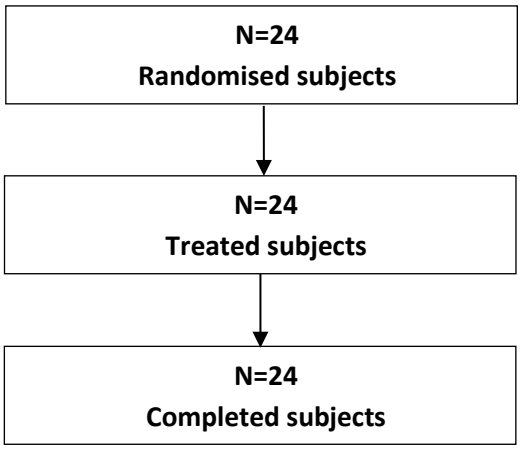
Participant flow



The two investigational products were orally administered as follows:

- Test product (T): one film-coated tablet of ibuprofen arginine 600 mg
- Reference product (R): one sachet of Espidifen® 600 mg granules for oral solution

Twenty-four (24) subjects were randomised in the study as planned, received the study treatment (T/R or R/T, according to the randomisation list and to the 2-way cross-over design) and completed the study per protocol.

Baseline characteristics

Demographic data	Randomised, safety and pharmacokinetic set N=24
Sex	
Female – n (%)	12 (50.0%)
Male – n (%)	12 (50.0%)
Age (years)	
Mean ±SD	42.0±9.6
Median (min-max)	44.0 (21-54)
Body weight (kg)	
Mean ±SD	68.34±12.39
Median (min-max)	68.50 (50.1-95.7)
Height (cm)	
Mean ±SD	167.8±9.2
Median (min-max)	168.5 (151-184)
Body Mass Index (kg/m^2)	
Mean ±SD	24.09±2.65
Median (min-max)	24.30 (18.7-29.0)
Race	
White – n (%)	24 (100.0%)

Outcome measures

Primary outcome

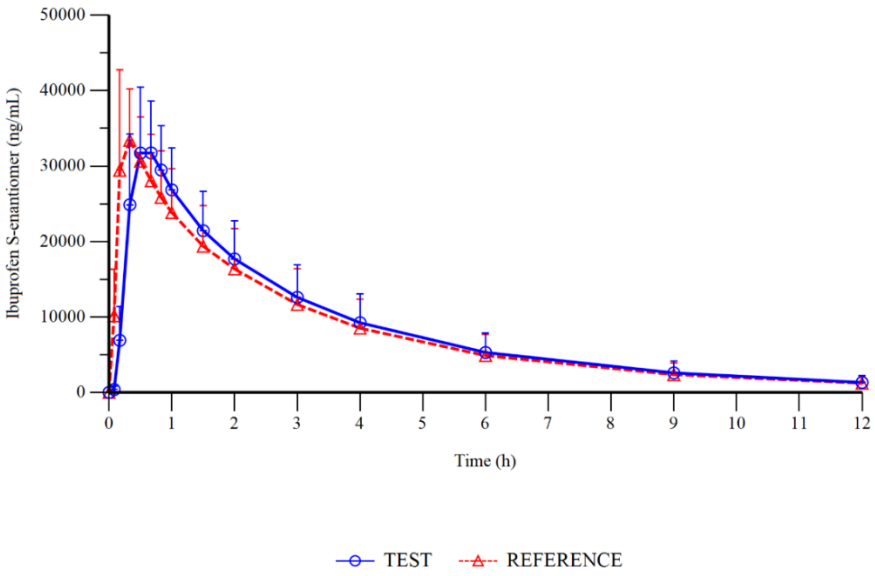
Results of the statistical comparison of plasma S(+)-ibuprofen pharmacokinetic parameters between T and R are presented in the table below:

S(+)-ibuprofen		Geometric mean ratio	
Treatment comparison	**Parameter**	**PE%**	**94.12% CI**
T vs. R	C_{max}	98.16%	93.29 – 103.29%
	AUC_{0-t}	104.21%	101.07 – 107.45%

T: Ibuprofen arginine 600 mg film-coated tablet; R: Espidifen® 600 mg granules for oral solutions.
PE: Point estimate, calculated as ratio of geometric means; CI: confidence interval; N=24.

