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Science and Applications of Skin Delivery Systems

The 28 chapters of this book, divided into six sections and covering more than 500 pages, represent a complete scientific review of cosmetic skin delivery systems written by experts in their specific delivery subjects. Based on the presentations of the Skin Delivery Advanced Technology Conference organized by Allured Publishing in Milan, Italy, in 2004, more novel developments were added to this text so that, unlike other publications describing various delivery systems available to formulators of topical products, *Science and Applications of Skin Delivery Systems* describes the science and application of skin delivery systems for the cosmetic and pharmaceutical industries being useful to the formulator in making the right choice in selecting the skin delivery system for a given application.

The book's editor, Johann Wiechers, is a well-known scientist with extensive experience in the industry and field of cosmetic science. Deeply involved in solving various problems in cosmetic science, Wiechers is also an industry consultant, specializing in topics such as skin delivery, skin sensory, topical formulation design, clinical trial design, skin bioengineering and biostatistics. Apart from this, due to his outstanding achievements, Wiechers has recently been elected as IFSCC President. Needless to say, his name recognition alone, displayed so prominently on the front cover, along with the names of other experts involved in writing the chapters included herein, can be taken as a token of a quite timely and useful book.

The six sections of this book are presented in a natural and logical manner, beginning with the principle and terminology of skin delivery systems, methods of measurement, a discussion of the various possible skin delivery systems and, last but not least, future perspectives.

The first section makes evident the basic principles of skin delivery so that the reader can easily understand what it is and why we need it. A delivery system is a method of holding, carrying and transporting an active. It is any type of vehicle that takes an active to a target site. A delivery system can control the releasing rate of an active from a formulation at an optimal rate. Attention is paid to some essential aspects on the subject, such as: the right site of action of a cosmetic ingredient, the right chemical, the right concentration of the components, and the correct application time of the products on the skin, known as the 4R's. At the same time, useful considerations are made on the action mechanism of the functional ingredients, such as the UV filters, antioxidants, skin lightening ingredients, and molecules with antiaging properties-acting either on the surface of the skin or in specific layers within the skin.

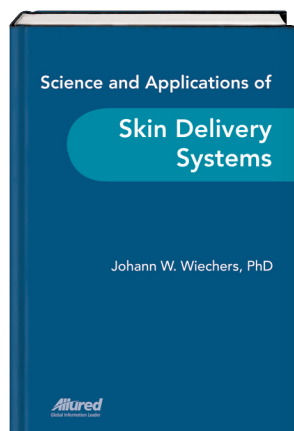
The skin penetration routes and the barriers encountered during this transport are then discussed. The fact is emphasized that apart from the inclusion of the active ingredients into cosmetics, the functionality claims are now brought into discussion; the cosmetic delivery must avoid transdermal delivery and keep the functional molecule in a specific skin layer. Later technologies that push the active ingredient into the skin rather than through the skin, enhancing the partition coefficient, achieve enhanced dermal delivery without causing irritation as usually happens with technologies that increase the diffusion coefficient. Delivery to the skin surface, the stratum corneum, the viable epidermis, the dermis and the sebaceous gland, other cosmetic delivery systems such as liposomes and patches are further made evident as topics connected with the site of action.

Measuring dermal and transdermal delivery of functional cosmetic ingredients is briefly characterized at the end of the first chapter; *in vitro* and *in vivo* studies are mentioned and their conclusions made evident. It is pointed out that more studies are to be performed moving forward because, although transdermal delivery is relatively well understood, the main factors affecting dermal delivery are still unknown, due to the measuring difficulties in this domain.

A discussion on the methods applied in measuring skin delivery is to be found in the second chapter, where the differences between *in vitro* and *in vivo* skin penetration techniques, animal and human skin as well as the need for more nondestructive methods to assess dermal delivery are discussed.

The methods for studying percutaneous absorption, discussed further, are characterized and the conclusion drawn of assessing dermal absorption by *in vitro* human skin permeation evaluation. The application of infrared spectroscopic imaging to skin delivery is the subject of the final chapter of the first section of the book.

