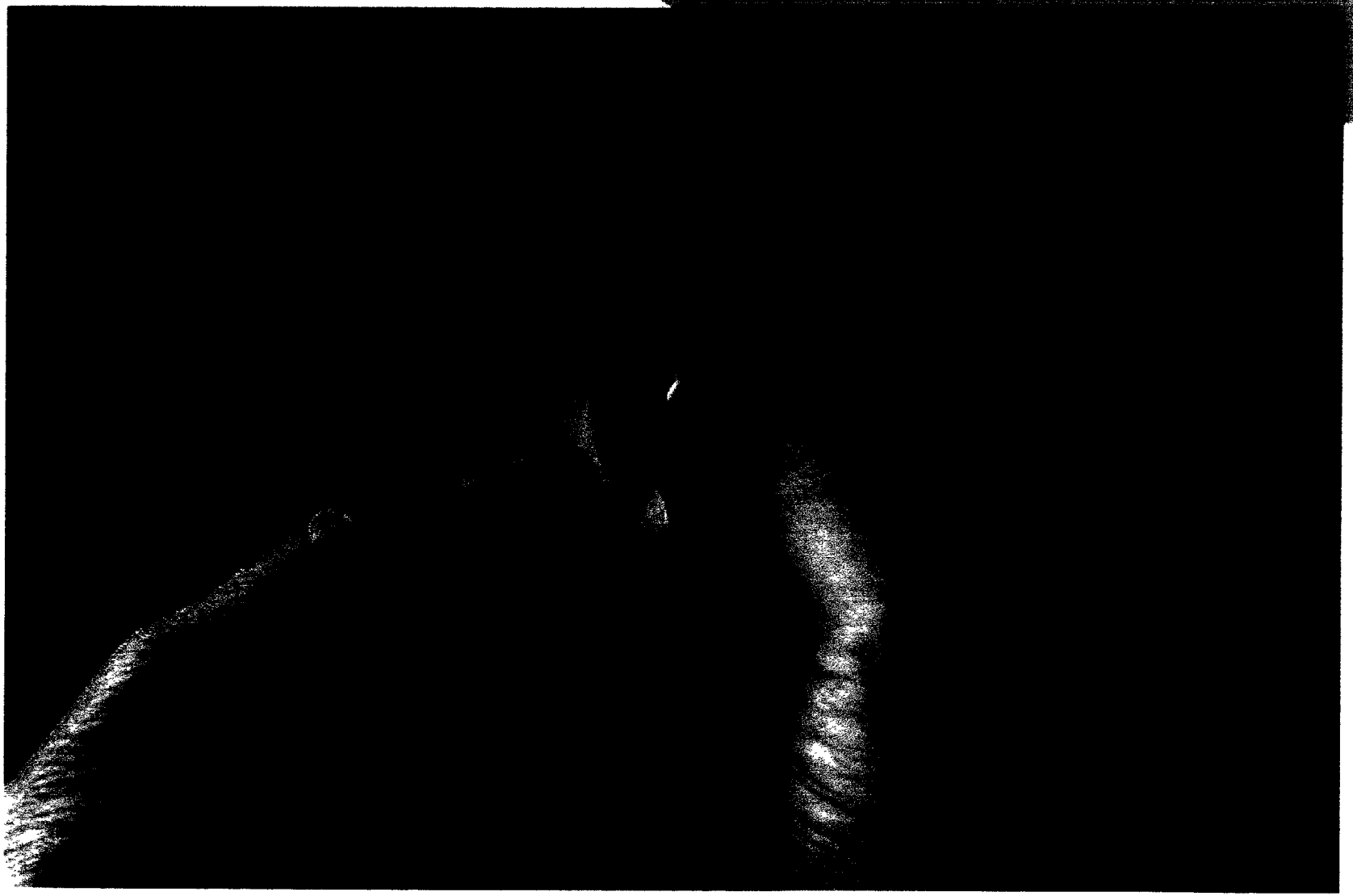
