Contents

Foreword xv
Preface xvii
Acknowledgements xix
List of contributors xxi

PART I Introduction 1

1 Cutaneous anatomy and function 3
   Robert P. Chilcott
   1.1 Introduction and scope 3
   1.2 Surface features 3
   1.3 Functional histology of the epidermis and associated structures 8
   1.4 Species differences 13
   Summary 15
   References 15

2 Biochemistry of the skin 17
   Simon C. Wilkinson
   2.1 Introduction and scope 17
   2.2 Protein synthesis and organisation during epidermal differentiation 18
   2.3 Lipid synthesis and organisation during epidermal differentiation 19
   2.4 Lipid classes in the stratum corneum 20
   2.5 Stratum corneum turnover 23
   2.6 Biotransformations in skin 24
   Summary 42
   References 42
3 Skin photobiology 51

Mark A. Birch-Machin and Simon C. Wilkinson

3.1 Introduction and scope 51
3.2 Photoprotection and melanogenesis 51
3.3 Increased environmental ultraviolet radiation exposure and its link with photoageing and skin cancer 55
3.4 Mitochondrial DNA as a biomarker of sun exposure in human skin 60
3.5 Apoptosis 61
3.6 Sun protection 63
Summary 65
References 65

PART II Skin Absorption 69

4 Skin as a route of entry 71

Simon C. Wilkinson

4.1 Salient anatomical features of the stratum corneum – the ‘brick and mortar model’ 71
4.2 Species and regional variation in skin structure 72
4.3 Species and regional variation in skin permeability 74
4.4 Intra- and inter-individual variation in percutaneous absorption 75
4.5 Effect of age on skin barrier function 76
4.6 Role of skin appendages 77
4.7 The in vitro skin sandwich model 78
4.8 Penetration of particles through appendages 79
Summary 80
References 80

5 Physicochemical Factors Affecting Skin Absorption 83

Keith R. Brain and Robert P. Chilcott

5.1 Introduction 83
5.2 Physicochemical properties 84
5.3 Exposure considerations 89
Summary 91
References 91

6 Principles of Diffusion and Thermodynamics 93

W. John Pugh and Robert P. Chilcott
CONTENTS

6.1 Introduction and scope 93
6.2 Some definitions pertaining to skin absorption kinetics 94
6.3 Basic concepts of diffusion 97
6.4 Fick's Laws of diffusion 97
6.5 Thermodynamic activity 98
6.6 Skin absorption of a substance from two different vehicles 99
6.7 Partitioning 101
6.8 Diffusivity 102
6.9 Skin absorption data and risk assessments 105

Summary 106
References 106

7 In vivo measurements of skin absorption 109
James C. Wakefield and Robert P. Chilcott

7.1 Introduction and scope 109
7.2 Why conduct in vivo studies? 110
7.3 Ethics and legislation 110
7.4 Standard methodology: OECD Guideline 427 115
7.5 Alternative in vivo methods 119

Summary 126
References 126

8 In vitro percutaneous absorption measurements 129
Ruth U. Pendlington

8.1 Introduction and scope 129
8.2 Regulatory guidelines 129
8.3 Why assess percutaneous absorption in vitro? 130
8.4 Basic principle of in vitro percutaneous absorption measurements 131
8.5 Choice of diffusion cell 131
8.6 Skin membrane considerations 136
8.7 Integrity measurements 137
8.8 Choice of receptor fluid and sampling considerations 138
8.9 Test material considerations 139
8.10 Application of test preparation to the skin 140
8.11 Examples of results from in vitro skin absorption studies 142
8.12 What is considered to be absorbed? 146
8.13 Micro-autoradiography 147

Summary 147
References 147
PART III Toxicological Assessment

9 Skin immunology and sensitisation

David A. Basketter

9.1 Introduction
9.2 Definitions
9.3 Skin sensitisation
9.4 Identification of skin sensitisers
9.5 Risk assessment
9.6 Other types of allergic skin reaction
9.7 Future prospects