Secondary outcome

Mean (+SD) S(+)-ibuprofen plasma concentration (ng/mL) vs. time profiles for T and R products are shown in the figure below:

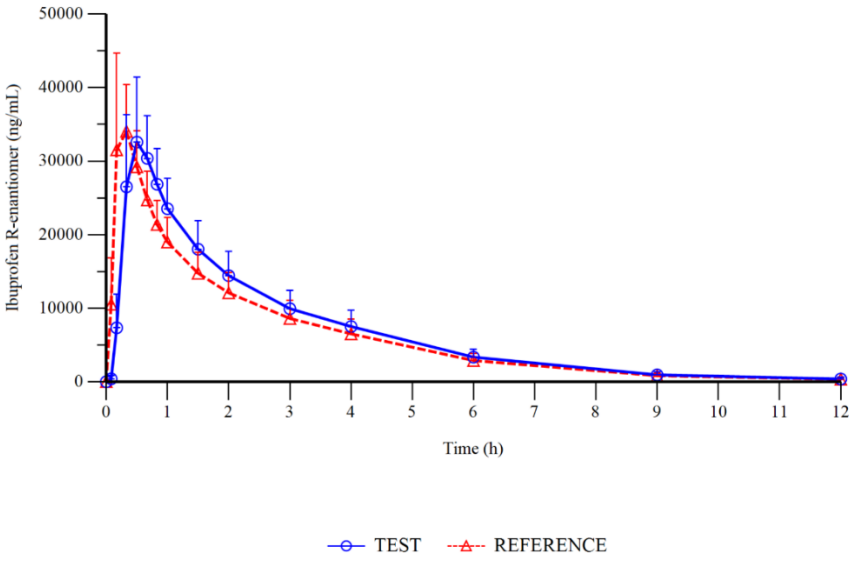


Descriptive statistics of S(+)-ibuprofen plasma pharmacokinetic parameters are presented in the table below:

Pharmacokinetic parameter	**T**	**R**
C_{max} (ng/mL)	34086.644±6716.221	35144.433±9775.391
AUC_{0-t} (ng/mL×h)	102842.339±33387.629	99622.556±36242.171
$AUC_{0-\infty}$ (ng/mL×h)	108850.458±38160.629	105193.591±40990.400
t_{max} (h)	0.500 (0.38–0.83)	0.330 (0.17–0.67)
$t_{½}$ (h)	2.855±0.522	2.841±0.572

T: Ibuprofen arginine 600 mg film-coated tablet; R: Espidifen® 600 mg granules for oral solution. Values are arithmetic means ± SD, except for t_{max}: median (min-max). N=24

Mean (+SD) R(-)-ibuprofen plasma concentration (ng/mL) vs. time profiles for T and R are shown in the figure below:



Descriptive statistics of R(-)-ibuprofen plasma pharmacokinetic parameters are presented in the table below:

Pharmacokinetic parameter	**T**	**R**
C_{max} (ng/mL)	34835.415±7230.013	36966.352±9314.980
AUC_{0-t} (ng/mL×h)	80802.605±17567.567	74224.077±16260.429
$AUC_{0-\infty}$ (ng/mL×h)	82141.029±17879.621	75411.630±16529.971
t_{max} (h)	0.500 (0.33–0.83)	0.330 (0.17–0.5)
$t_{½}$ (h)	1.891±0.447	1.945±0.434

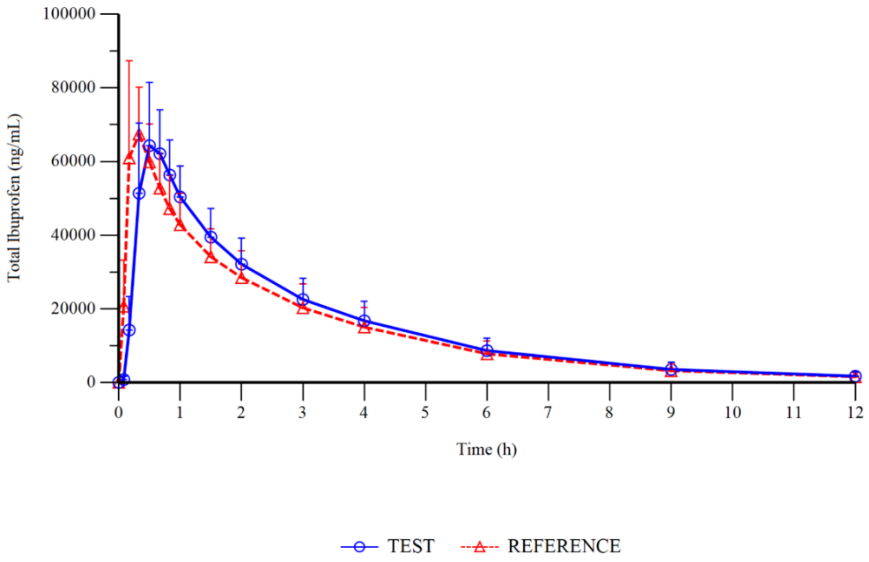
T: Ibuprofen arginine 600 mg film-coated tablet; R: Espidifen® 600 mg granules for oral solution. Values are arithmetic means ± SD, except for t_{max}: median (min-max). N=24

