	0.194	3.57	0.500	1890	6.93	11.1	37.3	6.99	1.36	2.27	5.21
			female	F016	0.9998	0.172	4.02	0.333	5550	15.0	25.9	42.0	3.35	0.579	2.12	5.77
				F017	0.9803	0.325	2.14	0.333	2140	6.45	8.24	21.7	5.61	1.82	2.06	3.37
				F018	0.9540	0.228	3.04	0.333	3770	10.0	14.6	31.5	4.50	1.03	2.04	4.35
			total	N	5	5	5	6	6	6	5	5	5	5	6	5
				Mean	0.975	0.248	2.98	0.417 (0.333, 2.00)	2968	8.83	13.3	30.4	5.46	1.40	2.12	4.35
				SD	0.0269	0.0712	0.840		1434	3.47	7.65	9.70	1.55	0.639	0.217	1.16
				CV%	2.8	28.7	28.1		48.3	39.4	57.3	31.9	28.4	45.7	10.2	26.8

Note: *T_{max} is expressed as the median (min, max).

Table 21: Results of pharmacokinetic parameters for multiple administration (ketorolac tromethamine tablets - D7).

Constituencies	route of administration	Dose administered (mg)	gender	Animal number	R2	LZ (1/h)	t1/2 (h)	Tmax,ss* (h)			Cmax (ng/mL)			Cmax,ss (ng/mL)	Cmin,ss (ng/mL)	Cavg,ss (ng/mL)
								D7 15 mg for the first time	D7 10 mg for the second time	D7 10 mg for the third time	D7 15 mg for the first time	D7 10 mg for the second time	D7 10 mg for the third time			
Ketorolac tromethamine tablets (R)	take orally	35	male	M013	0.9838	0.0486	14.3	0.500	0.500	1.00	2990	3100	2800	3100	233	1391
				M014	0.8773	0.154	4.50	0.167	0.333	4.00	2660	2840	2290	2840	171	1610
				M015	0.9853	0.0615	11.3	0.500	1.00	2.00	2440	2230	1740	2440	110	997
			female	F016	0.9764	0.0610	11.4	1.00	1.00	4.00	5920	5760	6180	6180	1460	4527
				F017	0.9946	0.0605	11.4	0.500	0.333	1.00	2650	2880	2510	2880	170	1316
				F018	0.8082	0.0764	9.07	1.00	0.500	1.00	4570	4340	4070	4570	257	2295
			total	N	6	6	6	6	6	6	6	6	6	6	6	6
				Mean	0.938	0.0770	10.3	0.500 (0.167, 1.00)	0.500 (0.333, 1.00)	1.50 (1.00, 4.00)	3538	3525	3265	3668	400	2023
				SD	0.0769	0.0388	3.30	18			1400	1296	1625	1433	522	1301
				CV%	8.2	50.4	31.9	1.00 (0.167, 4.00)			39.6	36.8	49.8	39.1	130.4	64.3

Note: *T_{max,ss} is expressed as the median (min, max);

The results of PK parameters after the first, second and third administration of D7 were calculated separately with each dose of 0 h, and the results of other parameters were comprehensively calculated.

Table 21: Results of pharmacokinetic parameters for multiple administration (ketorolac tromethamine tablets-D7) (Continued table).

Constituents	route of administration	Dosage administered (mg)	gender	Animal number	AUC0-5 (h*µg/mL)	AUC5-10 (h*µg/mL)	AUC10-82 (h*µg/mL)	AUC0-48 (h*µg/mL)	AUC0-t (h*µg/mL)	AUC0-t (h*µg/mL)	AUC _∞ (h*µg/mL)	AUC _{extrap} (%E)	CE _{0/F} (S)	CL _{ss} /F (L/hr)	MRT _{0-∞} (h)	DF (%)	R [#]	
					D7 for the first time	D7 for the second time	D7 for the third time											
Ketorlac tromethamine tablets (R)	take orally	35	male	M013	7.77	6.64	21.7	35.8	36.1	33.4	36.6	1.3	21.6	1.05	12.8	206.1	1.42	
				M014	9.91	6.41	23.7	40.0	40.0	38.6	40.1	0.4	5.88	0.906	11.8	165.8	1.09	
				M015	8.60	6.18	10.8	25.4	25.6	23.9	25.9	0.9	23.8	1.46	10.0	233.6	1.24	
			female	F016	19.9	23.2	123	156	166	109	168	1.2	5.28	0.322	25.2	104.3	1.33	
				F017	7.52	6.25	20.0	33.5	33.8	31.6	34.0	0.8	18.3	1.11	12.2	205.9	1.17	
				F018	17.2	13.9	27.7	57.3	58.8	55.1	59.3	0.9	8.32	0.64	10.5	187.9	1.72	
			total	N	6	6	6	6	6	6	6	6	6	6	6	6	6	6
				Mean	11.8	10.4	37.8	58.1	60.0	48.5	60.6	0.911	13.9	0.914	13.8	184	1.33	
				SD	5.34	6.95	42.1	49.3	53.1	31.2	53.7	0.309	8.32	0.396	5.69	45.0	0.224	
				CV%	45.2	66.6	111.3	84.9	88.4	64.3	88.6	33.9	60.0	43.3	41.3	24.5	16.9	

