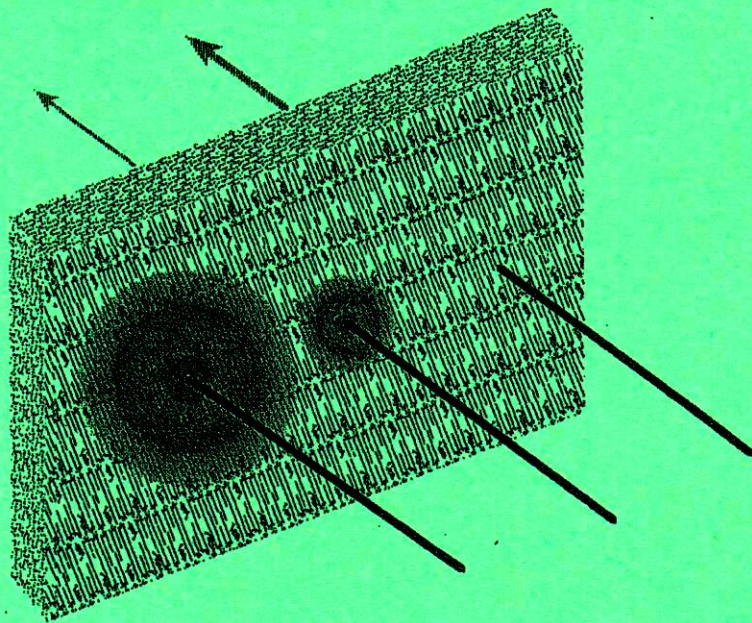


# Perspectives in Percutaneous Penetration

Volume 8a



Edited by K.R. Brain and K.A. Walters



# Abstracts of presentations at the Eighth International Perspectives in Percutaneous Penetration Conference held in Antibes-Juan-les-Pins April 2002

## Acknowledgements

The organisers are grateful to all of the organisations who have supported the Eighth Perspectives in Percutaneous Penetration Conference.

Acrux  
Alza Corporation  
An-eX  
Bioskin  
Clairol/Procter & Gamble  
Control Delivery Systems  
Covance  
Syngenta CTL

## Scientific Advisory Board

J. Bouwstra, Leiden, The Netherlands  
R. Bronaugh, Washington, USA  
C. Cullander, San Francisco, USA  
W. Dressler, Stamford, USA  
D. Esdaile, Sophia Antipolis, France  
K. Feld, Fort Washington, USA  
G. Flynn, Ann Arbor, USA  
J. Heylings, Alderley Park, UK  
N. Kitson, Vancouver, Canada  
H. Maibach, San Francisco, USA  
W. Meuling, Zeist, The Netherlands  
M. Ponec, Leiden, The Netherlands  
M. Roberts, Brisbane, Australia  
A. Watkinson, Galashiels, UK  
A. Williams, Bradford, UK

# TABLE OF CONTENTS

## INVITED CONTRIBUTIONS

<b>UPTAKE OF WATER IN THE STRATUM CORNEUM – THE CLEAR PICTURE</b>	1
JA BOUWSTRA, A DE GRAAFF, J NIJSSE and AC VAN AELST	
<b>METALLOPROTEINASES IN SKIN INFLAMMATION AND ANGIOGENESIS</b>	2
W HOLLERAN	
<b>ABSORPTION OF THALIDOMIDE AND ITS N-ALKYL ANALOGUES THROUGH HUMAN SKIN</b>	3
C GOOSEN, TJ LAING, J DU PLESSIS, TC GOOSEN and GL FLYNN	
<b>BIOTERRORISM AND THE SKIN</b>	4
RP CHILCOTT	
<b>TOPICAL IMMUNISATION-A REALITY</b>	5
HD PARTIDOS	
<b>SKIN BARRIER PROPERTIES FOLLOWING BURNS AND OTHER INJURIES</b>	6
GL FLYNN	
<b>CORNEODESMOSOMES AND XEROSIS</b>	7
G SERRE	
<b>ATTENUATED TOTAL REFLECTION-FTIR FOR SKIN BIOPHYSICAL INVESTIGATION</b>	8
L BRANCALEON	
<b>IN VIVO CONFOCAL RAMAN SPECTROSCOPY AND MOLECULAR CONCENTRATION PROFILES</b>	9
PJ CASPERS, GW LUCASSEN, HA BRUINING and GJ PUPPELS	
<b>PERMEATION OF PESTICIDES: THE USEFULNESS OF PROTECTIVE GLOVES</b>	10
JB NIELSEN	
<b>DOES DESQUAMATION REDUCE PERMEATION?</b>	11
MB REDDY and AL BUNGE	
<b>SYSTEMIC FATE OF CHEMICALS REMAINING IN THE SKIN</b>	12
RL BRONAUGH	
<b>DEFORMABLE LIPOSOMES?</b>	13
AC WILLIAMS	
<b>RECENT ADVANCES IN DERMAL DELIVERY WITH ETHOSOMES</b>	14
E TOUITOU	
<b>GENE DELIVERY TO SKIN</b>	15
JC BIRCHALL	