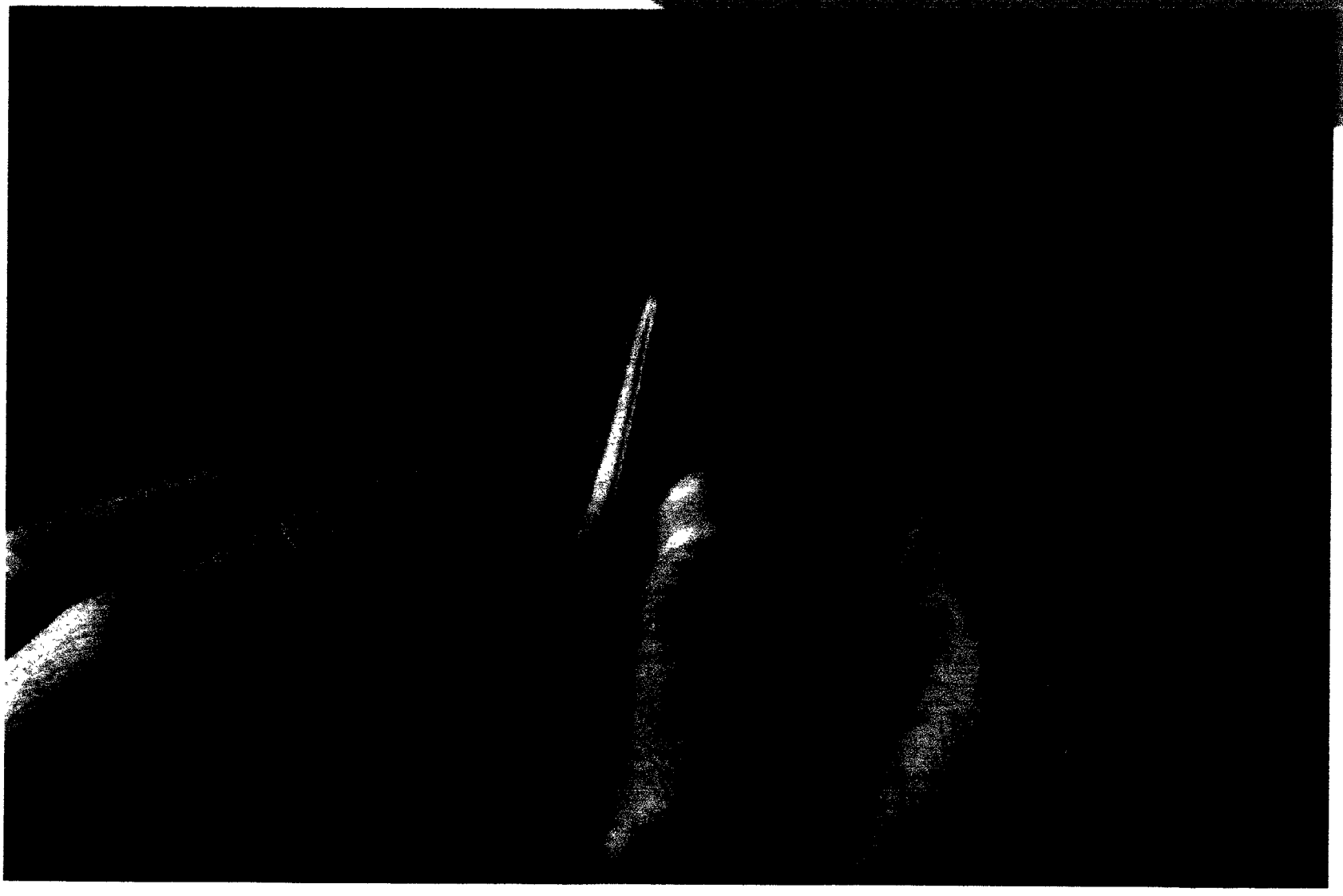
Attachment 2

