Annals of Pharmacology and Pharmaceutics

Short Communication
Published: 15 Sep, 2017

Vasoconstrictor Assay Method for the Bioequivalence Assessment of Topical Corticosteroid Applications: A Complex and Variable Approach

Mastan S[1], Shabana S[2]*

[1]*Department of Pharmacology, Siddhartha Institute of Pharmaceutical Sciences, India*

[2]*Department of Pharmacology, Venkatreddy Nagar, Ramalayam Road, India*

Short Communication

Skin blanching due to topical corticosteroids was initially observed by [1,2] introduced the assessment of bioequivalence (BE) of topical corticosteroids using Vasoconstrictor Assay (VCA)/ Skin Blanching Studies. Eventually, based on these findings, US-FDA issued interim guidance in 1992 and final guidance in 1995 on "Topical Dermatological Glucocorticoids: In vivo Bioequivalence" [3]. From 1995, these guidelines were adapted and recommended by all major regulatory authorities for the BE assessment of topical corticosteroids. In principle, this method relies on the unique ability of topical corticosteroids to produce a blanching response as a result of vasoconstriction of the skin microvasculature. The basis of this approach is the measurement of the pharmacodynamic

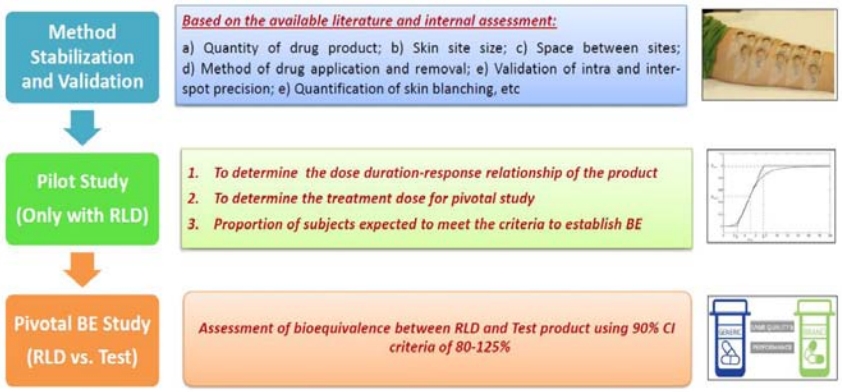

Figure 1: Main steps involved in the assessment of bioequivalence of topical corticosteroids using Vasoconstrictor Assay.

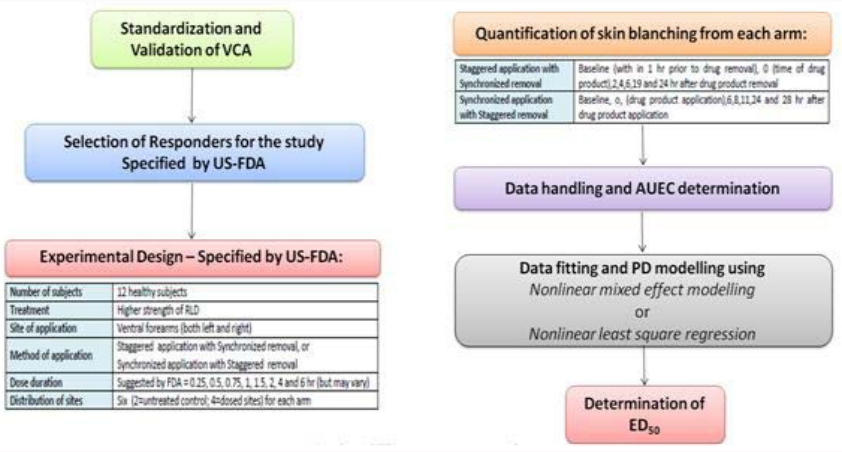

Figure 2: Main steps involved in the pilot study of Vasoconstrictor Assay VCA=Vasoconstriction Assay, US-FDA=United States Food Drugs Administration; AUEC = Area Under the Effective Curve, PD = Pharmacodynamic; ED_{50} = Dose Duration at which Effect is Half-maximal.

Correspondence:
Mastan Shaik, Department of Pharmacology, Siddhartha Institute of Pharmaceutical Sciences, India, E-mail: shkmastan@gmail.com

Received Date: *21 Jun 2017*
Accepted Date: *25 Aug 2017*
Published Date: *15 Sep 2017*

Citation:
Mastan S, Shabana S. Vasoconstrictor Assay Method for the Bioequivalence Assessment of Topical Corticosteroid Applications: A Complex and Variable Approach. Ann Pharmacol Pharm. 2017; 2(9): 1089.