## SUBMITTED CONTRIBUTIONS

<b>THE EFFECT OF SLOW EQUILIBRATION ON TRANSDERMAL ABSORPTION</b>	19
YG ANISSIMOV and MS ROBERTS	
<b>THE USE OF BSA SOLUTION FOR RECEPTOR PHASE TO PREDICT TRANSDERMAL ABSORPTION PARAMETERS FOR HIGHLY LIPOPHILIC DRUGS</b>	20
SE CROSS, YG ANISSIMOV and MS ROBERTS	
<b>USE OF ETHANOL IN RECEPTOR PHASE - A LUCKY ESCAPE?</b>	21
M SAUNDERS and W J PUGH	
<b>MODELLING OF OESTRADIOL:PROGESTOGEN INTERACTIONS</b>	22
M SAUNDERS, W J PUGH and J HADGRAFT	
<b>EFFECT OF SOLVENT PRE-TREATMENT ON EPIDERMAL FLUX</b>	23
WJ PUGH, C ROSADO, SE CROSS, MS ROBERTS and J HADGRAFT	
<b>QUANTITATIVE STRUCTURE-PERMEABILITY RELATIONSHIPS FOR PERCUTANEOUS ABSORPTION: RE-ANALYSIS OF STEROID DATA</b>	24
GP MOSS and MTD CRONIN	
<b>OPEN VERSUS CLOSED FOLLICLES</b>	25
H SCHAEFER, J LADEMANN, N OTBERG, H RICHTER and W STERRY	
<b>DELIVERY TO SEBACEOUS GLAND: IN-VIVO STUDY AND THEORETICAL MODELLING</b>	26
S MUKHERJEE, C SELLITTI, M CHAN, H KNAGGS and D THIBOUTOT	