Durogesic® SMAT





Elastischer Matrixaufbau

3 Schichten

[redacted]

51 µm

48 µm

➡ **Dicke des Pflasters < 0.1 mm!**

➡ **Keine Transportvermittler nötig**

Eigenschaften des Klebstoffs

Ziel:

Kontrollierte und gleichmäßige Wirkstofffreisetzung mit guten Trageeigenschaften

➡ Besonderer Klebstoff in Fentanyl D-Trans Matrix garantiert eine **gute Haftung** an der Haut und einen **optimalen Wirkstofffluss** durch die Haut.

Vergleich Reservoir/ D-TRANS® Matrix

Eigenschaft	Durogesic™ (Reservoir Pflaster)	D-TRANS® Fentanyl Matrix
Pflasteraufbau	Reservoirsystem mit gelartigem Inhalt; 5 Schichten	Elastischer Matrixaufbau; 3 Schichten
Pflastergröße	25 µg/h – 18.7 cm² 50 µg/h – 34 cm² 75 µg/h – 44.2 cm² 100 µg/h – 57.0 cm²	– 10.5 cm² – 21 cm² – 31.5 cm² – 42 cm²
Klebstoff	Silikon-Klebstoff	Polyacrylat-Klebstoff

Vergleich Reservoir/ D-TRANS® Matrix

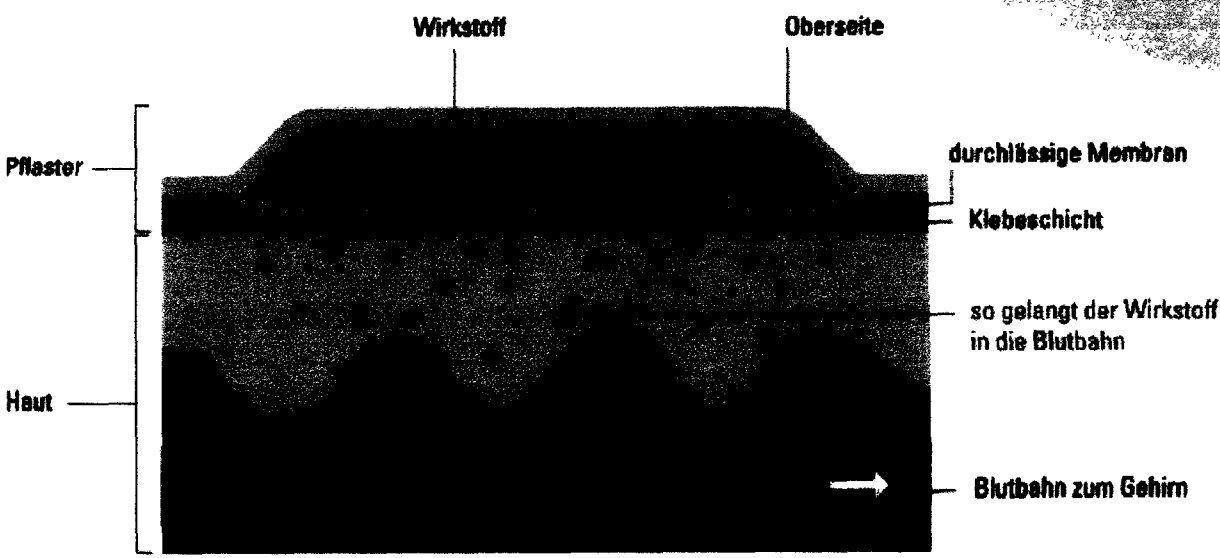
Eigenschaft	Durogesic™ Reservoir	D-TRANS® Matrix
Wirkstoff-schicht	Fentanyl suspendiert in Wasser/Ethanol und Hydroxyethylzellulose	Fentanyl direkt gelöst im Klebstoff
Kontrolle der Abgaberate	Durch Membran und Stratum corneum	Durch Matrix-Monomere und Stratum corneum
Transport-vermittler	Ethanol	Keiner
Abziehfolie	Polyethylenterephthalat = PET, ohne Schlitzung	PET, geschlitzt, einseitig silikonisiert

Durogesic SMAT: Pflastereigenschaften auf einen Blick

- **klein:** noch 26 – 44% kleiner als Durogesic
- **dünn:** über 80% dünner als Durogesic
- **flexibel:** elastischer Matrixaufbau
- **transparent:** bessere Trageeigenschaften
- **praktisch:** einfachere Handhabung
- **angenehm:** noch höherer Tragekomfort