Summary
References

10 In vitro phototoxicity assays

Penny Jones

10.1 Introduction and scope
10.2 In vitro strategies for phototoxicity testing
10.3 The UV/visible absorption spectrum as a pre-screen for phototoxicity
10.4 In vitro assays for phototoxicity using monolayer cultures
10.5 In vitro assays for photoallergenicity
10.6 In vitro assays for phototoxicity using human 3-D skin models

Summary
References

11 In vitro alternatives for irritation and corrosion assessment

Penny Jones

11.1 Introduction and scope
11.2 Acute dermal irritation/corrosion
11.3 Validation/regulatory status of in vitro assays for skin corrosion
11.4 In vitro tests for skin corrosion
11.5 Validation/regulatory status of in vitro assays for skin irritation
11.6 In vitro tests for skin irritation

Summary
References

12 Instruments for measuring skin toxicity

Helen Taylor

12.1 Introduction and scope
PART IV Clinical Aspects

13 Introduction to dermatology

Manjunatha Kalavala and Alex Anstey

13.1 Introduction and scope 223
13.2 Clinical assessment of patient with skin disease 224
13.3 Cutaneous manifestations of disease following exposure to chemicals and pharmaceutical formulations 234
13.4 Overview of standard treatments 241
Summary 243

14 Clinical aspects of phototoxicity

Anthony D. Pearse and Alex Anstey

14.1 Introduction and scope 245
14.2 UV-induced skin reactions 247
14.3 Phototoxicity (photoirritancy) reactions 247
14.4 Photosensitive reactions 251
Summary 256
References 256

15 Occupational skin diseases

Jon Spiro

15.1 Introduction and scope 259
15.2 Occupational skin disease 259
Summary 259
References 259
CONTENTS

15.1 Introduction and scope 259
15.2 Dermatitis 260
15.3 Development of occupational dermatitis 263
15.4 Patterns of occupational dermatitis 264
15.5 Incidence of occupational dermatitis 265
15.6 Effects of dermatitis on work 265
15.7 The outlook in occupational dermatitis 266
15.8 Identification of occupational dermatitis 266
15.9 Other occupational skin disorders 267
15.10 Investigation of a case of dermatitis at work 270
   Summary 276
   References 276

16 Prevention of occupational skin disease 279
   Chris Packham

16.1 Prevention of occupational skin disease 279
16.2 Defining the problem 280
16.3 Material safety data sheets 282
16.4 Chain of responsibility 283
16.5 Managing dermal exposure 284
16.6 Selection and use of personal protective equipment 289
16.7 Protective or ‘barrier’ creams: do they have a role? 294
16.8 The role of education and training 294
16.9 Conclusions 294
   Summary 294
   References 294

PART V Regulatory 297

17 Occupational skin exposures: legal aspects 299
   Chris Packham

17.1 Introduction and scope 299
17.2 Brief overview of current United Kingdom legislation 300
17.3 The employer’s perspective 303
17.4 Hazard identification 304
17.5 Risk assessment 306
17.6 Gloves: a note of caution 309
   Summary 310
   References 310
18 Safety assessment of cosmetics: an EU perspective 311
   Jo Lerner

18.1 Introduction and scope 311
18.2 Overview and scope of Cosmetics Directive 76/768/EC 312
18.3 Overview of the requirements of the EU Cosmetics Directive 315
18.4 Scientific advice 316
18.5 Influence of other legislation 317
18.6 Adverse effects from cosmetics 318
18.7 Toxicity of cosmetic ingredients 320
18.8 The safety assessment 326
18.9 A final consideration 328
   Summary 329
   References 329
   Appendix 18.1 Additional obligations for cosmetic suppliers 330

19 Regulatory dermatotoxicology and international guidelines 333
   Adam Woolley

19.1 Introduction 333
19.2 Regulatory context 334
19.3 Product groups and the human context 335
19.4 Dermal toxicology with the different product groups 336
19.5 Factors in dermal toxicity 338
19.6 Repeat dose dermal toxicology 339
19.7 Classic short-term dermal toxicity studies 341
19.8 Pragmatic considerations 344
   Summary 345
   References 345

20 Glossary of main terms and abbreviations 347
   James C. Wakefield

Index 358