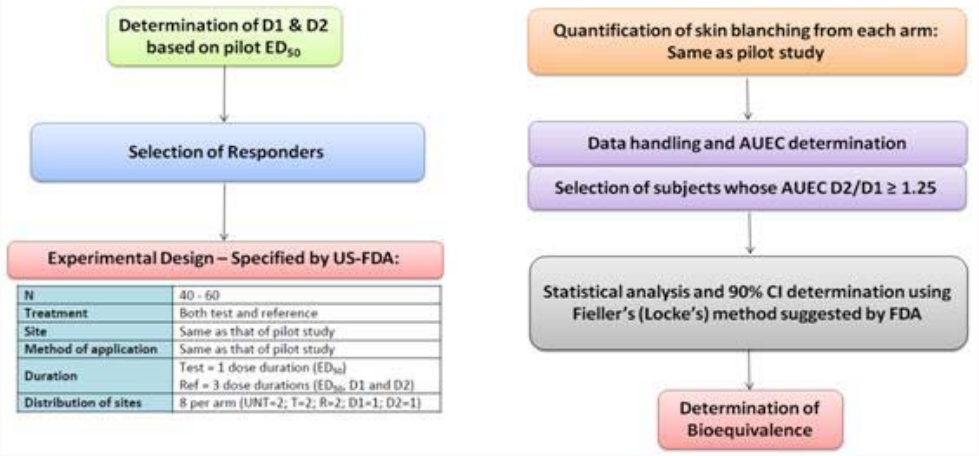

Figure 3: Main steps involved in the pivotal study of Vasoconstrictor Assay D1 = The shorter dose duration Reference Listed Drug calibrator, D2 = The longer dose duration Reference Listed Drug calibrator, US-FDA=United States Food Drugs Administration; AUEC = Area Under the Effective Curve, CI = Confidence Interval, UNT = Untreated.

Table 1: Major differences between pilot and pivotal studies in VCA.

Activity	Pilot study	Pivotal study
Sample size	12	40 - 60
Objective	To determine population ED50	To determine bioequivalence between test and reference product
Considered subjects	All	The subjects whose AUEC D2/D1 ≥ 1.25
Model	Pharmacodynamic modelling	Statistical analysis with 90% CI
Specific method	Emax suggested by FDA	Fieller's (Locke's) method suggested by FDA
Assessment	Reasonable ED50 value	90% CI of AUEC should be 80 – 125%

D1 = The shorter dose duration Reference Listed Drug calibrator, D2 = The longer dose duration Reference Listed Drug calibrator, AUEC = Area Under the Effective Curve, CI = Confidence Interval

effect of the drug being assessed as a function of time. The main steps involved in this study includes a) method stabilization and validation, b) pilot study with only reference product, and c) pivotal BE study with both test and reference products as represented in Figure 1. The workflow specified by the regulatory authorities for pilot and pivotal are represented in Figure 2 and Figure 3, respectively. The major difference between pilot and pivotal BE studies are presented in Table 1.

Even though these VCA methods are well adapted by various regulatory authorities, from a practical perspective there are several major limitations/concerns which make this method as a complex and variable. The major limitations/concerns includes – (i) suitable best with fair-skinned subjects who show good blanching response, (ii) works best with medium to high potency formulations and simpler formulations such as gels and ointments, (iii) mostly fail to control intra-subject variability via consistent Chromameter technique, (iv) even with good Chromameter technique , some products' data do not fit well to a simple Emax model or they have inherent high intra-subject variability that requires sample sizes > 60 (upper limit in US-FDA Guidance), (v) problematic for lower potency products and newer formulations such as sprays, tapes, foam, (vi) expected variability in skin blanching due to several physiological factors, (vii) many fluctuations due to impact of an environmental factors such as hot and humidity. Due to these major limitations/concerns, there is no much BE applications in this segment from Asia based pharmaceutical industries, in fact, which playing major role in the generic production in other therapeutic areas. Hence, there is a remarkable requirement for an alternative approaches in this area which would certainly enhance the overall generic production in an efficient manner in Pharmaceutical Research which intern facilitates pharmacoeconomic benefit to the patients.

References

1. Hollander JL, Stoner EK, Brown EM. The use of intra-articular temperature measurement in the evaluation of anti-arthritic agents. J Clin Invest. 1950;29(5):822-823.
2. McKenzie AW, Stoughton RB. Method for comparing percutaneous absorption of steroids. Arch Dermatol.1962;86(2):608-610.
3. US-FDA. Guidance for Industry. Topical Dermatoglogical Corticosteroids: *In Vivo* Bioequivalence.1995;1-36.