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Dry-swabbing/image analysis technique for the pharmaceutical equipment cleaning validation

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Abstract

This paper presents the development of a new technique using the dry-swabbing method for monitoring the contamination of pharmaceutical equipment. Black polyester wipes were used to improve the detection limit of the visual inspection. A standardized method of producing model impurity was used to produce known contamination of the model surface by a variety of compounds ranging from 0 to 500 µg.dm^{-2}. The sample contaminations were dry-swabbed and evaluated by measuring the intensity of contamination using the computer image analysis. The detected intensities of contamination were always proportional to the amount of the impurity applied. The dry-swabbing method has been proven to be at least by one order of magnitude more sensitive than mere visual check.

Keywords: Cleaning validation; dry-swabbing; image analysis; decontamination

1. Introduction

Cleaning validation is a collection of techniques and processes aimed at maintaining the cleanness standards for the pharmaceutical equipment regardless its processing history. The cleaning validation procedures are generally aimed at checking and proving, that the residues of the active pharmaceutical ingredient, remaining at the surface of the machinery are acceptable after finished cleaning; the

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acceptance value being related to the toxicity of API in question. In general, the acceptable level of residual contamination [1, 2] can vary depending on the compound from several hundreds μg per dm^2 of the equipment surface to several μg per dm^2. Unassisted human eye can only identify contamination levels of the several hundred μg per dm^2 magnitude [3], thus in most cases some instrumentation is required to improve sensitivity. The analysis (usually UV or HPLC) of wet swabs from the equipment surface or rinse water represents the industrial standard [4]. Common drawback of both approaches is the necessity to take the sample to laboratory and hence the inevitable delay in continued operation of the production equipment.

This study reports the development of a new technique using the dry-swabbing method for monitoring the contamination of pharmaceutical equipment that is more readily available for routine monitoring of the contamination. The dry-swabbing/image analysis (DSIA) technique employs black polyester wipes for dry-swabbing the equipment surface, so as to transfer all, or at least the representative portion of contamination to the wipe creating visible stain on its surface. Digital photography and computer image analysis can convert the visual information into the numerical intensity, which is proportional to the amount of contamination.

2. Materials and methods

The study involved a variety of tested compounds, including amlodipin, ibuprofen, paracetamol, caffeine, rutin, esculin, losartan etc. and pharmaceutical formulations thereof as a model substances and formulations for investigating the test performance. Those substances were provided by courtesy of Zentiva company (Czech Republic).

2.1. Testing equipment and procedure

The experiments were carried out in laboratory, using plain stainless steel plates, having marked square 1 dm^2 sample areas. Simulated contamination by any of the model contaminants was created by spraying the pre-determined amount of substance solution or suspension over the sample area (fig. 1a). The sprayed volume was maintained constant in order to improve reliability and the contamination level was changed using different concentration of sprayed solution/suspension. Steel plates were then left to dry. This procedure was used to produce a series of stainless steel plates containing known surface contamination by selected model contaminant. Contamination levels ranging from 0 to 500 $\mu g.dm^{-2}$ were generally used. Contaminations over 300 $\mu g.dm^{-2}$ were above the visually detectable limit for most compounds, on the other hand, the contaminations below 150 $\mu g.dm^{-2}$ were not visually detectable.

Then, each sample area was wiped by folded Black Inspection Wiper Class 10.000 (Vestilab SA, Spain) using forceps. The wiping proceeded in a scanning-like manner from left to right edge of the sample area and then again in the top-down direction. The contamination was transferred at least partially onto the wiper, producing a “dry-swab”, containing visible stain, if there was any contamination to be detected. Example of obtained dry-swabs is provided in fig. 2.

The figure shows, that the size and/or intensity of the stain generally increase with the increasing surface contamination. Therefore, it should be possible to use the swabs to quantify the contamination.