TRANSDERMAL DELIVERY OF ANTIOXIDANTS FROM DIFFERENT COSMETIC FORMULATIONS	89
S RICHERT, A SCHRADER and K SCHRADER	
INFLUENCE OF POLYMER STABILIZED/COSTABILIZED O/W EMULSIONS VISCOSITY ON DEXPANTHENOL RELEASE PROFILE AND ITS SHORT-TERM HYDRATION EFFECTS	90
S SAVIC, J MILJC and G VULETA	
IN VITRO PERCUTANEOUS ABSORPTION : INFLUENCE OF GALENIC AND MOLECULAR PARTITIONING	91
F OUVRARD-BARATON, B LE VARLET, L HENRY, F BROSSARD, B NOE, V ALARD and P COURTELLEMONT	
<b>PERCUTANEOUS ABSORPTION OF UV FILTERS VEHICULISED IN LIPOSOMES</b>	<b>92</b>
<b>E RAMON, L CODERCH, A DE LA MAZA, M DE PERA, O LOPEZ and JL PARRA</b>	
SIMULTANEOUS PENETRATION OF NSAID AND ESSENTIAL FATTY ACID ESTERS AS A DUAL-ACTION ANTI-ARTHRITIS THERAPY	93
CM HEARD, J HARWOOD, P MAGUIRE, G MCNAUGHTON and WJ PUGH	
DERMAL DELIVERY OF A NEW CLASS OF POTENT AND SELECTIVE INHIBITORS OF VARICELLA ZOSTER VIRUS	94
CA JARVIS, C McGUIGAN and CM HEARD	
TRANSDERMAL DELIVERY OF EXTRACT OF HYPERICUM PERFORATUM	95
C SEARS, CM HEARD and A MORRIS	
VIADERM™ A NOVEL MICROELECTRONIC SYSTEM ENHANCES SKIN PERMEABILITY OF DRUGS: IN VITRO AND IN VIVO PERCUTANEOUS PENETRATION OF DICLOFENAC AND GRANISETRON IN PIG AND RAT SKIN	96
G LEVIN, D DANIEL, T HANNAN, ZEEV SOHN, I KRYMBERK and AC SINTOV	
INVESTIGATION OF A MICROFABRICATED DELIVERY SYSTEM TO DELIVER NON-VIRAL GENE VECTORS THROUGH HUMAN SKIN	97
F CHABRI, K BOURIS, CJ ALLENDER, JC BIRCHALL, DA BARROW and KR BRAIN	
MOLECULARLY IMPRINTED POLYMER MEMBRANES FOR TRANSCUTANEOUS MONITORING DEVICES	98
A HILLBERG, CJ ALLENDER and KR BRAIN	
FLUX OF NICKEL SALTS vs NICKEL SOAP ACROSS HUMAN SKIN	99
JJ HOSTYNEK and W REIFENRATH	
IN VITRO PERCUTANEOUS ABSORPTION OF DIETHANOLAMINE (DEA) IN HUMAN SKIN	100
MEK KRAELING, CT JUNG, JJ YOURICK and RL BRONAUGH	
PENETRATION AND DISTRIBUTION OF DIETHANOLAMINE THROUGH HUMAN SKIN IN VITRO AFTER APPLICATION FROM COSMETIC VEHICLES UNDER IN-USE CONDITIONS	101
KR BRAIN, S BRAIN, DM GREEN, KA WALTERS, AC WATKINSON, S ALCASEY, K BLACKBURN, W BROCK, J BURDICK, D DAVIS, W DRESSLER, A DRIEDGER, W FUNG, S GETTINGS, S MANN, T RE and M RIOS-BLANCO	
IN VITRO PERCUTANEOUS ABSORPTION OF VENT VAPORS	102
IP DICK, E ROBINSON, B RAWSON and P GRIFFIN	
PERCUTANEOUS ABSORPTION OF TRICHLOROETHYLENE IN VOLUNTEERS	103
S KEZIC, C vd SCHOOR and J KRUSE	
PERCUTANEOUS ABSORPTION OF MEXORYL SX® IN HUMAN VOLUNTEERS: COMPARISON WITH IN VITRO DATA	104
F BENECH-KIEFFER, WJA MEULING, C LECLERC, L ROZA, J LECLAIRE and G NOHYNEK	
PERCUTANEOUS PENETRATION OF [ <sup>14</sup> C]-CAFFEINE IN HUMAN VOLUNTEERS: A MASS BALANCE APPROACH	105
WJA MEULING, JJM VAN DE SANDT and L ROZA	
SAFETY (DERMAL ABSORPTION) TESTING OF SUNSCREENS IN HUMAN VOLUNTEERS: A TIERED APPROACH	106
WJA MEULING and L ROZA	
PERCUTANEOUS PENETRATION OF POLYCYCLIC AROMATIC HYDROCARBONS (PAHs) FOLLOWING EXPOSURE TO DIESEL ENGINE EMISSIONS AT PETROL STATIONS	107
S KLEEFELD, E ELAHI, M BYRNE and P CLARK	
PENETRATION OF RADIONUCLIDES ACROSS THE SKIN. REDUCTION OF TRANSDERMAL CONTAMINATION	108
V KOPRDA, M HARANGOZO, Z KASSAI and P BENDOVA	
IN VITRO SKIN ABSORPTION AND DISTRIBUTION OF THE NERVE AGENT VX USING DOMESTIC WHITE PIG SKIN	109
RP CHILCOTT, CH DALTON, I HILL, CM DAVIDSON, KL BLOHM, ED CLARKSON and MG HAMILTON	

## PERCUTANEOUS ABSORPTION OF UV FILTERS VEHICULISED IN LIPOSOMES

E RAMÓN, L CODERCH, A DE LA MAZA, M DE PERA, O LÓPEZ and JL PARRA  
Instituto de Investigaciones Químicas y Ambientales de Barcelona (IIQAB), CSIC,  
Jorge Girona, 18-26, 08034 Barcelona, Spain

Following a standardised in vitro protocol to study dermal absorption and percutaneous penetration using pig skin<sup>1</sup>, the influence of several liposomic vesicles including UV filters has been investigated.

Two different sun filters have been considered: Ethylhexyl methoxycinnamate (lipophilic) and benzophenone-4 (hydrophilic). Multilamellar liposomes were formed either with unsaturated phosphatidylcholine (PC), saturated phosphatidylcholine (H-PC)<sup>2</sup> or a mixture of lipids isolated from wool fibres mimicking the lipid structure of the stratum corneum<sup>3</sup>. The two sun filters were adequately incorporated in the formation process of these different vesicles.