Results of the statistical comparison of plasma R(-)-ibuprofen pharmacokinetic parameters between T and R are presented in the table below:

R(-)-ibuprofen		**Geometric mean ratio**	
Treatment comparison	**Parameter**	**PE%**	**94.12% CI**
T vs. R	C_{max}	94.76%	87.77 – 102.31%
	AUC_{0-t}	108.73%	102.79 – 115.02%

T: Ibuprofen arginine 600 mg film-coated tablet; R: Espidifen® 600 mg granules for oral solutions. PE: Point estimate, calculated as ratio of geometric means; CI: confidence interval; N=24.

Total ibuprofen plasma concentrations were calculated as the sum of S- and R-ibuprofen plasma concentrations. Mean (+SD) total ibuprofen concentration (ng/mL) vs. time profiles for T and R are shown in the figure below:



Descriptive statistics of total ibuprofen plasma pharmacokinetic parameters are presented in the table below:

Pharmacokinetic parameter	**T**	**R**
C_{max} (ng/mL)	68665.063±13087.657	71829.893±18967.253
AUC_{0-t} (ng/mL×h)	183738.260±45585.210	173953.530±49455.325
$AUC_{0-\infty}$ (ng/mL×h)	190407.798±50570.554	180080.540±54177.849
t_{max} (h)	0.500 (0.38–0.83)	0.330 (0.17–0.50)
$t_{½}$ (h)	2.429±0.500	2.453±0.493

T: Ibuprofen arginine 600 mg film-coated tablet; R: Espidifen® 600 mg granules for oral solution. Values are arithmetic means ± SD, except for t_{max}: median (min-max). N=24

Results of the statistical comparison of total ibuprofen plasma pharmacokinetic parameters between T and R are presented in the table below:

R(-)-ibuprofen		**Geometric mean ratio**	
Treatment comparison	**Parameter**	**PE%**	**94.12% CI**
T vs. R	C_{max}	96.60%	90.73 – 102.84%
	AUC_{0-t}	106.34%	102.68 – 110.13%

T: Ibuprofen arginine 600 mg film-coated tablet; R: Espidifen® 600 mg granules for oral solutions. PE: Point estimate, calculated as ratio of geometric means; CI: confidence interval; N=24.

Adverse events

Number of treatment-emergent adverse events (TEAEs) and number and percentage of subjects with TEAEs by System Organ Class (SOC), preferred term (PT) and treatment after single dose of T and R. Safety set

SOC	**T N=24**		**R N=24**		**Overall N=24**	
PT	**n AEs**	**n (%) subjects**	**n AEs**	**n (%) subjects**	**n AEs**	**n (%) subjects**
All TEAEs – all SOCs	1	1 (4.2)	3	3 (12.5)	4	4 (16.7)
Investigations	1	1 (4.2)	2	2 (8.3)	3	3 (12.5)
Blood creatinine increased	1	1 (4.2)	2	2 (8.3)	3	3 (12.5)
Nervous system disorders	0	0 (0.0)	1	1 (4.2)	1	1 (4.2)
Presyncope	0	0 (0.0)	1	1 (4.2)	1	1 (4.2)

Number of treatment-emergent adverse events (TEAEs) and number of subjects with TEAEs after single dose of T and R. Safety set

Category	**T N=24**		**R N=24**		**Overall N=24**	
	n AEs	**n (%) subjects**	**n AEs**	**n (%) subjects**	**n AEs**	**n (%) subjects**
All TEAEs	1	1 (4.2)	3	3 (12.5)	4	4 (16.7)
Related	1	1 (4.2)	2	2 (8.3)	3	3 (12.5)
Not related	0	0 (0.0)	1	1 (4.2)	1	1 (4.2)
Leading to discontinuation	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
SAEs	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)