Open Access
Scientific Reports

Open Access Scientific Reports

Review Article Open Access

Abstractauthbstractun(r 96 >>vels)43(of)wtvels4.

Keywords: Dermatopharmacokinetic; Stratum corneum; Bioequivalence; Skin stripping

Introduction

Bioequivalence is a relative term which denotes that the drug substance in two or more identical dosage forms, reaches the systemic circulation at the same relative rate and to the same relative extent i.e. their plasma concentration pro les will be identical without signi cant statistical di erences. us in the case of topical formulations the drug has to penetrate through the layers of skin to reach the local site of action which is a complex process only due to the rate limiting barrier of the Stratum Corneum [1]. Stratum Corneum is the external layer of the skin composed of mainly corneocytes which are embedded in complex lipid matrix comprising of ceramides, cholesterol, and free fatty acids. is explains the behavior of Stratum Corneum as a barrier to the transport of hydrophilic substances.

e determination of the Bioequivalence of topical products involves the DermatoPharmacoKinetic (DPK) approach [2]. e DPK approach includes any measure of drug concentration in the skin, whether directly or indirectly related to the drug`s therapeutic action, which can be determined continuously or intermittently for a period of time. is may include the measurement of either drug concentration in Stratum Corneum over time and or drug concentration in serial biopsy samples. e measurement of the change in the Stratum Corneum drug concentration as a function of time is the objective of DPK approach and thus is a valid means of comparing a generic and innovator product for their ability to deliver drug to the deeper layers of the skin.

DPK studies o er certain advantages as it is painless, the active drug substances (moieties) are protected from gastric enzymes, it avoids rst pass e ect, and it is simple to terminate if any adverse or undesired e ect is observed.

SUPAC-SS:It is the FDA guidance for “Nonsterile Semisolid Dosage Forms, Scale –U and Post Approval Changes: Chemistry, Manufacturing and Controls,In Vitro Release Testing and In Vivo Bioequivalence Documentation” (SUPAC-SS). It is intended to lower the regulatory burden while assuring the safety and e ectiveness of the products under post approval changes. It de nes three levels of changes they are:-

*Corresponding author: Rahul Mayee, 10, Gurukunj Housing Society, Tilak Nagar, Aurangabad 431005 MS, India, E-mail: rahul.mayee@rediffmail.com

Received October 09, 2012; Published October 31, 2012

Citation: Mayee R, Rawat S, Joshi V (2012) Pharmacokinetic Studies of Topical Formulations - A Review. 1:441. doi: V F L H Q W L 4 1 F U H S R U W V V

Microdialysis: Microdialysis technique has been introduced to study the amount of drug a er topical drug administration. e method consists of placing an ultrathin semi permeable hollow ber, called the probe in the dermis and per fusing this ber with a tissue compatible sterile bu er at a very low rate with a Microdialysis pump. e probe functions as an arti cial vessel in the dermis and thus exchanges small, di usible molecules from the probe to tissue and vice versa. e recovery of the given compound closely re ects the concentration of unbound, that is, pharmacologically active compound in the intracellular uid of the tissue surrounding the probe.

Pharmacodynamic approach: Phamacodynamic approaches for certain selected corticosteroid drugs have already proved useful to document Bioequivalence, which is based upon the well- known skin blanching e ects of corticosteroids. Also another endpoint which proves useful is the increase in Trans Epidermal Water Loss (TEWL) and desquamation rate of the Stratum Corneum following the application of retinoic acid dose. is happens over the course of several days and the phenomenon is readily followed with respect to time.

In Vitro permeation assessment: In-Vitro experiments are performed using arti cial membranes or excised skin (from humans or an animal model) to screen and optimize topical formulations. e arti cial membranes such as silicone membrane or even pig ear skin are used to serve the purpose. As mentioned by Shah et al. [5] the evidence available suggests that the rate of permeation of drugs from their formulations and the temporal pro les of such permeation may be similar as long as the formulation themselves are the same. ough there are di erences in clinical end points the permeation rates have shown to vary and these nding still need investigation. In this method all comparisons must be performed with skin membranes cut from the same section of unblemished excised skin.

Confocal laser scanning: Confocal laser scanning microscopy appears to be a promissable tool for future DPK studies. is tool allows an investigator to focus a beam to a given depth within a tissue and to take reading of the concentration of an agent at the level of focus, thus a concentration pro le can be generated following topical application of drug product [6].

Validation procedures: DPK method should be validated and veri ed. Method validation should include all aspects of sampling e.g. Stratum Corneum stripping and measurement of drug concentration in Stratum Corneum, or any other analysis. At every critical step in the method development accuracy, precision, sensitivity, speci city, and other standard aspect of validating an assay methodology should be established. Following methods are used for assessing the validity of Stratum Corneum tape stripping method to determine the BE of topical formulations.

Cadaver skin permeation: As mentioned by the authors, this method validation procedure is done by selecting multiple sections of dermatome human trunk skin and mounted on Franz cells and placed in di usion apparatus consisting of dermal receptor solution which is constantly stirred and maintained at optimal temperature. Each sections integrity was veri ed by measuring its permeability to titrated water. Subsequently test product was applied to a required number of sections and multiple donors were used for each section. At di erent time intervals the solution is replaced with fresh solution, and aliquot taken for assay by HPLC.

Vasoconstrictor assay: e vasoconstrictor potency of the test product and positive control are tested using normal human volunteers. e test product and the control were applied and a er a speci c time it was removed and sites skin color was evaluated using Minolta Chroma Meter. e change in scale value between pre-dosing and post dosing a er the speci ed time was calculated for each site.

References

1. Sarigullu Ozguney I, Yesim Karasulu H, Kantarci G, Sozer S, Guneri T, et al. (2006) Transdermal delivery of diclofenac sodium through rat skin from various formulations. AAPS Pharm Sci Tech 7: 88.
2. Shah VP (2001) Progress in methodologies for evaluating bioequivalence of topical formulations. Am J Clin Dermatol 2: 275-280.
3. Lademann J, Jacobi U, Surber C, Weigmann HJ, Fluhr JW (2009) The tape stripping procedure--evaluation of some critical parameters. Eur J Pharm Biopharm 72: 317-323.
4. Benfeldt E, Hansen SH, Volund A, Menne T, Shah VP (2007) Bioequivalence