In each percutaneous absorption assay, six samples of dermatomed pig skin (thickness of  $700 \pm 50 \mu\text{m}$ ) were used. After 20 hr exposure time in Franz static diffusion cells, the excess remaining on the skin surface was recovered by an specific washing procedure. Afterwards, 10 strippings (D-Squame) were carried out on the skin surface by applying constant pressure (80 g/cm) for 5 sec. Epidermis was separated from dermis by heat treatment. The amounts of sun filters recovered in the SC (strips), epidermis, dermis, receptor fluid and washing solutions were determined by HPLC.

Depending on the fluidity of the liposomes<sup>2,4</sup>, the sun filters yielded different distribution profiles in the SC, epidermis and dermis as compared with the profiles obtained for the same sun filters incorporated in a conventional oil/water emulsion.

1. M Torres Fernandez, H-J Duesing, JL Parra and W Diembeck (1998) In vitro absorption and penetration of UV filters on fresh excised pig skin, *PPP Proc.*, Vol 6A, p 93
2. L Coderch, J Fonollosa, M de Pera, J Estelrich, A de la Maza and JL Parra (2000) Influence of cholesterol on liposome fluidity by EPR. Relationship with percutaneous absorption, *J.Control. Rel.*, 68, 85-95
3. M de Pera, L Coderch, J Fonollosa, A de la Maza, and JL Parra (2000) Effect of Internal Wool Lipid Liposomes on Skin Repair, *Skin Pharmacol.Appl.Skin Physiol.*, 13,188-195
4. N Perez-Cullell, L Coderch, A de la Maza, JL Parra and J Estelrich (2000) Influence of the fluidity of liposome compositions on percutaneous absorption, *Drug Delivery*, 7, 7-13

## INDEX

- 4-cyanophenol, 42  
 6-aminohexanoic acid 2-octylester, 69  
 Aciclovir, 29  
 Ahmed, 30, 31  
 Alache, 39  
 Akram, 123  
 Alard, 90  
 Alc Casey, 100  
 Alkanolamine, 99  
 Allender, 96, 97  
 Allergenic, 117  
 Alprazolam, 33  
 Amethocaine, 85  
 Ametop, 85  
 Andrian, 44  
 Angiogenesis, 2  
 Anissimov, 22, 19  
 Anthrax, 4  
 Antiperspirant, 110  
 Antiviral, 93  
 Antoniou, 48  
 Apomorphine, 52  
 Arbey, 34  
 ATR-FTIR, 8, 68  
 Audring, 48  
 Azo dyes, 113  
 Azone, 32, 70, 75, 76, 85  
 Bacitracin, 14  
 Baillet, 68  
 Baktir, 87  
 Baltenneck, 43  
 Barel, 51  
 Barrier, 6, 36, 117  
 Barrow, 96  
 Barry, 30, 31, 53  
 Basic red 76, 113  
 Basic yellow 57, 113  
 Basketter, 117  
 Bayer, 79  
 Beck, 124  
 Becket, 122  
 Behenic acid, 36, 54  
 Belyaev, 54  
 Bendova, 107  
 Benech-Kieffer, 43, 44, 103, 124  
 Ben-Zion, 64  
 Benzoate, 32  
 Benzodiazepines, 33  
 Benzoic acid, 125  
 Benzophenone-4, 91  
 Beyssac, 39  
 Bioavailability, 44  
 Bioequivalence, 61, 62  
 Biophysical, 8  
 Biopsy, 63  
 Bioterrorism, 4  
 Birchall, 15, 96  
 Blackburn, 100  
 Blohm, 108, 109  
 Boix-Montañes, 33  
 Bondía, 35  
 Bonner, 53  
 Bouris, 96  
 Bouwstra, 1, 50, 52, 57, 78  
 Brain, 27, 28, 29, 75, 96, 97, 100, 111  
 Brancaleon, 8  
 Brand, 26  
 Brock, 100  
 Bronaugh, 12, 99  
 Brossard, 90  
 Brown, 113, 114, 115, 116  
 Bruining, 9  
 BSA, 19, 112, 121, 125  
 Bunge, 11, 42  
 Bupivacaine, 32  
 Burdick, 100  
 Burns, 6  
 Butorphanol, 70  
 Butylparaben, 49, 85, 86  
 Byrne, 106  
 Caffeine, 43, 44, 56, 79, 90, 97, 104, 125  
 Cage, 125  
 Calpena, 85, 86  
 Cannabidiol, 14  
 Carmichael, 125  
 Carvacrol, 122  
 Caspers, 9  
 Castiel-Higounenc, 34  
 Catechol, 12  
 Ceramides, 32, 34, 35, 36, 54, 55, 59, 68, 71  
 Cetrimide, 27  
 Cevc, 83  
 Chabri, 96  
 Chan, 25  
 Chilcott, 4, 108, 109  
 Cholesterol, 32, 35, 36, 54, 55, 58, 59, 68, 84, 91  
 Chopart, 34  
 Chromameter, 61  
 Chu, 123  
 Cioni, 120  
 Ciurlizza, 86  
 Clark, 106  
 Clarkson, 108, 109  
 Clarys, 51  
 Clobetasol, 46, 61  
 Cocera, 60  
 Coderch, 35, 60, 91  
 COLIPA, 124  
 Colom, 37  
 Confocal, 9, 14, 43, 57  
 Corish, 81  
 Corneocytes, 1, 7, 8, 22, 46, 60  
 Corneodesmosomes, 7  
 Corticosteroid, 61, 84  
 Cosmetic, 24, 35, 36, 43, 44, 46, 48, 50, 57, 75, 78, 79, 88, 90, 99, 100, 105, 124  
 Courtellemont, 90, 124  
 Cox, 87, 92  
 Cronin, 23