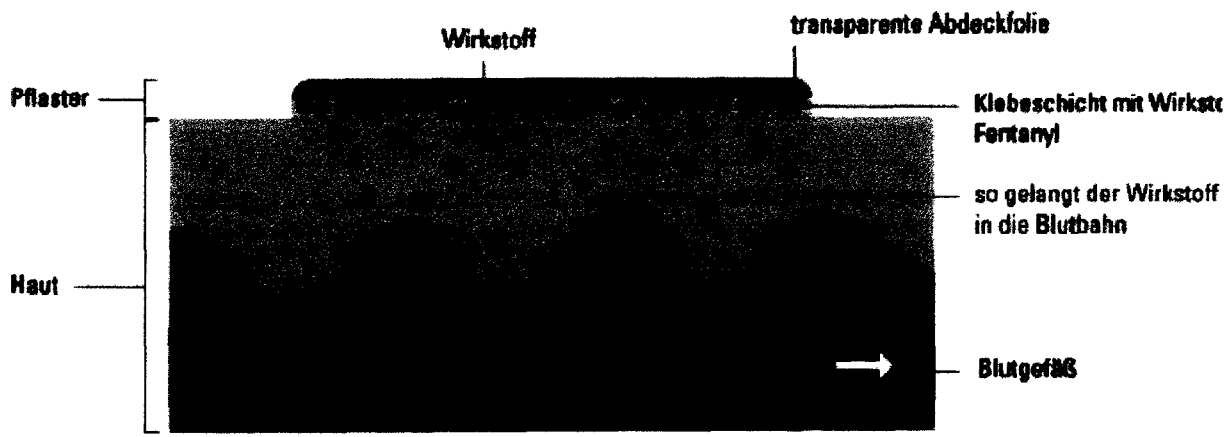
Durogesic SMAT

Schematischer Aufbau



Durogesic-Reservoir

Durogesic SMAT



D-TRANS® FENTANYL MATRIX

Klinisch-pharmakologische Studien

D-TRANS® Fentanyl MATRIX

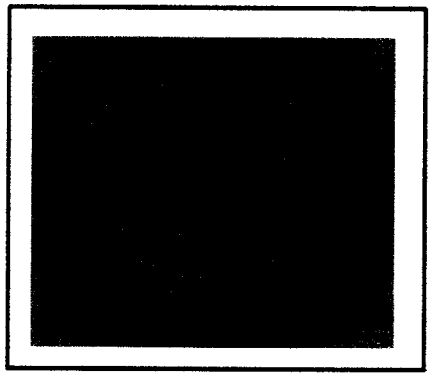
Bioäquivalenz

Mehrfachdosis

Dosisproportionalität

Demographische Einflüsse

D-TRANS® Fentanyl MATRIX



25 µg/h

Gleiche Abgaberaten

➡ **Bioäquivalenz** ✓

Bioäquivalenz-Studie

Pflastersysteme:

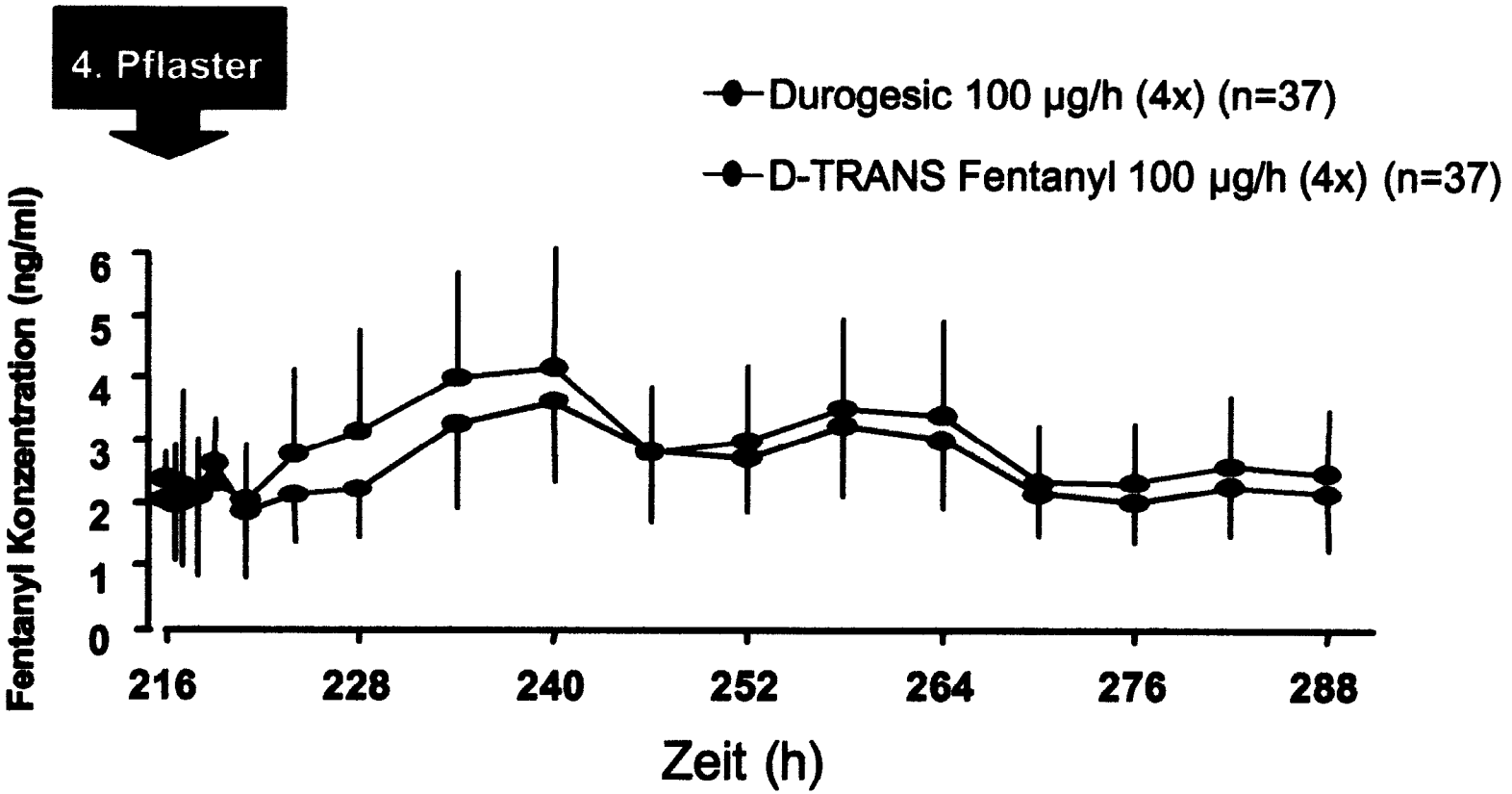
Durogesic-Reservoir; 100 µg/h

D-TRANS® Fentanyl Matrix; 100 µg/h

Studiendesign: Randomisiert, Crossover

Ergebnis (n=37): Bioäquivalenz ✓

Bioäquivalenz im Steady State - Mehrfachdosierung



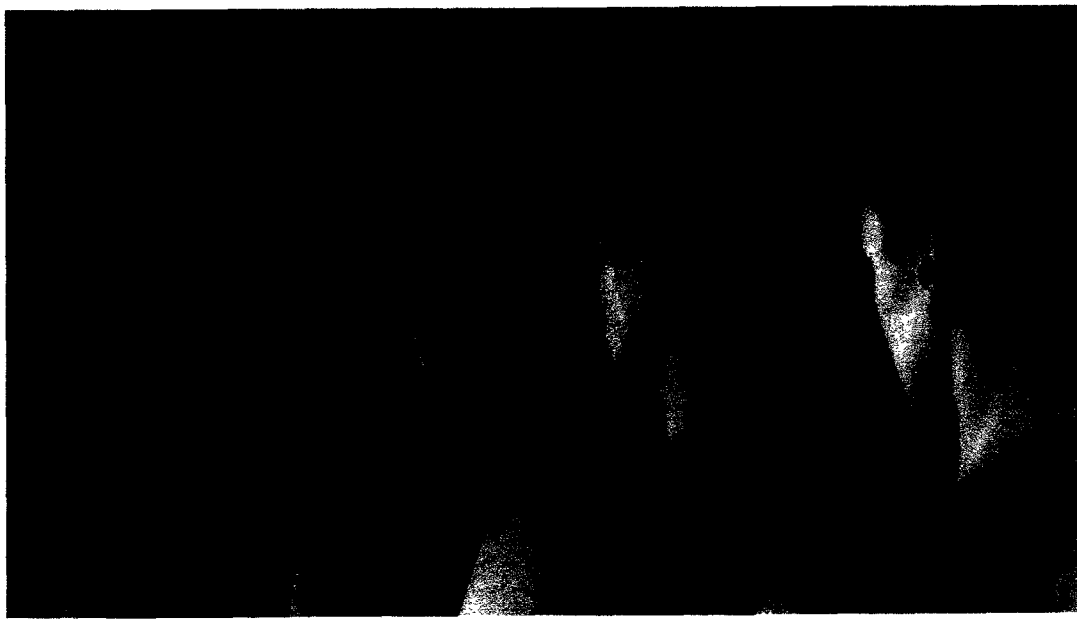
Dosisproportionalität

[redacted]