Note: [#]R=AUC0-5 (G4 group D7)/AUC0-t (G4 group D1 first).

1. Figures

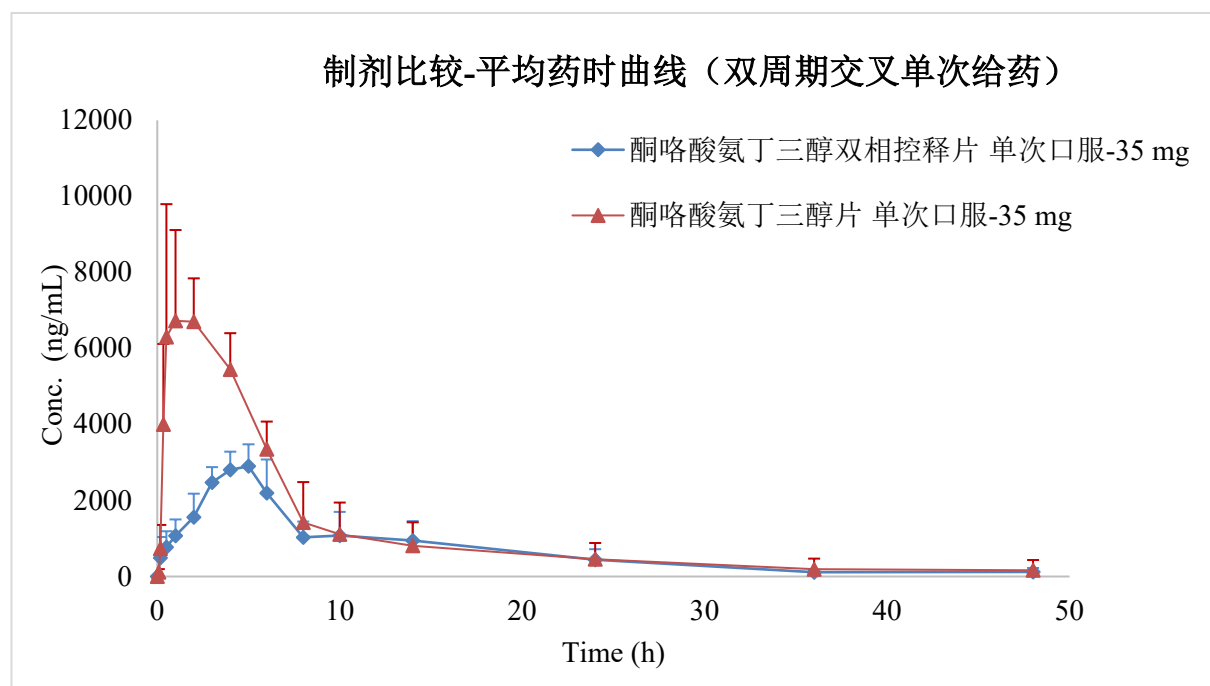


Fig-1 Comparison of preparations with the average plasma concentration-time curve of a single dose of a single dose in two cycles