Cross, 19, 22  
 Cruz, 83, 84  
 Cryopreserved, 120  
 Dalton, 108, 109  
 Danhof, 52  
 Daniel, 95  
 Daty, 43  
 Davidson, 108, 109  
 Davis, 30, 31, 100  
 De Graaff, 1, 78  
**De la Maza, 35, 60, 91**  
 De Paepe, 36  
 De Pera, 35, 91  
 DEA, 99, 100  
 Deformable liosomes, 13  
 Dellarco, 41  
 Demaret, 37  
 Desquamation, 11  
 Detergents, 10  
 Dettmar, 111  
 Dexpanthenol, 89  
 Dextran, 32  
 Diazepam, 22, 33  
 Dick, 101, 125  
 Diclofenac, 37, 81, 95  
 Diembeck, 124  
 Diethanolamine, 12, 99, 100  
 Diethylenetriaminepenta-acetic acid, 115, 116  
 Diez-Martin, 33  
 Diffunisal, 22  
 Disperse blue 1, 12  
 Dithranol, 84  
 DMSO, 9  
 DNA, 15  
 Doblhofer, 83  
 Dolezal, 69, 70, 71  
 Domenech, 33, 37, 85, 86  
 Domenech-Berrozpe, 33  
 Doucet, 79  
 Dreher, 44  
 Dressler, 100  
 Driedger, 100  
 DSC, 21, 32, 59, 68, 71  
 Du Plessis, 3  
 Dupuis, 124  
 Duragesic, 77  
 Duran-Hortola, 33  
 Earl, 112  
 Elahi, 106  
 Electrical resistance, 45, 56  
 Electroporation, 54  
 Embil, 87  
 Enantiomers, 69  
 Enhancers, 10, 36, 69, 70, 71, 75, 76, 77, 81, 85, 86  
 Epiderm, 44  
 Eoiskin, 44  
 Equilibration, 22  
 Escribano, 85, 86  
 Essa, 53  
 Esterases, 28, 29  
 Estradiol, 13, 53  
 Ethosomes, 14  
 Eudragit, 31  
 Exposure, 41, 45, 66, 79, 106, 119  
 Fasano, 45  
 Fatouros, 50  
 Fentanyl, 76, 77  
 Fentem, 113  
 Fenvalerate, 119  
 Ferraro, 119  
 Figueiredo, 62  
 Fimiani, 120  
 Finnin, 76, 77  
 FITC, 14  
 Fitzpatrick, 81  
 Flynn, 3, 6  
 Follicles, 13, 24, 25, 53, 57, 107, 112, 122  
 Fonollosa, 35  
 Fouchard, 43, 44, 79  
 Fragrance, 46, 75  
 Frank, 47  
 Freeze-fracture, 60, 90  
 Freixa, 33  
 FTIR, 8, 32, 59, 67, 68  
 Fung, 100  
 Furusawa, 65  
 Fuzzy logic, 26  
 Gaetani, 34  
 Gallagher, 74  
 Garcia, 79  
 Garcia, 37  
 Garson, 43  
 Geh, 125  
 Gene delivery, 15  
 Genes, 15, 92  
 Gettings, 100  
 Gloves, 10, 119  
 Glycerolized, 120  
 Goddard, 111  
 Goosen, 3  
 Grams, 57  
 Granisetron, 95  
 Greaves, 56  
 Green, 100, 111  
 Griffin, 101  
 Groenink, 78  
 Guey, 34  
 Haas, 47  
 Hachem, 36  
 Hadgraft, 21, 22  
 Hadjur, 43  
 Haigh, 38, 39, 40, 61  
 Haloperidol, 27  
 Hamilton, 108, 109  
 Handwash, 111  
 Hannan, 95  
 Harangozo, 107  
 Harwood, 92  
 Hasegawa, 65  
 Hassler, 66  
 Hatanaka, 49  
 Heard, 27, 28, 29, 74, 75, 92, 93, 94, 111  
 Henry, 90