Demographische Einflüsse

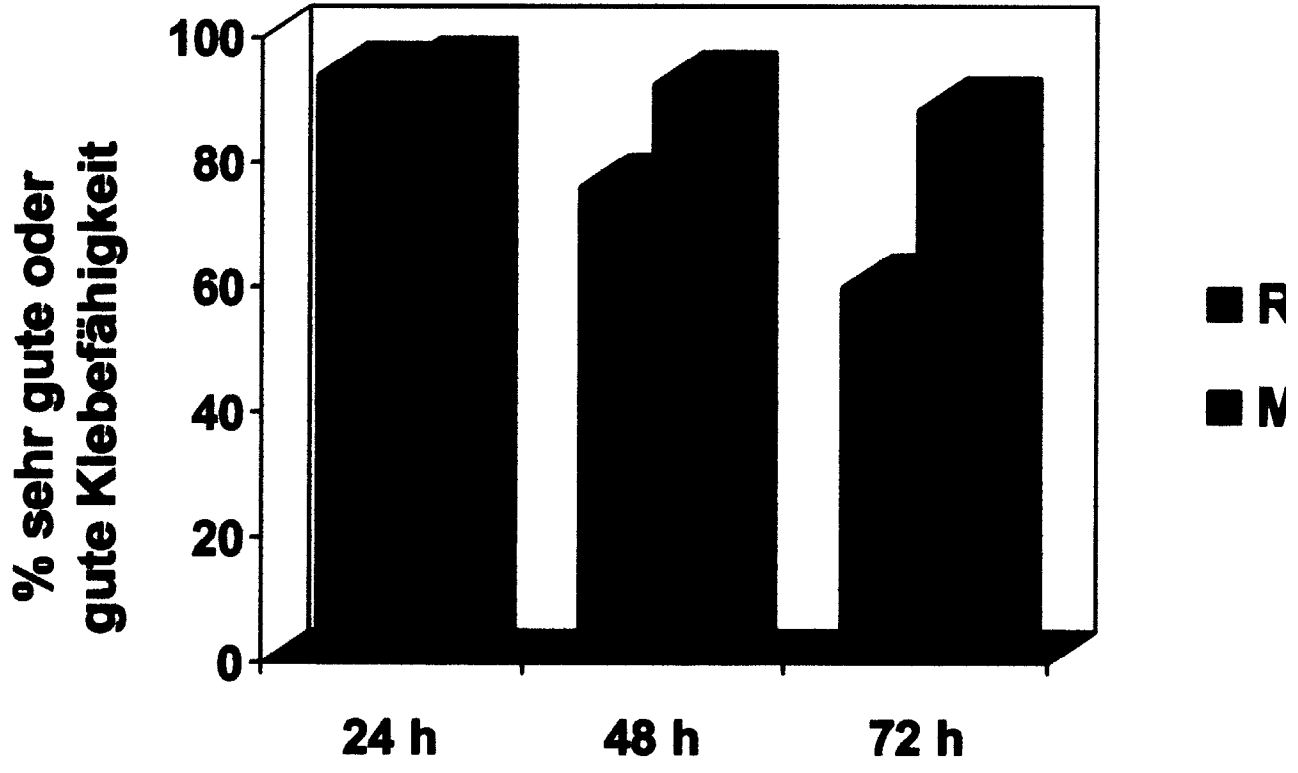
Pharmakokinetik

unabhängig vom Hauttyp



Durogesic SMAT

D-TRANS:
Ausgezeichnete Kle



Hautverträglichkeit

Studie Kontakt-Sensibilisierung (D-TRANS Placebo; n=201):

21 Tage Expositionsphase

14 Tage Ruhephase

48 Stunden Re-expositionsphase

➡ **Keine Kontakt-Sensibilisierung**

Hautverträglichkeit

Studie Phototoxizität (n=37):

