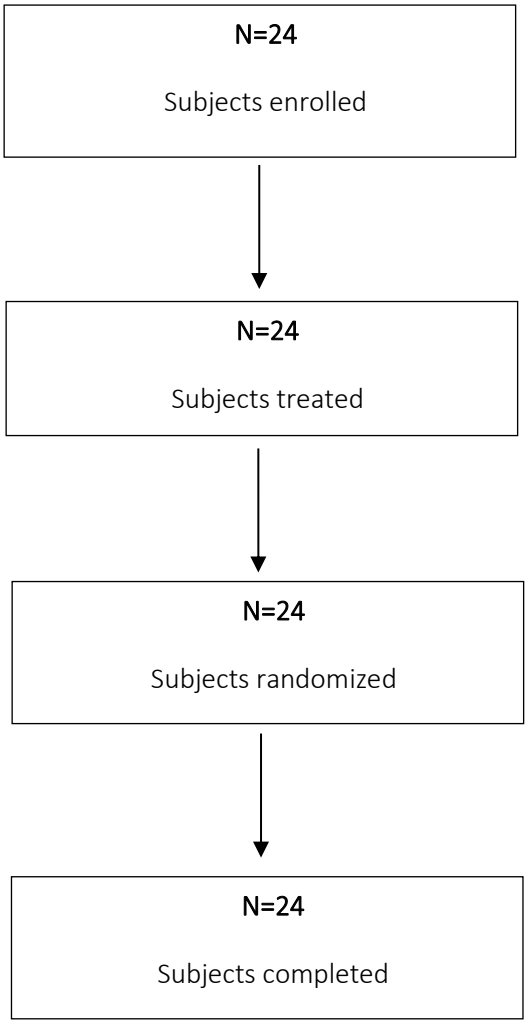
Participant flow



Baseline characteristics

Demographic data	Safety, Adhesion and PK set – N=24
Sex	
Women – n (%)	12 (50%)
Men – n (%)	12 (50%)
Age (years)	
Mean ± SD	54.3±5.5
Median (range)	54.5 (46-64)
Body weight (kg)	
Mean ± SD	68.64±8.86
Range	66.55 (53.8-88.5)
Height (cm)	
Mean ± SD	168.9±8.7
Median (range)	169.5 (154-184)
BMI (kg/m^2)	
Mean ± SD	24.06±2.50
Median (range)	23.55 (20.0-29.2)
Race	
White – n (%)	24 (100.0%)

Outcome measures

Primary outcomes

Adhesion assessment for DHEP 2.6% medicated plaster applied with and without reinforcement

Time	Actual adhesion percentage - Mean±SD		
	PW (N=24)	PRT (N=12)	PRN (N=12)
Day 1 - 4 h	95.5±20.4	99.0±1.3	96.5±4.1
Day 1 - 8 h	95.1±20.3	98.3±1.9	96.0±4.2
Day 1 - 12 h	94.8±20.2	98.3±1.9	95.8±4.8
Day 1 – 16 h	94.3±20.2	98.1±2.1	92.9±5.8
Day 1 – 20 h	91.0±20.5	97.5±2.8	91.8±6.4
Day 1 – 24 h*	88.0±22.4	92.6±13.0	87.6±10.4
Overall – Day 1	93.1±20.5	97.3±5.9	93.4±6.9
Day 3**	96.6±4.0	92.3±17.6	96.8±2.7
Day 4**	95.8±9.0	94.5±11.5	95.9±3.5
Day 5**	94.8±7.5	97.0±5.8	95.2±3.7
Day 6**	95.9±4.8	96.4±8.4	96.3±3.6

*PW: Plaster without reinforcement; PRN: Plaster reinforced using elastic net; PRT: Plaster reinforced by corner taping; * corresponding to Day 2 before plaster removal; **Before plaster removal*

Pharmacokinetic profile of diclofenac in plasma after once a day (o.d.) application of DHEP 2.6% medicated plaster for 5 consecutive days (N=24)

Diclofenac PK parameters – N=24	
$C_{max0\text{-}24h}$ (ng/mL)	3.167±1.283
C_{24h} (ng/mL)	2.892±1.228
AUC_{τ} (ng/mL×h)	59.592±24.576
$t_{max0\text{-}24h}$ (h)	4.00 (0.00-24.00)
$C_{min0\text{-}24h}$ (ng/mL)	1.843±0.813
$C_{ave0\text{-}24h}$ (ng/mL)	2.483±1.024
$Flu_{(0\text{-}24h)}$ (%)	54.458±10.775

Secondary outcome

If feasible, pharmacokinetic profile of epolamine and epolamine N-O after once-a-day application of DHEP 2.6% medicated plaster for 5 consecutive days

Epolamine plasma levels were below the quantification limit (BLQL) of the analytical method for all subjects at all assessment time points, while epolamine-N-oxide levels were BLQL at all assessment times for 9 of the 24 subjects in the study. The other 15 subjects showed few sporadic concentrations just above the lower quantification limit of the analytical assay.

Adverse events

No adverse events and no unexpected nor unfavourable local tolerability findings were reported during the study.
No significant effects of the study treatment on vital signs or laboratory parameters were observed.