- Hexylnicotinate, 51  
 Hill, 108, 109  
 Hillberg, 97  
 Holleran, 2  
 Honeywell-Nguyen, 78  
 Hostynek, 98  
 Houben, 36  
 Hrabálek, 69, 70, 71  
 Huebner, 59, 71  
 Human skin model, 65  
 Humberstone, 77  
 Hyde, 113, 114, 116  
 Hydration, 1, 8, 9, 13, 37, 44, 51, 53, 64, 89  
 Hydrocortisone, 32, 75  
 Hypericum, 94  
 Ibuprofen, 30, 31, 38, 39, 40, 86, 92  
 Imanidis, 62  
 Immunisation, 5  
 Indenbom, 54  
 Inflammation, 2  
 Infrared, 67, 79  
 Insulin, 13, 55, 82  
 Integrity, 10, 21, 35, 45, 56, 85, 86, 90, 96, 120  
 In-use conditions, 100, 111  
 Iontophoresis, 29, 50, 51, 52, 53, 55, 81, 97  
 Iontophoretic, 15, 50, 51, 52, 53, 55, 81  
 Ishibashi, 65  
 Ivermectin, 47  
 Jain, 72  
 Janicki, 32  
 Jarvis, 93  
 Jasmonates, 75  
 Jones, 26  
 Jung, 99  
 Junginger, 78  
 Kara, 87  
 Kassai, 107  
 Katzung, 47  
 Kawasaki, 49  
 Kawashima, 49  
 Kenyon, 125  
 Ketoprofen, 74  
 Ketorolac, 37  
 Kezic, 102  
 Kleefeld, 106  
 Klose, 77  
 Knaggs, 25  
 Koprda, 107  
 Korinth, 125  
 Kraeling, 99  
 Kruse, 102  
 Krymberk, 95  
 Kunz, 115  
 Kurosaki, 49  
 Lademann, 24, 46, 47, 48  
 Laing, 3  
 Lambrecht, 51  
 Larese, 125  
 Latex, 10, 30, 31, 117  
 Lau, 32  
 Laugel, 68  
 Lauroba, 37  
 Le Varlet, 90  
 Leave-on, 75, 99, 100  
 Leclaire, 43, 44, 103  
 Leclerc, 43, 103  
 Lee, 80, 110, 112, 118  
 Levin, 95  
 Ley, 42  
 Li, 52, 67  
 Lignoceric acid, 36  
 Limasset, 125  
 Lindemann, 46, 47, 48  
 Lipo-microdialysis, 49  
 Liposomes, 13, 35, 36, 53, 58, 72, 84, 91, 96  
 Löffler, 66  
 Logic, 26  
 Long, 80, 110  
 Loperamide, 73  
 Lopez, 60, 91  
 Lopez-iglesias, 60  
 Lorazepam, 33  
 Lovell, 124  
 Lpd, 96  
 Lse-high, 65  
 Lucassen, 9  
 Maas, 125  
 Madry, 43  
 Maeda, 49  
 Maeder, 62  
 Maguire, 92  
 Mann, 100  
 Manning, 45  
 Mannitol, 122  
 Martindale, 110  
 Martins, 83, 84  
 Mass spectrometry, 58  
 McGuigan, 93  
 McNaughton, 29, 92  
 MDTs, 77  
 Menthol, 122  
 Merly, 73  
 Metalloproteinases, 2  
 Methiocarb, 10  
 Methyl ethyl ketone, 101  
 Methyl paraben, 42  
 Methyleugenol, 12  
 Methylnicotinate, 51  
 Meuling, 103, 104, 105  
 Mexoryl<sup>®</sup> sx, 103  
 Meykadeh, 46  
 Microchannels<sup>™</sup>, 95  
 Microelectronic, 95  
 Microemulsion, 85, 86  
 Microfabrication, 15, 96  
 Microneedles, 15, 96, 97  
 Microscopy, 14, 24, 40, 43, 48, 57, 72, 122  
 Microspectrometer, 9  
 Milic, 89  
 Minter, 112, 113, 114, 116, 118  
 Mio, 67  
 Mirza, 73  
 Mitchem, 67  
 Mitin, 54