- Zwei 2.4 µg/h D-TRANS Fentanyl Pflaster (1cm²
  TRANS Plazebos (1cm²) für 24 h auf dem Rück
- 2 beklebte (1x wirkstoffhaltig und 1x Plazebo) ar
  unbeklebte (Kontrolle) Hautstelle/n UV-A Licht a

➡ **Keine Phototoxizität**

Durogesic SMAT

Die Vorteile auf einen Blick:

- bewährte gute Wirksamkeit und Verträglichkeit
- ausgezeichnete Klebeeigenschaften
- hervorragende Hautverträglichkeit
- einfache Handhabung
- hoher Tragekomfort
- unempfindlich gegen Beschädigung

Noch sicherer Therapieerfolg durch Patientenzufriedenheit

Durogesic SMAT

ist das einzigartige 3-Tage-Schmerzpf

das die Verlässlichkeit von Durogesi

allen Vorteilen der fortschrittlichsten D

-Technologie verbindet.

DUROGESIC® SMAT

Translation Sheet

Page 4:

Elastic Matrix Structure
3 Layers
Transparent cover layer
Adhesive layer of poliacrylate with fentanyl
<0.1 mm! Thick
No carriers needed

Page 5:

Adhesive Properties
Goal:
Ensure the continuous controlled release of the active substance keeping the patch on the skin all the time
- The adhesive/glue guarantees the adherence to the skin and optimal absorption through it

Page 6:

Reservoir Patch vs. D-TRANS® Matrix

Features	Reservoir Patch	D-TRANS®
Patch Structure	Reservoir System with a gelatine substance contained and 5 coats	Matrix structure with 3 coats
Patch Size		
Adhesive	Silicon	Poliacrylate

Page 7:

Reservoir Patch vs. D-TRANS® Matrix

Features	Reservoir Patch	D-TRANS®
Active substance layer	Fentanyl suspended in water/Ethanol and Hydroxiethil-cellulose	Fentanyl dissolved directly in the adhesive
Control of the release rate	Through a membrane and the *stratum corneum*	Through a matrix monomere and the *stratum corneum*
Carrier	Ethanol	None
Protective layer	Smooth	One side of silicon the other is rough

Page 8:

Patch Properties "at first sight"
Small: 26-44% smaller than DUROGESIC
Thin: 80% thinner than DUROGESIC
Flexible: Elastic matrix structure
Transparent: Better adherence properties
Functional: Easy to handle (put on/take off)
Comfortable: More comfortable when using it

Page 9:

Structure Scheme

Active substance Upper part

Patch

Adhesive

That is how the active substance achieves the bloodstream

Skin

Bloodstream to the CNS

Upper transparent layer

Adhesive layer with fentanyl

Page 10:

Clinical-Pharmacological Studies

Page 11:

Bioequivalence
Multiple doses

Dose proportionality

Dermatological influences

Page 12:

Same release rate control
Bioequivalence

Page 13:

Bioequivalence Study
Patch Systems
Design of Studies: Randomised, crossover
Result (n=37): Bioequivalence

Page 14:

Bioequivalence in Steady State
Dose Multiple
4 Patches
time (h)

Page 15:

Dose Proportionality
The four sizes are proportional to the doses

Page 16:

Dermatological Influences
Pharmacokinetic
Not affected by the different types of skin

Page 17:

D-TRANS: Outstanding adhesive properties
% Adhesive Property

Page 18:

Skin Tolerance
Study of skin sensibility
21 days of Exposure Phase
14 Days of non-exposure
48 h of re-exposure phase
Without altering skin sensibility after contact with the patch

Page 19:

Skin Tolerance
Photo-toxicity study (n=37)
2 DTRANS Fentanyl patches and 2DTRANS Placebos around 24h on the back
2 skin areas with patch (one with fentanyl and the other with placebo) and 1 area without patch (control area) exposed to UVA light.
No photo-toxicity.

Page 20:

Advantages at first sight:

- Proven good efficacy and tolerance
- Outstanding Adhesive Properties
- Outstanding skin tolerance
- Easy to handle
- High comfort whilst using it
- Resistant

The success of the therapies is even more ensured due to the increased patients' satisfaction

Page 21:

Durogesic SMAT is the only 3 days analgesic patch that combines the safety of Durogesic® with all the advantages of the D-Trans Technology®.

DUROGESIC® SMAT

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