The second section is devoted to skin delivery from emulsions as a complex phenomenon influenced by many factors, including composition, formulation type and manufacturing conditions. A systematic study is reported herein on the basis of an investigation of the transdermal and dermal delivery of active ingredients from different formulation types, and guidelines are advanced for supporting further investigation in the field. Skin delivery of active ingredients and drugs from semi-solid product forms such as emulsions were, for quite some time, less studied, the difficulties being partially caused by the many parameters to be taken into account in the formulation process. The topics approached regard the influence of the formulation type, the influence of formulation polarity via the choice of emollients, the influence of stratum corneum polarity via the use of adjuvants, the influence of skin lipid organization via the choice of emulsifiers, the influence of liquid crystalline emulsion structure, and the influence of droplet size on skin delivery. The last chapter of section two describes how to measure and control some additional



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aspects of formulation science such as stability. The experiments are clearly described and the results systematically presented in tables and graphs. The conclusion is pointed out that microemulsions are on average quite an effective vehicle for the transdermal delivery of active ingredients although often these ingredients need dermal delivery, and a formulation map is given in the book for certain formulations .

Soft and hard encapsulation techniques are discussed in section three. Vesicles as skin delivery vehicles, namely conventional vesicles and their interaction with animal and human skin, novel types of vesicles used as delivery vehicles, and the mode of action of vesicles in skin transport enhancement represent interesting subjects developed by the authors leading to the conclusion that the vesicles are much used as skin delivery vehicles for pharmaceutical and cosmetic purposes. Elastic vesicles showed superior properties in comparison with the conventional, rigid vesicles as regard the therapeutic potential and the interactions with the human skin. Solid lipid nanoparticles (SLN) and nanostructured lipid carriers (NLC) are much investigated for cutaneous administration, as revealed in chapter 13. The use of lipid nanoparticles in aqueous SLN and NLC dispersions as carriers in cosmetic skin delivery systems is also discussed. Microencapsulation and cosmetics, discussed in chapter 14, bring into discussion essential subjects such as microcapsule structures and the principles of the microencapsulation methods as yet unavailable for use on an industrial scale, being only published as patents. Flexible liposomes for topical applications in cosmetics, their structure, properties and ability to transport active substances into the deeper skin layers, as well as the benefits of liposomal encapsulation of active, are covered by chapter 15.

Chapter 16 deals with Pheroid technology and delivery system, defined as a colloidal system that contains unique and stable lipid-based submicron- and micron-sized structures, called Pheroids, uniformly distributed in a dispersion medium. By using colloidal systems as carriers of drugs or cosmetic compounds, their efficacy is enhanced and the side effects reduced. The Pheroid is particularly advantageous as a delivery system due to the high effectiveness and to the fact that the system is based on the naturally occurring molecules of the body being thus pharmaceutically safe.

Two chapters are then subsequently devoted to micro- and nano-encapsulation of water- and oil-soluble actives for cosmetic and pharmaceutical applications. Encapsulation and other topical delivery systems are discussed, as are the advantages of different encapsulation technologies made evident.

In the last chapter of section three, another essential subject is brought to the reader's attention, namely the chemical stability of active ingredients. Linoleic acid is taken as a good example of such compounds, showing beneficial skin properties but low chemical stability. This shortcoming can be overcome by the molecular inclusion of the linoleic acid in β -cyclodextrin, which gives sufficient stability to oxidation for being used in cosmetic formulations.

Chapters 20–22, in section four, deal with alternative ways to enhance skin delivery. Topical delivery of cosmetic ingredients by sonophoresis and iontophoresis is presented after the description of the basic techniques to enhance penetration. These methods are safe and effective means for treating the photo-damaged skin.

Special delivery routes are discussed in section five, along three chapters where experimental studies on important subjects are described: delivery from rinse-off products, novel ways of measuring the transfollicular transport of active ingredients across the skin, and significance of follicular delivery and ways to measure it.

The last part of the book deals with the legal perspective on cosmetic and drug skin delivery systems. Legal responsibilities are discussed, and the marketing and dermatological perspectives of said responsibilities are also taken into account. The increased interest of the cosmetic industry in cosmeceuticals or functional cosmetics is pointed out in connection with the interest promoted in botanicals and natural products that affect the biochemical pathways underlying skin reactions, and the discovery and development of new agents that can be used in formulations with topical actives.

Science and Applications of Skin Delivery Systems, written by prestigious specialists in the cosmetic science field, succeeds in elaborating a complete scientific review of cosmetic and skin delivery systems on the basis of extensively cited literature and properly commented chapters where theoretical and experimental aspects are so joined as to create a useful guidance for the cosmetic and pharmaceutical formulators for the consumer's benefit. The fact is made evident that the particularly complex character of cosmetic science needs a good cooperation between the specialists in various fields, such as chemists, pharmaceutical chemists, chemical engineers, botanists, dermatologists, physicists, and economists to offer their contribution to the progress of a field vital to all of us.