- Model, 11, 14, 15, 20, 23, 25, 26, 30, 31, 32, 33, 42, 49, 53, 54, 65, 67, 68, 69, 71, 72, 73, 83, 88, 90, 94, 104, 107, 108, 110, 114, 118, 122  
 Modelling, 22, 18, 21, 25  
 Montinaro, 119  
 Montomoli, 119, 120, 125  
 Moody, 123  
 Moore, 111  
 Morris, 27, 94  
 Moss, 23, 80, 110  
 Mukherjee, 25  
 Musk xylol, 12  
 Mustard gas, 4  
 Mycotoxins, 4  
 Naproxen, 28  
 Neubert, 58, 59, 71  
 Neumannova, 71  
 Nicholls, 116  
 Nickel, 98, 114, 116  
 Nicotines, 51  
 Nicotine, 67  
 Nielsen, 125  
 Nijse, 1  
 Nimesulide, 87  
 Nitroglycerin, 67  
 Noe, 90  
 Nohynek, 103  
 Nonylphenoethoxylate, 10  
 NSaid, 87, 92  
 Nussinovitch, 64  
 Obach, 85  
 Occlusion, 9, 13, 52, 63, 80, 125  
 Occupational health, 66  
 Octyl salicylate, 76  
 OECD, 88, 124  
 Oestradiol, 20, 21  
 Okahata, 65  
 Oliveira, 84  
 Orcet, 79  
 Otberg, 24  
 Ouvrard-Baraton, 90  
 Paclobutrazol, 10  
 Padimate O, 76  
 PAHs, 106  
 Pannier, 26  
 Parra, 35, 60, 91  
 Patouillet, 44  
 Payan, 125  
 Paye, 124  
 PCMX, 111  
 Pele, 43  
 Pendlington, 80, 113, 114, 115, 116, 118  
 Peptides, 5, 55, 83  
 Peraire, 33, 37  
 Peraire-Guitart, 33  
 Pesticides, 10  
 pH, 19, 22, 27, 32, 33, 37, 38, 39, 40, 50, 53, 57, 70, 85, 87, 89, 99, 112, 114, 115, 116, 125  
 Pharmacokinetics, 49, 77, 102  
 Phenol, 21, 22  
 Photoacoustic spectroscopy (, 67  
 Pianigiani, 120  
 Pig skin, 27, 83, 91, 92, 108, 122, 124  
 Pinazepam, 33  
 Pirmicarb, 10  
 Plätzer, 58  
 Polar pathways, 55  
 Polydimethylsiloxane, 20, 42  
 Polypeptide, 14, 82  
 Polyvinylpyrrolidone, 30  
 Pressure-sensitive adhesive, 64  
 Pretreatment, 22, 32, 51, 52, 55, 95  
 Prodrugs, 27, 28, 29  
 Progesterone, 39, 40  
 Progestogen, 21  
 Propranolol, 122  
 Propylene glycol, 29, 31, 70, 73  
 Protective gloves, 10  
 Pugh, 20, 21, 22, 92, 111  
 Puppels, 9  
 Purdon, 38, 39, 40  
 Pyrethroids, 119  
 QSPRS, 23  
 Qureshi, 123  
 Rades, 122  
 Radioluminography, 66  
 Radionuclides, 107  
 Raman, 9  
 Ramón, 91  
 Rastogi, 55  
 Raudenkolb, 59  
 Rawlings, 80  
 Rawson, 101  
 Re, 100  
 Receptor phase, 19, 20  
 Reconstructed human skin models, 44  
 Reddy, 11  
 Reed, 76  
 Reifenrath, 98  
 Reservoir, 12, 46, 112, 113, 118, 121  
 Retinoids, 2  
 Retinol, 12  
 Rettig, 71  
 Richert, 88  
 Richter, 24  
 Rinse-off, 100  
 Rios-blanco, 100  
 Roberts, 22, 19  
 Robinson, 101, 125  
 Rodrigues, 63  
 Rogiers, 36  
 Roguet, 44  
 Rosado, 22, 63  
 Rosales, 86  
 Roseeuw, 36  
 Roza, 103, 104, 105  
 Sanders, 113, 114, 115, 116  
 Sano, 49  
 Sarin, 4  
 Sartorelli, 119, 120, 125  
 Saunders, 20, 21  
 Savic, 89