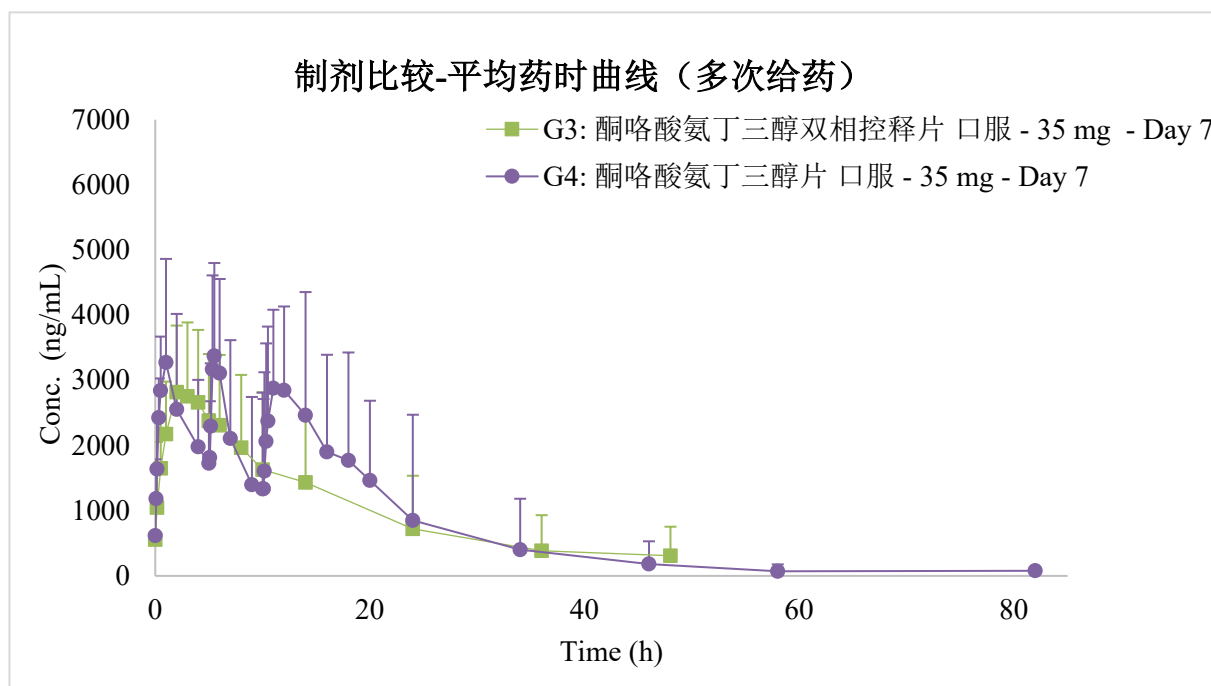


Fig-2 Comparison of preparations with the average plasma concentration-time curve of repeated dosing

2. Appendix

Appendix 1: Single-dose animal weight information

cycle	Weighing date	Constituencies	Test article	Mode of administration	Dosage administered (mg)	Animal number	gender	weight (kg)
P1	2024/08/22	G1	Ketolac tromethamine biphasic controlled-release tablets	take orally	35	M001	male	9.08
						F002	female	9.82
						F003		8.82
		G2	ketorolac tromethamine tablets	take orally	35	M004	male	9.52
						M005		9.46
						F006	female	7.48
P2	2024/08/28	G1	ketorolac tromethamine tablets	take orally	35	M001	male	9.12
						F002	female	9.86
						F003		8.46
		G2	Ketolac tromethamine biphasic controlled-release tablets	take orally	35	M004	male	9.54
						M005		9.24
						F006	female	7.54

Appendix 2: Weight information on multi-dosed animals

Weighing date	Constituencies	Mode of administration	Dosage (mg)	Animal number	gender	weight (kg)
2024/08/27	G3 (D1 pre-dose).	take orally	35	M007	male	10.42
				M008		9.72
				M009		8.74
				F010	female	8.40
				F011		10.80
				F012		9.86
2024/09/02	G3 (D7 pre-dose).	take orally	35	M007	male	10.32
				M008		9.72
				M009		7.74
				F010	female	7.58
				F011		10.32
				F012		9.56
2024/08/27	G4 (D1 pre-dose).	take orally	35	M013	male	8.82
				M014		10.04
				M015		10.02
				F016	female	7.70
				F017		12.40
				F018		9.46
2024/09/02	G4 (D7 pre-dose).	take orally	35	M013	male	8.94
				M014		9.80
				M015		9.96
				F016	female	7.02
				F017		12.06
				F018		9.10