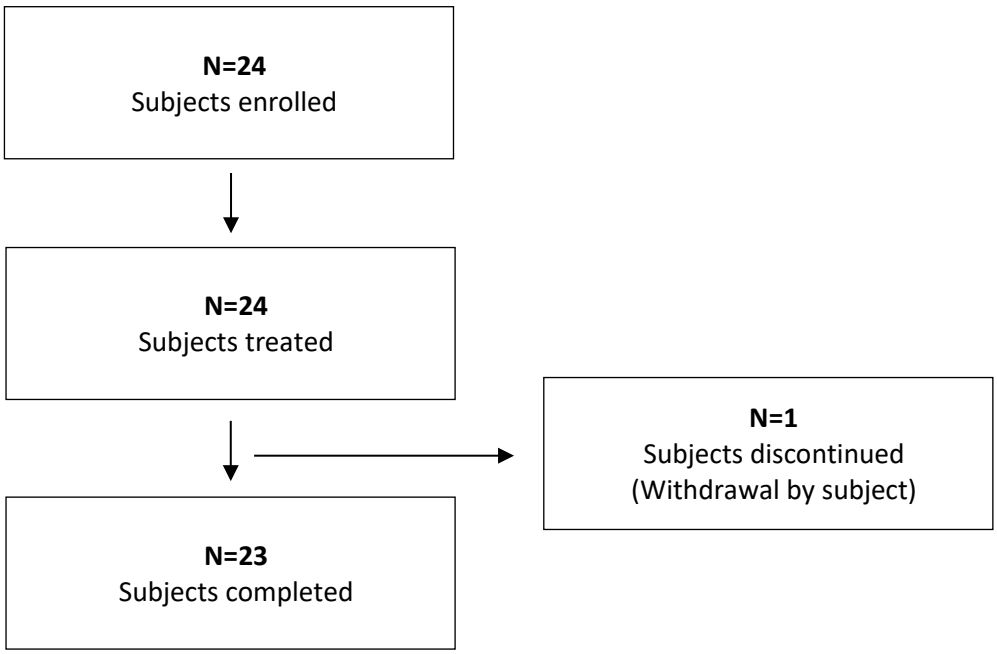
Participant flow



Baseline characteristics

Demographic data	**Safety set N=24**
Gender	
Female – n (%)	11 (45.8%)
Male – n (%)	13 (54.2%)
Age (years)	
Mean ± SD	35.6±8.9
Median (range)	39.0 (18 – 45)
Body weight (kg)	
Mean ± SD	67.48±12.24
Range	65.25 (48.9 – 96.1)
Height (cm)	
Mean ± SD	169.0±8.8
Median (range)	170.0 (153 – 187)
Body Mass Index (kg/m^2)	
Mean ± SD	23.51±2.88
Median (range)	23.30 (19.6 – 29.3)
Race	
White – n (%)	24 (100.0%)

Outcome measures

Primary outcome

Local tolerability of the study products, evaluated as adverse drug reactions at the application site (erythema, dryness, swelling and exfoliation), observed by the Investigator or spontaneously reported by the subjects after once a day application for 2 consecutive days of DHEP medicated plasters (T1: DHEP 360 mg/140 cm^2 plaster, T2: DHEP 180 mg/70 cm^2 plaster, R: Flector EP Tissugel® 182 mg/140 cm^2)

	T1 N = 24		**T2 N = 23**		**R N = 23**	
Treatment-emergent Adverse Events related to the IMP	**TEAEs n**	**Subjects n (%)**	**TEAEs n**	**Subjects n (%)**	**TEAEs n**	**Subjects n (%)**
Application site erythema	0	0 (0.0)	1	1 (4.3)	0	0 (0.0)

Secondary outcome

Diclofenac plasma pharmacokinetic parameters for DHEP 360 mg/140 cm^2 plaster (T1), DHEP 180 mg/70 cm^2 plaster (T2) and Flector EP Tissugel® plaster (DHEP 182 mg/140 cm^2; R) applied once a day for 2 consecutive days

PK parameter	**Diclofenac**		
	T1 N=11	**T2 N=11**	**R N=11**
C_{max} (ng/mL)	3.75 ± 2.29	1.87 ± 1.38	3.80 ± 2.70
AUC_{τ} (ng/mL×h)	68.26 ± 38.68	33.15 ± 23.76	67.94 ± 39.10
C_{min} (ng/mL)	2.18 ± 1.20	1.03 ± 0.78	2.10 ± 1.29
C_{ave} (ng/mL)	2.84 ± 1.61	1.38 ± 0.99	2.83 ± 1.63
t_{max} (h)	16.00 (0.00 – 24.00)	12.00 (0.00 – 24.00)	4.00 (0.00 – 24.00)
Flu% (%)	58.29 ± 22.19	66.25 ± 26.73	57.53 ± 19.56

Values are arithmetic means ± SD, except for tmax: median (min-max)

Adverse events

Number of subjects reporting and number of reported TEAEs by treatment, system organ class (SOC) and preferred term (PT) after applications of DHEP 360 mg/140 cm^2 plaster (T1), DHEP 180 mg/70 cm^2 plaster (T2) and Flector EP Tissugel® plaster (DHEP 182 mg/140 cm^2; R) once a day for 2 consecutive days. Safety set

MedDRA description SOC and PT term	T1 N=24		T2 N=23		R N=23		Overall N=24	
	TEAEs n	Subjects n (%)	TEAEs n	Subjects n (%)	TEAEs n	Subjects n (%)	TEAEs n	Subjects n (%)
Total number of AEs and of subjects with at least one AE	1	1 (4.2)	1	1 (4.3)	0	0 (0.0)	2	2 (8.3)
Gastrointestinal disorders	1	1 (4.2)	0	0 (0.0)	0	0 (0.0)	1	1 (4.2)
Diarrhoea	1	1 (4.2)	0	0 (0.0)	0	0 (0.0)	1	1 (4.2)
General disorders and administration site conditions	0	0 (0.0)	1	1 (4.3)	0	0 (0.0)	1 (4.2)	1 (4.2)
Application site erythema	0	0 (0.0)	1	1 (4.3)	0	0 (0.0)	1 (4.2)	1 (4.2)

Number of TEAEs and number of subjects with TEAEs after applications of DHEP 360 mg/140 cm^2 plaster (T1), DHEP 180 mg/70 cm^2 plaster (T2) and Flector EP Tissugel® plaster (DHEP 182 mg/140 cm^2; R) once a day for 2 consecutive days. Safety set

Category	T1 N=24		T2 N=23		R N=23		Overall N=24	
	N AEs	n (%) subjects	N AEs	n (%) subjects	N AEs	n (%) subjects	N AEs	n (%) subjects
All TEAEs	1	1 (4.2)	1	1 (4.3)	0	0 (0.0)	2	2 (8.3)
Related	0	0 (0.0)	1	1 (4.3)	0	0 (0.0)	1	1 (4.2)
Not related	1	1 (4.2)	0	0 (0.0)	0	0 (0.0)	1	1 (4.2)
Leading to discontinuation	0	0 (0.0)	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)	0	0 (0.0)