- SCCNFP, 124  
 Schaefer, 24, 46, 47, 48  
 Schaller, 125  
 Schmidt, 34  
 Schrader, 88  
 Sears, 94  
 Sebaceous gland, 25  
 Sebum, 8, 24, 25, 47  
 Sellitti, 25  
 Senorkyan, 87  
 Serre, 7  
 Shunt route, 13, 53  
 Simões, 83, 84  
 Simonnet, 44  
 Singh, 55  
 Sintov, 95  
 Sisinni, 119, 120  
 Smith, 38, 39, 40, 61, 62  
 Smith Pease, 112, 113, 114, 115, 116, 117, 118  
 Snake skin, 40  
 Snook, 67  
 Snow, 114, 115, 116  
 Sodium lauryl sulphate, 10, 32  
 Soil, 41  
 Solvents, 12, 32, 55, 56, 63, 80, 101  
 Songkro, 122  
 Spengler, 124  
 St John's Wort, 94  
 Stelling, 124  
 Stepina, 54  
 Stereoselective, 69  
 Steroid, 23  
 Steroids, 20, 23  
 Sterry, 24, 46, 47, 48  
 Stoddart, 28  
 Stolyhwo, 32  
 Stratum corneum, 1, 4, 6, 7, 8, 9, 11, 13, 15, 19, 28, 29, 32, 34, 35, 40, 43, 44, 46, 47, 48, 49, 52, 53, 54, 57, 58, 59, 60, 62, 63, 66, 68, 69, 71, 75, 76, 78, 79, 80, 81, 83, 90, 93, 95, 96, 97, 98, 103, 107, 111, 112, 114, 115, 116, 117, 121, 122  
 Structure-permeability relationships, 23  
 Sugibayashi, 65  
 Sunscreens, 24, 46, 62, 75, 76, 103, 105  
 Surber, 61, 62  
 Svozil, 70  
 Sweat, 24, 42, 47, 53  
 Sznitowska, 32  
 Tack test, 64  
 Takahashi, 65  
 Tape stripping, 24, 28, 29, 46, 47, 48, 62, 78, 93, 98, 100, 111, 114, 115, 123  
 Tassopoulos, 62  
 Taylor, 80, 110  
 Tea, 99  
 Teichmann, 46  
 Testosterone, 32, 112, 121, 125  
 TEWL, 6, 35, 36, 37, 52, 85, 86  
 Thalidomide, 3  
 Theophylline, 69, 97  
 Thiboutot, 25  
 Timolol, 50  
 Topical immunisation, 5  
 Torres, 85  
 Toutou, 14  
 Transfersomes, 72, 83  
 Transkarbam 12, 70, 71  
 Traversa, 76  
 Trichloroethylene, 101, 102  
 Triclosan, 111, 121  
 Trommer, 58  
 Trotter, 73, 74  
 Tsikrikas, 48  
 Tubek, 80  
 Ultradeformable, 72  
 UV, 6, 33, 37, 46, 58, 70, 85, 86, 91, 96, 103, 105  
 Validation, 20, 121  
 Van Aelst, 1  
 Van Burgsteden, 125  
 Van de Sandt, 104, 125  
 Van der Spek, 52  
 Van der Steeg, 52  
 Vasoconstriction, 61  
 Vávrová, 69  
 Vd Schoor, 102  
 Verdier, 43  
 Vesicles, 13, 58, 72, 78, 84, 91  
 Viaderm™, 95  
 Von Pelchrzim, 46  
 Vuleta, 89  
 VX, 4, 108, 109  
 VZV, 93  
 Walters, 100  
 Wartewig, 59, 71  
 Watanabe, 65  
 Water, 1, 41  
 Watkinson, 100  
 Weigmann, 46, 48  
 White, 117  
 Whitehead, 57, 80  
 Wilkins, 75  
 Wilkinson, 56, 125  
 Williams, 13, 30, 31, 32, 56, 110, 112, 118, 121, 125  
 Winckle, 111  
 Wolf, 58  
 Xenobiotic, 62, 66, 98  
 Xerosis, 7  
 Xylene, 101  
 Yasunaga, 49  
 Yourick, 99  
 Zastrow, 79  
 Zeev Sohn, 95  
 $\alpha$ -tocopherol, 44